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REVIEW ARTICLE

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Effect of glutamine supplementation in elderly people with emphasis on sarcopenia, immunity and hypertrophy: a concise systematic review

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Abstract

Currently, the aging of the population is no longer a forgotten subject for health professionals in Brazil. This is due to the decrease in the birth rate in the country and the improvement in quality of life, this first factor was boosted after the ease of access to information on contraceptive methods and their distribution by the health system. As a result, the Nutrition area has been studying more diligently ways to provide elderly people with methods that contribute to a more comfortable, healthy, and long-lasting life. The nutritionist is essential to identify the deficits and disharmonization of the body of the elderly caused naturally over the years in people's lives, such as loss of muscle mass, and lack of nutrients, among others. Given this scenario, this work will be focused on showing that the use of oral Glutamine supplementation contributes to the gain of muscle mass in the elderly since this natural amino acid present mainly in the muscle tissue of the human body is greatly reduced due to loss of mass skin and body weight gain caused by the slow metabolism found in older people. In this way, supplementation along with a well-designed nutritional table and an exercise routine will promote less chance of injury to the elderly due to a lack of nutrients and greater physical resistance. To reinforce and prove this study, we will use the literature review method distributed in topics.

Keywords: Glutamine. Sarcopenia. Immunity. Hypertrophy.

Introduction

The aging process brings significant and degenerative changes to the body, sarcopenia, which is presented as an intrinsic process of aging, as a process of tonus reduction, and as a progressive loss of muscle mass. Directly, sarcopenia brings with it significantly impacts the quality of life, contributing to the reduction of strength, mobility and subsequent indirect risks, which lead to interference in the individual's experience and independence, which can trigger from small accidents to chronic diseases, taking into account because of the reduction of tone and muscle mass **[1]**.

Glutamine supplementation in the elderly is a major topic of discussion in contemporary times, especially when the focus is on the aging process from the point of view of Nutrology and the scope that this approach requires in a multidisciplinary way. However, hormones need to be correlated in this analysis similar to what is arranged by metabolic and energy functions in addition to the entire composition of the human body that demonstrates different singularities during the aging phase **[2]**.

The imbalances and dynamics must be understood by the nutrology professional, while the patients can be directed to the treatment and the practice of exercises according to their existing conditions **[1]**. By the way, the necessary demand for the body is commonly absorbed in the practice of physical exercises and other activities, requiring supplementation on the part of this individual, however, divergences and adversities require medical follow-up in the case of supplementation in the elderly, especially those who already have conditions special **[2]**.

Although the main searches for food supplements are directed towards improvements in physical size, when the focus is on the elderly, there is a greater demand for the consumption of nutritional supplements due to their positive effects both on quality of life and well-being **[1]**. In this way, it is expected to define legitimate means for glutamine supplementation in the

elderly based on safe dosages across age groups where both an increase in strength (hypertrophy) and improvements in the sarcopenia process are allowed **[3,4]**.

In this sense, the main objective of this study was to determine the general direct effects of glutamine supplementation in elderly people of different age groups. The specific objectives, equally, are intended to questions such as: demonstrating the benefits generated by this type of supplementation, defining the appropriate dosages for practitioners of physical activities over 60 years of age, examining the barriers imposed on this type of consumption, and verifying how sarcopenia, immunity, and hypertrophy affect the lives of elderly Brazilians.

Methods

Study Design

The present study followed a concise systematic review model, following the systematic review rules - PRISMA (Transparent reporting of systematic review and meta-analysis: //www.prisma-statement.org/). A documentary bibliographical review was carried out through qualitative research directed to texts, works, and Brazilian and international scientific articles published in a specific time scale regarding the last 10 years.

Search Strategy and Search Sources

The literary search process was carried out from September to October 2022 and was developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, addressing scientific articles from various eras to the present day. The descriptors (MeSH Terms) were used: "Glutamine. Sarcopenia. Immunity. Hypertrophy", and using the Boolean "and" between MeSH terms and "or" between historical findings.

Study Quality and Risk of Bias

Quality was rated as high, moderate, low, or very low for risk of bias, clarity of comparisons, accuracy, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analysis of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument through the analysis of the Funnel Plot graph (Sample size versus Effect size), using Cohen's test (d).

The theoretical basis consists of the following factors, "Aging Process: Relationship between Hypertrophy, Immunity and Sarcopenia" and "Glutamine: Possibilities and Benefits of Supplementation in the Elderly". Still, on this topic, there is a reverberation about this modality of supplementation in the elderly of different age groups and the main pre-existing conditions that demand special precedent attention. The growing search for this theme aggregates the values elucidated during this study, given that the areas of Nutrology demonstrate a great modern scope regarding the health of the elderly and the different scales of nutritional supplementation.

Results and discussion

Summary of Findings

As a corollary of the literary search system, a total of 110 articles were found that were submitted to the eligibility analysis and, then, 11 of the 41 final studies were selected to compose the results of this systematic review. The listed studies showed medium to high quality (Figure 1), considering in the first instance the level of scientific evidence of studies in types of study such as meta-analysis, consensus, randomized clinical trial, prospective and observational. The biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with I 2=98.8%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 23 studies with a high risk of bias and 28 studies that did not meet GRADE.

Figure 1. Flowchart showing the article selection process.

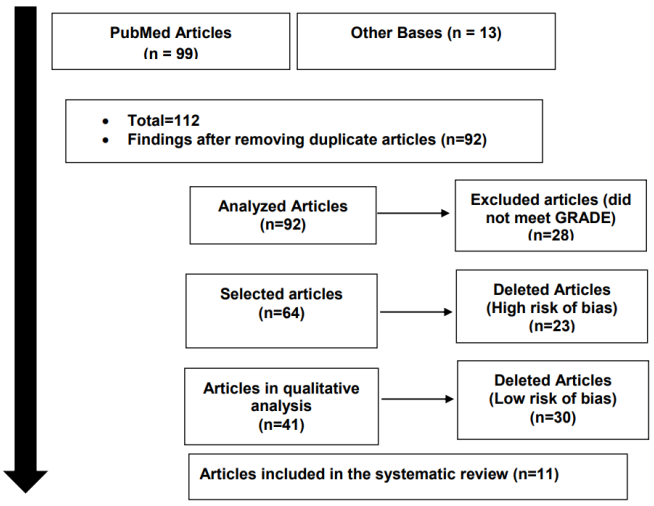
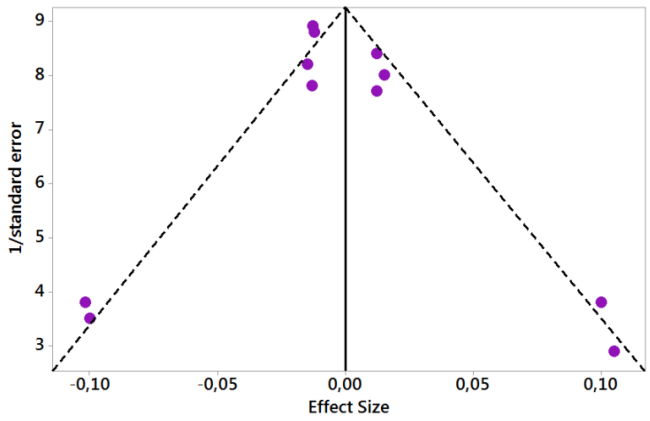


Figure 2 presents the results of the risk of bias of the studies through the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the

difference) using the Cohen Test (d). Precision (sample size) was indirectly determined by the inverse of the standard error (1/Standard Error). This chart had a symmetrical behavior, not suggesting a significant risk of bias, both between studies with small sample sizes (lower precision) that are shown at the bottom of the chart and in studies with large sample sizes that are shown at the top.

Figure 2. The symmetrical funnel plot does not suggest a risk of bias among the small sample size studies that are shown at the bottom of the plot. High confidence and high recommendation studies are shown above the graph (n=11 studies).



Source: Own authorship.

Glutamine: The Essential and Non-Essential Amino Acid for Muscle Reconstruction in the Elderly

Amino acids are the main protein builders in our body, especially when we talk about muscle protein:

> In nature there are about 300 amino acids, some amino acids are special and only appear in some types of proteins (hydroxyproline=collagen). Therefore, amino acids are the fundamental units of proteins. All human proteins are formed from the binding as a result of just 20 types of amino acids encoded by DNA. They perform several important functions in addition to forming proteins such as: neurotransmitters, hormone formation, drugs, methylation, etc. **[3]**.

Chemically speaking, "amino acids are molecules formed by a carbon atom (alpha carbon) covalently bonded to a carboxyl group (-COOH), an amino group (-NH2), a hydrogen atom (-H) and a side chain (- R)" **[4]**. These are divided into 5 groups: non-polar, aliphatic amino acids; polar, uncharged amino acids; polar, positively charged amino acids; polar, negatively charged amino acids and aromatic amino acids.

Roughly, the amino acids are the elements that constitute the protein, being able to observe that each protein, has in its composition, the combination of 20 amino acids. Amino acids in the human body are divided into essential and non-essential, as shown in Table 1.

Table 1. Division of Amino Acids.

ESSENTIALS	NON-ESSENTIALS
✓ Arginine	✓ Alanine
✓ Phenylalanine	✓ Asparagine
✓ Histidine	✓ Aspartate
✓ Isoleucine	✓ Cysteine
✓ Leucine	✓ Glycine
✓ Lysine	✓ Glutamate
✓ Methionine	✓ Glutamine
✓ Threonine	✓ Proline
✓ Tryptophan	✓ Serine
✓ Valine	✓ Tyrosine

As you can see in Table 1 above, Glutamine is on the list of non-essential amino acids, however, it is essential for the functioning and development of body muscles. Non-essential amino acids are so called because "they are synthesized by the body and do not depend on an external source to obtain them. This occurs in healthy individuals, not affected by certain pathologies." **[5]**.

Glutamine is the most abundant free amino acid in plasma and muscle tissue. In its composition ($C_5H_{10}N_2O_3$), it is an L-α-amino acid and even being classified as a non-essential amino acid, it is present in 20% of free amino acids in plasma and 50% (or more) of amino acids in skeletal muscle, as it can be synthesized by all body tissues. In a reduced form, the synthesis of glutamine takes place from glutamate in catalysis and its conversion into glutamine occurs with the consumption of ATP (adenosine triphosphate).

Namely, quantitatively, skeletal muscle tissue is responsible for the "production", storage, and release of Glutamine. In this context, the connection between sarcopenia and glutamine: The use of this amino acid in its oral replacement/supplementation, is a way to stop the process of muscle deterioration. However, with aging, these percentages decrease and this leads to the factors mentioned above: weight loss, ease of injury, and fragility in health. Thus, once again, we reinforce that the oral intake of glutamine for the elderly will complement the percentage that is missing from the body of these patients.

The researcher Angélica Freitas, in her doctoral defense work, for the University of São Paulo (2014), brings promising results on the use of glutamine by the

elderly. In her text, she states that "glutamine supplementation in elderly people at risk of frailty showed variations that can be interpreted as possible benefits to intestinal functioning and body composition" **[6]**. Without fail, the ingestion of functional foods, which contain in their composition a substance capable of modulating metabolic processes, leads to the improvement of physiological processes, as well as the nutraceutical administration of certain amino acids, works as a way of replacing compounds that could not be replaced only by bodily production. Namely, a nutraceutical dose is the administration of a compound that exceeds the normal dose of exposure to that agent in food **[7]**.

In the present case, the nutraceutical dose of Glutamine is applied, in a way, in a kind of immunonutrition, with the administration of larger doses, with monitoring by a multidisciplinary team, thus seeking protein and amino acid replacement that are no longer produced or finding production deficits in the human body.

Aging Process: Relationship between Hypertrophy, Immunity, and Sarcopenia

The demographic readjustments demonstrated in the last decades are consistent with a better quality of life, in the same way, that life expectancy registered an increase both among men and among women **[8]**. In recent data shown by the Ministry of Health in mid-2016, recent life expectancies were seen to be 75 years for women and 72 years for men, on an approximate scale **[1]**.

On the other hand, the low fertility rate recorded during the same period shows an older population, following patterns very similar to data from several European countries **[8]**. In this way, the pathologies correlated to the process of continuous aging of the population become adversity of great proportions. From the perspective of the individual himself, nutritional care is essential to achieve a healthy and safe life, based on well-being **[2]**.

Brazil, like other developing countries, is in a process marked by social inequalities and difficulties regarding access to efficient free treatments, which asserts the aging process and the other risks that encompass this phase. In general terms, Severino and Santos **[1]** point out that, although it is a natural process, "this factor characterizes a new problem for public health policies since the demand for services in this field no longer corresponds to the needs of the elderly. generating an exorbitant accumulation of elderly people in queues to get appointments at medical clinics, cardiologists, and ophthalmology, among others" (p. 197).

From the age of 65, several profound changes in body composition can be evaluated, one of which is the increase in body fat mass, with attention to the increase in this mass in the abdominal region and, consequently, a decrease in mass. This decrease in a lean mass called sarcopenia imposes its symptoms mainly on physically inactive individuals, among other factors such as hormonal changes, loss of motor neurons, inadequate nutrition, physical inactivity, and a low degree of chronic inflammation. Thus, sarcopenia causes the decrease in muscle strength and power to be incisive in the loss of autonomy, well-being, and quality of life of the elderly, making mobility difficult, as well as other essential factors for the experience of aging with quality [...] In this way, the increased demand for preventive alternatives, drugfree and even for the treatment of some diseases through changing dietary patterns and consumption of supplements throughout life has been the subject of much research in recent years, leaving It is clear why the use of dietary supplements in the elderly is being discussed, with a focus on their use to improve body weight, lean mass, and physical performance, as well as preventing morbidity and mortality rates and improving quality of life **[2]**.

Still according to the literature **[2]**, "there are many doubts about the consumption of supplements by patients from the most varied population groups, as well as there, are doubts about the true risks and benefits related to their use" (p.12). The loss of muscle strength is evidenced by hypertrophy and sarcopenia, although it is similarly correlated with low immunity. Nevertheless, such diseases are less silent than other chronic pathologies, given that their consequences include direct reverberations to physical performance, especially in terms of strength **[9]**.

For Rebelo **[8]**, singularly about sarcopenia, a direct relationship with dynapenia is visualized. This proportionality indicates that "changes in muscle mass are directly and fully responsible for the decrease in strength. However, several studies show that elderly people have their strength reduced even before they lose muscle mass and muscle gain does not nullify this effect" (p.13). Therefore, such adversity must be worked on by professionals, from prescription to guidance and consumption stem from a robust base **[10]**.

Glutamine: Possibilities and Benefits of Supplementation in the Elderly

Nutritional supplements are presented as elements of great value for Brazilians interested in complementing

the nutrients that are consumed in conventional meals. However, glutamine supplementation has been the subject of different discussions among scholars from different areas **[9]**. Nutrition in the elderly is more complex due to the natural changes that the human body undergoes, including the decrease in lean body mass, the greater difficulty in developing hypertrophy, and the possibility of systemic aggravation due to lower immunity **[11]**.

Thus, the consumption of nutritional supplements has increased in recent years due to indications of improvement according to the degree of what is ingested and the specific conditions of each user. However, the practice of physical exercises in gyms or different sports favor improvements in metabolism and energy functions **[9]**.

In general terms, glutamine has some practical effects on the human body. In harmony with the prisms exposed by Severino and Santos **[1]**, glutamine is "responsible for optimizing the nitrogen balance and maintaining muscle protein synthesis, it is also an important energy source for the immune system, as it acts by stimulating the production of T lymphocytes, B and immunoglobulin A (IgA)" (p. 199).

Sanches **[9]** classifies glutamine as "the most abundant free amino acid in the human body, mainly in plasma and muscle tissue, and is also found in relatively high concentrations in other various body tissues1,2. It is an L - amino acid composed of carbon, hydrogen, oxygen and nitrogen atoms, nutritionally classified as non-essential, and can be synthesized by all body tissues" (p. 8).

Drug interactions and guidance regarding the use of nutritional supplements, as well as glutamine, need to follow a safe and effective dosage for practitioners of physical activities. In the case of the elderly, that is, men and women over 60 years of age, the indications are 0.3g a day. Thus, this dosage is lower than that indicated for healthy adults, where guidance is given on a scale of 7g to 15g daily **[11]**.

In metabolism, tissues, and organs undergo a different interaction with glutamine ingested via nutritional supplementation, which must be analyzed by the Nutrology professional in each case, especially when the patient is elderly and presents some clinical worsening **[10,11]**. In a similar study developed by Paixão **[10]** in 2021, it was found that supplementation via glutamine is beneficial to the elderly due to the ability of this amino acid to amplify the protective effects of vaccines, especially concerning the Influenza virus, either as L-glutamine or as a placebo.

Conclusion

The data elucidated in this article indicate the singular effects of glutamine supplementation in the elderly, especially in men and women aged 60 years or more, demonstrating the need for an initial medical follow-up regarding the conditions already present in each organism. Supplementation via glutamine in harmony with the practice of physical exercises corroborates for an expansion of practical results, but the indications regarding activities need to follow the patient's clinical condition or even his predispositions. The Nutrology professional, in turn, has excellent representativeness in this scenario for bringing a superior study of the treatment to these individuals in a comprehensive way, appropriating adequacy of the consumption routine from the presented degree of hypertrophy or sarcopenia. The purposes established at the beginning of this study were achieved with the help of theoretical bases and practical research developed by important authors in the areas of Nutrology, opening space for future studies and new investigations according to the appropriate scientific and technological advances. At this juncture, it was validated that glutamine supplementation on a safe and appropriate scale for the patient is of great value for their muscle performance, bringing direct improvements both in strength and in the reduction of harm related to sarcopenia. In addition, this type of nutritional supplementation generates advantages in the immunity of the elderly, preventing the occurrence of aggravating pathologies and infections, while the body's response to both drugs and vaccines becomes intensified.

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Ethics approval

Not applicable.

Informed consent

Not applicable.

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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