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EFEITO DO CONSUMO DO LEITE EM VARIADAS PARTICULARIDADES FISIOLÓGICAS: REVISÃO DA LITERATURA
EFFECT OF MILK CONSUMPTION ON VARIOUS PHYSIOLOGICAL PARTICULARITIES: LITERATURE REVIEW
EFECTO DEL CONSUMO DE LECHE EN DIVERSAS PARTICULARIDADES FISIOLÓGICAS: REVISIÓN DE LA LITERATURA

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RESUMO

Introdução: O consumo de leite é significativo no dia a dia das pessoas, independentemente da fase da vida, sendo um alimento que contém alto valor biológico, portanto possui todos os aminoácidos essenciais em quantidades adequadas para suprir as necessidades diárias. Além disso, o leite é de fácil digestão para a maioria das pessoas e possibilita uma melhor absorção de vitaminas e minerais em comparação com outros produtos lácteos. Porém, este tema de estudo sobre os efeitos do consumo diário de leite de vaca traz discussões controversas e divergentes.

Objetivo: Esta análise tem como objetivo examinar diversos estudos que investigaram os impactos do consumo regular de leite de vaca na saúde humana, abordando tanto os potenciais benefícios como os riscos associados a esta prática.

Métodos: Revisão de literatura simples em que foram pesquisados 29 artigos na base de dados Science Direct e Pub Med, em busca de argumentos com base científica em que fossem considerados os efeitos do consumo regular de leite, quanto aos benefícios ou malefícios que esse hábito pode trazer. A metodologia de busca utilizou as palavras-chave: alergias ao leite; consumo diário de leite; leite e inflamação. Os critérios utilizados para seleção dos trabalhos foram artigos que explorassem os diferentes contextos nos quais o consumo habitual de leite pode interferir. Os artigos estudados são de diversas nacionalidades como britânica, norte-americana, irlandesa, argentina ou portuguesa.

Resultados: Estudos têm demonstrado que as patologias estudadas são cada vez mais comuns e determinantes, influenciando a história natural das doenças. Observou-se ainda que ingerir leite na frequência e quantidade adequada, ajuda a fortalecer o organismo e o sistema imunológico, além de proporcionar uma ingestão adequada de cálcio ou vitamina D. Contudo existe um potencial alergênico não negligenciável, considerando que o leite de vaca contém inúmeras proteínas, oito das quais apresentam potencial alergênico. Também a intolerância à lactose representa um problema para alguns consumidores.

Conclusão: Os estudos revistos enfatizam a contribuição fundamental do consumo de leite e seus significativos benefícios para a melhoria da qualidade de vida, desempenhando um papel crucial em diversas condições fisiológicas do corpo humano. É fundamental destacar, porém, que o potencial benéfico do leite pode ser contraproducente em casos de alergias ou intolerâncias aos seus componentes. Portanto, a inclusão do leite na dieta deve ser considerada com sensibilidade, considerando as necessidades individuais de cada pessoa.

Palavras-chave: alergia ao leite; dieta láctea; componentes do leite

ABSTRACT

Introduction: The consumption of milk is significant in people's daily routine, regardless of their stage of life, because cow's milk is a food that contains a high biological value; therefore, it has all the essential amino acids in adequate amounts to meet our daily needs. In addition, the milk is easily digested and better at absorbing vitamins and minerals compared to other dairy products. However, this topic of study regarding the effects of daily consumption of cow's milk brings controversial and divergent discussions.

Objective: This analysis aims to examine several studies that investigated the impacts of regular consumption of cow's milk on human health, addressing both the potential benefits and risks associated with this practice.

Methods: Simple literature review in which 29 articles were searched in the Science Direct and Pub Med databases in search of scientifically based arguments in which the effects of regular milk consumption were considered regarding the benefits or harms that this habit can bring. The search methodology used the keywords: milk allergies, daily milk consumption, milk, and inflammation. The criteria used to select the works were articles that explored the different contexts in which habitual milk consumption can interfere. The articles studied are from different nationalities, such as British, North American, Irish, Argentine, and Portuguese.

Results: Studies have shown that the pathologies studied are increasingly common and determining, influencing the natural history of diseases. It was also observed that ingesting milk at the appropriate frequency and quantity helps to strengthen the body and the immune system, in addition to providing an adequate intake of calcium or vitamin D. However, there is a non-negligible allergenic potential, considering that cow's milk contains numerous proteins, eight of which have allergenic potential. Lactose intolerance also represents a problem for some consumers.

Conclusion: The studies reviewed emphasize the fundamental contribution of milk consumption and its significant benefits for improving quality of life, playing a crucial role in various physiological conditions of the human body. It is essential to highlight, however, that the beneficial potential of milk can be counterproductive in cases of allergies or intolerances to its components. Therefore, the inclusion of milk in the diet should be considered sensitively, considering each person's individual needs.

Keywords: milk allergy; dairy diet; milk components

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RESUMEN

Introducción: El consumo de leche es significativo en la vida diaria de las personas, independientemente de su etapa de vida, ya que es un alimento que contiene alto valor biológico, por lo tanto cuenta con todos los aminoácidos esenciales en cantidades adecuadas para cubrir las necesidades diarias. Además, la leche es fácil de digerir para la mayoría de las personas y permite una mejor absorción de vitaminas y minerales en comparación con otros productos lácteos. Sin embargo, este tema de estudio sobre los efectos del consumo diario de leche de vaca trae discusiones controvertidas y divergentes.

Objetivo: Este análisis tiene como objetivo examinar varios estudios que investigaron los impactos del consumo regular de leche de vaca en la salud humana, abordando tanto los posibles beneficios como los riesgos asociados con esta práctica.

Métodos: Revisión bibliográfica simple en la que se buscaron 29 artículos en las bases de datos Science Direct y Pub Med, en busca de argumentos con base científica en los que se consideraran los efectos del consumo regular de leche, respecto de los beneficios o daños que este hábito puede traer. La metodología de búsqueda utilizó las palabras clave: alergias a la leche; consumo diario de leche; leche e inflamación. El criterio utilizado para seleccionar los trabajos fueron artículos que exploraran los diferentes contextos en los que puede interferir el consumo habitual de leche. Los artículos estudiados son de diferentes nacionalidades como británica, norteamericana, irlandesa, argentina o portuguesa.

Resultados: Los estudios han demostrado que las patologías estudiadas son cada vez más comunes y determinantes, influyendo en la historia natural de las enfermedades. También se observó que ingerir leche en la frecuencia y cantidad adecuada ayuda a fortalecer el organismo y el sistema inmunológico, además de proporcionar un aporte adecuado de calcio o vitamina D. Sin embargo, existe un potencial alergénico no despreciable, considerando que la leche de vaca La leche contiene numerosas proteínas, ocho de las cuales tienen potencial alergénico. La intolerancia a la lactosa también representa un problema para algunos consumidores.

Conclusión: Los estudios revisados enfatizan el aporte fundamental del consumo de leche y sus importantes beneficios para mejorar la calidad de vida, desempeñando un papel crucial en diversas condiciones fisiológicas del cuerpo humano. Es fundamental destacar, sin embargo, que el potencial beneficioso de la leche puede resultar contraproducente en casos de alergias o intolerancias a sus componentes. Por tanto, la inclusión de leche en la dieta debe considerarse con sensibilidad, teniendo en cuenta las necesidades individuales de cada persona.

Palabras Clave: alergia a la leche; dieta láctea; componentes de la leche

INTRODUCTION

There is a worrying trend for a social perception regarding the consumption of dairy foods according to which they contain high levels of saturated Fatty Acids and cholesterol, which are considered harmful to human health as they are associated with a high risk of cardiovascular diseases (CVD). CVDs are the leading cause of death in developed societies and are associated with factors such as diet, obesity, physical inactivity, diabetes, stress, and smoking. Controlling the intake of cholesterol and saturated fats of animal origin has been a fundamental dietary strategy to reduce the incidence of CVD, and therefore, reducing the consumption of products has been recommended (Siurana & Calsamiglia, 2016).

However, milk has been a source of food for humans since prehistoric times. Its primary function is to nourish and provide immunological protection for the mammalian offspring. The human being is the only mammal that drinks milk as an adult, whether for cultural reasons, eating habits, or personal preference. Consumption of milk is significant in people's daily routine, regardless of their stage of life, because cow's milk is a food that contains a high biological value. In its composition, it contains numerous proteins and minerals, including essential elements like calcium, magnesium, and phosphorus. These are crucial for training, strengthening, and maintaining muscles, preventing osteoporosis, aiding in weight loss, and providing all the necessary amino acids in sufficient quantities to meet our daily nutritional requirements (Haile & Headey, 2023; Pereira, 2014). In the composition of milk, it can also be found vitamin A (retinol), vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B12 (cyanocobalamin), vitamin C (ascorbic acid), vitamin D (cholecalciferol) and enzymes such as peroxidase, catalase, phosphatase and lipase. The aforementioned nutrients help maintain healthy eyesight and participate in the wound healing process. Because it is a highly digestible food, these minerals and vitamins are absorbed quickly (Faria et al., 2010).

The regular consumption of milk is a subject of study that brings controversial and divergent discussions. Although the nutrients in milk provide many health benefits, if consumed in excess, it can increase the incidence of acne on the dermis and abdominal discomfort in situations where the individual has irritable bowel syndrome, lactose intolerance, and Cow's Milk Protein Allergy (CMPA) (Faria et al., 2010).

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1. METHODS

In this work of simple bibliographic review, scientific articles were collected on the ScienceDirect and Pub Med platforms to analyze and discuss milk consumption, consumption habits, and its effects on health. Both the benefits and inconveniences are addressed, for those who are lactose intolerant or not, such as how much daily consumption alters their health, the possible physiological inflammations due to consumption, and what the treatment alternatives for individuals who have CMPA, its role in traditional medicine and the relation of its physiologically active nutritional components with beneficial effects to human health, through scientifically verified information. During the bibliographic review, it was noticed that milk has more benefits than negative effects on health, especially when there is no excessive consumption. In this work, 29 scientific articles were collected, including review articles and research articles. The articles studied are from different nationalities, such as British, North American, Irish, Argentine, and Portuguese. Using inclusion criteria to search for articles with the following keywords: milk consumption, milk and inflammation, and lactose intolerance.

2. RESULTS

Milk consumption is an individual and complex choice, as it involves several aspects, including nutritional, environmental, ethical, and cultural influencing factors. Consumption varies widely in different cultures and regions of the world. Some societies have a long tradition of consuming milk, while others do not incorporate it into their traditional diets.

Calcium is essential for carrying out important bodily functions such as providing rigidity to bones and teeth, supporting nerve functionality, and maintaining a normal heart rhythm. Adverse health impacts can arise with a prolonged calcium deficiency, such as osteopenia, marked by a decrease in bone mass and weakened bones, leading to osteoporosis, characterized by increased bone fragility, deterioration, and compromised bone strength (Balk et al., 2017).

Appropriate calcium intake has been correlated with a number of health benefits, namely a reduction of hypertensive disorders in pregnancy, lower blood pressure particularly among young people, prevention of osteoporosis and colorectal adenomas, lower cholesterol values, and lower blood pressure in pregnant women (Cormick & Belizán, 2019). Regarding calcium supplementation, some possible side effects have been reported, such as the formation of renal stones and myocardial infarction in older people (Pu et al., 2016), but those have been proven false (Cormick & Belizán, 2019).

Balk et al. (2017) developed an interactive world map, showing countries according to the average calcium intake and allowed them to identify intake differences on some sociodemographic variables, such as age, sex, and socioeconomic status. For this, they used reported calcium intake across 74 countries based on data from nearly a thousand studies. They found that the average national dietary calcium intake is very variable, ranging from 175 to 1233 mg/day. However, these intakes are different according to the region of the world. In Asia and several other countries, the average dietary calcium intake is lower than 500 mg/day. Also, in Africa and South America, a great number of countries have low calcium intake, in the range of 400 – 700 mg/day. On the other hand, average dietary calcium intakes greater than 1000 mg/day were observed only in Northern European countries. Regarding the variability of calcium intake according to sex, it is generally lower in women than men. As for the effect of other sociodemographic variables, namely age or socioeconomic status, no clear patterns across countries were found.

Study baseline measurements were taken from 2004 to 2013, and follow-up examinations were performed from 2012 to 2016. A total of 65642 general participants visited 38 general hospitals and health examination centers in eight regions of South Korea for the questionnaire and anthropometric and clinical measurements. Overall, participants who consumed more milk had higher intakes of total energy, carbohydrates, protein, and fat than those who consumed less milk. However, the percentage of energy from carbohydrates decreased, and that from proteins and fats increased according to milk consumption. Both men and women in the highest milk consumption group had lower sodium and calcium levels than those in the lowest milk consumption group (Lee et al., 2019).

Having in mind the key roles of vitamin D and calcium in adolescent bone health, the work by Cashman et al. (2022) investigated the nutritional status of calcium and vitamin D in a sample of Irish teenagers aged between 13 and 18 years. Their results showed that 94% of the teenagers had intakes of calcium and vitamin D below the Estimated Average Requirement values. These results confirm the inadequacy of intake for both micronutrients, with particular incidence in the group of female teenagers as compared with males.

Milk protein allergy and lactose intolerance

Adverse reactions to food are characterized as: allergic reactions, mediated by immunological mechanisms in which IgE may or may not participate (IgE or non-IgE mediated food allergy), and those due to other forms of hypersensitivity/intolerance; the latter includes metabolic/enzymatic, pharmacological, toxic and idiopathic causes (Johansson et al., 2001). The clinical presentation of food allergy is variable, and mucocutaneous manifestations, urticaria and angioedema, respiratory and gastrointestinal manifestations, and, in some cases, anaphylaxis may occur. Gastrointestinal manifestations are common (vomiting, diarrhea, esophagitis) (Couto et al., 2012).

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Cow's Milk Protein Allergy (CMPA) is an immune system reaction to proteins present in cow's milk, such as casein. The conventional treatment of CMPA consists of the avoidance of cow's milk proteins, in addition to the resolution of acute episodes. The immunological mechanisms involved in the appearance of food allergy are still not fully understood. However, it probably results from a lack of oral tolerance, that is, the lack of an active response of the immune system to an antigen presented by the gastrointestinal mucosa (Couto et al., 2012).

Cow's milk contains numerous proteins, eight of which have allergenic potential, with caseins and lactoglobulins being the most frequently responsible for CMPA (Wal, 2002). Table 1 shows the four main whey proteins with the greatest allergenic power and the portion of milk where they can be found.

Table 1 - potencial allergenic proteins in milk.

| Type of Protein | Part of the milk where it is found |
|--------------------|------------------------------------|
| S1 alpha casein | Solid Fraction |
| Beta casein | Solid Fraction |
| Casein k | Solid Fraction |
| Beta-lactoglobulin | Whey fraction |

The IgE-mediated forms constitute more than half of CMPA cases (Nowak-Wegrzyn & Sampson, 2006), usually presenting immediate symptoms a few minutes after ingestion, with conditions ranging from just skin symptoms (hives, angioedema) or gastrointestinal symptoms (vomiting, abdominal pain, diarrhea), to potentially fatal anaphylaxis, even with the ingestion of small doses. This particularity was discussed in a case study of a 16-year-old teenager, who from the 1st year of life, was diagnosed with CMPA, having been followed up in consultation with an immunoalergologist, in which he was recommended to avoidance of cow's milk proteins and the addition of soy-based foods (Couto et al., 2012). In the context of the clinical case under analysis, after the occurrence of an anaphylactic reaction after ingesting a hidden allergen, the medical team suggested to the teenager and his family the possibility of starting a protocol aimed at inducing tolerance to cow's milk proteins. This recommendation, supported by the assessment of the clinical picture, was preceded by a detailed explanation of the risks and benefits of the procedure. The proposal aimed to establish a protocol that replicated, in a physiological way, the natural process of tolerance, in which the body gradually becomes accustomed to the allergen, avoiding adverse reactions. This approach would involve controlled administration of the allergen, preferably into the digestive tract, orally or sublingually. The dosage would be started minimally, progressively increasing according to the body's acceptance capacity, in order to avoid abrupt reactions and promote a safe transition to tolerance to cow's milk proteins (Couto et al., 2012).

Currently, methodologies used for the progressive introduction of increasing amounts of cow's milk in the treatment of allergies still show considerable variability, especially during the induction phase. In conventional protocols, a dose increase is observed daily or at intervals of a few weeks, while in rapid protocols, no rush, dose increments occur at intervals ranging from minutes to hours. In addition to these approaches, there are mixed protocols that combine elements of both methodologies. It is important to highlight that the occurrence of side effects has been a characteristic frequently observed in rapid oral protocols. Given this scenario, an innovative protocol of a mixed nature was presented that was developed with the aim of overcoming some of the limitations associated with conventional methods (Couto et al., 2012). This presupposes a rapid induction phase followed by a slightly slower approach, with a sublingual and oral route of administration, using undiluted cow's milk as an allergenic extract, but foreseeing dose adaptations. This protocol has shown excellent efficacy (with the acquisition of tolerance for 200 ml of cow's milk in less time) and safety even in cases with clinical signs of severe anaphylaxis and without the need for adjuvant immunological therapy, regardless of the levels of specific IgEs, as occurred in the case under discussion, these having no predictive value for the success of the protocol; in the follow-up of this case, an immediate reduction in specific IgE for CM and casein was observed, but with an increase in specific IgE for α -lactalbumin and β -lactoglobulin.

One of the articles under study also analyzes daily calcium intake among 55 study participants who lived in the United States and included parents or caregivers of a child diagnosed with milk allergy (experimental group) and parents of a child without milk allergy (control group). This study is of great relevance since milk allergies can impact dietary calcium intake, which can represent an obstacle to achieving individuals' daily needs for this mineral. Calcium intake was assessed using the Calcium Assessment Tool, a validated, self-administered food frequency questionnaire (FFQ) that assesses daily dietary calcium intake (Dubrovsky et al., 2023). Cow's milk is among the most common food allergens in infants and young children; 1% to 5% of children worldwide have been diagnosed with a milk allergy (Flom & Sicherer, 2019). Childhood milk allergies are also associated with more severe reactions. They are a leading cause of food-induced anaphylaxis, a systemic response marked by vasodilation, vascular permeability, tissue swelling, and/or fluid retention. Food allergies have been shown to be associated with a reduction in overall quality of life, impacting children's school and social environments and nutritional status (Mehta et al., 2013).

Lactose intolerance is a gastrointestinal symptom caused by a deficiency or decreased activity of the lactase enzyme in the intestine, which makes it difficult to completely digest the lactose in breast milk or cow's milk. This is characterized by abdominal pain and distension, flatulence, and diarrhea after lactose ingestion. It usually occurs due to impaired production of the enzyme

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β -galactosidase (lactase), which is genetically determined to cease after weaning or during childhood. The development of symptoms depends on several individual factors, including diet, oro-cecal transit time, distribution and fermentation capacity of the intestinal flora, sensitivity to chemical and mechanical stimulation of the intestine, and psychological factors (Roškar et al., 2017). Due to the discomfort caused by ingesting foods containing lactose for individuals with intolerance, this study identified a lower dietary calcium intake among parents or caregivers of children with milk allergies, compared to those who care for children without allergies. The implications of this study are significant for nutritional education, particularly for parents or caregivers of children with food allergies, highlighting the importance of a thorough assessment of micronutrient consumption. Some probiotics, especially selected strains of *Lactobacillus* and *Bifidobacterium* species, have been shown to alleviate symptoms of lactose intolerance (Almeida et al., 2012; He et al., 2008, Saltzman et al., 1999).

Milk consumption and cancer risk

There has been evidence of an association between decreased risk of colorectal cancer and milk consumption, based on studies that included a large series of colorectal cancer cases. This inverse association of milk intake with colorectal cancer risk has been attributed to its calcium content, as dietary calcium intake is also inversely related to colorectal cancer risk (Godos et al., 2020). There are several potential mechanisms by which calcium may be protective, including neutralizing the carcinogenic effects of free fatty acids and bile acids, inhibiting mucosal cell proliferation and promoting cell differentiation and apoptosis, suppressing oxidative DNA damage, and modulation colorectal disease, cancer-related cell signaling pathways (Papadimitriou et al., 2021).

In an analysis of daily milk intake and its association with an increased risk of cancer, there was research that used phenotypic and genetic data, applying extensive touchscreen questionnaires, verbal interviews, physical measurements, and collecting some samples, such as blood, saliva, and urine. These data were collected from British white UK Biobank participants. For the Mendelian Randomization (MR) analyses, information from the FinnGen trial and all available consortium meta-analyses were also included. Cancers with more than 1000 cases from the UK Biobank and FinnGen cohort databases were included, and some rarer cancers were also investigated where previous meta-analyses from observational studies suggested risk differences associated with milk consumption. Mendelian randomization helps narrow unwanted influences by using genetic variants from the germline established at birth to represent an exposure (Lumsden et al., 2023).

When Magnetic Resonance Imaging (MRI) analyses were performed in pre-and postmenopausal women in the UK Biobank cohort for female cancers, it was observed that hormone levels may influence, and an association was revealed between the consumption of genetically modified milk and a higher risk of uterine cancer among pre-menopausal women. This is due to a potential mechanism that could be the menopause delaying effects of milk consumption since late menopause is a risk factor for uterine cancer (Lumsden et al., 2023). In a study before this, there was the suggestion that steroid hormones and growth factors, such as estrogens present in milk and dairy products, may increase the risk of uterine cancer in postmenopausal women, particularly in cases where there was no hormone replacement. The authors observed a low association between dairy intake and endometrial cancer, but the association was stronger among postmenopausal women who were not on hormonal therapy (Ganmaa et al., 2012).

For the effect of milk consumption on bladder and urinary tract cancer, a positive association was observed through the observational analysis of the UK Biobank but not for the MR analyses, confirming the result of previous studies (Larsson et al., 2020).

Effect of milk on hypertension

Hypertension is defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg (Lee et al., 2019). Several factors influence the development of hypertension, including an unhealthy diet and lifestyle, such as high sodium or low potassium intake, being overweight or obese, excessive alcohol consumption or smoking, and lack of physical activity (Iqbal & Jamal, 2023). To better understand the relationship between the incidence of hypertension and milk intake, there was a study that applied a validated food frequency questionnaire (FFQ), including 106 food items. Participants reported the frequency and quantity of food or drink they consumed during the previous year. This sample was selected from the Health Examinees (HEXA) study, a large-scale genomic cohort study conducted in South Korea (Jung et al., 2022). The authors concluded that higher milk intake was inversely related to the risk of increased blood pressure, thus diminishing the risk of hypertension events. In the study by Jung et al. (2022), 10.3% of participants consumed over 1 serving of milk daily. A high total energy intake, a low percentage of energy from carbohydrates, and a high percentage of energy from protein are accompanied by high milk consumption. In the group with the highest milk consumption, between men and women, lower probabilities of worsening trends in blood pressure were observed in the follow-up analysis than at the beginning of the study. Furthermore, women showed a more apparent trend towards a greater likelihood of blood pressure improvement trends. In addition, participants with higher milk consumption had a lower incidence of hypertension than non-consumers (Jung et al., 2022).

The antihypertensive effect of milk consumption can be attributed to the presence of caseins and whey proteins in milk, such as α -, β -, γ - and κ -casein; α -lactalbumin; and β -lactoglobulin, which contains peptides. Specific milk proteins exert vascular effects that reduce the risk of hypertension. Consumption of casein and whey protein reduces concentrations of soluble vascular cell

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adhesion molecule-1 (sICAM-1) and soluble vascular cell adhesion molecule 1 (sVCAM-1), leading to decreased vascular dilation and improved vascular reactivity (Jung et al., 2022). This meta-analysis showed an inverse association between the consumption of dairy foods and milk and the incidence of hypertension. Furthermore, increased milk consumption was associated with a lower prevalence of cardiovascular disease in men and women in South Korea, and milk consumption was associated with a reduced risk of coronary heart disease in South Korean postmenopausal women.

Effect of milk consumption on acne

According to the observation of Stroup et al. (2000), done through a comprehensive literature search, carried out by a complete meta-analysis following the guideline of the Meta-analyses Of Observational Studies in Epidemiology, the dose-response analysis was meticulously conducted to examine the complex relationship, both linear and non-linear, between milk intake and the potential risk associated with the development of acne. The proposition arises that dietary patterns, particularly those linked to the Western model, combined with a diet characterized by a high glycemic index (GI) and enriched in omega-6 fatty acids, play a preponderant role in triggering acne. In this context, cow's milk and its derivatives, highlighted as prominent elements in the Western diet, emerge as significant contributors to the pathogenesis of acne, as indicated by Melnik (2012).

Casein and whey protein in dairy products act as boosters, elevating insulin-like growth factor-1 (IGF-1) levels and insulin concentrations. IGF-1, playing a crucial role in enhancing the mammalian target of rapamycin activity and sebaceous lipogenesis, emerges as a significant player in the development of acne, as Smith et al. (2008) discussed. The present meta-analysis carefully incorporated 14 observational studies, which thoroughly investigated the relationship between different types of dairy products, such as whole milk, skimmed milk, yogurt/cheese, and the development of acne. The results showed a substantial association between these dairy products' consumption and acne's presence. Linear dose-response analysis revealed that each increase in servings of dairy, whole milk, and skim milk was associated with a significant 83%, 13%, and 26% increase in acne risk, respectively. On the other hand, results from no linear dose-response analysis indicated no linear relationship between dairy product consumption and acne development, while yogurt/cheese intake did not demonstrate a significant association.

Strict controls were employed to clarify the acnogenic properties of milk and its derivatives, with some analyses highlighting a notable increase in the concentration of IGF-1. Milk and its derivatives, which contain IGF-1, have the particularity of not being hydrolyzed by intestinal enzymes, resulting in the plasma release of this growth factor. Additionally, the casein content of these products stimulates the hepatic release of IGF-1, leading to a subsequent increase in plasma levels. This elevation of both exogenous and endogenous IGF-1 acts as a stimulus to sebocytes, triggering the development of acne, as indicated by Adebamowo et al. (2005).

Subsequent studies showed that the ingestion of milk and its derivatives, through the IGF-1/phosphoinositide-3-kinase (PI3K)/Akt pathways, exerts a significant influence on the expression of the transcription factor Forkhead box (Fox) O1, triggering, thus, a manifestation of acne. FoxO1, an essential regulator of acne-related genes, is secreted by the sebaceous glands, and its upregulation plays a central role in acne control, as highlighted by Agami et al. (2016). Furthermore, FoxO1 acts as a modulator of the mTOR complex 1 (mTORC1), participating in the activation and analysis of sebocytes. Milk, by increasing branched-chain amino acids (BCAA), stimulates mTOR activity. IGF-1, in turn, intensifies androgen receptors, boosting the production of testosterone and dihydrotestosterone (DHT), resulting in increased androgenic activity and promoting the growth of follicular cells, events associated with the genesis of acne.

CONCLUSION

This bibliographic review concluded that, nutritionally, milk is a rich source of essential nutrients such as calcium, protein, B and D vitamins, phosphorus, and potassium. These nutrients are critical to bone development, muscle function, cardiovascular health, and other body functions. However, some individuals are intolerant to lactose, the natural sugar in milk, which can cause digestive discomfort. Moreover, other individuals in the case studies were allergic to cow's milk proteins, which can lead to severe allergic reactions. In these cases, it is essential to avoid milk consumption or consume it according to medical advice. In other situations, in the studies analyzed, moderate consumption did not bring about significant regulatory changes, even in organisms with diseases such as high blood pressure or cancer.

For individuals with hypertension, the analysis revealed that with milk consumption, there was a lower incidence of high blood pressure episodes compared to non-consumers, as the presence of caseins and whey proteins contributed to an antihypertensive effect, reducing molecules associated with hypertension. vascular dilation. These results highlight the relevance of milk consumption in preventing cardiovascular diseases, highlighting its beneficial properties.

Regarding the association between milk intake and the incidence of acne, the relevance of the various signaling pathways and biochemical factors involved is highlighted. The results of the dose-response analysis highlight significant increases in acne risk associated with additional dairy consumption. These findings offer valuable insights to guide dietary considerations and management strategies in acne-focused clinical settings.

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AUTHOR CONTRIBUTIONS

Conceptualization, R.G.; data curation, I.B. and R.G.; formal analysis, I.B. and R.G.; funding acquisition, R.G.; investigation, I.B. and R.G.; methodology, R.G.; project administration R.G.; resources, R.G.; supervision, R.G.; validation, R.G.; visualization, R.G.; writing-original draft, I.B.; writing-review and editing, R.G.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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