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The use of whey protein in the post-fracture bone formation process

El uso de proteína de suero en el proceso de formación ósea postfractura

O uso do whey protein no processo de formação óssea pós-fratura

ABSTRACT
Milk has one of its proteins, Whey, which has several components in its composition that bring benefits to bone formation, by suppressing osteoclasts and stimulating osteoblasts. Having as objective of the article to expose in a clear and succinct way, the importance of Whey as an adjuvant in the bone healing process. Methodo: A bibliographic review was carried out in a PubMed and Biblioteca Virtual de Saúde (BVS) database, using some descriptors and inclusion criteria for selecting articles. Results: Studies have demonstrated the ability of Whey to create an anabolic environment for bone tissue, by stimulating factors that were bone and canceling factors of bone absorption. Conclusion: With that, for all factors presented in the results, this substance is effective in bone healing.
DESCRIPTORS: Whey protein; Osteoblast.

RESUMEN
La leche tiene una de sus proteínas, el suero de leche, que tiene varios componentes en su composición que aportan beneficios a la formación ósea, al suprimir los osteoclastos y estimular los osteoblastos. Teniendo como objetivo el artículo exponer de forma clara y sucinta, la importancia del Whey como coadyuvante en el proceso de cicatrización ósea. Metodo: Se realizó una revisión bibliográfica sobre el tema en una base de datos PubMed y Biblioteca Virtual de Saúde (BVS), utilizando algunos descriptores y criterios de inclusión para la selección de artículos. Resultados: Los estudios han demostrado la capacidad de Whey para crear un ambiente anabólico para el tejido óseo, estimulando factores que eran los huesos y cancelando los factores de absorción ósea. Conclusión: Con eso, para todos los factores presentados en los resultados, esta sustancia es efectiva en la curación ósea.
DESCRIPTORES: Proteínas de suero; Osteoblasto.

RESUMO
O leite apresenta uma das suas proteínas o Whey, que apresenta vários componentes em sua composição que trazem benefícios para formação óssea, por meio de supressão dos osteoclastos e estimular os osteoblastos. Tendo como objetivo do artigo, expor de maneira clara e sucinta, a importância do Whey como adjuvante no processo de consolidação óssea. Metodo: Realizou-se uma revisão bibliográfica sobre o tema em banco de dados da PubMed e Biblioteca Virtual de Saúde (BVS) com uso de alguns descritores e critérios de inclusão para seleção dos Artigos. Resultados: Estudos demonstraram a capacidade do Whey em criar um ambiente anabólico para o tecido ósseo, por estimular fatores que foram o osso e anular fatores de absorção óssea. Conclusão: Com isso, por todos fatores apresentados nos resultados, tal substância é eficaz na consolidação óssea.
DESCRITORES: Proteínas do soro do leite; Osteoblasto.

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INTRODUCTION

Milk is an inexpensive source of compounds necessary for bone development and regeneration, containing two main sources of protein: casein and whey proteins (whey);[1] therefore, it is possible to report that whey protein is more effective than casein in conditions of its faster digestion capacity, since the rate of hydrolysis is slower and the kinetics have better absorption when linked to the presence of bioactive components. [2]

Whey protein is considered a complete protein, since its components are β-lactoglobulin, α-lactoalbumin, bovine serum albumin, immunoglobulins, lactoferrin, lactoperoxidase, glycomacropeptide; where they have multiple biological actions and advantages for improving health, as well as for the treatment of pathologies, cancer prevention, combating microbials, mutagens; and is responsible for increasing the level of glutathione, increasing the satiety response, enhancing the activity of pre-gastric esterase and also serves for the regulation of phosphorus. [2]

Whey protein has also been shown to suppress osteoblast-mediated bone resorption and osteoclast formation, thus using the pre-existing and newly formed osteoclast and hematopoietic cell system. [2] With this in mind, it is important to know that osteoblasts originate in a method that encompasses multipotent mesenchymal cells that breed and undergo a sequential differentiation of the progenitors into proliferating osteoblasts, osteoblasts that produce bone matrix, and finally osteocytes (bone cells). Osteoblast progress and maturation require several inducing factors, including bone morphogenetic protein (BMPs) and insulin-like growth factor I (IGFI). [3]

There are studies showing that isolated milk protein increases osteogenic cell proliferation and differentiation,[2] also assisting in the bone healing process, in which it occurs in three closely integrated and sequential phases: 1) inflammatory, during which the necrotic tissue is removed; 2) reparatory, when the rapid synthesis of a new matrix occurs; and 3) remodeling, in which the disorganized matrix of the repair phase undergoes a maturation process, becoming a compact and functionally efficient structure. [4]

In parallel to this, vascular lesions occur, which promote variable bleeding, in addition to providing the formation of a hematoma that involves the focus of the fracture, causing the injured segments to be, at their ends, lacking in nutrition and evolve to necrosis. The hematoma is organized, with an influx of polymorphonuclear cells and pluripotential cells, causing the fibrovascular tissue of the clot to be replaced by collagen fibers. This is followed by the reabsorption of necrotic tissue and the proliferation and differentiation of osteogenitor cells, in the periosteum, in the endosteum and in the bone marrow in fibroblasts and chondroblasts and or osteoblasts. [4]

That is, whey protein - whey protein - is formed by a group of basic whey proteins and is also effective in preventing bone loss, stimulating bone deposition (bone formation) and suppressing removal (bone resorption);[5] such protein, is also being used abundantly by individuals as a dietary supplement [2], because there is a balance between bone resorption by osteoclasts and formation by osteoblasts that supports bone homeostasis through a process called bone remodeling.[3] Therefore, it can be concluded that whey protein is effective in reducing the occurrence of diseases associated with bones, including osteoporosis. [2]

The objective was to clearly and succinctly expose the importance of Whey Protein as an adjuvant in the bone healing process, in addition to reporting its benefits to the general population.

METHOD

This material constitutes a systematic literature review study, in which it proposes to analyze scientific productions with a common theme in order to gather the central information of them in a single location and facilitate the explanation of the use of whey protein as a cofactor in osteogenesis. The making of

this work followed the following order: guiding question, data collection, data evaluation, analysis of publications and discussion of results.

The first phase, the guiding question of the study, was: "does the use of a protein supplement with whey bases have an important role in bone development more effectively?". And, from this questioning, it was possible to continue the following phases. In this context, data collection, second phase, was carried out within the Virtual Health Library (VHL), and PUBMED, during 11/19/2020 to 12/12/2020, taking as a starting point the analysis of DeCS-Descriptors in Health Science, in the quick search, to verify the existence of the following logical sequences: whey proteins and osteoblast. In view of the existence of these terms, the search for the material continued using the advanced search option. In it, the analyzed descriptors associated with Boolean sum operators were inserted. Therefore, it was researched: whey protein AND osteoblast. 96 documents were found. Thus, to refine the specificity of the collection obtained, the following exclusion criteria were used to filter that group of files: full text available, year of publication (2011 to 2020) and language: Portuguese, English and Spanish. After this action, 53 articles remained.

In the third phase, time to evaluate the data, after reading the obtained productions in full, it was possible to apply the exclusion criterion for: data that do not match the proposed theme because they present explanations about the use of whey in other species, texts that had duplication of its replicas and works that did not present the selected language, thus leaving 6 articles. These were selected by the inclusion criterion because they have medium and high relevance for this work.

In sequence, the fourth phase was the moment used to evaluate the publications available in order to certify that they contained all the selected criteria and the expected quality. Here, there was 100% success and a careful study of the 6 publications found began, extracting data from the articles independently. The fifth and last phase, discussion of the results, was the propitious space to describe the importance of highlighting the use of whey protein as a factor of osteogenesis, a topic of global interest, which is of interest to all human beings, in view of the fact that the general population needs healthy bone growth.

The fifth and last phase, discussion of the results, was the propitious space to describe the importance of highlighting the use of whey protein as a factor of osteogenesis, a topic of global interest, which is of interest to all human beings, in view of the fact that the general population needs healthy bone growth.

Chart 1: Presentation of the place of action of whey protein and the respective benefit presented for the acceleration of the bone healing process.[6]

WHEY INTERACTION	BENEFIT
Action on Osteoblasts	Increased proliferation and differentiation of osteoblasts, increases calcium deposition and decreases bone resorption
Action on Alkaline Phosphatase	Increases mineralization in osteoblasts
Action on Osteoclasts	Decreases proliferation

RESULTS AND DISCUSSION

Many studies have demonstrated the benefits of whey in bone metabolism, both in vitro and in vivo. These studies showed that whey and its derivatives had the potential to stimulate the proliferation and differentiation of the osteoblast MC3T3E1, regarding the increase in the protein and hydroxyproline content, this maturation being induced by factors such as bone morphogenetic protein (BMPs) and the factor similar growth to type 1 insulin (IGF1). In addition, whey has also been shown to suppress osteoclast-mediated bone resorption.[1]

Another benefit presented by whey was the increase in the activity of alkaline phosphatase in demineralized bone implants, indicating a positive effect on bone formation. [2] However, the most evident action of whey in bone repair is the action on MC3T3E1 osteoblasts, increasing the proliferation of these osteoblasts, being a concentration-dependent process, whey was used at 62.5 to 500 μg/mL. Also having an increase in the action of alkaline phosphatase (ALP) in these cells, the action of ALP in osteoblasts is essential for mineraliza-

tion, in this case whey was used in the concentration of 250 to 500 μg/mL. In addition, there is an increase in the deposition of calcium in MC3T3E1 cells, which is an essential mineral for bone formation. [6,7]

In another study carried out in mice, lactoferrin - glycoprotein found in whey - showed improvement in bone mineral density by stimulating the growth of osteoblasts and by inhibiting pre-osteoclastic cells in vitro. [8] In addition, it demonstrated an ability to act as a growth factor and proved to be an anabolic agent for bone tissue, both in vitro and in vivo. [9] Another research carried out, sought to measure the increase in bone mineral density in children, showing an increase of 5% in the whole body, decreasing the chances of fracture in childhood by approximately 9%. [10]

Thus, it is observed that whey protein has several benefits for the human body, in addition to its action on bone tissue, it also has an increase in the level of the antioxidant glutathione, helps in the prevention of cancers, has antibacterial activity and increased passive immunity. [6]

CONCLUSION

Therefore, in an attempt to better understand how the use of whey would be beneficial for patients in recovery after a fracture, it was concluded that whey, as it is considered a complete protein, has many advantages for improving health, disease prevention and treatment. Its main action found for better and faster bone consolidation was the suppression of bone resorption by osteoblasts and the suppression of osteoclast formation. These studies, carried out in vitro and in vivo, showed that there is also a stimulus for the proliferation and differentiation of osteoblasts MC3T3E1, induced by BMPs and IGF1. Therefore, the use of whey protein can be considered, to improve the efficiency of osteoblasts in the post-fracture period.

However, more research should be done on the subject, considering different patient profiles, in a comparative bias, considering the effectiveness of this alternative in patients of different ages, sex, regarding the mechanism and energy of the trauma. ■

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