Health & Nutrition Research

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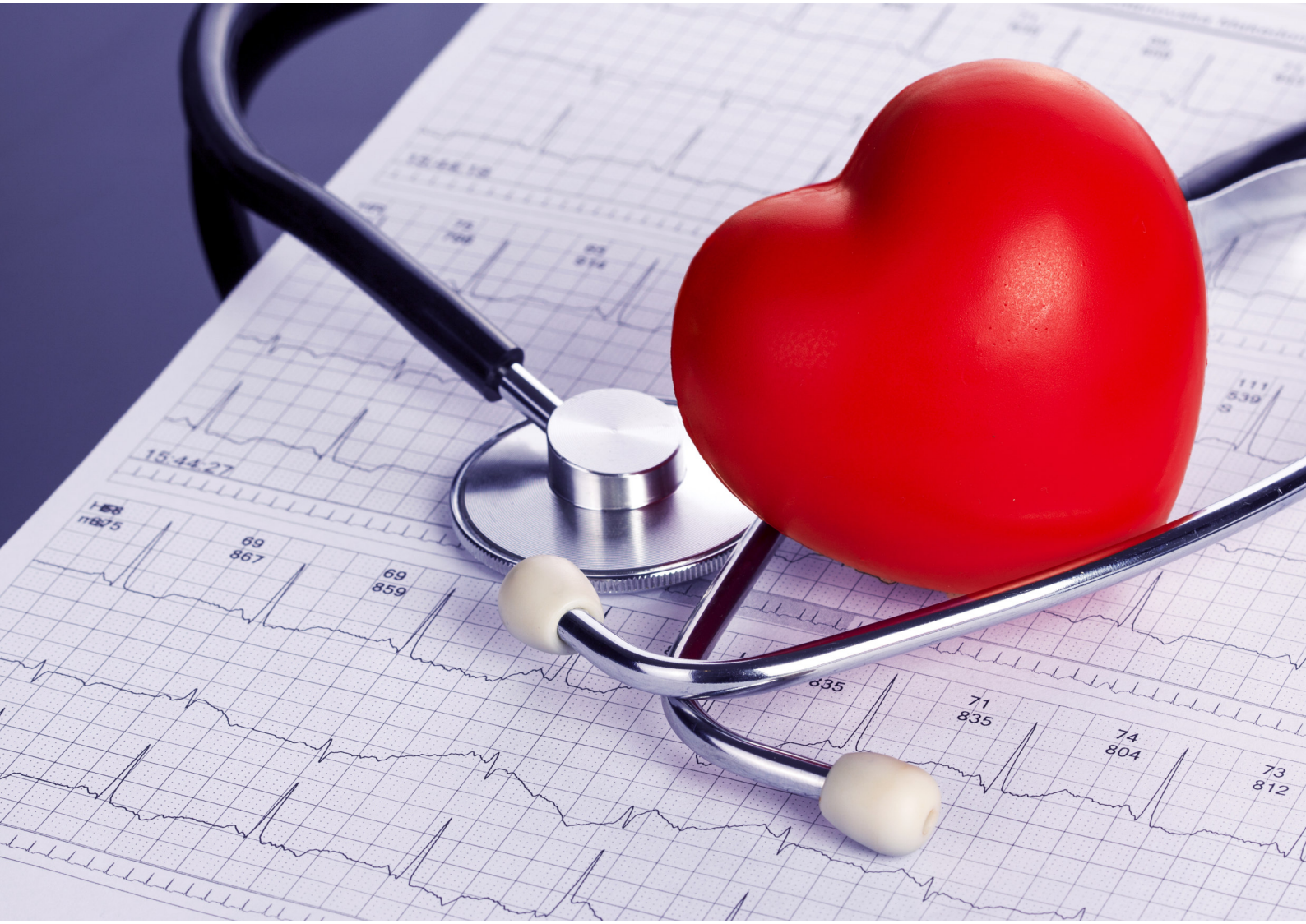

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SUMARIO • SUMMARY • RESUMO

RESEARCH

Editorial

From the Editorial Board of the MLS Health and Nutritional Research Journal we would like to announce the launching of the first number, which aims to be an instrument of scientific knowledge transfer in the field of health, nutrition and food. Through original articles or scientific reviews, in basic as well as applied and methodological areas, which represent a scientific contribution to the advancement of knowledge.

The first article deals with "New dietary-nutritional treatments in type 2 diabetes mellitus: a narrative review". The increase in the prevalence of type 2 diabetes mellitus is closely related to current unhealthy eating and living habits.

The following article discusses "Dual effect of branched-chain amino acids and their relationship with insulin resistance". Insulin resistance is a complication present in subjects with obesity among and has been identified as a key factor in the onset and progression of type diabetes mellitus. Numerous studies highlight the benefits of a high-protein diet for both the treatment of obesity and insulin resistance.

From the field of pediatric nutrition, “Ponderal gain of newborns feed with exclusive human milk vs. mixed breastfeeding entered in the Neonatal Special care Unit of the Regional Hospital of Autlan de Navarro, México".

Related to COVID-19, "Medical Nutritional Treatment in patients with COVID-19". Coronaviruses are a large family of viruses that can cause disease in both animals and humans. Medical nutritional treatment is of great importance, given the high energy and protein requirements associated with the energy expenditure associated with the disease, AND in the recovery phase, which can be lengthy.

The following study is within the field of food innovation and development. "The elaboration and sensory evaluation of a cookie based on yellow pitahaya (Selenicereus megalanthus) shell flour flavored with basil (Ocimum basilicum) and rosemary (Rosmarinus officinalis)". This research was carried out with the purpose of providing humans with natural products rich in nutrients. The objective was the fortification (sensory) of the classic wheat flour with yellow pitahaya shell flour, because this fruit is of high nutritional value.

Finally, "The influence of parents on the sexuality of female adolescents in low-income families in Bolivia". Studies highlight the influence of the family on adolescent sexuality, since they could help delay the beginning of sexual life and encourage safer sexual behaviors among adolescents, in the city of Cochabamba, Bolivia.

We cannot end this editorial without thanking the Fundación Universitaria Iberoamericana (FUNIBER) and the different sponsoring Universities for the material and human support that have contributed in a good way so that the first number of this journal can be published. We would also like to thank the entire team that has supervised and contributed to the success of this project.

Editor Jefes
Dr. Iñaki Elío Pascual

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NEW DIETARY-NUTRITIONAL TREATMENTS IN TYPE 2 DIABETES MELLITUS: A NARRATIVE REVIEW

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Abstract. Introduction: The increase in the prevalence of type 2 Diabetes Mellitus is closely related to current bad eating and lifestyle habits. Dietary-Nutritional strategies, such as intermittent fasting or high protein diet, could be new treatment options effective and safe in order to improve glycaemic control in people with type 2 Diabetes Mellitus. Objective: Assess the effectivity and safety of intermittent fasting and high protein diet as new dietary-nutritional strategies in the treatment of type 2 Diabetes Mellitus. Method: A bibliographic review was carried out, for which 12 scientific articles from the Pubmed database published in the last 5 years (from April 2015 to April 2020) were selected and analysed, 6 referring to intermittent fasting and 6 to high protein diet. Results and discussion: Both intermittent fasting and high protein diet, with a hypocaloric approach, are dietary-nutritional strategies effective and safe for glycaemic control in adults with type 2 Diabetes Mellitus due to the fact that they cause weight loss which reduces insulin resistance. In the case of intermittent fasting, it is advisable to adjust the medication at the time of intakes to improve its safety, while high protein diet is safe as long as there is no previous kidney damage. Future research is needed to show that both strategies have effects on glycaemic control independent of weight loss.

Keywords: Type 2 Diabetes Mellitus, intermittent fasting, high-protein diet, glycaemic control, weight loss.

NUEVOS TRATAMIENTOS DIETÉTICO-NUTRICIONALES EN DIABETES MELLITUS TIPO 2: UNA REVISIÓN NARRATIVA

Resumen. Introducción: El aumento de la prevalencia de Diabetes Mellitus tipo 2 está muy relacionada con los hábitos actuales de alimentación y vida poco saludables. Estrategias dietético-nutricionales como el ayuno intermitente y la dieta hiperproteica, podrían ser nuevas opciones de tratamiento efectivas y seguras para mejorar el control glucémico en personas con Diabetes Mellitus tipo 2. Objetivo: Evaluar la efectividad y seguridad del ayuno intermitente y la dieta hiperproteica como nuevas estrategias dietético-nutricionales en el tratamiento de la Diabetes Mellitus Tipo 2. Método: Se realizó una revisión bibliográfica, donde se analizaron un total de 12 artículos científicos de la base de datos Pubmed publicados en los últimos 5 años (de abril 2015 a abril 2020), 6 referentes a ayuno intermitente y 6 a dieta hiperproteica. Resultados y discusión: Tanto el ayuno intermitente como la dieta hiperproteica, con un enfoque hipocalórico, son estrategias dietético-nutricionales efectivas y seguras para el control glucémico en adultos con Diabetes Mellitus tipo 2, debido al hecho de que provocan una bajada de peso la cual disminuye la resistencia a la insulina. En el caso del ayuno intermitente es recomendable ajustar la medicación a la hora de las ingestas para mejorar su seguridad, mientras que la dieta hiperproteica es segura siempre y cuando no exista daño renal previo. Se necesita futura investigación para demostrar que ambas estrategias tienen efectos sobre el control glucémico independientemente de la pérdida de peso.

Palabras clave: Diabetes Mellitus tipo 2, ayuno intermitente, dieta hiperproteica, control glucémico, pérdida de peso.

Introduction

The term Diabetes Mellitus (DM) encompasses a group of chronic diseases whose common characteristic is hyperglycemia due to a defect in insulin production, in its action, or in both. Ninety percent of the total diagnosed cases of DM belong to type 2 (DM2), although it is worth noting that a large percentage of cases are undiagnosed (1).

Prevalence and incidence rates have increased in recent years worldwide, especially among young people as reflected by the International Diabetes Federation in its 2019 atlas (2). In Spain, the results of the first part of the study di@bet.es (3) reported a prevalence of DM2 of 13.8% in 2010, implying that more than 4.5 million Spaniards were diagnosed with this disease. In the second part of the study (4) carried out in 2015, the incidence of DM2 in Spanish population was analyzed, being 11.6 cases/1000 persons/year.

The increase in the number of cases of DM2 worldwide seems to be caused by the aging of the population, the increase in sedentary behavior, and the increase in the consumption of unhealthy foods, factors that have been related to the development of obesity and insulin resistance in peripheral tissues (1,5).

DM2 is a major public health problem due to the high human, social, and economic costs derived from medical treatment, in addition to the need to treat the acute and chronic complications generated. Among the acute complications is the appearance of hypo- and hyperglycemia, where the latter can lead to the appearance of diabetic hyperosmolar hyperglycemic syndrome (HHS). Chronic complications include microvascular complications (diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy) as well as macrovascular complications (arterial hypertension, dyslipidemia, cardiovascular disease, and diabetic arteriopathy). DM2 is considered the main cause of cardiovascular disease, blindness, non-traumatic amputations, and renal failure in developed countries (1).

Despite these data, there are several publications that affirm that the establishment of good lifestyle habits by following a healthy, adapted, varied, and balanced diet, together with the practice of regular physical activity, they play a key role in preventing the development of DM2, as well as in controlling its signs and symptoms and the appearance of associated complications. It can be stated that the development and progression of DM2 is strongly influenced by dietary and nutritional habits (6). However, the American Diabetes Association (ADA) has not established a consensus on the most appropriate nutritional treatment to apply in DM2, with special emphasis on the importance of individualizing dietary patterns (7).

Several meta-analyses, literature reviews, and studies (8-10) have shown that following a Mediterranean-type diet, characterized by a high consumption of plant-based foods and quality fats, can act as a protective factor against the main chronometabolic diseases that affect our society today, including DM2 (8). Following this dietary pattern has been shown to improve the cardiometabolic profile (9), reduce blood pressure levels, normalize blood glucose, and reduce body mass index (BMI) in people with DM2 (10).

The effectiveness of a dietary pattern in the treatment of a disease lies in the capacity of adherence and adaptation that the affected person generates on it. Currently, different research groups are increasing their interest in the search for new dietary patterns, different from following a conventional Mediterranean diet, to help control chronic diseases related to diet, including DM2. Within these new dietary-nutritional patterns, intermittent fasting (11) and the hyperproteic diet (12) are currently being strongly investigated and discussed within the scientific community as possible treatments in DM2 due to the potential benefits found in both types of dietary patterns.

The main objective of this review is to evaluate the effectiveness and safety of following an intermittent fasting or a hyperproteic diet as a dietary-nutritional treatment in people with DM2.

Method

A search for scientific articles related to the topic was conducted, giving priority to human clinical trials, review articles, and meta-analyses using the Pubmed database. The search for articles began in January 2020 and ended in April 2020.

To locate articles relating intermittent fasting and DM2 we applied the 5 years old filter and used the different search strategies: ("Fasting" [MeSH] or "Intermittent Fasting" [in title and abstract]) AND ("Diabetes Mellitus type 2" [MeSH], or "Diabetes Mellitus type 2" [in title and abstract], or "Glycemic Control" [in title and abstract], or "Hypoglycemia" [in title and abstract], or "Insulin Resistance" [in title and abstract], or "Weight Control" [in title and abstract]).

To locate articles relating Hyperproteic Diet and DM2, the 5 years old filter was applied and the following search strategies were used: ("Hyperproteic Diet" [MeSH] or "Hyperproteic Diet" [in title and abstract] AND ("Diabetes Mellitus type 2" [MeSH], or "Diabetes Mellitus type 2" [in title and abstract], or "Glycemic Control" [in title and abstract], or "Hypoglycemia"

[in title and abstract], or "Insulin Resistance" [in title and abstract], or "Weight Control" [in title and abstract]).

Once the titles and summaries of the different articles were obtained, the inclusion criteria were observational studies, clinical trials, reviews, or meta-analyses in which an intermittent fasting protocol or a high-protein diet was applied in persons diagnosed with DM2 or pre-diabetes, with or without overweight/obesity, and interventions of at least 1 month's duration.

The exclusion criteria were articles that did not fit the topic were carried out in cellular models, animal models; the sample that was not diagnosed with DM2 or pre-diabetes, the interventions were of very short duration or it was impossible to read beyond the title/abstract.

Finally, a total of 12 articles were selected and included in the review; 6 related to Intermittent Fasting and DM2 and 6 related to Hyperproteic Diet and DM2, which were analyzed in depth.

Results

Intermittent Fasting

Intermittent fasting is understood as the alternation of periods of voluntary abstention from food intake with periods of free intake for a certain period of time (11).

Fasting is a practice that has been used since ancient times, due to the religious and medical properties that have been attributed to it (11). Currently, the interest of the world population in this practice has increased in recent years, producing an exponential increase in internet searches (13). This fact has led numerous lines of research to focus on investigating the health effects of intermittent fasting and its use as a possible medical treatment (14).

Intermittent fasting is not a dietary plan per se, so the type of food consumed during the period of intake and its quality are not taken into account (13). Depending on the duration of the period of intake restriction, a classification of different types of intermittent fasting is established (13,16-19). The main types of fasting and their description, assuming that there are many possible variants, are summarized in Table 1. It should be emphasized that it is difficult to make a classification since there is no consensus on the part of any national or international scientific body.

Table 1. Summary of the main types of feeding patterns in intermittent fasting (11, 13-17).

Name	Abbreviation	Description
Food restricted time	TRF	Fasting 16 h - Feeding 8 h Fasting 12h - Feeding 12h
Early restricted time feeding	eTRF	Feeding allowed from 6:30-8:00h until 14:00-15:00 h.
Fasting alternate days	ADF	Alternates: 1 full day fasting - 1 day normal food intake
Modified alternate-day fasting	ADMF	Alternates: 1 day intake of 20-25% Total Energy Expenditure (TEE) - 1 day total intake of TEE
Periodic fasting	PF	Alternates: 2 non-consecutive days per week intake 20-25% of GET - remaining days of the week total intake of GET

TRF: Time-Restricted Feeding; eTRF: Early-Time Restricted Feeding; ADF: Alternated-Day Fasting; ADMF: Alternated-Day Modified Fasting; PF: Periodic Fasting.

In the following sections we will analyze different mechanisms through which following different intermittent fasting strategies can produce beneficial effects on the control of DM2, the most significant of which are efficacy in weight loss, improvements in markers of glycemic control, and reduction of insulin resistance. At the same time, the risks and contraindications of following an intermittent fasting protocol in people with DM2 will be presented.

Intermittent fasting and weight loss

As previously mentioned, one of the main risk factors for the development of DM2 is being overweight or obese (1). It has been shown that a reduction in body weight can improve and even reverse DM2 in a large percentage of diagnosed individuals (6), so that a main objective in the treatment of DM2 is to reduce body weight, especially in those individuals who, in addition to DM2, are also overweight or obese.

The hourly restriction of food intake can facilitate the consumption of fewer calories at the end of the day (11). For this reason, several professionals prescribe a hypocaloric diet within an intermittent fasting protocol, with the aim of creating an energy deficit in a simpler way that favors weight loss. However, several studies have been carried out which reject this belief that intermittent energy restriction favors weight loss more than a continuous hypocaloric diet (13,16,18,19).

In 2018, Harris L et al. (16) performed a meta-analysis where they analyzed a total of 6 clinical trials, which evaluated the efficacy of following different intermittent energy restriction protocols in reducing body weight during a time period of 3-12 months in different samples of

people older than 18 years with BMI ≥ 25 kg/m^2. In 4 of the trials, the control groups performed a continuous hypocaloric diet during the same time periods. The results obtained were that intermittent energy restriction and continuous energy restriction resulted in weight loss without significant differences (-1.03 (-2.46, -0.40) kg; 95% CI; p = 0.156).

In the review by Seimon RV et al. (18), they reached the same conclusion as the previous meta-analysis. After analyzing a total of 40 clinical trials evaluating the effectiveness of following different intermittent fasting protocols (specifically different ADF protocols) to reduce body weight and control blood glucose for a mean of 12 weeks, they stated that different intermittent fasting protocols produce similar effects to continuous energy restriction in reducing body weight and glucose metabolism.

Intermittent fasting and glycemic control

In humans, the main mechanism by which intermittent fasting improves glycemia is the reduction of insulin resistance in peripheral tissues; this mechanism being dependent on weight loss, which means that continuous energy restriction, when also producing weight loss, achieves the same effects on glycemia. Few studies have directly evaluated the effect of intermittent fasting on glycemic control in humans (20-22).

A randomized clinical trial by Carter S et al. (20) addressed this relationship. A total of 137 individuals aged 61 ± 9.1 years with obesity (BMI of 36.0 ± 5.8 kg/m^2) and DM2 (HbA_{1c} 7.3 ± 1.3%) participated. The objective was to compare the effects of following an intermittent energy restriction protocol with continuous energy restriction on glycemic control and weight loss in individuals with DM2 for 12 months. The intervention group was subjected to a 5:2 FP (on fasting days the number of calories was 500 - 600 kcal), while the control group followed a continuous hypocaloric diet (1200 - 1500 kcal/day), both diets had the same foods and were elaborated by dieticians-nutritionists, who offered advice to both study groups. During the one-year follow-up of the study, no significant differences were found between the control group and the intervention group in the decrease of HbA_{1c} levels (- 0.5 ± 0.2% vs - 0.3 ± 0.1%; 90% CI; p = 0.65) and weight loss (-5.0 ± 0.8 kg vs - 6.8 ± 0.8 kg; 90% CI; p = 0.25) between both groups.

One year after the end of the intervention, the same authors (21) measured the same variables again in both groups one year after the end of the intervention. As results they found that HbA_{1c} levels increased in both the control group (0.4 ± 0.3%) and the intervention group (0.1 ± 0.2%) although without significant differences between the two groups (CI 90%; p = 0.32). Weight loss was maintained at -3.9 ± 1.1 kg in both groups, with a difference between the two groups of 0.07 (-2.5, 2.6) kg; 90% CI).

Cho Y et al. (22) pooled in a meta-analysis, 12 clinical trials (a total of 545 participants with DM2) comparing the effectiveness of different intermittent calorie restriction protocols (TRF, ADF, ADMF and PF) in reducing BMI and improving glycemic metabolism with a continuous hypocaloric diet. After the end of the intervention periods of the different studies, which ranged from 4 to 24 months, it was found that there was a significant decrease in fasting glucose levels in those groups that followed an intermittent fasting protocol compared to the control groups (-4.16 (-6.92, -1.40) mg/dL; 95% CI; p = 0.003). A significant decrease in BMI was also observed in the intervention group compared to the control group (-0.75 (-1.44, -0.06) kg/m^2; 95% CI; p = 0.033). In this investigation, variation in insulin resistance levels was also assessed in 6 of the studies using the homeostatic model assessment marker of insulin resistance

(HOMA-IR). The decrease in mean insulin resistance was significantly greater in the groups following an intermittent energy restriction protocol (0.54 (-1.05, -0.03) %; 95% CI; p = 0.038).

Sutton EF et al. (17) sought to demonstrate that early intermittent fasting (eTRF), in tune with circadian metabolic rhythms, has benefits in improving insulin resistance independent of weight loss. To this end, they conducted a 5-week randomized clinical trial in which they divided the sample of 12 adults aged 56 ± 9 years with obesity (BMI = 32.2 ± 4.4 kg/m^2) and prediabetes (fasting glucose 102 ± 9 mg/dl). Individuals in the intervention group performed an eTRF with 6 hours of early feeding (from 8:00 am until 2:00 pm), and those in the control group a TRF similar to the feeding pattern of the average American citizen with 12 hours of feeding (from 8:00 am until 8:00 pm), 12 hours of fasting, of which only 8 individuals completed the test. The diet in both groups was normocaloric, adjusted to the needs of each individual and was not focused on weight loss. Among the results, it was obtained that the application of an eTRF significantly improved basal insulin levels (3.4 ±1.6 mU/l; p <0.005) and insulin resistance (36 ± 10 U/mg; p <0.005), independently of weight loss. In addition, it was the first intermittent fasting study to show the weekly menu with its respective foods, although not the amounts, since these depended on the energy needs of each individual.

Risks and Contraindications

Following an intermittent fasting protocol is not risk-free, both in the short and long term, and even less so in ill persons, as is the case of patients with DM2 (24).

The most frequent short-term risk in patients with DM2 who practice intermittent fasting is the occurrence of episodes of hypoglycemia (24). The patients most at risk are those under treatment with insulin and/or sulfonylureas (11). Other types of antidiabetic medication are not usually associated with episodes of hypoglycemia (25,26). The results obtained in the clinical trial by Corley BT et al. (27) show that any fasting protocol, whether scheduled or not, increases the risk of hypoglycemia compared to a regular meal schedule in patients with DM2 without other pathologies. However, in those patients who receive more nutritional education and have more frequent blood glucose monitoring, hypoglycemia episodes are lower (28).

Hyperproteic Diet

The recommended daily intake (RDA) of protein for a sedentary adult, regardless of age and sex, is 0.8 g/kg body weight per day, which represents 10-15% of total calories (29). Diets with this protein content are considered normoproteic for adults, although the needs vary with age, physical activity, and state of health (30). This amount is considered the minimum to avoid protein deficiency; however, in recent years it has been proposed that providing higher amounts of protein can be beneficial for the control of metabolic diseases (12,31).

It is difficult to establish the limit for a diet to be considered high-protein. In general, a high-protein or hyperprotein diet is defined as one that provides more than 20% of total calories in the form of protein, which represents an amount of about 1.2 g/kg bw/day, the same as the amount recommended for the elderly (29,30).

The following sections will show the possible beneficial effects of following a high-protein diet in the management of DM2 by aiding weight loss and improving glycemic control. At the same time, the risks and contraindications of following a high protein diet in people with DM2 will be presented.

Hyperproteic diet and weight loss

The use of a high protein diet has been considered an effective protocol for weight loss in cases of overweight and obesity (31).

Wycherley TP et al. (31) evaluated in a meta-analysis 24 clinical trials comparing the differences in weight loss between following a low-fat, high-protein diet, and a diet with the same calories low in fat but normoproteic. Data were collected from a total of 1063 individuals over 18 years of age. The mean duration of the interventions was 12.1 ± 9.3 weeks. Compared with a normal protein diet, the hyperprotein diet produced a significant, albeit moderate, reduction in body weight (-0.79 (-1.50, -0.08) kg; 95% CI; $p < 0.005$).

However, other studies did not reach these results. In a review and meta-analysis of the literature, Zhao T et al. (12) analyzed 18 clinical trials, where they found no significant difference in whether the amount of protein in a normocaloric diet is related to greater or lesser weight loss in adults with DM2 (-0.09 (-0.21, -0.04) kg; 95% CI; $p = 0.17$).

In 2015, Tay J et al. (32) conducted a clinical trial where they evaluated in 115 adults with obesity (BMI 34.6 ± 4.3 kg/m^2 and DM2 (HbA1c 7.3 ± 1.1%) the differences in weight loss between following a hyperproteic hypocaloric diet and a normoproteic hypocaloric diet together with the same physical exercise program. After 52 weeks of intervention, no significant differences were found in the resulting weight loss between the two groups (-9.3 (-10.6, -8.0) kg; 95% CI; $p = 0.18$).

The same results were obtained by Campos-Nonato I et al. (33) where in a sample of 105 adults and after 6 months of intervention they found no significant differences in the percentage of weight lost between following a hypocaloric diet with a standard amount of protein (0.8 g protein / kg weight) and a hypocaloric hyperprotein diet (1.34 g protein / kg weight) -2.1(-7.5-3.2) (95% CI; $p = 0.427$). However, a higher percentage of weight loss was observed in those individuals with high adherence to the prescribed diet (considered those who complied with the prescribed diet at least 75% of the time), being higher in the individuals in the intervention group (-9.5%) than in the individuals in the control group (-5.8%) (99% CI; $p < 0.001$).

High-protein diet and glycemic control

Different systematic reviews and meta-analyses have analyzed different clinical trials studying the effects of following a high-protein diet on glycemic control in people with DM2 (12,34,35).

In the meta-analysis of clinical trials presented above, Zhao T et al. (12) also collected data on different markers of glycemic metabolism. No significant differences were found between following a hyperprotein and a normal protein diet in changes in fasting glucose (-0.08 (-0.21, -0.06); 95% CI; $p = 0.25$), fasting insulin (-0.04 (-0.24, 0.17); 95% CI; $p = 0.71$), and HbA1c (-0.07 (-0.20, 0.06); 95% CI; $p = 0.27$), suggesting that the amount of protein present in the diet does not affect long-term glycemic control in adults with DM2.

In another meta-analysis, Yu Z et al. (34) analyzed 13 clinical trials studying the effect of following a high-protein diet on glycemic control in different samples with a total of 1138 adults with DM2. The results showed no significant differences in changes in fasting glucose (-0.13 (-0.46, 0.19); 95% CI; p = 0.43) and HbA1c (-0.05 (-0.18, 0.08); 95% CI; p = 0.92) between following a high-protein diet and a normal protein diet. However, significant differences were observed in the reduction of insulin resistance, measured by the HOMA-IR marker (-0.27 (-0.47, -0.06); 95% CI; p = 0.01).

The results of the two previous publications also correlate with the conclusions obtained in the systematic review recently carried out by Malaeb S et al. (35), where after analyzing a total of 21 clinical trials they concluded that, in randomized studies with a large number of participants and long term, following a high-protein diet does not provide greater benefits in glycemic control in patients with DM2 than a diet with a normal protein content associated with abandonment or non-follow-up of the diet.

Risks and Contraindications

As previously mentioned, a protein intake above the RDA may be beneficial for the control of metabolic diseases (12,31). However, excessive intake is not without risk (36-39).

First, it has been postulated that long-term consumption of a high-protein diet can produce a series of alterations in renal function that can lead to the development of renal diseases (36-38). The potential renal damage associated with a high protein diet appears to be glomerular hyperfiltration, proteinuria, nephrolithiasis, increased renal acid load, and decreased long-term glomerular filtration rate (38).

Diabetic nephropathy is a frequent complication in DM2, mainly caused by poor long-term control of blood glucose and blood pressure (36). In turn, it has been proposed that a high protein diet, by causing glomerular hyperfiltration, can lead to damage in the structure of the glomerulus, deteriorating renal function, so that for years it has been advised against following a high protein diet in persons with DM2 to avoid deterioration of renal function (37).

However, more recent studies suggest that following a high-protein diet does not adversely affect long-term renal structure and function in patients with DM2 (32,40). Tay J et al. (32) also studied the effects of following a high-protein diet for 52 weeks on renal function markers in subjects with obesity and DM2. They concluded that, performing a long-term hyperproteic diet does not worsen renal function in subjects with DM2 without previous renal disease.

On the other hand, in a retrospective cohort study, Kaji A et al. (40) analyzed the association between protein intake and changes in urinary albumin levels and glomerular filtration rate, observing no significant differences between the amount of protein in the diet and the changes produced in renal function markers in persons with DM2 without macroalbuminuria.

Second, a cross-sectional study suggested an association between consumption of a high-protein diet and an increased risk of hypertension (OR = 1.16 (1.02-1.30); CI:95%; p = 0.02) since some foods containing high protein are also high in sodium (41). However, in three recent systematic reviews and meta-analyses presented above, the authors observed no significant differences between the amount of dietary protein and increased blood pressure in patients with DM2 (12,34,35).

Discussion

The effectiveness of a feeding protocol on glycemic control in people with DM2 can be achieved directly through a decrease in body weight or through mechanisms independent of this weight loss by decreasing markers such as insulin resistance (1).

In reference to intermittent fasting, 6 of the articles included in this review directly address the relationship between following an intermittent fasting protocol and its effects on weight or glycemic control in adults with DM2 (16-18,20-22).

In relation to weight loss, most evidence shows that following intermittent fasting strategies with a hypocaloric approach does not offer greater weight loss compared to other protocols with longer feeding periods (16,18,18,20,21). Several authors state that other factors are more influential in weight loss than feeding schedules, such as adherence to a healthy diet and the type of foods that are part of the diet (11,13,15,16). Cho Y et al. (22) did demonstrate that intermittent energy restriction is more effective as a strategy to reduce BMI in people with DM2 than a continuous hypocaloric diet. The authors state that this is due to the fact that during a period of fasting lipolysis processes are stimulated, stimulating the use of fat deposits as the main source of energy, added to the fact that, by concentrating the diet in a diurnal time slot, the activity of the circadian rhythms of the organism is improved, having a positive impact on body weight loss (22).

Some authors argue that this weight loss is the direct cause of the improvement in glycemic control in people with DM2 who are overweight or obese (20-22). Weight loss reduces inflammation in peripheral tissues decreasing insulin resistance. These effects do not seem to be shown in individuals with DM2 and normal weight (14-16). The favorable results of intermittent fasting on glycemic control, independently of weight loss, seem to occur only in animal studies (42,43) or in interventions with a very small population sample and short duration (17).

In human clinical trials using intermittent fasting as a strategy to improve glycemic control, a variety of results were found (20-22). Carter S et al. (20) showed that there are no significant differences in glycemic control in patients with DM2 and overweight or obesity between any diet focused on weight loss, either intermittent energy restriction or continuous hypocaloric diet. However, after one year after discontinuation of intermittent fasting, HbA_{1c} increased again in both groups, despite the fact that the patients did not regain the lost weight (21). On the other hand, Cho Y et al. (22) did find a significant reduction in fasting glucose levels among the group that performed intermittent energy restriction versus the group that followed a continuous hypocaloric diet. Even so, in both groups this reduction in blood glucose was attributed to weight loss by reducing central adiposity and improving insulin resistance. Further research in humans is needed to determine whether the use of any of the different variants of intermittent fasting may have additional effects on glycemic control beyond weight loss in patients with DM2.

Regarding the safety of intermittent fasting, although no study directly confirms it, experts suggest that any fasting practice increases the risk of suffering hypoglycemia, both in patients without any pathology and in patients with DM2, by increasing the number of hours

spent without ingesting food (26). However, adequate nutritional education and medication readjustment seem to significantly reduce the occurrence of hypoglycemia episodes in patients with DM2 who practice intermittent fasting (11,24,25,27).

Regarding the high protein diet, 6 articles were reviewed that directly related the effects of a high protein diet on weight (12,31-33) and/or glycemic control in adults with DM2 (12,34,35).

In relation to weight loss, most authors state that a hypocaloric hyperproteic diet is as effective as a hypocaloric normoproteic diet for long-term weight loss. Therefore, the protein content of the diet would not be related to weight loss and the number of total calories in the diet would (12,32). On the other hand, Wycherley TP et al. (31) found a greater weight loss in the group that followed a high protein diet, which was attributed, among other causes, to a greater feeling of satiety (44). Campos-Nonato I et al. (33) found that, although weight loss was similar in both groups, individuals with high adherence to the hyperprotein diet experienced greater weight loss than individuals with high adherence to the normoproteic diet, pointing once again to the importance of good adherence to any dietary protocol.

In relation to the hyperprotein diet and glycemic control in persons with DM2, no additional benefits have been found in the reduction of glucose or HbA_{1c} levels other than those directly caused by weight loss (33). However, Yu Z et al. (34) did observe a greater reduction in insulin resistance by following a hyperprotein diet. They attribute this result to a lower insulin release by increasing the amount of protein in the diet and reducing the amount of carbohydrate (34). The increase in the amount of protein seems to cause greater weight loss at the beginning of its follow-up, but in the long term its effect seems to be similar to that of other diets with a lower amount of protein.

Traditionally, a high protein diet has been associated with the occurrence of renal damage (37,41). However, both Tay J et al. (32) and Kaji A et al. (40) did not find that a high protein diet is associated with greater renal damage in patients with DM2 as long as there are no previous renal pathologies. Several authors are of the opinion that other factors, such as failure to maintain an adequate weight or high blood pressure are more important for the development of renal disease (38,39).

Regarding the limitations of the study since there is no consensus on the definition of intermittent fasting, each research group defines its own protocol, making it difficult to compare results between different publications. In addition, each research group uses one or more different markers to assess glycemic control (glucose levels, insulin, HbA1c, insulin resistance, etc.), which makes it difficult to compare results. Finally, no clinical trials of sufficient duration have been carried out to evaluate the long-term safety of following an intermittent fasting protocol and/or a high-protein diet in people with DM2.

With a view to future studies, we recommend that food professionals prepare a document containing the definition and characteristics of the main intermittent fasting protocols, which would allow standardization and comparison of results between different research groups. Finally, we propose the elaboration of a long-term clinical trial to study the effects of following an intermittent fasting protocol and/or a high-protein diet on glycemic control in patients with DM2, using HbA1c as the standard marker of effectiveness since it is the only indicator of long-term glycemic control.

Conclusions

On the basis of the review carried out, we conclude that both intermittent fasting and a high-protein diet with energy restriction, adequately planned and monitored by a health and nutrition professional, can be effective dietary-nutritional strategies for weight loss. It is this weight loss that directly results in improvements in glycemic control in people with DM2 by decreasing inflammation and thus insulin resistance in peripheral tissues. Further research is needed to determine whether both feeding protocols exert an effect on improving glycemic control in people with DM2 independent of weight loss.

Intermittent fasting protocols have not been shown to cause a greater number of episodes of hypoglycemia compared to continuous feeding. Nor has it been shown that a high-protein diet increases the risk of developing renal disease in persons with DM2 as long as there is no previous renal damage.

Therefore, any variant of intermittent fasting or following a hyperproteic diet are safe dietary-nutritional strategies to be applied in people with DM2 as long as they are monitored by a health professional who applies nutritional education strategies and a readjustment in medication, especially in the distribution of fast-acting insulin in the case of practicing an intermittent fasting protocol.

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DUAL EFFECT OF BRANCHED-CHAIN AMINOACIDS AND THEIR RELATIONSHIP WITH INSULIN RESISTANCE

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Abstract. Insulin resistance is a complication present in subjects with obesity and has been identified as a key factor in the appearance and progression of diabetes mellitus. Numerous studies highlight the benefits of a high-protein diet for both the treatment of obesity and insulin resistance. However, despite these benefits, a high protein diet has been linked to worse metabolic dysfunction, and even worsened insulin resistance. Thanks to studies in metabolomics, it has been postulated that branched-chain amino acids may be mediating these contradictory effects of a high protein intake and its relationship with insulin resistance. This narrative review compiles emerging evidence regarding the paradoxical effect that branched-chain amino acids can have on body homeostasis. Different contexts such as the presence of obesity, dietary patterns, origin of proteins that contain branched-chain amino acids, physical exercise, intestinal microbiota, sex as well as genetic load, are variables to take into account to evaluate the role of these amino acids.

Keywords: BCAA, branched-chain amino acids, insulin resistance, obesity, diabetes mellitus.

EFECTO DUAL DE LOS AMINOACIDOS DE CADENA RAMIFICADA Y SU RELACION CON LA RESISTENCIA A LA INSULINA

Resumen. La resistencia a la insulina es una complicación presente en sujetos con obesidad y se ha identificado como un factor clave en la aparición y progresión de la diabetes mellitus. Numerosos estudios resaltan los beneficios de una dieta con alto contenido de proteínas tanto para el tratamiento de la obesidad como para la resistencia a la insulina. No obstante, a pesar de dichos beneficios, una dieta hiperproteica se ha relacionado con una peor disfunción metabólica, e incluso empeorando la resistencia a la insulina. Gracias a estudios en metabolómica se ha postulado que los aminoácidos de cadena ramificada pueden estar mediando estos efectos contradictorios de una alta ingesta de proteínas y su relación con la resistencia a la insulina. En la presente revisión narrativa se recopila la evidencia emergente en cuanto al efecto paradójico que pueden desempeñar los aminoácidos de cadena ramificada en la homeostasis del organismo. Diferentes contextos como la presencia de obesidad, patrones dietéticos, origen de proteínas que contengan aminoácidos de cadena ramificada, ejercicio físico, microbiota intestinal, sexo, así como la carga genética, son variables a tener en cuenta para evaluar el rol de estos aminoácidos.

Palabras clave: BCAA, aminoácidos de cadena ramificada, resistencia a la insulina, obesidad, diabetes mellitus.

Introduction

Insulin resistance (IR) is a common characteristic that can present pathologies such as obesity and type 2 diabetes mellitus (DM2); in addition to atherosclerosis, dyslipidemia, and hypertension, which are commonly included in the metabolic syndrome, which has a great impact on the mortality and morbidity of individuals (1) (2). In order to alleviate this situation, it is common to perform dietary-nutritional interventions with a modification of macronutrients, usually by increasing the number of proteins and decreasing carbohydrates or fats. All this with the aim of reducing the fat percentage and consequently improving other parameters such as IR (3).

Proteins are one of the three macromolecules present in food. Due to their great structural diversity, they are capable of performing a large number of crucial functions in the homeostasis of the human organism such as body composition, food intake, satiety, protein synthesis, among others (4) (5). In the short term, diets with a high protein intake can influence weight control; in addition, thanks to their insulinotropic effect, they can help glycemic control (6) (7). However, paradoxically, different studies have related a high dietary protein intake with poorer metabolic health (8). Similarly, in some long-term investigations, a greater association has been found between a diet rich in protein and the risk of insulin resistance (9) (10).

For some time now, the results of various investigations have pointed to the structural units of proteins as possible mediating agents of this association and, specifically, to the branched-chain amino acids (BCAA) (11) (12). BCAAs comprise leucine, isoleucine, and valine, which are essential amino acids, which implies that the organism can only obtain them through food or through muscle catabolism. In comparison with other essential amino acids, BCAAs are found in greater proportion in dietary proteins, ranging from 17% to 30% in some food groups, with some dairy products such as cheese (30.41%), fish and seafood (17.57%), red meat and poultry (29.73%) having the highest content (13). Potential beneficial effects of BCAAs on adiposity and metabolic syndrome have been reported (14). These results have been supported by mechanistic research in rats where it has been reported that BCAAs improve glucose uptake in muscles (15).

Despite the potential benefits of BCAAs, in recent years, metabolomic studies have shown a significant relationship between high circulating levels of BCAAs and insulin resistance. It is noteworthy that obese subjects presented a higher level of 20% and 14% for valine and leucine/isoleucine, respectively, compared to lean subjects (16).

The aim of this narrative review is to describe the dual effect that, depending on the context, branched-chain amino acids can have on human health. It will also describe the different specific aspects that can modulate the role of these amino acids.

Method

A search for articles was conducted during the period February to May 2020 with a subsequent update from December 1 to December 10, 2021. All articles reviewed were in English. The PubMed database as the main source and Google Scholar as a complementary source. Articles were included where the potential beneficial as well as detrimental effects of high consumption of branched-chain amino acids on health were analyzed, with a special emphasis on their relationship with insulin resistance. Boolean operators such as AND were used to narrow the results. The reference list of these as well as the list of recommended "related articles" in PubMed were consulted. Some search terms used were "excessive consumption AND branched-chain amino acids," "insulin resistance AND branched-chain amino acids," "obesity AND branched-chain amino acids." A total of 85 original articles were obtained, of which 14 articles were used to discuss their results. The characteristics taken into account for the selection of the latter 14 articles were that the interventions were in humans, original articles no more than 10 years old, quantification of branched-chain amino acids either by plasma analysis or dietary intake to analyze their impact after the experiment.

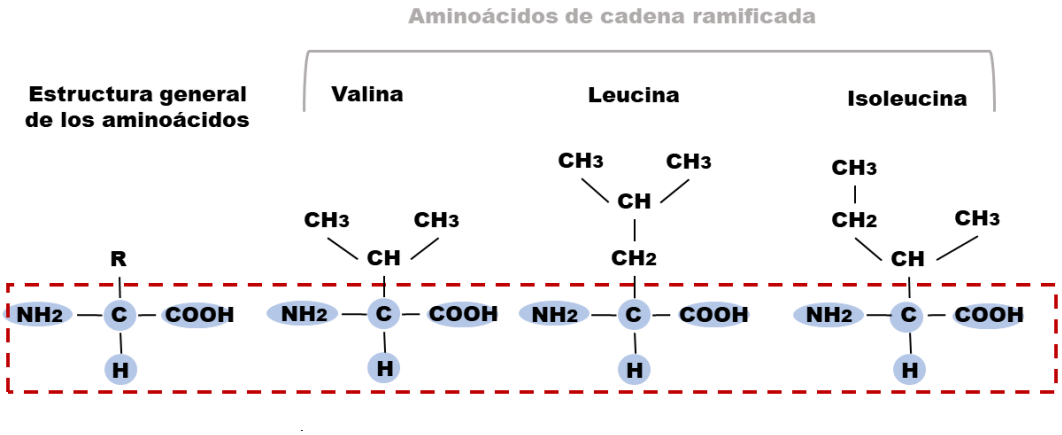
Results

A search for articles was conducted during the period February to May 2020 with a subsequent update from December 1 to December 10, 2021. All articles reviewed were in English.

Digestion, absorption, and catabolism of branched-chain amino acids

Proteins, after being ingested in the diet, are broken down in the gastrointestinal system. First, digestion begins in the stomach mediated by pepsins, and it then continues in the small intestine with the help of pancreatic proteases released by the exocrine pancreas. As a result of these processes, the proteins are transformed into amino acids and smaller oligopeptides. Finally, brush border peptidases finish digesting the oligopeptides into free amino acids, dipeptides, and tripeptides, which are taken to the enterocyte where they undergo further digestion. BCAAs, unlike other essential amino acids, differ in having aliphatic side chains with a branch point as shown in Figure 1.

Figure 1. Chemical structure of BCAAs. The dotted rectangle indicates the basic structure of all amino acids. Generic BCAAs have an aliphatic side chain with a branching point. [Source: Own elaboration]

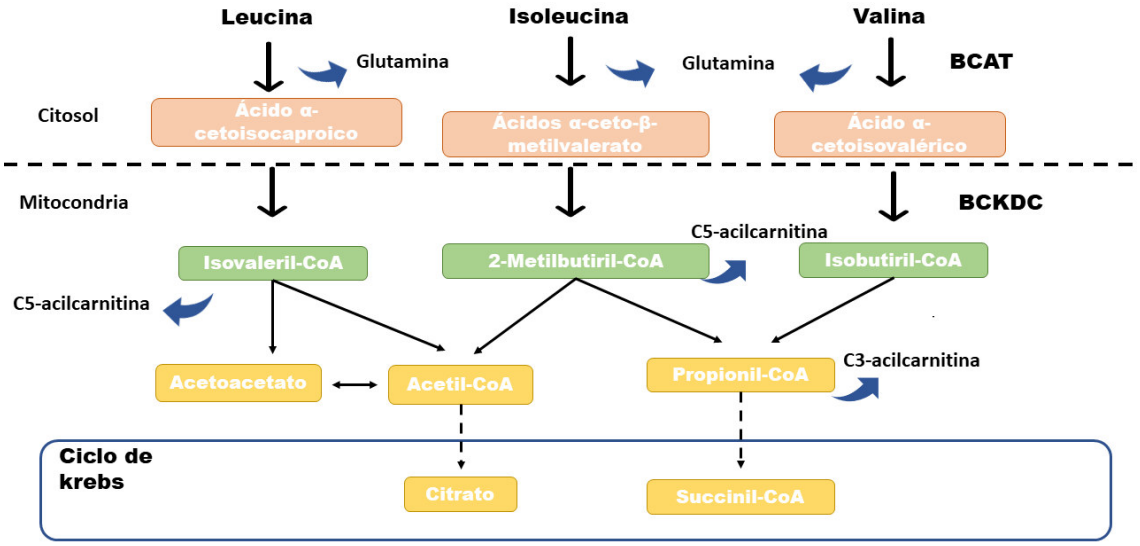


In blood plasma, after a meal rich in BCAAs, these amino acids increase approximately 2 to 3 times and then decrease to their initial value after approximately 3 hours. Furthermore, it should be noted that the kinetics of their absorption will differ according to the source of protein ingested (17) (18). After absorption, BCAAs are not taken to the liver to be metabolized as is the case with other amino acids. About 80% of BCAAs are transported to the blood circulation to be directly absorbed by peripheral tissues, such as skeletal muscle and adipose tissue, where they are directly metabolized (8).

Already in the extrahepatic tissues (mainly muscle and adipose tissue), BCAAs can undergo further catabolism. In their first reactions BCAAs are metabolized simultaneously. First, BCAAs undergo reversible transamination by branched-chain amino acid aminotransferases (BCATs), which convert them to branched-chain alpha-ketoacids (BCKAs), alpha-ketoisocaproate, alpha-ketoisovalerate, and alpha-keto-beta-methylvaleric for leucine, valine, and isoleucine, respectively. BCKAs can be released into the bloodstream and absorbed by other tissues; however, the normal pathway they take is to continue to the next step in their catabolism, which involves irreversible oxidative decarboxylation, mediated by the branched-chain keto acid dehydrogenase complex (BCKDC) located on the mitochondrial surface. It is noteworthy that BCKDCs have a higher activity in the liver and lower activity in muscle, adipose tissues, and brain (20). This fact is of great relevance since, as will be discussed later, the defects in BCAA catabolism in extrahepatic tissues have been postulated as a potential pathway for the development of insulin resistance.

Finally, oxidized alpha-keto acids diverge into alternate metabolic pathways to produce branched-chain acyl-CoA esters: acetyl-CoA and Succinyl-CoA for leucine, valine, and isoleucine, respectively, as depicted in Figure 2 (21) (22).

Figure 2. Catabolism of branched-chain amino acids. BCAAs undergo a first reaction in the cytosol mediated by BCAT producing α-ketoacids. Next, the keto acids undergo an irreversible oxidative decarboxylation by BCKDC at the mitochondrial membrane. Finally, BCAAs can be incorporated into the Krebs cycle for energy production. Depending on the context, BCAAs can produce glutamine or acylcarnitines, the latter of which are related to the genesis of IR. [Source: Image adapted from: Holeček M. Nutr Metab (Lond). 2018 May 3;15:33. (23)]



Actions of branched-chain amino acids on the health of the body

Undoubtedly, due to their characteristics, BCAAs play very relevant roles in the homeostasis of the organism. Therefore, it is important to maintain a correct balance of these amino acids.

BCAAs are of particular relevance in health due to their close relationship with important metabolic pathways. Among these, protein synthesis is one of the most recognized functions performed by proteinogenic amino acids, including BCAAs. Which is of particular importance for muscle proteins that are in constant protein turnover. BCAAs induce an anabolic state as long as there is a good availability of all essential amino acids for muscle protein synthesis; representing up to 35% of essential amino acids present in muscle (24) (25). This has been studied especially during training to achieve a greater synthesis of muscle proteins during exercise (26). Furthermore, because of their ability to be incorporated into the Krebs cycle, BCAAs are involved in energy production where, through their catabolites, they can act as metabolic substrates (23).

Likewise, in recent years it has been demonstrated the important role that BCAAs can have in different aspects of health such as the functioning of the gastrointestinal tract, blastocyst development, fetal growth, immune function, among others, which indicates the important role that BCAAs play in the homeostasis of the organism (27).

Reduced branched-chain amino acid balance

The extrahepatic tissues, as well as the enzymes involved in the processing of BCAAs, play an important role in maintaining the levels of these amino acids at optimal levels. However, in certain situations where these variants are put out of balance, a marked role is observed in the clinical manifestations of various diseases. An excess of BCAAs has been related to important metabolic disorders, while in other scenarios their contribution is crucial to improve the prognosis of serious pathologies. Therefore, it is necessary to know the specific context of

health or disease in order to determine the different variables where BCAAs can play a dual role.

Several studies highlight the therapeutic effects that BCAAs can have in different conditions characterized by a basic catabolic state, where the concentrations of these amino acids are diminished. Such is the case of liver cirrhosis (LC), which is characterized by alterations in the structure and function of the liver (28). In this pathology there is a marked decrease in plasma BCAA concentration that may be caused by reduced food intake, hypercatabolism, and ammonia detoxification in skeletal muscle. Because some tissues are able to utilize BCKAs to produce the amino acid glycine. This reduces ammonia accumulation and, consequently, the concentration of BCAA (29). Although there are divergences in clinical studies on the use of BCAA in LC, supplementation with these amino acids when their requirements are not reached in the diet results in a greater regulation of ascites, cachexia, hepatic encephalopathy, and even insulin resistance (30) (31) (32) (33).

Similarly, other diseases that present low urea and high ammonia levels in the blood, such as urea cycle disorders, result from the detoxification of ammonia in the liver. In these disorders it is common to find an increase in the amino acid glycine, as well as a decrease in BCAA levels, especially when acute metabolic decompensation occurs. These alterations support the important role that BCAAs may play in homeostasis (34) (35). Similarly low levels of both BCAAs and α-keto acids have been reported in blood plasma and skeletal muscle in patients with untreated chronic renal failure, and during dialysis (36). The metabolic acidosis present in CKD, together with hemodialysis, represent the main factor for the depletion of proteins in general and specifically of BCAA and their catabolites (37). The normalization of BCAA together with α-ketoacids in plasma, through oral supplementation, was associated with an improvement in appetite and nutritional status (38) (39).

High branched-chain amino acid balance

Elevated BCAA levels and their negative role in health are evidenced by inborn errors of BCAA metabolism such as maple syrup urine disease (MSUD). In this pathology, alterations in BCAA catabolism occur, affecting the action of BCKDCs, thus causing a marked elevation of both BCAAs and their catabolites in urine, blood, and tissues. These higher levels are toxic to the brain and lead to irreversible neurological complications or even death for patients. In animal models with MSUD, it has been shown that BCAA administration can cause hippocampal DNA damage (40). Therefore, the exhaustive control of BCAAs in the diet is essential to improve the clinical and prognostic outcome of this disease (41).

On the other hand, abnormally elevated BCAA levels have been reported in obese subjects since the 1960s (42). Subsequent metabolomic studies have correlated these elevated BCAA levels with the risk of insulin resistance and future type 2 diabetes mellitus (43) (16). These results were confirmed by animal studies where administration of BCAAs together with a high-fat diet resulted in increased insulin resistance (16). The above conclusions are in line with another study which concluded that a BCAA-restricted diet improved insulin sensitivity in skeletal muscle of rats (44).

Additionally, in another study, this time in humans, a decrease in plasma BCAA was found in obese subjects when they underwent weight loss surgery. These changes were paralleled by an increase in mitochondrial BCAT and BCKD in omental and subcutaneous fat (45). Another study described a reduction of BCAA and acylcarnitines after weight reduction

in obese adolescents, resulting in improved insulin sensitivity (46). In addition, after an overnight fast, high levels of BCAA are still observed (47).

These results seem to point to excess adiposity as a potential mediator in the detrimental effects of BCAAs. Obesity, along with chronic excessive dietary energy intake, are the main predisposing factors for the development of IR (48) (49). Although there are multiple factors that contribute to the development of obesity, it is well known that energy intake in excess of expenditure is a major contributor to its development. Likewise, obesity triggers inflammation that affects multiple organs crucial in insulin action and glucose regulation (such as skeletal muscle, adipose tissue, and liver) and in the development of IR (50). The accumulation of excessive energy in the form of fat causes mechanical stress on the adipose cell, resulting in chronic low-grade inflammation caused by activation of the innate immune system (51) (52).

Apart from adipose tissue, this inflammation is also present in other peripheral tissues. The liver may also experience activation of inflammatory pathways during obesity, as macrophages increase along with local production of chemokines and inflammatory cytokines that may predispose to IR in hepatocytes (53) (54). For their part, myocytes in skeletal muscle are another cell type that is associated with increased obesity-related inflammation through the infiltration of immune cells that may contribute to IR locally in this tissue (55).

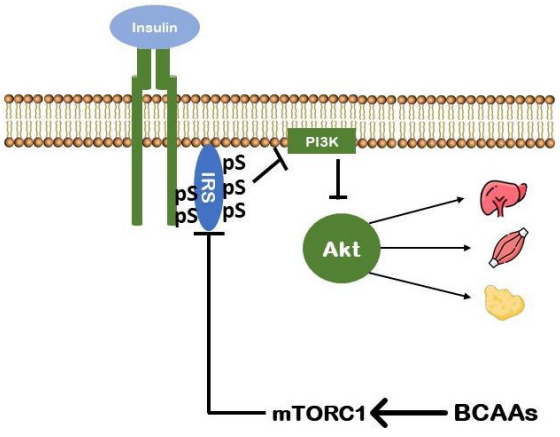
Branched-chain amino acids and their relationship to insulin resistance

In some research, like BCAAs, other amino acids have been associated with an increased risk of IR. However, in the case of BCAAs, there are mechanisms described by which increased BCAAs may contribute to future metabolic problems such as IR. Therefore, further understanding of the pathways that may be mediating between BCAAs and the development of IR is needed.

Mammalian target of rapamycin pathway

The mTOR complex is a serine/threonine of the PI3K-related kinase family. The mTOR pathway is the main pathway capable of coordinating local nutrients for cell growth and proliferation. The mTOR is the component of two multiprotein complexes known as mTORC1 and mTORC2 (56). The function of mTORC1 is to maintain a balance between anabolism and catabolism in response to various stimuli, including the concentration of BCAA. BCAAs, through the Rag family of GTPases, can act as a nutrient signal and activate the mTORC1 pathway at the lysosomal surface (57). Chronic activation of mTORC1 causes negative feedback leading to serine phosphorylation of the insulin receptor substrate (IRS), which impacts on Akt and consequently leading to IR in different tissues such as skeletal muscle, liver, and adipose tissue (58).

Figure 3. Proposed mechanism by which branched-chain amino acids contribute to insulin resistance through activation of mTORC1**.** After insulin binding to the α-subunit of the insulin receptor, it recruits IRS which triggers a signaling cascade activating the phosphatidylinositol-3-kinase (PI3K)/Akt pathway responsible for most of the metabolic actions of insulin in tissues such as liver, skeletal muscle, and adipose tissue. BCAAs, through chronic stimulation of mTORC1, are able to phosphorylate different IRS serines, resulting in decreased insulin actions such as glucose uptake and glucose synthesis in tissues crucial in their metabolism. [Source: Image adapted from: Yoon MS. Nutrients. 2016 Jul 1;8(7):405. (59)]



Altered branched-chain amino acid catabolism in peripheral tissues

The catabolism of BCAAs in the different peripheral tissues such as skeletal muscle, adipose tissue, and liver is well regulated to maintain a correct negative and positive balance of BCAAs. Interestingly, these same tissues are key organs in the metabolization of glucose and in the normalization of fasting and postprandial plasma insulin levels. Impairment of BCAA catabolism would occur in a manner similar to a domino effect, with excess fat being a major catalyst. Obesity through various pathways, including inflammation, could impair catabolic pathways in tissues, including adipose, leading to an overload on other tissues as discussed below.

Excess fat in adipose tissue, by mechanisms yet to be further explored, may exert an influence on genes encoding key enzymes in BCAA metabolism such as BCAT and BCKDH, leading their enzymes to decrease their transcription and activity (45). This is supported by studies where down-regulation of BCAA enzyme mRNA was seen to be caused by selective overexpression in adipose tissue of Glut4 in animals with an obese phenotype (60).

In several investigations in transgenic rats with alterations in mitochondrial BCAT, as well as in BCKD, cause sustained changes in plasma BCAA concentrations (61) (62) Therefore, the reduction of these enzymes may have an impact on BCAA catabolism in this tissue causing other tissues such as muscle and liver to have to break down a greater amount of BCAA.

By increasing BCAA catabolism in the ME, an intermediate in valine catabolism, 3-hydroxy-isobutyrate (3-HIB) is formed. 3-HIB regulates transendothelial transport as well as uptake of free fatty acids from plasma into muscle cells. This leads to an elevated accumulation of lipid oxidation products within muscle fibers such as diacylglycerides and ceramides triggering insulin resistance in this tissue (63).

In skeletal muscle, the expression of BCKDH is very low, which hinders the complete breakdown of the BCKA previously generated. Therefore, BCKA are transported to the liver since this organ has a higher expression of BCKDH compared to skeletal muscle (64). They can then be broken down to produce acyl-CoA and propionyl-CoA, which are then introduced into the Krebs cycle for oxidation. However, if the production of acyl-CoA and propionyl-CoA exceeds the oxidative capacity of the mitochondria, acylcarnitines can be produced, impairing mitochondrial CAT. Consequently, the liver's ability to oxidize fatty acids and glucose is reduced causing these products to accumulate excessively, altering insulin, signaling and causing hepatic IR.

In addition, the production of acetyl-CoA is able to increase gluconeogenesis and lipogenesis, which added to the oxidative stress of mitochondria, further promotes IR in this organ (65). Although mechanistic studies in rats supplemented with BCAA have highlighted positive effects such as improved glucose tolerance, decreased inflammation in adipose tissue, and improved insulin signaling in adipose tissue in insulin-resistant db/db mice.

In primates, including humans, BCAA metabolism is less active in the liver than in rats (66) (67). This is because the activity of catabolic enzymes is much higher in rats than in primates, so the capacity to eliminate branched-chain alpha-ketoacids is much higher. Specifically, 83%, 3%, and 1% of BCKDs in rats are expressed in liver, skeletal muscle, and brain, respectively. Whereas in primates, 13%, 54%, and 20% are expressed in liver, muscle, and brain, respectively. Therefore, the best models for testing BCAA overdoses would be in nonhuman primates (68).

Other aspects to take into account

High BCAA levels as a consequence of IR

The question remains as to whether the consumption of foods rich in BCAA is capable of increasing IR; or, on the contrary, the increase in BCAA is a subsequent consequence of IR. Since the antiproteolytic action of insulin is altered and as a consequence protein catabolism increases secondary to IR (69). However, in the study conducted by Asghari et al. (70), it was described that a high BCAA intake is related to an increased risk of IR in overweight adults followed for 2.3 years. Another study by Zhen et al. (71) prospectively analyzed the association between long-term BCAA intake and DM2 incidence. The population consisted of normal-weight and overweight Americans. The study showed a strong correlation of BCAA intake with an increased risk of DM2. Notably, total BCAA intake was positively associated with BMI and protein intake. However, it was not clearly distinguished whether these effects were mediated by BCAA, total protein, or animal protein. In contrast to the above results, in the trial conducted by Woo et al. (72), where they selected 12 heterogeneous individuals between 20 and 60 years of age, obese and prediabetic, no significant differences were observed for body weight, fat mass, muscle mass, BMI, fasting plasma glucose and insulin, and HOMA-IR after BCAA supplementation for 4 weeks. In addition, BCAA consumption did not cause an increase in plasma BCAA. However, as the authors point out, BCAA concentrations could have been affected by the gut microbiome, as gut bacteria are capable of synthesizing fatty acids from AA including BCAA (73). Additionally, the final results of the study by Nagata et al. (74) suggest that high intakes of BCAAs were associated with a decreased risk of diabetes in women. While in men, total BCAA intake was not significantly associated with diabetes risk after controlling for covariates. In addition, higher leucine intake was significantly associated with a decreased risk of diabetes. Interestingly, in another study (75), after analyzing more than 8000 Chinese individuals predisposed to have DM2 with normal weight and overweight, it was found that higher BCAA intake and DM2 risk depended on the context of dietary patterns and not only on BCAA intake.

Modification of BCAA concentrations by diet

Another important factor is whether the amounts of BCAA in the diet will have an impact on plasma concentrations. Some studies have addressed this question such as the one conducted by Karusheva et al. (76), where they investigated whether lower BCAA intake improved short-term insulin sensitivity in overweight and obese subjects aged 40 to 60 years.

The sources of BCAA were both foods available from grocery stores and markets as amino acid supplements. After the intervention, it was found that the basal plasma BCAA level went from 507±90 to 422±56 µmol/L, representing a decrease of 17%. In addition, we found a decrease in insulin secretion; increased postprandial insulin sensitivity; increased stimulation of mitochondrial efficiency in adipose tissue and, finally, we found alterations in the composition of the intestinal microbiome in favor of bacteroidetes.

Another study with a larger sample size concluded that BCAA concentrations are directly related to the risk of DM2. High BCAA concentrations were positively related to the consumption of legumes and red meat. In addition, it was shown that basal BCAA concentrations were significantly higher in men than in women. Also, BCAA levels decreased in participants receiving the intervention (411±113 to 363±80.5 nmol/nL), and the improvement in BCAA concentration occurred independently of weight loss, although there was a greater decrease in subjects with greater weight loss (77).

Similar results were obtained by Ruiz Canela and collaborators (78), who investigated the association of one-year changes in BCAA and aromatic amino acids (AAA) in 892 patients with type 2 diabetes, overweight, or slightly obese within the PREDIMED trial. It was concluded that the Mediterranean diet + extra virgin olive oil intervention was associated with significant reductions in BCAA after one year.

In contrast to these results, another study evaluated that a specific short-term dietary intervention modestly modified fasting BCAA levels in healthy individuals. The researchers used diets low in BCAAs, using plant foods and supplements free of these amino acids; on the other hand, in the high BCAA diet, they used foods such as meat and supplements high in BCAAs. However, the authors point out that it is possible that dietary manipulation of BCAA may be more effective in obese people or those with insulin resistance who are known to have dysregulation of BCAA metabolism (79).

Recently, an isocaloric dietary intervention with BCAA restriction (-50%) was performed on 12 healthy individuals for 7 days. For this purpose, the participants followed diets low in BCAA while consuming a BCAA-free supplement. At the end of the study, the initial plasma BCAA value was significantly reduced from 437±60 to 217±40 µmol/L. Similarly, there was an improvement in insulin resistance. It is worth mentioning that the low number of subjects and the short intervention are important factors to take into account for the interpretation of their results (80).

Genetic variability

Genome-wide association studies (GWAS) are showing results on how the genetic variability of each individual plays a key role in the changes and effects of plasma BCAAs. Specifically, it has been described that some polymorphisms such as rs1440581 may be related to insulin resistance (81). In this line, it has been described that increased BCAA intake is associated with an increased predisposition to DM2 when the genetic predisposition was high (82). Similarly, these amino acids were found to be able to increase the risk of both DM2 and glycosylated hemoglobin in incident diabetes patients with high genetic susceptibility for altered BCAA metabolism (83).

Physical exercise

Physical exercise can be another very potent factor in mediating the effects that BCAAs and their catabolites can trigger in the body. Physical exercise is able to act on the ME and affect the major organ in the regulation of BCAA catabolism. Although more research is needed, some actions such as improving the oxidative potential of mitochondria may lead to increased elimination of BCAA intermediates, in turn, improving IR (84). Similarly, it has been described that physical exercise triggers mechanisms for more efficient elimination of BCAA- and acylcarnitine-derived catabolites in the ME via glycine conjugation in the liver in obese individuals (85).

Conclusion

Emerging evidence points to the great relevance that a high intake of dietary BCAAs can play in the health of people particularly with metabolic disorders such as insulin resistance. High plasma levels of branched-chain amino acids lead to a worsening of metabolic health, while their limited intake has an impact on the improvement of some parameters such as blood glucose homeostasis. It is important to emphasize that these effects become noticeable in people who present a basic alteration, as is the case of excess adiposity. Therefore, a dietary pattern that not only quantifies the proportions of macronutrients but also the quality and quantity of their functional units. In this case, branched-chain amino acids could be a therapy to be considered to combat the complications associated with obesity such as insulin resistance. Future studies should take into account variables such as physical exercise, genetic load, as well as gut microbiota, sex, and dietary patterns in both the quality and type of protein and other accompanying dietary components such as fats.

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PONDERAL GAIN OF NEWBORNS FEED WITH EXCLUSIVE HUMAN MILK VS MIXED BREASTFEEDING ENTERED IN THE NEONATAL SPECIAL CARE UNIT OF THE REGIONAL HOSPITAL OF AUTLAN DE NAVARRO, MEXICO

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Abstract. Introduction: This research addresses the analysis of the weight gain of neonates fed with exclusive breastfeeding and mixed breastfeeding in the Neonatal Special Care Unit of the Autlan Regional Hospital. Method: It is a prospective, cross-sectional, descriptive-comparative and experimental investigation, identifying the type of breastfeeding and the modification of body weight from birth to one month of life. The universe is made up of 961 newborns in the institution, 112 correspond to those admitted to the UCEN. The sampling technique was non-probabilistic through the Census, discarding those neonates with hospital stays <5 days, the total sample was 64 children. Results: 59% were male, 41% female. 28% of neonates were exclusively breastfed, 72% mixed breastfeeding. Of the 100% of infants fed EBF, 39% increased their weight, the remaining 61% decreased. Of those with mixed lactation, 48% had a negative modification, 52% had a positive modification with respect to the initial weight. Discussion: Children fed with mixed breastfeeding show greater weight gain, compared to those fed with exclusive breastfeeding. EBF allows normal functional growth and development, fully covering nutritional needs and requirements, providing hormonal and / or nutritional components, protecting and stimulating the newborn's immune system; it also plays a protective role against obesity. In contrast, the dairy formula presents nutritional components in high amounts according to the nutritional requirements of the newborn, which stimulates accelerated weight gain.

Keywords: lactation, neonates, weight.

GANANCIA PONDERAL DE NEONATOS ALIMENTADOS CON LECHE HUMANA HOMÓLOGA EXCLUSIVA VS LACTANCIA MIXTA INGRESADOS EN LA UNIDAD DE CUIDADOS ESPECIALES NEONATALES DEL HOSPITAL REGIONAL DE AUTLÁN DE NAVARRO, MÉXICO

Resumen. Introducción: La presente investigación aborda el análisis sobre la ganancia ponderal de neonatos alimentados con lactancia materna exclusiva y lactancia mixta en la Unidad de Cuidados Especiales Neonatales del Hospital Regional Autlán. Método: Es una investigación prospectiva, transversal, descriptiva-comparativa y experimental, identificando el tipo de lactancia y la modificación de peso corporal desde el nacimiento hasta el mes de vida. El universo es compuesto por 961 recién nacidos en la institución, 112 corresponden a los ingresados en la UCEN. La técnica de muestreo fue no probabilística a través de Censo, descartando aquellos neonatos con estancia hospitalaria < 5 días, la muestra total fue de 64 niños. Resultados: El 59% corresponde al sexo masculino, 41% sexo femenino. El 28% de neonatos llevó lactancia materna exclusiva, 72% lactancia mixta. Del 100% de neonatos alimentados con LME, el 39% aumentó su peso, el 61% restante disminuyó. De aquellos con lactancia mixta el 48% tuvo modificación negativa, el 52% modificación positiva respecto al peso inicial. Discusión: Los niños alimentados con lactancia mixta presentan mayor ganancia de peso, comparados con los alimentados con lactancia materna exclusiva. La LME permite un crecimiento y desarrollo normo funcional, cubriendo totalmente necesidades y requerimientos nutricionales, aportando componentes hormonales y/o nutricionales protegen y estimulan el sistema inmune del neonato; además cumple un papel protector contra la obesidad. A diferencia, la fórmula láctea presenta componentes nutricionales en cantidades elevadas de acuerdo a los requerimientos nutricionales del neonato, lo cual estimula la ganancia acelerada de peso.

Palabras clave: lactancia, neonatos, peso.

Introduction

Neonatal feeding is a fundamental pillar to achieve the correct growth and development of the infant (9). It is known that human milk is the best food for them, it contains all the nutrients in the right amount to sustain and protect the child's life (10-11); however, sometimes it is necessary to use breast milk substitutes to complement the neonate's diet, due to the mother's or newborn's state of health, their residence, among other factors, which does not allow that, at hospital level in a Neonatal Special Care Unit, the total energy requirement of the infant is covered 100% with human milk (14). Infants who receive either total or partial artificial breastfeeding may present differences in the contribution of both macro and micronutrients in the daily intake, which could cause a significant difference in the growth and development of the newborn (1). Breast milk has been evolving and adapting to the characteristics and environment of the human being, providing all the necessary nutrients, offering protection, health and well-being. Currently, the percentage of exclusive breastfeeding in our country is lower than global rates and it is worrying that Mexico occupies the first place in child obesity worldwide (2), which has been reflected from infants.

The hypothesis proposed is that mixed breastfeeding allows a faster weight gain compared to exclusive breastfeeding in newborns at the Neonatal Special Care Unit of the Autlan Regional Hospital, due to the high protein content of breast milk substitutes causing an increase in the secretion of Growth Factor 1, facilitating greater adiposity in the infant. The objective of this study is to analyze the relationship between the weight gain of neonates fed

with exclusive homologous human milk vs. mixed breastfeeding admitted to the Neonatal Special Care Unit of the Regional Hospital of Autlan de Navarro, Mexico.

Analysis of the literature

The neonatal period includes from birth to 28 days of life, during this time the neonate undergoes changes to adapt to extrauterine life, and close monitoring by the multidisciplinary team is needed to achieve timely detection of alterations and global clinical conditions of the newborn (7).

In 1961 the first Neonatal Special Care Unit was created worldwide (5), this area is responsible for the specialized treatment in neonatology with the use of prenatal steroids, ventilatory techniques, use of surfactant, use of orogastric tubes for better nutrition, if necessary parenteral nutrition is administered which has improved the physiological state of newborns who for some reason need intensive care (6).

The main risk factors for anatomical or functional deviation in a preterm newborn are the immaturity of its apparatus and systems and its clinical characteristics (11). Significant changes of adaptation, extrauterine nutrition, intestinal function and intermediate metabolism arise in the newborn. Sánchez M, Arévalo M, Figueroa M., in their work state the following (5): "It has been proved that enteral feeding after birth stimulates the increase of circulating intestinal hormones (gastrin, duodenal secretin and jejunal cholecystokinin), which induce the nutritional adaptation of the premature newborn and favor its development and maturity". Neonatal feeding is a pillar for growth and development, in premature newborns it is necessary to closely monitor the sucking reflex, swallowing, assessment of respiratory effort during feeding and identification of signs of feeding intolerance (vomiting, gastric residue and abdominal distention), as well as the presence of bronchial aspiration (6).

The evaluation of the neonatal nutritional status in the NICU aims to establish the patient's feeding behavior from the moment of admission, determining the nutritional diagnosis for the nutritional therapeutic plan. The nutritional evaluation takes information in relation to the clinical history, identifying (8): weight, length, head circumference, gestational age. Serial measurements of these parameters will allow us to identify the growth pattern in an individualized manner, identify neonates with alterations and therefore act in a timely manner (9,10). Plascencia J, Villalobos G, Márquez M. (8), state that: "Weight reflects the total mass of all body compartments: lean tissue, fat, intra and extracellular fluids. Weight reflects changes in body composition, as well as development". Marín A, Jaramillo B, Gómez R, Gómez U. (7) determine that weight gain is the result of various physiological and nutritional factors, the most significant increase is observed up to 4-6 months of life, then the curve flattens and although each child has a different weight gain over time, a relative increase is estimated as follows:

- 1st trimester: 20-30 g/day
- 2nd trimester: 15-20 g/day
- 3rd trimester: 12-15 g/day
- 4th trimester: 10-12 g/day
- 5th month: doubles birth weight
- 8th month: 8 kg - 11th month: triples birth weight.

A newborn has an average gain of 1 g per hour, and this increase is prolonged during the first three months of life; at the end of this trimester the gain decreases with an approximate of 0.8 g per hour, and it is in the third trimester when approximately 0.5 g/hour is gained, relatively a weight gain for half that occurred in the first trimester (7,8). A child who does not gain weight should not always be considered as sick, since several considerations such as pathological, psychological, social and nutritional influence the growth, so that there is no unified definition of the problem. Delayed gain should be considered if the child presents one of the following percentile adjustments:

- Weight below the 3rd percentile on the weight-for-age charts.
- The child's weight-for-age is less than 80% of his or her ideal weight.
- If the child's weight falls two percentiles over time on a conventional chart (7).

The neonatal period is a vulnerable stage, since it is a critical time for the transition from the fetal stage (in which the placenta supplies the necessary nutrients) to birth, during which several changes occur for adaptation to the new environment.

Breast milk is the best food for a newborn, since it is the ideal source of nutrients and energy; it completely covers the requirements of the newborn, thus guaranteeing a correct growth and development, strengthening its immune system every day. Compared to breast milk substitutes, it has a lower protein intake, but it completely covers its requirements, avoiding an excessive protein intake which is a predominant agent for obesity in later life and a renal overload caused by artificial feeding (1). Its contribution of macronutrients stands out, with two groups of proteins: caseins and whey proteins, whey proteins being present in greater quantity in the first 10 days (90%) and even up to 8 months (60%); these proteins are made up of alpha lacto albumin, lactoferrin and IgA immunoglobulins. The total protein content of breast milk is 1.1 g/100 ml (1). Fats are the macronutrient that varies the most in breast milk since there is a higher lipid intake in the afternoon. Human milk contains lipase, which is stimulated by bile salts that favor its absorption. It contains an excellent supply of omega 3 and 6 fatty acids, which enable neurological and visual development. Its cholesterol content favors the differentiation and proliferation of adipocytes in later life, which promotes a lower risk of cardiovascular disease (1, 9). The main carbohydrate is lactose, which promotes the growth of lactobacilli and acidifies the intestinal pH favoring the growth of intestinal flora; it increases calcium absorption and promotes lactase synthesis. Human milk contains oligosaccharides that act as soluble receptor analogues, preventing pathogenic microorganisms from binding to the receptors of the infant's brush border cells, thus modulating epithelial and immune responses inhibiting pathogenic bacterial colonization and growth (1), thus preventing and combating bacteria, viruses, fungi and parasites such as: E. coli, salmonella, campylobacter jejuni, vibrio cholerae, hemophillus influenzae, clostridium botulinum, rotavirus, respiratory syncytial virus, poliovirus, influenza, cytomegalovirus, HIV, giardia lamblia, candida albicans (1, 9).

Samples of human milk have been taken from mothers with preterm infants, as well as full-term breast milk, showing that the former has high levels of: total nitrogen (increased by 20%), proteins, long, medium and short chain fatty acids, cholesterol and phospholipids; and they are justified because they have an indispensable role to mature, increase and form tissues and organs. Similarly, IgA, sodium, magnesium, magnesium, chloride and iron levels are

elevated, but lactose levels are low, since nature is wise and adapts breast milk to the needs of the newborn, as preterm patients have insufficient levels of lactase (1, 11, 18).

Breastfed infants have a lower protein intake and metabolize fewer calories. There is a close relationship between high protein intake at an early age and "adipocyte rebound" as well as elevated BMI in adulthood. Breast milk has approximately 60-70% less protein and 10-18% less caloric density compared to a human milk substitute. The high protein intake of breast milk substitutes causes an increase in the secretion of insulin-like growth factor 1 (IGF-1), leading to increased adiposity in the infant.

Method

This research takes place at the Autlán Regional Hospital, located in the municipality of Autlán de Navarro, Jalisco, offering services to the population of the 19 municipalities of the Sierra de Amula and Costa Sur Region of Jalisco. This institution is accredited as a Baby and Child Friendly Hospital, by the international strategy launched by the WHO, has key areas of care to promote and protect the health of the mother and child binomial, among which are the NICU, labor and delivery department, Emergency, two operating rooms and the Lactarium, which aims to provide training in breastfeeding to postpartum mothers, as well as to guide and assist them in the extraction of breast milk so that it can be provided in a homologous way to the newborns in the NICU.

This research was conducted in four sequenced moments, namely: literature review, reading of journals and specialized articles, collection of field information and systematization and interpretation of the material through statistical methods, to obtain the results of weight gain of neonates fed with exclusive homologous breast milk and those fed with mixed breastfeeding in the institutions of the NICU of the Autlan Regional Hospital in the period from June to December 2016.

This research aims to analyze the weight gain according to the type of feeding of neonates hospitalized in the UCEN, it was necessary to review in detail the standards of weight gain for healthy and sick neonates, as well as the physiological characteristics of children of this age, biochemical composition of human milk and breast milk substitutes through a literature review in order to determine the reason for weight gain related to dietary intake.

Research approach

A two-stage model was used. First, a quantitative approach was applied in which the weight gain of hospitalized neonates during their stay in the NICU was analyzed statistically, taking data 5 days after admission, 10, 20 and 30 days later, a process that was carried out by means of a technical file that collected the data of each neonate. Subsequently, the data was plotted and then a qualitative approach was applied, which made it possible to go deeper into the results found. At the end, a synthesis was made to include the results of both phases of the research process.

Research design and scope

It is a prospective, cross-sectional, descriptive-comparative and experimental research, identifying the type of breastfeeding and the modification of body weight from birth to one month of life. This study meets the two requirements to achieve control and internal validity since a group of newborns were compared according to established variables such as weight,

type of feeding, medical diagnosis, gestational age, milliliters of milk indicated per feeding at the beginning and at each measurement, and sex. Likewise, we worked with pre- and post-test data when taking weight measurements at a determined time from birth to one month of life, as long as the infant was still in the NICU for each weight-taking session, and thus could be related to the type of feeding for the determination of weight gain.

Universe, population and sample

The universe is composed of 961 newborns in the institution, 112 correspond to those admitted to the NICU. The sampling technique was non-probabilistic through census, discarding those neonates with hospital stay < 5 days, the total sample was 64 children. Similarly, during data collection it was identified that of the total number of newborns studied, only 3 had a hospital stay of 30 days, and 5 were admitted for 20 days, so the results are based on a hospital stay of 0 to 10 days.

The data collected were taken from the medical records of each newborn admitted to the NICU during the period from June to December 2016; likewise, data were obtained from the records of the Feeding Logs and the records of the institution's Lactary Feeding Census.

Instrument

The measurement instrument used to determine the weight gain of neonates admitted to the NICU was a technical sheet which, as a data sheet, was a key element for the research because it facilitated the collection of information by means of variables that made it possible to identify the amount and type of food received by the newborn admitted to the Neonatal Special Care Unit of the Autlan Regional Hospital, as well as the weight gain secondary to medical and nutritional treatment during their hospital stay. This instrument is detailed in Table 1 below.

Table 1. Measuring instrument.

Recién nacido	Sexo	Fecha de ingreso	Edad Gestacional	Diagnóstico Médico	Tipo de Alimentación	ml inicial espoma	Peso inicial Kg	ml por toma al los 5 días de vida	Peso en kg al los 5 días de vida	ml por toma al los 10 días de vida	Peso en kg al los 10 días de vida	ml por toma al los 20 días de vida	Peso en kg al los 20 días de vida	ml por toma al los 30 días de vida	Peso en kg al los 30 días de vida	Ganancia de peso a los 5 días	Ganancia de peso a los 10 días	Ganancia de peso a los 20 días	Ganancia de peso a los 30 días

Note*: Own elaboration.*

The Data Processing Technique

We worked with pre- and post-test data with the control group by taking weight data at baseline and between each specific measurement.

Data validation

The results were validated by means of a specialized database in Excel, where the collected data were concentrated and through statistical formulas it was possible to obtain the weight gain of the neonates admitted to the NICU of the Autlan Regional Hospital.

Results

According to the aforementioned methodology, field work was carried out in which the Census was applied, where it was necessary to eliminate from the research those newborns that did not meet the parameter of days of hospital stay to corroborate the weight change, those whose days of hospitalization were less than 5 days were discarded, therefore, the total sample was 64 newborns. Once the information was collected, it was necessary to take as a research parameter a hospital stay of no more than 10 days, because of the total number of newborns studied, only 3 had a hospital stay of 30 days, and 5 were admitted for 20 days.

Thus, we obtained the results of the type of feeding that each neonate received from the first day of hospital stay to the day of discharge, which is detailed in Table 2, highlighting that

28% of the newborns admitted to the NICU received their diet based on exclusive breastfeeding. However, 72% of the total number of neonates were fed with mixed breastfeeding.

Table 2. Classification of neonates according to their type of feeding.

Type of feeding	No. of neonates	Percentage
Exclusive Breastfeeding	18	28
Mixed Breastfeeding	46	72
Total	64	100

Note: Own elaboration.

Tabla 3. Clasificación de neonatos de acuerdo al sexo.

Sex	N° of neonates	Percentage
Male	38	59
Female	26	41
Total	64	100

Note: Own elaboration

Of the 64 infants studied, 38 corresponded to the male sex with a percentage of 59%, while the female sex was represented by 26 newborns, 41% of the sample studied.

Taking into account the type of feeding, Table 4 classifies the newborns admitted to determine weight gain or loss during their hospital stay, showing that of the 100% of the infants fed exclusively with human milk, 39% had an increase in weight, compared to the remaining 61% who had a reduction in body weight. Meanwhile, 52% of the infants fed with mixed breastfeeding showed weight gain, compared to the remaining 48% who showed weight loss.

Table 4. Neonatal weight change with exclusive breastfeeding during a hospital stay of 5 to 10 days.

Weight change	N° of newborns	Percentage
Weight gain	7	39
Weight loss	11	61
Total	18	100

Note: Own elaboration.

In order to identify more concretely the weight gain of each newborn, the weight at birth and the weight of each programmed measurement were taken into account to determine the percentage of weight gain in relation to the birth weight. However, as mentioned in the theoretical framework within the evolution of weight in the first days, it is normal that in the first week there is a loss of 7 to 10% of the birth weight, which should be recovered on the seventh day. Therefore, Table 5 shows in detail that, of the 18 neonates fed exclusively with breast milk, 39% showed weight gain; however, this gain was never greater than 10% of their

birth weight. The remaining 61% decreased their weight, but this loss was not greater than 10% of their initial weight.

Table 5. Change in neonatal weight compared to birth weight, according to exclusive breastfeeding.

Weight change	N° of neonates with wl or wg	Percentage
wl > 10% at birth	0	0
wl < 10% at birth	11	61
wg > 10% at birth	0	0
wg< 10% at birth	7	39
Total	18	100

Note: *wl: weight loss. **wg: weight gain. Source: Own elaboration

Considering the 46 infants studied with mixed breastfeeding, Tables 6 and 7 show that, as in the case of exclusive breastfeeding, the weight change does not include more than a gain or loss of more than 10% of their birth weight. However, 48% presented a decrease in weight of less than 10% of their birth weight and the remaining 52% of children with mixed breastfeeding had a market weight gain of no more than 10% of their birth weight.

Table 6. Neonatal weight modification with mixed breastfeeding.

Weight modification	No. of neonates	Percentage
Weight gain	24	52
Weight loss	22	48
Total	46	100

*Note:*Own elaboration

Table 7. Change in neonatal weight compared to birth weight, according to mixed breastfeeding.

Modificación de peso	N° of neonates with wl or wg	Percentage
wl > 10% at birth	0	0
wl < 10% at birth	22	48
wg > 10% at birth	0	0
wg< 10% at birth	24	52
Total	46	100

Note: *wl: weight loss. **wg: weight gain. Source: Own elaboration

In relation to the weight gain of the newborns with their medical diagnosis, Table 8 shows that of the 64 newborns studied, 19 of them had a diagnosis of Acute Pulmonary Disease corresponding to 29% of the sample, while 23 infants corresponding to 35% of the total were diagnosed with Sepsis, 16 infants, corresponding to 24% of the sample, were premature and finally, there is a different case of jaundice, syphilis, hydroelectrolyte imbalance, convulsive crisis, hypoglycemia, and genopathy/congenital malformations, each of them representing 2%

of the total sample. Likewise, the type of feeding is presented according to the grouping by medical diagnosis.

Table 8. Classification of neonates according to medical diagnosis and type of feeding.

Medical Diagnosis	N° of neonates studied	Percentage	Exclusive Breastfeeding	Mixed Breastfeeding
Acute Lung Disease	19	29	21%	79%
Sepsis	23	35	35%	65%
Prematurity	16	24	19%	81%
Jaundice	1	2	100%	-
Syphilis	1	2	100%	-
Seizures	1	2	-	100%
Genopathy/congenital malformations	1	2	100%	-
Hydroelectrolyte imbalance	1	2	-	100%
Hypoglycemia	1	2	-	100%
Total	64	100		

Note: Own elaboration

According to the type of feeding and medical diagnosis, Table 9 shows that those exclusively breastfed infants with sepsis, prematurity and syphilis gained < 10% of their weight at birth, while those infants who were mixed breastfed with a diagnosis of acute pulmonary disease, sepsis, prematurity, convulsive crisis, hydroelectrolyte imbalance and hypoglycemia also showed weight gain of < 10% at birth, prematurity, seizures, hydroelectrolyte imbalance and hypoglycemia, also showed weight gain < 10% with respect to birth, coinciding with the results obtained in the research "Comparison between weight gain of preterm infants fed exclusively breastfed and those of mixed breastfeeding or substitutes"; directed by Velásquez G. , where he followed the nutritional study including anthropometry of 48 patients, obtaining as a result that the average daily weight gain of those who received exclusive breastfeeding was 32.4 + 9.2g; while the infants who received breast milk substitutes presented an increase of 36.2 + 7.3 g. (26).

Table 9. Modification of neonatal weight in relation to Medical Diagnosis and Type of Feeding.

	Weight modification with SML	Weight modification with LM

Medical Diagnosis	Exclusive Breastfeeding	Mixed Breastfeeding	**wl > 10 % al na ci mi ent o**	**wl < 10 % al na ci mi ent o**	**wg > 10 % al na ci mi ent o**	**wg < 10 % al na ci mi ent o**	wg < 10 % al na ci mi ent o	wl < 10 % al na ci mi ent o	wg > 10 % al na ci mi ent o	wg < 10 % al na ci mi ent o
Acute Pulmonary Disease	21%	79%	0%	100%	0%	0%	0%	67%	0%	33%
Sepsis	35%	65%	0%	37%	0%	63%	0%	27%	0%	73%
Prematurity	19%	81%	0%	67%	0%	33%	0%	62%	0%	38%
Jaundice	100%	-	0%	100%	0%	0%	0%	0%	0%	0%
Syphilis	100%	-	0%	0%	0%	100%	0%	0%	0%	0%
Seizures	-	100%	0%	0%	0%	0%	0%	0%	0%	100%
Genopathy/ congenital malformations	100%	-	0%	100%	0%	0%	0%	0%	0%	0%
Hydroelectrolyte imbalance	-	100%	0%	0%	0%	0%	0%	0%	0%	100%
Hypoglycemia	-	100%	0%	0%	0%	0%	0%	0%	0%	100%

Note: Own elaboration

Discussion and conclusions

In this research work, an analysis has been made through a methodology to be followed at different times, in this way it is possible to reach the conclusion about exclusive breastfeeding, which allows supporting the newborn in its growth and normal functional development, covering all the nutritional needs and requirements, providing hormonal and/or nutritional components that allow protecting, developing and reinforcing the immune system of the newborn; it also plays a protective role against obesity (10-12). In contrast, breast milk substitutes have nutritional components in high amounts according to the nutritional requirements of the newborn, which is why they stimulate accelerated weight gain. It can be identified that a newborn has an average gain of 1 g per hour since it oscillates between 20 and 30 g per day, and this increase increases during the first three months of life; however, at the end of this trimester the increase decreases with an approximate 0.8 g per hour, and it is in the third trimester when approximately 0.5 g/hour is gained, (4) relatively a weight gain for half that which occurred in the first trimester.

It is important to note that changes occur in the first week of life, as there is a decrease of up to 10 and 15% of the total weight respectively in term and preterm newborns. In extremely low birth weight newborns, i.e., below 1000 g., a greater decrease can be expected. This weight

loss is recovered by two weeks of life; however, for newborns born below 27 weeks of gestation, the estimated weight gain ranges between 10 and 20 g/kg/day, while neonates born after 27 weeks of gestation reach a weight gain between 20 and 35 g/kg/day (5).

Breast milk is the best food for a newborn, since it is the ideal source of nutrients and energy; it also completely covers all the requirements of the newborn and the infant, thus guaranteeing a correct growth and development, strengthening their immune system every day.

Most human milk substitutes provide a very high percentage of protein compared to breast milk, maintaining approximately 1.45 to 1.8 g/100 ml, which represents 50% more than in human milk. The total protein content of breast milk is 1.1 g/100 ml (1). The predominant protein in cow's milk is alpha-lactoglobulin, which is an allergenic component, while in breast milk alpha-lactalbumin is the most important. There is a marked difference between breast-fed and formula-fed children, with the latter showing higher serum levels of threonine, phenylalanine, valine and methionine (7,9). Breast milk substitutes generally contain lactose as an available carbohydrate, as does breast milk.

Breast milk in comparison to artificial feeding, plays a basic role in the development of the immunology of the newborn as it contains immunoglobulins, lactoferrin, lactoferricins B and H, lysozyme, lactoperoxidase, nucleotide hydrolysing antibodies, k-casein, α-lactalbumin, haptocorrin, mucins, lactadherin, free secretory component, fatty acids, leukocytes, maternal cytokines, SCD14, complement, complement receptors, β-defensin 1, Toll-like receptors, bifidus factor; and all of them together make human milk work as an antimicrobial agent against infections, as long as its consumption persists. It has been proven that colostrum and human milk serum present high doses of IgG, IgA and IgM (12).

Regarding the contribution of micronutrients, the contribution of calcium and phosphorus is described in detail, highlighting a greater contribution in infant formulas; however, 75% of the calcium in breast milk is absorbed, compared to 20% in human milk substitutes, which is essential for the development of bone tissue in the newborn. The same is true for the iron supply, since the iron contained in breast milk has a bioavailability of 49%, compared to only 4% in artificial breastfeeding. Breast milk also contains a complete hormonal profile, including oxytocin, prolactin, leptin, ghrelin, adiponectin, insulin, IGF-2, cortisol, prostaglandins, thyroid-stimulating hormone and thyroxine; it should be noted that, in the first six months of life, the high concentrations of insulin, leptin, IL 6 and TNFa in breast milk will help to avoid overweight, excess fat mass and consequently accelerated weight gain (3).

According to the results obtained, it can be concluded that most of the neonates admitted to the Neonatal Special Care Unit are fed with mixed breastfeeding and a very low percentage are exclusively breastfed. However, when taking into account the type of diet to compare the parameters in neonatal weight gain, only 39% of the total number of infants exclusively breastfed had weight gain <10% of the weight at birth, compared to the infants fed with mixed breastfeeding where more than 50% had weight gain compared to the weight at birth. For this reason we can conclude that, regarding the type of feeding, there is a higher incidence of accelerated weight gain in infants fed with human milk substitutes, compared to infants who exclusively received milk from their mothers; however, in addition to breaking the balance of their normal growth and development, the fact of consuming more protein than required in a milk substitute may represent a health risk due to the renal load of solutes that this implies.

Taking into account the weight gain of the neonates with their medical diagnosis, we found a limitation, since, in terms of jaundice, syphilis, hydroelectrolyte imbalance, seizures, hypoglycemia, and genopathy/congenital malformations, only one case per pathology was presented, which is why it is not possible to make a comparison of weight gain. Regarding the 19 neonates diagnosed with Acute Pulmonary Disease, all the exclusively breastfed infants showed weight loss, and more than half of the mixed breastfed infants also showed a marked weight loss. While 63% of the children who were diagnosed with sepsis and exclusively breastfed gained weight, 73% of the mixed breastfed children gained weight in relation to their birth weight.

Of the preterm neonates who were exclusively breastfed, only 33% of them achieved a weight gain of <10%, and of the preterm neonates who were sustained with mixed breastfeeding, 38% of them had a weight gain in relation to birth. Therefore, it can be emphasized that, of the medical diagnoses presented in neonates admitted to the Neonatal Special Care Unit of the Autlan Regional Hospital, Mexico, in the period from June to December 2016; Acute Pulmonary Disease and Prematurity have greater metabolic demand, a situation that makes it more difficult for neonates to gain weight, regardless of the type of feeding they receive.

As mentioned in the analysis of the literature, the medro is influenced by pathological, psychological, social and nutritional considerations, therefore, the weight gain may also be conditioned by the pathology or medical condition of the neonate, This is also mentioned by Murillo Fajardo in his research on weight gain in premature infants hospitalized in the Neonatal Intensive Care Unit from January 1 to December 31, 2018, in which he states that "in order to achieve optimal weight gain in the newborn, it will depend on the expertise of health personnel in both the nutrition received and the resolution of diseases in the newborn that hinder their growth" (28). It will be interesting to start a new research correlating the pathology of the newborn, type of feeding and weight gain.

In spite of the fact that most of the population has empirical knowledge about the benefits of breastfeeding for newborns, in many occasions they choose to use industrialized feeding, either with mixed breastfeeding or artificial breastfeeding in its totality, ignoring the risk factors involved in its consumption, especially when it comes to obesity and its complications in adulthood.

It is important to raise awareness among healthcare staff and the population in general about the indiscriminate use of human milk substitutes, in order to favor and increase the statistics of exclusive breastfeeding during the first six months of life, which will result in a generation of healthier children.

In spite of knowing that breast milk is the best neonatal food, since it fulfills the nutritional requirements of both macro and micronutrients, favoring the growth and normal development of the infant, protecting and favoring its immune system and preventing it from chronic diseases such as obesity, diabetes and hypertension in adulthood; there are situations in which breast milk is not available or is contraindicated for infant feeding, either because of maternal or newborn illness, or because of a shortage of breast milk in the institution's lactation center, or because of the mother's decision; in these cases, the use of human milk substitutes will be acceptable. It may be interesting to carry out an investigation in which the causes of abandonment of exclusive breastfeeding in patients admitted to the Neonatal Intensive Care Unit of the Autlan Regional Hospital are determined, and thus be able to support the mother in

the factors that are preventing this feeding, which will undoubtedly favor the health of the binomial.

Knowing the standards of weight gain of the newborns while they were admitted to the Neonatal Special Care Unit of the Autlan Regional Hospital, Mexico, it is important to follow a line of research by monitoring these patients for at least 6 months, since this is the period of time that the World Health Organization (WHO) establishes as a period of exclusive breastfeeding; In addition, as health professionals we have the capacity to influence as breastfeeding advisors, thus supporting the mother in difficult situations that she considers a risk to abandon this practice of neonatal feeding, which contributes to the health of the infant and the mother herself, both in the short and long term.

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NUTRITIONAL MEDICAL TREATMENT IN PATIENTS WITH COVID-19

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Abstract. Introduction. Coronaviruses are a large family of viruses that can cause disease in both animals and humans. In humans, several coronaviruses are known to cause respiratory infections that can range from the common cold to more serious illnesses such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Methods. Nutritional medical treatment is of the utmost importance, given the high energy and protein needs associated with the energy expenditure that the disease entails, and in the recovery phase, which can be long. An inadequate diet, whether it is associated with overweight or obesity or malnutrition, can significantly influence the evolution of Covid-19. Therefore, patients hospitalized for Covid-19 must be properly nourished.

Keywords: Keywords: COVID-19, Treatment for COVID-19 patients, Nutrition for COVID-19 patients.

TRATAMIENTO MÉDICO NUTRIMENTAL EN PACIENTES CON COVID-19

Resumen. Introducción. Los coronavirus son una extensa familia de virus que pueden causar enfermedades tanto en animales como en humanos. En los humanos, se sabe que varios coronavirus causan infecciones respiratorias que pueden ir desde el resfriado común hasta enfermedades más graves como el síndrome respiratorio de Oriente Medio (MERS) y el síndrome respiratorio agudo severo (SARS). Método. El tratamiento médico nutricional es de suma importancia, dado las altas necesidades energéticas y proteicas asociadas al gasto energético que conlleva la enfermedad, Y en la fase de recuperación, que puede ser larga. Una alimentación poco adecuada, tanto si se asocia a un cuadro de sobrepeso u obesidad como a un cuadro de desnutrición, puede influir notablemente en la evolución de la Covid-19. Por ello, a los pacientes ingresados por Covid-19 hay que nutrirles adecuadamente.

Palabras clave: COVID-19, Tratamiento para pacientes con COVID-19, Nutrición para pacientes con COVID-19.

Introducción

There is a long family of viruses that were identified in the mid-1960s, causing various diseases in humans. Some types of coronaviruses are common in people and others in animals. Earlier examples of these viruses such as SARS and MERS were spread by cats or camels.

The first cases of COVID-19 were reported on December 31, 2019, in Wuhan city in Hubei province, China, where a cluster of pneumonia cases with unknown etiology was reported.

On January 30, 2020, the Director-General of the World Health Organization (WHO) declared the outbreak to be a public health emergency of international concern (PHEIC), accepting the advice of the Emergency Committee of the International Health Regulations (IHR).

On February 11, following World Health Organization (WHO) best practices for naming new human infectious diseases, it named the disease, COVID-19, short for coronavirus disease 2019.

On the same day, the International Virus Taxonomy Committee announced "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" as the name of the new virus causing COVID-19. Finally, on March 11, 2020, the WHO Director-General declared the pandemic associated with COVID-19 (2).

As of April 19, 2020, 2,241,778 confirmed cases of COVID-19 have been reported globally, which were reported by 212 countries, areas, or territories. Of the total number of reported cases, the number of deaths included has exceeded 100,000 with 152,5511 deaths reported. There has been a decrease in the number of new COVID-19 cases and deaths reported from China since February and an accelerated increase in the number of cases and deaths reported from countries outside China, mainly driven by some European countries and the United States of America (2,3).

This disease primarily affects the respiratory tract, but can deteriorate to multi-organ failure and be fatal. Prolonged stays in the Intensive Care Unit are a major cause of morbidity and mortality in patients with COVID-19. Older adults and poly morbid individuals have worse outcomes and higher mortality.

Signs and Symptoms

Coronaviruses are respiratory viruses that replicate in the airways. And, throughout the course of the disease, people may be asymptomatic, i.e., without symptoms or symptomatic usually causing mild to moderate upper respiratory tract illnesses, such as the common cold.

Common symptoms are fever, cough, and tiredness. And about 5% of people who become severely ill have difficulty breathing. And they can include runny nose, headache, sore throat, fever, a general feeling of malaise, loss of taste, smell, and appetite, among others. These human coronaviruses can sometimes cause respiratory tract diseases, such as pneumonia or bronchitis in more severe cases and without timely treatment.

People who already have a pathology such as cardiopulmonary disease, weakened immune systems, infants, and older adults may be at higher risk.

Two other human coronaviruses, MERS-CoV and SARS-CoV, have been known to cause severe symptoms frequently. Symptoms of MERS generally include fever, cough, and shortness of breath that often progress to pneumonia.(4)

The symptoms, in any case, are similar in all these pathologies. The main difficulty in comparing them is the variability in which the flu can present itself. Fever, cough, and shortness of breath are some of the most common.

Thus, for example, fever can occur in 83 to 98 percent of coronavirus cases and in virtually all cases of SARS (99-100 percent) and MERS (98 percent of cases). For influenza, however, it can occur in 36 to 100 percent of cases.

Similarly, cough affects 76 to 82 percent of Covid-19 cases; 62 to 100 percent of SARS cases; 83 percent of MERS cases; and 40 to 100 percent of influenza cases.

Pathophysiology

Currently, there is little information about it; however, the initial infection will be caused by the virus entering the respiratory tract, then the binding of AC2 receptors and multiplication causing cellular injury. And with this, the immune response begins together with the great capacity of viral dissemination or contagiousness (5).

The major structural proteins found on the membrane surface of SARS-Cov-2 viral particles are: Membrane (M) and envelope spike (S).

Particularly, the SARS-Cov-2 receptor anchor domain is located in the membrane protein S. The ACE2 receptor is a type I membrane receptor; under normal conditions, its main function is the proteolytic cleavage of angiotensin 1 into angiotensin 1-9, while under pathological conditions, it is the protein binding site of several coronaviruses (5).

Protein S has two subunits: S1 and S2, the first one is the one that binds to the host cell receptor by possessing the anchor domain. SARS-CoV-2 and when the stability of the S protein is broken, a link is formed that enters by endocytosis to release its RNA and initiate the viral replication cycle.

The cells with the highest receptor capacity are the ACE2 cells, which are present in humans regardless of age or gender. They are distributed throughout the body and can be found in type II pneumocytes of the pulmonary alveolus, stratified epithelial cells of the esophagus, absorptive enterocytes of the ileum and colon, myocardial cells, epithelial cells of the renal proximal tubule, and urothelial cells of the bladder. Therefore, symptomatology in these devices must be taken into account.

Passing to the pulmonary infection phase, the virus moves to the alveolus, causing a lesion in the wall, inflammatory reaction, and activation of immunity in general. Macrophages will be activated, presenting alveolitis related to edema and alteration in the small vessel that triggers an alteration in perfusion (5).

Later in the pulmonary infection and hyperinflammatory phase, it can cause respiratory distress and endothelial injury, which can be associated with thrombosis, myocarditis, diarrhea, renal failure, liver failure, or acute necrotizing encephalopathy in the bloodstream.

Transmission

The disease is spread primarily from person to person by droplets that are ejected from the nose or mouth of an infected person when coughing, sneezing, or talking. There are various estimates of the incubation period for SARS-CoV-2, but the most widely accepted are 4 to 5.1 days. Human coronaviruses are most commonly transmitted from an infected person to others through the air by coughing and sneezing. Close personal contact, such as touching or shaking hands.

Obesity, risk, and severity of COVID-19

There is some discussion as to how obesity may increase the risk for severe cases of viral disease, and there are several explanations for this. The nutritional status of a given person may alter the immune response to a virus. And some comorbidities are risk factors for progression to the severe spectrum of COVID-19.

In the first instance, it is considered that obesity modifies the humoral and cellular responses of immunity by being a proinflammatory state. If this is examined in microenvironments, such as the lung, it is observed that there are alterations in the function of macrophages and T cells, favoring viral expansion at that site, increasing the possibility of serious damage.

In addition to the above, it has been said that in patients with obesity and respiratory viral infections there is a higher viral load due to a delay in viral clearance or a higher viral elimination in the symptomatic phase of the infection (6).

All this is relevant, given that in the current SARS-CoV-2 pandemic, which causes coronavirus pneumonia or COVID-19, obesity has been reported as one of the risk factors associated with the development of severe pneumonia.

In a recent analysis in New York City, of 4,103 patients confirmed with COVID-19, 26.8% were obese (body mass index ≥ 30 kg/m2), and 15% had diabetes. Furthermore, 39.8% of the patients who required hospitalization were obese, compared with 14.4% of the positive cases who were not hospitalized. In the multivariate analysis, grade 3 obesity (≥ 40 kg/m2) was one of the factors most associated with the risk of critical illness (hazard ratio: 6.2; 95% CI: 4.2 - 9.3), defined as admission to intensive care, use of mechanical ventilation, or death (6).

Prevention and Treatment

Health measures and strategic objectives should be generated to limit the spread among individuals and contain the epidemic or encourage its progression. Pay close attention to the promotion of prompt and adequate clinical care, and social distancing to avoid contagion. Some very important sanitation measures according to WHO to avoid contagion are to wash hands often with soap and water for at least 20 seconds.

Avoid touching your eyes, nose, or mouth with unwashed hands. Covering your mouth and nose with a tissue when coughing or sneezing, or with the angle of your elbow, are good preventive measures, as well as avoiding close contact with sick people and staying home if you are symptomatic, cleaning and disinfecting frequently touched objects and surfaces, wearing facemasks, and people who have symptoms of Covid-19 should wear facemasks to help prevent the spread of the disease to others. Facemask use is also essential for health care workers and people caring for someone in a closed environment (at home or in a health care facility). If soap and water are not available, use a hand sanitizer containing at least 70 percent alcohol.

There is no specific antiviral treatment recommended for Covid-19 coronavirus. People with Covid-19 should receive supportive care to help relieve symptoms.

The most frequent symptoms are fever, dry cough, and general malaise, representing 98%, 76%, and 44% of patients, respectively. Gastrointestinal symptoms, such as diarrhea and neurological symptoms, such as headache, are also reported. The increased prevalence of reports of anosmia and ageusia will also be considered among the primary symptomatology to be considered during the presumptive diagnosis.

In severe cases, treatment should include medical care to support vital organ function. It is very important that persons who believe they may have been exposed to Covid-19 should contact their health care provider immediately.

Vaccination

Considered one of the most important inventions in the history of mankind, vaccines represent the simplest and most cost-effective intervention to protect against epidemics and pandemics. Basically, the benefits are related to the reduction of mortality and morbidity, and include, in turn, economic benefits by avoiding hospitalization, preventing long-term disability, and sustaining the economy.

There are currently vaccines developed against SARS-CoV-2, and those licensed are Oxford-AstraZeneca, Pfizer-BioNtech, Sputnik V, CanSino, SinoVac, Janssen, Sinopharm, and Bharat.

Equitable access to safe and effective vaccines is critical to ending the COVID-19 pandemic, so it is hugely encouraging to see so many vaccines in testing and development. WHO is working tirelessly with partners to develop, manufacture, and deploy safe and effective vaccines.

Safe and effective vaccines are a game-changing tool; however, for the foreseeable future we must continue to wear masks, clean our hands, ventilate indoor spaces well, maintain physical distance, and avoid crowded places.

Being vaccinated does not mean that we can disregard precautionary measures and put ourselves and others at risk, especially since the extent to which vaccines protect not only against disease, but also against infection and transmission, is still under investigation.

Nutritional treatment

Nutrition-based treatment includes checking a person's nutritional status and giving appropriate foods or nutrients to treat conditions, such as those caused by diseases, such as diabetes, heart disease, and cancer or communicable diseases.

It may involve simple changes in a person's diet, or intravenous or tube feeding. Medical nutrition therapy can help patients recover faster and spend less time in a medical center or intensive care.

Nutritional support for patients with COVID-19 according to the ESPEN and ASPEN guidelines indicates that energy needs can be assessed using indirect calorimetry or weight-based prediction equations and formulas.

For patients at risk of refeeding syndrome, it is recommended to start with 25% of the total caloric expenditure and monitor the serum phosphorus, potassium, and sodium level of these patients. It is recommended between 15-20 kcal/kg/day and 1.2 to 2 grams/kg/day of protein (7).

27 kcal per kilogram of body weight of total expenditure is used for polyomorbid patients over 65 years of age and 30 kcal per kilogram of body weight for severely underweight polyomorbid patients.

The calculation of proteins, carbohydrates, and lipids should be 1 gram of protein per kilogram of body weight and more than 1 gram for hospitalized patients (7).

In terms of carbohydrates and lipids, both are adapted to the energy needs of each patient with Lp: 30% and CHO: 50%.

Take great care in the adequate supply of vitamins to potentially reduce the impact of the disease. Vitamin D and its deficiency has been associated with viral diseases, such as influenza, HIV, and Hepatitis, and it has been observed that patients with a good supply of Vitamin D have had better disease outcomes. Vitamin A has been shown that adequate supplementation can reduce morbidity and mortality in infectious diseases.

Deficiencies of minerals such as selenium, zinc, and polyunsaturated fatty acids, such as Omega-3, should be considered in the evaluation for these patients (8).

Glutamine is not recommended for enteral supplementation, Omega-3 formulas have been shown to improve intensive care stays. Arginine has been shown to have a possible replacement benefit for the patient with COVID-19. Vitamin C, a water-soluble vitamin with a recognized antioxidant effect, may be administered in short periods. Vitamin D, which is severely deficient in sepsis, may help reduce mortality (8).

Enteral and Parenteral Nutrition

The most important issue is the timing of initiation of nutritional therapy. The goal should be to initiate early enteral nutrition (EN) within 24-36 hours of ICU admission or within 12 hours after intubation and placement on mechanical ventilation. In the patient who is unable to maintain voluntary oral intake, early EN is recommended by the SCCM / ASPEN 2016 and ESPEN 2019 guidelines.

Parenteral nutrition (PN) should be initiated as early as possible in the high-risk or moderately to severely malnourished patient for whom early gastric EN is not feasible.

Enteral nutrition should always be preferred over parenteral nutrition due to lower infectious and non-infectious complications.

Nutrition is a basic concept for all living beings. In general terms, it is responsible for our organism to obtain the necessary elements to carry out its vital functions as well as the energy we require in the execution of daily activities.

Although it seems a simple process, which all people do on a daily basis, sometimes, due to various circumstances such as illnesses and even accidents, it cannot be done in a natural way. In these cases, it becomes essential to administer supplements, either by enteral or parenteral route.

Parenteral nutrition is performed intravenously, through a catheter that provides the body with a solution containing about 40 essential nutrients for human beings, such as proteins, crystalline amino acids, carbohydrates, lipids, and electrolytes.

Providing adequate nutritional support is very important in the evolution and recovery of hospital patients. Health institutions report that up to 70% of them are in some stage of malnutrition, which increases infectious complications, length of stay in the health center, and mortality (9).

In people affected by COVID-19, nutrition must be one of the central measures of an integral treatment to optimize its results since a sufficient supply of nutrients is essential to survive the severe aggression that this virus produces in the organism.

Although coronavirus is a recent disease and there are few studies on the subject, it has been detected that it can have repercussions in several organs, in addition to the lungs, especially during the acute phase.

When critically ill patients with COVID-19 present complications in the stomach and/or intestines, manifesting inflammation in the abdomen, diarrhea, vomiting, among other symptoms, enteral nutrition is not functional.

Although clinical guidelines approved by the Society of Critical Care Medicine and the American Society for Parenteral and Enteral Nutrition (ASPEN) indicate that the enteral route should be the first choice, in cases of gastrointestinal intolerance, such as those mentioned above, adequate parenteral nutrition may be beneficial during the pandemic under certain variables. (10)

In general, it provides a practically complete nutritional supply to critically ill patients and favors the rehabilitation of those who are recovering.

In addition, with the correct use of personal protective equipment, parenteral nutrition implies a lower risk of contagion by saliva and secretions for health professionals since, as it is performed intravenously, it avoids the contact involved in the placement and maintenance of the oral device used in enteral nutrition.

On the other hand, the European Society for Clinical Nutrition and Metabolism (ESPEN) has pointed out that parenteral nutrition with state-of-the-art lipid-based formulations, such as olive oil, as opposed to soybean oil emulsions, does not contribute to disease-induced inflammation or the development of liver disorders. (11)

Recommendations

The world is currently experiencing the Coronavirus-19 pandemic. Given the circumstances and one of the main recommendations is quarantine, which in medicine is a term to describe the isolation of people for an unspecified period of time to prevent or limit the risk of the spread of a disease.

And one of the things that can be associated with the disruption of our normal routine can lead to generate types of feelings and conditions of our mental health.

Therefore, increase energy intake, the consumption of higher amounts of fats, carbohydrates, and proteins.

In which certain behaviors are united, such as the emotional, which is the intense desire to eat, the behavioral, which is the search for food, and the cognitive, which are the thoughts we develop about food, and without forgetting the physiological, which includes salivation (12,13).

It is important to consume foods that contain or promote the synthesis of serotonin and melatonin in the diet. This includes a considerable variety of plant species, including roots, leaves, fruits, and seeds, such as almonds, bananas, cherries, and oats.

Protein foods such as milk and dairy products are the main sources of the sleep-inducing amino acid tryptophan. In addition, tryptophan is involved in the regulation of satiety and calorie intake through serotonin, which primarily reduces carbohydrate and fat intake and inhibits neuropeptide Y, the most potent hypothalamus mineral peptides (14).

During quarantine, increased macronutrient intake may also be accompanied by micronutrient deficiency as occurs in obesity.15, which is commonly associated with impaired immune responses, particularly cell-mediated immunity, phagocyte function, cytokine production, secretory antibody response, antibody affinity, and the complement system, making them more susceptible to viral infections (15,16).

Therefore, during this time, it is important to take care of nutritional habits, following a healthy and balanced nutritional pattern containing a large amount of minerals, antioxidants, and vitamins. Several studies reported that fruits and vegetables that supply micronutrients can boost immune function.

Sources of vitamin C include red peppers, oranges, strawberries, broccoli, mangoes, lemons, and other fruits and vegetables. The main dietary sources of vitamin E are vegetable oils (soybean, sunflower, corn, wheat germ, and walnuts), nuts, seeds, spinach, and broccoli. In addition, quarantine may be associated with less time outdoors, less sun exposure, and reduced vitamin D production as a result of lower levels of 7-dehydrocholesterol in the skin.

Vitamin D deficiency in winter has been reported to be associated with viral epidemics. In fact, adequate vitamin D status reduces the risk of developing several chronic diseases, such as cancers, cardiovascular diseases, diabetes mellitus, and hypertension, which significantly increase the risk of death from respiratory tract infections that otherwise cure people (17,18).

Since time spent outdoors and consequently sun exposure is limited, it is recommended to get more vitamin D from the diet. Foods containing vitamin D include fish, liver, egg yolk.

Another essential trace element that is crucial for the maintenance of immune function is zinc. Zinc has been reported to inhibit the binding and elongation of the severe acute respiratory syndrome (SARS) RNA polymerase (RdRp) template in Vero-E6 cells. Although oysters contain the highest amount of zinc per serving, the most common foods for zinc are represented in poultry, red meat, nuts, pumpkin seeds, sesame seeds, beans, and lentils (19).

Method

A search was carried out in the main bibliographic databases of peer-reviewed articles, in search engines of scientific articles that are in the process of peer review, in generic internet search engines, and in COVID-19 development follow-up platforms of academic institutions; where treatments are described in the acute stage of the disease in stable patients in adult population.

Table 1. Search strategy: The search was based on the following databases: PubMed, Biblio Xplora and ScienceDirect.

PubMed	Xplora Library	ScienceDirect
10 results	100 results	10 results
5 included	9 included	6 included
Excluded - 3 Per title in case of - 1 Per abstract - 1 Restricted	Excluded - 50 Per title - 40 Per abstract - 1 Repeated	Excluded - 2 Per title - 2 Per abstract - 2 Repeated

Inclusion criteria

- Articles in English and Spanish
- 2019-2020 Updated Studies

Exclusion criteria

- Languages other than English or Spanish.

Results

The search yielded a total of 120 articles, of which 102 were excluded because of title, abstract, or year of publication. In total, as a result of this search, 20 articles were included which met at least one of the criteria. Based on the results of the study, these show a great diversity in the changes and recommendations for patients showing the pathology.

Discussion and conclusions

There is currently no vaccine or specific antiviral treatment to prevent or treat COVID-19 infection. The only proven methodology to prevent infection is to avoid exposure to the virus; therefore, uninfected persons (with the exception of appropriately protected health care professionals) should avoid contact with affected persons. In general, persons infected with COVID-19 should receive supportive treatment depending on their clinical presentation, i.e., to help alleviate symptoms in relatively mild cases or to ensure respiratory function in more severe cases.

The response to COVID-19 has demonstrated a much clearer understanding of mental well-being as a central consideration compared to previous emergencies.

Wellness has been a common part of media and public discourse, with workplaces, health systems, and civil society rising to the challenge of finding innovative ways to maintain social support, communication, and provision of basic needs. There has been a considerable amount of high quality, evidence-based resources available to guide mental health and wellness support for specific groups.

Thus, a healthy lifestyle and wellness support in terms of health, mental health, and nutrition is essential to reduce susceptibility and long-term complications of Covid-19.

Now more than ever, wider access to optimal nutrition should be a priority, and people should be aware of the importance of healthy lifestyle to reduce susceptibility and long-term complications of Covid-19.

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PREPARATION AND SENSORY EVALUATION OF BISCUIT BASED ON YELLOW PITAHAYA PEEL FLOUR (SELENICEREUS MEGALANTHUS) FLAVORED WITH BASIL (OCIMUM BASILICUM) AND ROSEMARY (ROSMARINUS OFFICINALIS)

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Abstract. This research was done in order to provide humans with natural and nutrient-rich products. The objective is the fortification (sensory) of the classic wheat flour with flour from the yellow pitahaya peel, because this fruit is of high nutritional value. In Ecuador there is enormous production of rosemary and basil, however, little consumption, these raw materials were applied a technological process such as dehydration (hot air drying). For the preparation of the biscuit, 3 formulations with different dosages of aromatic herbs were used: (T1, T2, T3) containing T1: 15% HP, 5% A and 5% R; T2: 15% HP, 7% A and 3% R; T3: 15% HP, 3% A and 7% R, where the percentage of the flour of the pitahaya shell is maintained, which changes are the percentages of the flavorings, which is basil and rosemary. The sensory evaluation was performed using a 4-aspect hedonic scale by a panel of 30 untrained evaluators who scored from 1 (I dislike it) to 4 (I like it very much). The properties evaluated are: color, texture, flavor and aroma in the 3 treatments achieved. A (DBCA) completely randomized block design was applied in the 3 treatments and 3 repetitions, with a study of variances and Tukey's test at 5% probability. The results showed that the T2 treatment (15% HP, 7% A and 3% R) has the highest agreement due to the evaluators, for which a microbiological and physical study was carried out.

Keywords: Yellow pitahaya, cracker, sensory attribute, rosemary, basil.

ELABORACIÓN Y EVALUACIÓN SENSORIAL DE GALLETA A BASE DE HARINA DE CÁSCARA DE PITAHAYA AMARILLA (SELENICEREUS MEGALANTHUS) SABORIZADA CON ALBAHACA (OCIMUM BASILICUM) Y ROMERO (ROSMARINUS OFFICINALIS)

Resumen. Esta investigación se hizo con la finalidad de brindar al ser humano productos naturales y ricos en nutrientes. Como objetivo la fortificación (sensorial) de la harina de trigo clásico con harina de la cascara de pitahaya amarilla, debido a que esta fruta es de alto valor nutricional. En el Ecuador existe enorme producción de romero y albahaca, sin embargo, poco consumo, a estas materias primas se les aplicó un proceso tecnológico como es la deshidratación (secado de aire caliente). Para la preparación de la galleta se usaron 3 formulaciones con diferentes dosificaciones de hierbas aromáticas: (T1, T2, T3) conteniendo T1: 15% HP, 5% A y 5% R; T2: 15% HP, 7% A y 3% R; T3: 15% HP, 3% A y 7% R, donde se mantiene el porcentaje de la harina de la cascara de la pitahaya lo cual cambia son los porcentajes de los saborizantes que es albahaca y romero. La evaluación sensorial ha sido ejecutada utilizando una escala hedónica de 4 aspectos por un panel de 30 evaluadores no entrenados que calificaron del 1 (me desagrada) al 4 (me gusta mucho). Las propiedades evaluadas son: color, textura sabor y aroma en los 3 tratamientos conseguidos. Se aplicó un (DBCA) Diseño de bloque completamente al azar en los 3 tratamientos y 3 repeticiones, con estudio de varianzas y prueba de Tuckey al 5% de probabilidad. Los resultados mostraron que el tratamiento T2 (15% HP, 7% A y 3% R) tiene el más grande asentimiento a causa de los evaluadores por lo cual se le realizo estudio microbiológico y físico.

Palabras clave: Pitahaya amarilla, galleta, atributo sensorial, romero, albahaca.

Introduction

Cookies are defined as a versatile and perishable food obtained by adding ingredients such as wheat flour, water, salt, sugar, fats, and enriching ingredients that provide proteins, complex carbohydrates, fiber, vitamins, and minerals in low quantities (1). The combination of a cereal with organic waste and aromatic herbs has made it possible to have fortified foods for human consumption with high nutritional value (2). The shell of the yellow pitahaya is an organic waste that is not used for industrialization because it contains nutrients such as calcium, phosphorus, iron, and dietary fiber that facilitates nutritional transit (3).

Wheat flour is one of the staple foods for many countries and among the most important cereals in Ecuador due to its high consumption in products such as bread, biscuits, noodles, etc. Ecuador is being very dependent on imports; internal import requirements are at 98%, while local production is 2% (4).

The wide variety of foods available to the population, which are consumed as fresh food or used as raw material to obtain new agro-industrial products. However, the mixture of a cereal with fruits and aromatic herbs made it possible to have fortified foods for human consumption, with a correct balance of nutrients and important amino acids (5).

Despite the fact that the combination of foods is a source of relevant nutrients, important portions of different fruits, vegetables, cereals, pseudo cereals, aromatic herbs are used, that is, they are not exploited to their full potential. Among these are mentioned certain native foods in the coast and highlands such as quinoa, amaranth, rosemary, basil, also bearing in mind that organic rejects such as the yellow pitahaya husk are not exploited and industrialized (6).

Man has depended on plants throughout his history to take care of his health. Nowadays, it is very difficult to find references to the first uses of medicinal plants in prehistoric times (7). The rosemary plant has had a very important weight throughout history due to its tributes and diversity of minerals such as potassium, calcium, iron, and vitamins B6; it is a refreshing digestive, a depurative, decongestant, tonic, and stimulant (8).

Basil is a natural pain reliever and relaxant. The oils contained in the fiber of its leaves contribute to alleviate the effects of arthritis and are curative for the joints. These leaves are an intestinal anti-inflammatory and favor the correct functioning of the urinary system and are an excellent insect repellent (9). In Ecuador, bibliographic information on basil and rosemary production, industrialization, and consumption is still scarce. Nevertheless, in the universal field, the tendency of its consumption and production shows a sustained growth throughout the last decades (10).

In Ecuador, there is a great variety of fruits that are not commercialized or known in the local and international market, as is the case of Pitahaya (11). The relevant reasons for its consumption are the properties attributed to its use, such as nutrients, minerals, and vitamins (12).

The objective of the population is to lead a healthy life by consuming natural products rich in nutrients. Currently, the processing of by-products, such as cookies, has been included with the intention of taking advantage of the dietary fiber present (13).

Dehydration is one of the oldest forms of food preservation and its objective is to eliminate most of the moisture from the products. Dehydrated foods retain a large proportion of their nutritional value if the process is carried out properly (14).

Flours in the food industry represent an important raw material for obtaining many foods and are generally made from barley, corn, or wheat. Their process consists of milling the grain, but dehydrated milled fruits are currently being used as an alternative to conventional flours (15).

These factors were considered at the time of conducting this research, which pursued the following objectives: to produce a high-quality cookie with attractive organoleptic characteristics obtained from pitahaya peel flavored with different percentages of basil and rosemary. To estimate consumer acceptance with information obtained through a panel of evaluators, to carry out microbiological analysis of the cookie obtained with the highest sensory acceptance.

Method

Location of research

The research was carried out at the facilities of the pilot plant of the Faculty of Agricultural Sciences of the Agrarian University of Ecuador, Milagro campus, located at coordinates 2°8.042' S south latitude and 79°35.649' W west longitude.

Product formulation

Three products were developed (T1, T2, and T3), whose independent variables were the amount of dehydrated aromatic herbs, such as rosemary and basil (Table 1). The dependent variable was the microbiological characteristics. Three replicates were carried out for each treatment under the same conditions. For the statistical analysis of the data, a completely randomized complete block design (CRBD) was used.

Treatments

Table 1. Formulation for the production of traditional cookies.

	PRODUCT		
Ingredients	**Witness g**	**Unit**	**Absolute % Absolute**
Wheat Flour	400	g	45. 97 %
Pitahaya Flour	00	g	00 %
Basil Leaves	00	g	00 %
Rosemary Leaves	00	g	00 %
Lard	200	g	22,99 %
Butter	50	g	5,74 %
Sugar	200	g	22,99 %
Salt	20	g	2,29 %
Total	870	g	100 %

Based on the traditional formula, we will consider the total wheat flour as 100% of the wheat flour in the formula, and on this we will work the difference in the percentages of the yellow pitahaya shell flour and the aromatic herbs.

Table 2. Treatment 1. Formulation for the production of cookies.

	PRODUCT		
Ingredients	**T1 g**	**Unit**	**Absolute % Absolute**
Wheat Flour	300	g	75 %
Pitahaya Flour	60	g	15 %
Basil Leaves	20	g	5 %
Rosemary Leaves	20	g	5 %
Total	400	g	100 %

Table 3. Treatment 2. Formulations for cookie production.

	PRODUCT		
Ingredients	**T2 g**	**Unit**	**Absolute % Absolute**
Wheat Flour	300	g	75 %
Pitahaya Flour	60	g	15 %
Basil Leaves	28	g	7 %
Rosemary Leaves	12	g	3 %
Total	400	g	100 %

Table 4. Treatment 3. Formulations for cookie production.

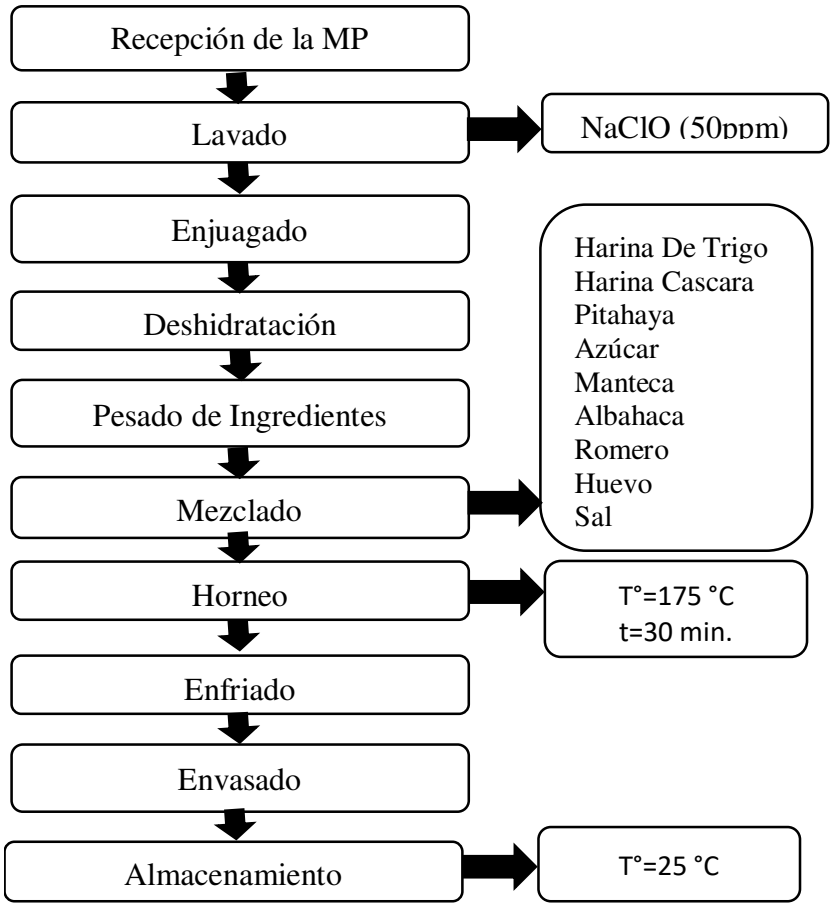
	Product		
Ingredients	**T3 g**	**Unit**	**Absolute % Absolute**
Wheat Flour	300	g	75 %
Pitahaya Flour	60	g	15 %
Basil Leaves	12	g	3 %
Rosemary Leaves	28	g	7 %
Total	400	g	100 %

The sensory evaluation of the treatments was carried out by a panel of untrained evaluators for the 3 formulations. The evaluators were students of the Agricultural Engineering career, agro-industrial mention, Milagro campus, of both sexes, between 18 and 25 years of age. Each panelist was trained based on the hedonic evaluation of 4 points of view that they applied to all treatments, and were given a glass with water, samples of each cookie, and an evaluation form. The water was used to rinse off any residue after each tasting. The data obtained were evaluated using the INFOSTAT statistical program.

Obtaining the product

The process is briefly explained in Figure 1. The materials used were selected based on their quality. The yellow pitahaya, basil, and rosemary hulls were washed using a solution of sodium hypochlorite (50 ppm concentration), then rinsed with pasteurized water. Then, the yellow pitahaya peel was dehydrated at a temperature of 53 °C for 23 hours, after which the peel was milled to obtain a good quality flour. In addition, the rosemary and basil leaves were dehydrated at a temperature of 53 °C for 5 hours, then the raw materials to be used were weighed, once the materials were weighed, the elements were mixed for the preparation of the cookies, Afterwards, the cookies were baked at a temperature of 175°C for 30 minutes. Finally, the product was cooled for its respective packaging in polyethylene bags, the cookies were stored at room temperature from 24 to 28°C, having a shelf life of 9 days for consumption.

Figure 1. Flow diagram of the cookie manufacturing process. [Source: Own elaboration.]



Results

The pitahaya shell flour was obtained by dehydration, which consisted of a gradual increase in temperature to reduce the water in the food. The main factors involved in dehydration were time (23 hours) and temperature (53 °C), in a tray dehydrator, followed by milling to reduce sizes and thus obtain a good quality flour.

For aromatic herbs, it was obtained by dehydration, which consisted of a gradual increase in temperature with a time of (5 hours and temperature of (53 °C), in order to eliminate the water from these leaves.

The butter type cookie was made with 3 formulations of different dosages of basil, 20g, 28g and 12g; and of rosemary, 20g, 12g, and 28g, keeping the same quantity of the pitahaya shell flour that is observed in tables 1, 2, and 3. The industrial type equipment used for the elaboration of the cookie was a laminator whose function was to lengthen the dough and stretch it, it is composed of metal rollers whose advantage is to increase the warmth of the product and decrease the physical effort. In relation to the INEN 2945 norm, it complied with the established or stipulated requirements, the organoleptic part, specifically the external aspects, complied with the characteristics according to the different formulations and dosages of the pitahaya shell flour.

Table 4 shows the results of the sensory evaluation carried out on 30 untrained evaluators. The cookie made with flour obtained from pitahaya husk flavored with aromatic herbs has a good acceptance mainly in the characteristics of flavor, odor, color, and texture where there is no significant difference in the treatments.

Table 5. Sensory analysis results.

Answer Option		Features				Total
		Taste	Odor	Color	Texture	
Treatment 1	I like it very much	10	13	15	19	57
	I like it	14	12	8	10	44
	I do not like it	5	4	5	1	15
	I dislike it	1	1	2	0	4
Treatment 2	I like it very much	**16**	**17**	**21**	**24**	**78**
	I like it	12	11	6	5	**34**
	I do not like it	2	2	3	1	**8**
	I dislike it	0	0	0	0	**0**
Treatment 3	I like it very much	11	12	13	19	55
	I like it	13	13	10	10	46
	I do not like it	4	1	5	1	11
	I dislike it	2	4	2	0	8
Total		**90**	**90**	**90**	**90**	**360**

Table 5 shows a comparison between treatment 1, treatment 2, and treatment 3 of the averages with respect to flavor, which have a great acceptance. Differences are evident in the results of table 4 between treatments 1, 2, and 3 in each of the attributes. And, for this reason, the second treatment was the accepted one. Therefore, the microbiological and physical analysis was carried out.

Table 6. Results of microbiological and physical analysis.

Parameters	**Unit**	**Results**	**Requirements**	**Methods**
Total coliforms	CFU/g	1×10^1	1×10^2 CFU/g	NTE INEN 1529-10
Staphylococcus aureus	CFU/g	<3	<3 CFU/g	NTN INEN 1529-6
Molds	CFU/g	Absence	.....	NTN INEN 1529-6
Humidity	%	9,13 ± 0.10	12	INEN ISO 6496
Ash	%	13,92 ± 0.11	24	INEN ISO 5984

Table 6 shows the microbiological and physical results where they are within the permitted range, according to the INEN standard.

Discussion and conclusions

Currently, it has been possible to make several partial substitutions of wheat flour for other types of flours to produce biscuits, bakery products, noodles, for example: soy, breadfruit, spinach, rice, chickpea, banana, etc.

According to Barreto (16), "in which he elaborated a gourmet bread based on chickpea and wheat flour" was incorporated, basil with improved nutritional qualities with percentages of wheat flour substitution in: 25%, 50%, and 75% of chickpea flour and 100% wheat flour, the formulation that obtained better results in the nutritional part was 25% wheat flour and 75% chickpea flour presenting high protein, minerals (potassium, magnesium, calcium, phosphorus, and iron) ethereal extract and crude fiber. While this study of cookie with the yellow pitahaya shell flour treatment 2 of 300 g of wheat flour corresponding to 75% and 100 g of the remaining 25% (100 g) is divided into three sections, first section which is 15% (60 g) of the yellow pitahaya shell flour, 7% (28 g) of basil and 3% (12 g) of rosemary.

According to Cabrera (17), where they elaborated cookies with freeze-dried vegetables, the result of the analysis had an increase in the nutritional, physicochemical and sensory attribute of the product. In addition, since most of the vegetables have inside antioxidant in a natural way, with them the oxidation of the cookie was diminished, it had a procedure of dehydrated in this situation the lyophilization, perfecting the characteristics of color and smell. As results of the analysis showed that the cookie with flour obtained from the yellow pitahaya shell and the combinations of aromatic herbs, such as basil and rosemary increased its organoleptic property because they were subjected to dehydration at drying temperature to preserve the aroma of freshness since, in the sensory evaluation, the third procedure comparatively with the above mentioned obtained similar results in color and texture.

According to Silva (18), in which several percentages of wheat flour were replaced in 20, 15, and 10% by soy flour and soluble fiber, by means of the sensory study, the consumer's favorite was selected, and then the nutritional characteristics of the cookie were evaluated. After making the sensory research the formula chosen by the panelists has been the one made with 20% soy flour and 80% wheat flour. The preferred scoring components were texture, color, and flavor, while the smell was not so much liked by the panelists, taking as an allusion the INEN rule (19), Venezuela COVENIN 226-88. In what for this analysis the element of approval has been the smell, in procedure 1 of 60 gr of yellow pitahaya shell flour, 20 gr of basil, and 20 gr of rosemary because the color had assent in the 3 treatments.

According to Tapia (20), whose research was based on "obtaining cookies with partial substitution of chontaduro flour (Bactris gasipaes Kunth)" and the percentage of substitution has been in wheat flour of 5, 10, 20% by chontaduro flour and wheat flour at 100%. In the sensory analysis, the formulation that had the highest level of acceptability was the 5% of chontaduro flour, among the attributes of pleasure were flavor, color, texture, after the physicochemical analysis was made, and its nutritional benefits were known, there was a growth in humidity, in the results of protein reduced the proportion of the same compared to the one elaborated with wheat flour at 100%, and the fat content grew in the chontaduro bread. Meanwhile, in this analysis the cookie with flour obtained from the yellow pitahaya shell and the combinations of aromatic herbs in procedure 2 of 75% wheat flour, 15% of pitahaya shell flour, 7% of dehydrated basil, and 3% of dehydrated rosemary have had similar results in the sensory part, and, in the microbiological part, the results have been within the established parameters.

In the same way, a comparative analysis is made with the standard under the parameters of microorganisms that is assimilated to the analysis made by the laboratory generating the microbiological parameters; whose results are favorable since it is seen the compliance that they are within the parameters in the same way the mold is analyzed in which in the analysis they maintain absenteeism. According to Arando (21), indicates that, from the compositional analysis, digestibility tests and microbiological quality of this compared with a conventional raw material, such as fish meal; corresponding to the quality control of food and ingredients for animal consumption, with counts of aerobic mesophiles, total coliforms. According to Ramos (22), the study carried out with insects' proportion of conventional raw materials that have antibacterial substances; and, therefore, the possibilities of pathogenic microorganisms are limited. Microbiological quality indicators provide timely warning of inadequate handling or contamination that increases the risk of the presence of pathogenic microorganisms in food (23).

From the present analysis it can be concluded: 3 types of cookies containing different percentages of basil and rosemary were formulated and elaborated; the products presented attractive and innovative organoleptic properties for the consumer; it is recommended to carry out an investigation using the yellow pitahaya shell flour as an alternative for animal feed.

Sensory acceptance was evaluated by an untrained panel for the three cookie formulations. In general, the degree of acceptance of the three cookies was quite satisfactory. The cookie of treatment 2 with 300 grams of wheat flour, 60 grams of flour obtained from the yellow pitahaya shell, 28 grams of basil, and 12 grams of rosemary in its composition, which in total gives 400 grams, 75% of wheat flour, and the remaining 25% is derived from 15% flour from the pitahaya shell in combination with 10% of aromatic herbs, deriving 7% in basil and 3% in rosemary. In the microbiological and physical analyses, the results obtained for mold, total coliforms, Staphylococcus aureus, humidity, and ash are within the parameters established in NORMA INEN; and, therefore, the product is safe and suitable for the consumer.

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INFLUENCE OF PARENTS ON THE SEXUALITY OF ADOLESCENT WOMEN IN LOW-INCOME FAMILIES OF BOLIVIA

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Abstract. Introduction. Studies highlight the influence of the family on the sexuality of adolescents, since they could help delay sexual intercourse and promote safer sexual behaviors among adolescents, so this study will explore the role that parents play in sexuality and in the sexual experiences of adolescent women living in disadvantaged environments in the city of Cochabamba, Bolivia. Methods. The data were collected as part of the Global Study of Early Adolescence, and were based on in-depth semi-structured interviews among 20 female adolescents between the ages of 10 and 14, who were studying at the "Gerardo Vargas Vidal" school, as well as with their selected parents. The interviews were transcribed verbatim and uploaded to the Atlas.ti Program. An ethnographic design was used for the analysis, within the interpretive paradigm. Results. The adolescent analysis of the influence that family composition has on sexuality and sexual health of women; The role that parents play, and especially the mother in addressing these issues, is also evident, so proper communication is important; on the other hand, domestic violence is perceived as something natural among adolescent girls and has a negative influence on the sexual development and behavior of adolescent women. Discussions and conclusions. It is important to consider the participation of parents, especially the role of mothers in the design of sexuality programs for adolescent women.

Keywords: sexual development, adolescent, sexual behavior.

INFLUENCIA DE LOS PADRES EN LA SEXUALIDAD DE LAS ADOLESCENTES MUJERES EN FAMILIAS DE BAJOS INGRESOS DE BOLIVIA

Resumen. Introducción. Estudios destacan la influencia de la familia en la sexualidad de los adolescentes, puesto que podrían ayudar al retraso del inicio de la vida sexual y fomentarían conductas sexuales más seguras entre los adolescentes, por lo que este estudio pretende explorar el papel que desempeñan los padres en la sexualidad de las adolescentes mujeres que viven en entornos desfavorecidos en la ciudad de Cochabamba, Bolivia. Métodos. Los datos fueron recolectados como parte del Estudio Global de Adolescencia Temprana, y se basaron en entrevistas semiestructuradas en profundidad entre 20 adolescentes mujeres comprendidas entre los 10 a 14 años, que cursaban estudios en un colegio público de Bolivia, así como con sus respectivos padres. Las entrevistas fueron transcritas textualmente y subidas al Programa Atlas.ti. Para el análisis se utilizó un diseño etnográfico, dentro del paradigma interpretativo. Resultados. El análisis reveló la influencia que tiene la composición familiar en la sexualidad y en la salud sexual de las adolescentes mujeres; asimismo se evidencia el papel que juegan los padres, y en especial la madre en el abordaje de estas temáticas, por lo que una adecuada comunicación es importante; por otro lado, la violencia doméstica tiene influencia negativa en el desarrollo y comportamiento sexual de las adolescentes mujeres. Discusiones y conclusiones. Es importante considerar la participación de los padres, destacando el rol de las madres en el diseño de los programas de sexualidad de las adolescentes mujeres.

Palabras clave: desarrollo sexual, adolescente, comportamiento sexual.

Introduction

Sex and sexuality are complex processes in the lives of adolecents, especially for the construction of their being (1), and are often considered taboo subjects in the Latin American population.

The study of early adolescence (10 to 14 years of age) is transcendental because it is a stage in which there is greater physical, cognitive, emotional, psychological and social development (2). It is a period in which adolescents seek their own sexual identities, influenced by interactions with friends, family and the media (3).

This makes this period the most vulnerable to high-risk behaviors (4), among which early sexual initiation stands out, exposing them to STIs/HIV, unplanned pregnancies and abortions (5); which especially affect female adolescents due to maternal conditions such as pregnancy and maternity (6), which could lead to obstetric problems that could even result in death.

Several studies suggest that the construction of sexuality is transmitted in the family system and in a society's culture (7), so the family and especially communication with parents about sexuality could help the health of adolescents by delaying the beginning of sexual life and the exercise of safer sexual behaviors (8), so studies have found that adolescents from married families with two biological parents are less likely to have unprotected sex and early sexual initiation compared with adolescents from single-parent families, cohabiting stepparents,

and married stepparents (9); however, adolescents and their parents are often hesitant to talk to each other about sex, and only half of adolescents report talking to their parents about this topic. (8)

It is known that adolescents who have a positive relationship with their parents are less likely to initiate early sexual relations (10). There is evidence that associates several dimensions of parenting such as connection, love, material support, behavioral control, follow-up and communication between parents and adolescents positively with the reduction of risk levels among adolescents (10), hence the importance of studying this influence in Bolivia.

In Bolivia, the percentage of adolescents aged between 15 and 19 years who were already mothers or who have been pregnant for the first time in 2016 was 14.8% (11), so we can say that unplanned and early pregnancy affects the health of adolescent women and impacts the development of their potential; the complexity of this problem is based on a mixture of social, individual and legal-normative factors that affect maternal mortality in the adolescent population (12). Among the factors that predispose to early pregnancy we could mention poverty (12), lack of knowledge of contraceptive methods, lack of information on sexuality, sexual violence (13), family treatment, socioeconomic and cultural factors (14) and negatively affect female adolescents, since when an adolescent pregnancy occurs, mothers and fathers in many cases tend to expel adolescents from their homes or confine them to their homes, invalidating their human rights (12).

Several of these pregnancies that occur at an early age end in abortion, with the risk of it being performed in inadequate sanitary conditions, exposing adolescents to greater risks of morbidity, infertility and death (11), this being a fundamental public health problem in the country because it puts the lives of adolescent women at risk; on the one hand, the birth rate in women between 15 and 19 years of age was 116 per 1. 000 pregnancies (15), on the other hand we must highlight the maternal mortality ratio per 100,000 live births which in 2011 was 160 (16), deaths resulting from misconducted abortion which, for the most part, are preventable.

Another problem is violence against women, which should be considered when analyzing the sexual health of adolescents since it constitutes a substantial problem of early unions, the rate of pregnancies due to sexual violence in children under 15 years of age is around 11.1% (17), which mostly occur in the family environment, registering 14 thousand cases of women raped every year, of which 60% have been victims of rape within their own homes (12).

According to the Demographic and Health Survey (2016), the knowledge of contraceptive methods that women between 15 and 19 years of age have is important, exceeding 90%, although the term "know" does not necessarily mean that the person has a good level of information about the method, it is enough that they can identify it (11), but only 9.4% of young women use some method of contraception (11). Therefore, despite the apparent knowledge of contraceptive methods, this situation is not reflected in their use and application (18), possibly

because they do not know how to use them, because they do not consider their use appropriate or because they are not easy to acquire.

In Bolivia, there are many myths and prejudices among parents who think that talking about sexuality with their children encourages early sexual initiation in adolescents (19), thus creating a distance. UNAIDS recommends intervening early, before adolescents become sexually active, and asks for an understanding of sexual and reproductive health communication between parents and adolescents to promote healthy sexual behavior (20).

For the present analysis, the "Multilevel Approach to Adolescent Pregnancy" (6) was used as a guide to examine more clearly how the family influences the Sexual and Reproductive Health outcomes of female adolescents.

Thus, this research pursues the following objective: (1) To explore the role of the parent/daughter relationship in the sexual experiences of female adolescents living in disadvantaged environments in Cochabamba.

Method

Study design and sample

Bolivia was part of the Global Early Adolescence Study (GEAS), which allowed examining how gender norms evolve and influence the health of early adolescents in 14 sites around the world. Between 2015 and 2016 the individual semi-structured in-depth interviews were conducted, the sample for this study was by convenience and 20 interviews were used with female adolescents aged 11 and 14 years, in order to have a diversity of the sample, obtaining the following distribution: 11 years (3), 12 years (9), 13 years (7), 14 years (1), all of them were students of a public school in the city of Cochabamba. We also obtained 20 interviews with their parents/guardians: mothers (19) and fathers (1).

Inclusion criteria included being between 11 and 14 years of age, being a student registered in a public school in Cochabamba, as well as having authorization to participate in the study from both the adolescent and the parents. The exclusion criteria were being outside the age range of 11 to 14 years, studying in another school in the area and not agreeing to participate in the research.

An ethnographic design was used for the thematic analysis, within the interpretative paradigm.

Data collection

The adolescents were approached personally and in order to increase trust among the participants, the interviews were conducted in the same school, the researchers also explained the purpose of the study and two research methods were used at the beginning of the sessions consisting of: "Timeline" which was conducted in groups of four adolescents, and the "Venn

Diagram" which was conducted individually prior to the in-depth interview. The timeline consisted of drawing the important events in the life of a typical adolescent from birth to adulthood. The discussion focused on gender differences (events that might be different between males and females). For the Venn diagram, adolescents were individually asked to indicate the relationships they had with key people in their lives by drawing circles on a sheet of paper, with the larger circles representing the most important relationships, in addition they were asked to mark positive (smiley face) and negative (sad face) relationships. (21)

The categories were developed within the framework of the GEAS project and, for one part, the interviews with adolescents were organized into: a) becoming an adolescent, b) community influences, c) family influence, d) relationships among friends, e) gender norms, f) gender socialization and g) romance and sexuality, with the category of family influence being analyzed for the present study, in order to have a greater understanding and comprehension of the influence of parents on adolescent sexual behavior.

On the other hand, we have the categories developed with the parents, which in addition to the categories developed with the adolescents, the category of parenting was added, again the matrices of these codes were related to family influence on adolescent health and parenting that influence sexual behavior.

The questions were framed as stories about how interpersonal relationships change as they grow up and how they learned about certain "rules" and behaviors about adolescence. The semi-structured interviews lasted an average of 60 min.

Data analysis

Interview recordings were transcribed verbatim and uploaded to Atlas.ti. A final set of "core" codes was developed with the consensus of all participants.

Ethical and safety considerations

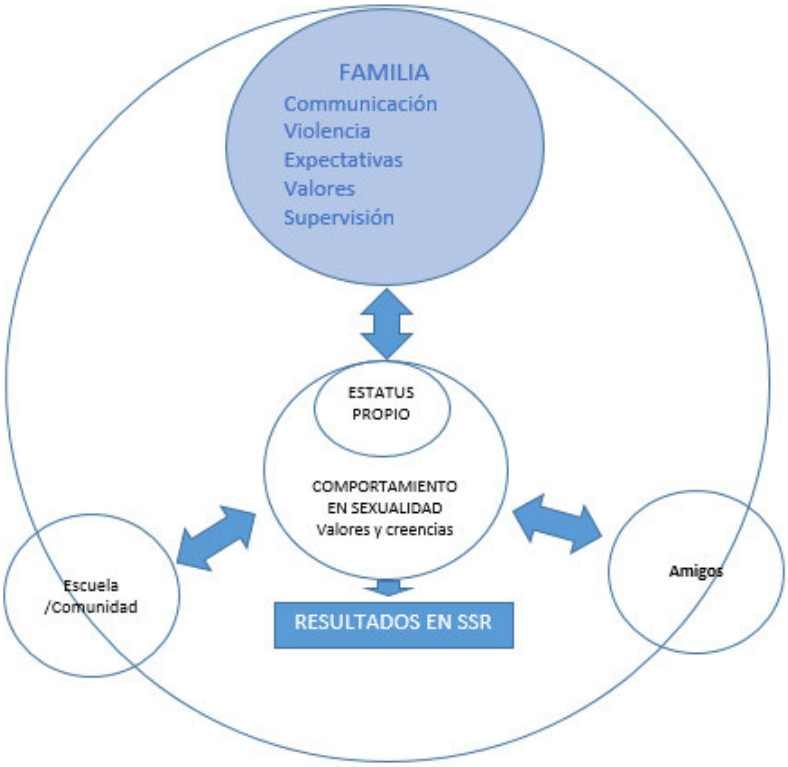
Written consent was requested from parents and female adolescents. At the departmental level, approval was obtained from the Bioethics Committee of the Universidad Mayor de San Simón in the city of Cochabamba, Bolivia.

Results

Intermittent Fasting

According to previous studies it is important to know the role played by the family, taking greater interest in mothers and fathers to understand the influences on sexual risk behaviors among adolescent women from low-income households, the analysis of the findings was based on the multilevel approach to teenage pregnancy developed by Chung (2018), which takes into account family influence and the subsections: communication between parents/adolescents, the expectations they have of their daughters, the values they transmit, the supervision exercised by parents on adolescents and intrafamily violence.

Figure 1. Diagram to organize the results [Source: Own elaboration based on the Multilevel approach to adolescent pregnancy].



Parental communication with adolescent daughters

More than half of the parents/guardians interviewed consider their daughters of that age as children, so they do not consider it necessary to communicate and address issues of sexuality with their daughters, this influences the healthy decision making of adolescents regarding their sexuality and has an impact on the prevention of premature and unplanned pregnancies.

> *"According to the teacher, they should always be treated as children, even if they are a little older, but they should always be told, they should be treated as children, so that they feel like children, so that they don't say that I am grown up and can do whatever I want. The teacher tells us they have to take it like a child, so that they continue to feel like children, not*

> *grown-ups".* ***Mother of female adolescent, 13 years old, Bolivia, MOMI_A_12***
>
> *"So, if parents don't talk to them, how should we explain to them what is really going on with them. They can fail in life, that's why".* ***Mother of female adolescent, 12 years old, Bolivia, MOMI_A_38***

The lack of communication, according to the results found in this research, was especially present in disintegrated families, that is, in homes where adolescents live only with the father or only with the mother, the stepfather/stepmother, a situation that is very frequent among the participants of the study due to the migration that parents recur to in order to assume family economic responsibilities.

Almost all the adolescents interviewed mentioned having better communication with their mothers than with their fathers, which coincides with the opinion of the mothers. Something that is noteworthy is that none of the adolescent girls participating in the study mentioned communication regarding sexuality issues with extended family (considering among them: uncles, aunts, cousins, cousins, grandparents, grandmothers).

> *"My mom is affectionate with me and my brother, she is affectionate, eh always when we tell her something, sometimes they say no see, our mom is our best friend they say no see, I always tell my mom my things, how I am doing at school, if something has gone wrong, when I have done well, or when something I can't understand, she explains to me, when I am already, when I was a child, when I was a child my mom, normal, she only bought me toys like that, Now when I'm a little older, a little bit older, she tells me that there are some girls that when they are starting to, others say rule, I don't know, when we are starting that, my mom knows how to explain, you don't have to be afraid, she tells me, it's normal sometimes, my mom knows how to tell me, she knows how to explain things, she knows how to support me, when I'm sad she tells me daughter what are you sad about, she gives me advice, she knows how to talk to me".* ***Female adolescent, 13 years old, Bolivia FI_13_A12.***
>
> "*I have been this, my children's friend. Look at their father, he has dedicated himself more to work".* ***Mother of female adolescent, 11 years old, Bolivia MOMI_A_16.***
>
> *"Because sometimes a dad maybe, the strong hand of the house. So he is the one who supports us in that. Then with the girls, not much because I am the one who is most interested in my daughters. The father, not much, he is not interested. I don't make him take much interest in my daughters, because they see so many things".* ***Mother of female adolescent, 12 years old, Bolivia MOMI_A_38***

Almost half of the interviewees indicated that the limited communication they have with their parents is due to the limited time they have for work reasons and sometimes because of their parents' temper.

> *"Sometimes he gets like that, he yells a lot, because he is always angry about something, and because of that, then he yells at me too, at my mom too, because he is always angry for some reason".* ***Female adolescent, 13 years old, Bolivia FI_13_A14***

Parents who indicated talking with their daughters did not refer to having extended to a meaningful discussion about healthy sexual behavior, most of them referred that they gave information to understand the emotional and physical consequences of sexual initiation or early pregnancy telling many times their experiences, but they did not refer to talk about contraceptive methods, sexually transmitted diseases, so they would not be adequately providing them with information about healthy relationships and safe sexual practices.

> *"Of course, we have all known how to fall in love. I also almost at the age of 19 I got my husband, because I had no one to talk to me too, no; but now I tell my daughter, I talk to my daughter because of that, that if she wants to get married at least she should have a boyfriend when she is already in her 20s, something like that".* ***Mother of female adolescent, 12 years old, Bolivia MOMI_A_07***

On the other hand, all the female adolescents participating in the study are aware that unplanned pregnancy has a negative impact on them, because pregnancy develops in their bodies, putting them at a disadvantage, so they worry about not getting pregnant, but above all about not having a boyfriend, preferring to focus on their studies to increase their job opportunities, seeking greater social acceptance.

> *"But also as when you have these relationships, you run the risk of getting pregnant, and some men when they find out that their girl is pregnant, do not want to take responsibility and blame her, why you have not protected yourself, however he is also to blame for, because the two of you are together".* ***Female adolescent, 13 years old, Bolivia FI_13_A14***

Domestic Violence

The interviews revealed that violence among adolescent females is a common practice; adolescent females are victims of different forms of domestic violence such as verbal, psychological and physical violence. Almost half of the adolescent girls perceive violence and disrespect as normal occurrences and even see it as acceptable behavior and this limits communication with adolescent girls in a transcendental way.

> *"Sometimes he gets like that, he yells a lot, because he is always angry about something, and because of that, then he yells at me too, at my mom too, because he is always angry for some reason".* ***Female adolescent, 13 years old, Bolivia FI_13_A14***

Young adolescent girls talk naturally about the violence they receive from their parents, seeming that violence against women is part of their lives.

> *"My mom has always hit me and my dad once touched me, but he cried because he hit me, and since then he has not hit me, he just scolds me, that's all".* ***Female adolescent, 12 years old, Bolivia FI_13_A15***

Expectations they have of their daughters

On one hand, most parents/guardians agreed with the importance of education in their daughters' lives, and revealed their fear of early sexual relations and pregnancy, so they prohibit their daughters from approaching adolescent boys, which does not result in an adequate solution.

> *"Sometimes I am afraid to take care of a little woman, there are times, maybe if they don't get pregnant".* ***Mother of female adolescent, 12 years old, Bolivia MOMI_A_06***

> *"Well, my daughter's goal is really just to study. Then she dedicates herself to having a profession. Afterwards, they have a house, or if you are going to do something that they see, they see it as something that will give them economic earnings. That's what my daughters focus on now".* ***Father of female adolescent, 12 years old, Bolivia DADI_A_01***

> *"When it has to be a boy, he has to take responsibility, not take a gamble, because I explain to you, right? Look how your father has left us, if he really can be a boy, he can be responsible for you, if he can love you too, I know that maybe he does not love you, that is why he has left and does not even talk to you, he does not know where you are or how you are, if you eat or do not eat, if you are bad or not bad, he does not ask you anything about you. So in order for this not to happen to you, you have to get ahead, I always tell you to study, every day you have to study, even if it is just for a little while, you have to study, not all day too, you have to have time to eat lunch, to play, to study, I also tell them, so they tell me yes mommy"* ***Mother of adolescent female, 13 years old, Bolivia MOMI_A_12***

On the other hand, the social roles imposed on women could be seen in most of the adolescents interviewed, since they must perform domestic chores such as washing, cleaning, cooking and caring for the children, in other words, they have to prepare themselves to assume this responsibility in the future, another example is the role in the home where they have to serve food first to the men, perhaps responding to cultural or traditional values, reinforcing gender inequalities.

> *"My mom used to tell me -little daughter if you are not going to learn to wash, cook, take care of your husband, you are going to do the talking for me, what your mother has taught you they are going to say- and that is what you have to do with daughters.".* ***Mother of female adolescent, age 12, Bolivia MOMI_A_5***

> *"First we serve the food to my dad, just me, my brother, just my sister, just my sister, just my sister, me and my nephew last".* ***Female adolescent, 12 years old, Bolivia FI_12_A01***

> *"Women always suffer more than boys, because boys only know how to make babies, perfect. And women have to wash clothes, they have to provide for their children, they have to give them milk, everything, food. They have to send food to their husbands, wash their clothes, all that".* ***Female adolescent, 12 years old, Bolivia FI_12_A06***

Values they transmit to their daughters

Most of the parents/guardians interviewed emphasized the expressiveness of affection that their daughters should have, they said that they should be sensitive, tender and expressive and with good behavior, this becomes important in SRH because they learn to assume a passive and often subordinate role in romantic relationships, with submissive attitudes and little empowerment in relation to the decisions of adolescent boys, preventing them from freely choosing what they want to do with their own bodies and how to regulate their reproduction, highlighting cultural beliefs, family traditions and transgenerational inheritance. (22)

> *"I tell her sometimes, you don't have to be aggressive, you have to have a little patience, and you don't have to be, you have to behave like a little woman more than anything else, you have to be gentle, you have to have that self-esteem, not like other girls running around, making a fuss or pulling boys around, none of those things. I talk to her about those things".* ***Mother of female adolescent, 13 years old, Bolivia MOMI_A_12***

> *"Ah, you have to be moderate, you have to help, that way you make people like you, and they say that girl is good, she helps you, you have to choose, while when you sit down and just look at her, and you don't help her, you make your mom and yourself look more, sometimes you don't teach your daughter anything, a woman has to know how to cook, iron, wash clothes, everything; For example, at home I make cakes, I know how to bake chicken, I make cakes, I do everything, my mother has taught me, that's what a woman and a man have, men mostly go on the internet, they don't do much, sometimes when they come to school they go on the internet, they play, they go to the tilines and so on".* ***Female adolescent, 12 years old, FI_12_A05***

This is also reflected in some of the adolescent girls' comments, as quoted below:

> *"Because men are always half, I don't know, they are other kinds or they don't want to be with you it's just for an annoying, for, to get you pregnant, whatever".* ***Female adolescent, age 12, FI_12_A04***

> *" mean, women always suffer more than boys, because boys only know how to make babies, perfect. And women have to wash clothes, they have to support their children, they have to give them milk, everything, food.*

> *Their husbands they have to send them food, wash their clothes, all that".* ***Female adolescent, age 12, FI_12_A06***

Supervision

Most of the parents/guardians interviewed referred to applying greater supervision to their daughters, likewise they give them less freedom of movement, establishing when and where they can go, although they said that this control is not always possible due to long working hours, this coincides with the interviews with adolescents who frequently noted that parents were often absent, and referred to lack of emotional support.

> *"I see some mothers instead of guiding them and other situations, they are more dedicated to the business".* ***Mother of female adolescent, age 11, Bolivia MOMI_A_16***

> *"Sometimes the girls drink because their parents are not at home, they neglect them, they don't take care of them, that's why they dedicate themselves to other things".* ***Mother of female adolescent, 12 years old, Bolivia MOMI_A_05***

Likewise, most of them referred to the importance of friends among their daughters, so most of them indicated that they take control of their daughters' friends. What is reflected in the interviews with adolescents where more than half of the interviewees stated that they prefer to distance themselves from friends who have sentimental interests, this influences their behavior as a risk factor, it is clear that they avoid conversations about sexuality.

> *"Yes, I believe because every girl, every boy or every adolescent, both female and male, friendships influence a lot; for good boys, good girls, sometimes they are easily corrupted".* ***Mother of female adolescent, 13 years old, Bolivia MOMI_A_14***

> *"Sometimes there are bad friends and they divert them".* ***Mom of female adolescent, age 12, Bolivia MOMI_A_07***

> *"My mom tells me that you shouldn't hang out with friends like that, with bad friends, who lead you astray".* ***Female adolescent, 13 years old, Bolivia FI_13_A11***

Regarding control of technology, most of the parents/guardians interviewed indicated that they are unaware of the use of technology, but recognize the influence it has on their daughters' sexuality, especially through the use of pornographic pages, and spoke of television, which often transmits inappropriate messages that induce the initiation of premature sexual relations.

> *"They are more alert, they want now, for example, to get into technology, they want to go on the Internet, they want to meet new friends".* ***Mother of female adolescent, 11 years old, Bolivia MOMI_A_16***

Discussion and conclusions

This research analyzed the influence of the relationship parents/adolescent daughters on the sexuality of their daughters and although many times, the family, is confused about how to deal with the sexuality of adolescents, it is not understood that they are sexually active and even less that they have the right to be so (23), as we could analyze in this research there is little communication between parents/guardians and daughters regarding sexuality, and although mothers express their experiences around sexuality, but there is no direct communication about contraceptive methods, sexually transmitted infections or HIV. A study conducted in Nigeria in 2017 recommended greater involvement of parents in communicating and monitoring the sexual behavior of female adolescents, taking into account the consequences of risky sexual behaviors on the health of adolescents and society in general (24); the solution to the problem of unwanted pregnancies, STIs, HIV / AIDS and abortions, is not in banning sex, but it is helping our young people to express their sexuality without risk (23). Another study conducted in Romania found that the family approach to sex education is positively associated with healthy sexual initiation (25).

Although the family influences the health behavior and well-being of adolescents, it is often interfered with by the corrective measures that are applied within the adolescent's family; these practices, often related to psychological violence, are very frequent and are often conceived as everyday practices in the home; one study highlights the influence that family formation has on violence in relationships (26). According to another study, violence may have contributed to a greater extent to female sexual experience in two-parent households (9).

In terms of expectations, parents want their daughters to develop in the academic field, but indirectly prepare adolescents to assume the role of caregiver at home, according to a study the lack of agency exposes them to get pregnant, by following existing norms, peer pressure, limited negotiating power in their relationship and poor acceptance of contraceptive use among their partners, impacting on the economic retribution of women.(27)

The values that parents transmit to their daughters regarding the expressiveness of their feelings and the experience of their sexuality respond to a transgenerational transmission as expressed by Neireitter (2017): "most mothers transmitted unfavorable and rejection messages regarding early motherhood. However, the intergenerational transmission of adolescent motherhood perpetuated a series of unfavorable variables in the daughters of these women.(28)

According to cultural beliefs and family traditions, when an adolescent becomes pregnant she suffers rejection by her partner and family; this coincides with a study carried out in Colombia where it was found to be common practice to abandon the partner after the first trimester; this male decision to abandon was linked to the position of his family of origin.(29)

Finally, we can conclude by highlighting the need for adolescent women to have the support of their parents/guardians in order to achieve a full and harmonious development of their sexuality.

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