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Protein supplements and excessive protein consumption during adolescence: Effects and consequences

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Abstract
Protein supplements are substances added to the diet to meet and/or complement nutritional deficiencies or improve physical performance. They are currently widely consumed by individuals of all ages, especially adolescents and young adult males, with the primary purpose of building a muscular and defined body as a standard of aesthetics and health. Although they are widely advertised as products that help the body meet certain nutritional needs in specific situations and in body remodeling processes when combined with physical activity, protein supplements should be consumed with caution, carefully prescribed, and under the supervision of qualified professionals, as excess intake can cause complications and adverse health effects. Adolescents are in phase of organ, system, and personality development, where excessive protein consumption can have undesirable consequences and should be avoided. This narrative review presents the main changes that can occur in metabolism and in different organs and systems of the human body resulting from excessive protein consumption from the diet and from products used in the form of protein supplements.

Keywords: Protein, protein supplement, protein metabolism, amino acids

Introductions
Adolescence is a period characterized by numerous physical, emotional, social, behavioral, and cognitive changes that occur as a child grows and develops toward adulthood. In this context, adolescents, while vulnerable to relational, cultural, and environmental factors that contribute to their health, learn to develop independence and life skills, such as establishing personal relationships with peers, assuming responsibilities, and planning for the future. However, this transitional phase, due to the immaturity of the central nervous system and protective mechanisms, is also associated with some types of risky behaviors associated with impulsivity and external influences [1]. One of the inherent aspects of this phase of life is the development of body image. While still in the process of emotional maturity, adolescents are influenced by peer groups and the media, leading them to seek ways to achieve the idealized body. In this sense, especially among boys, there is a high demand for gyms with more time and physical activity. In this space, they are often influenced and led to the consumption of nutritional supplements, more specifically, protein concentrates [2].
In general, adolescents can be considered nutritionally vulnerable and at-risk individuals, as they are at a stage of life with significant nutritional needs, both quantitatively and qualitatively, due to rapid growth and changes in body composition associated with puberty. In addition to adequate nutrient intake to meet all physical needs, adolescents are subject to peer influence, concerns about body image, and increased physical activity, which certainly contribute to the establishment of eating habits that can persist throughout life. Specifically regarding protein intake, recommendations to meet daily needs range from 0.95 to 1.0 g/kg of body weight, or 46 g/day for girls and 52 g/day for boys. This should also consider gender, weight, height, and physical activity level. The daily amount of protein intake should correspond to 15% of the total energy value of a balanced diet [3]. Studies have revealed that in more developed countries, adolescents consume more protein than recommended, especially of animal origin, which becomes relevant when considering that even with this type of diet, many adolescents regularly use protein supplements [4, 5].

Protein and protein supplements

Proteins are biomolecules of animal and plant origin, composed of long chains of amino acids linked by peptide bonds. They play an important metabolic role in the growth and maintenance of the body's vital processes, acting as catalysts (enzymes), components of the immune system (antibodies and cytokines), hormones (insulin, glucagon, growth hormone), transporters (hemoglobin, albumin), and storage (ferritin), among others. Although they contribute little to energy intake, proteins should be part of the daily diet, as the human body does not maintain reserves and the intake of the nine essential amino acids depends on them [4, 6, 7]. The protein digestion process begins in the stomach through the action of pepsin, which is responsible for 10% to 20% of total digestion, converting protein into proteoses, peptones, and other peptides. The proteolytic enzymes trypsin, chymotrypsin, carboxypolypeptidase, and proelastase continue the digestive process in the duodenum and jejunum, producing smaller fractions such as dipeptides and tripeptides. In the final stage of digestion, these peptides are subject to the action of peptidase enzymes, which are present in the microvilli of enterocytes, transforming them into amino acids, which constitute almost the entire final product of digestion [8]. This process results in absorption in the form of amino acids and a few dipeptides and tripeptides. After absorption, amino acids are actively transported by transport proteins to the sites where protein synthesis will occur. Amino acids not required for protein synthesis are converted to glucose or metabolized to produce energy [8]. Protein digestion takes between 2 and 3 hours, resulting in a slow increase in amino acids in the blood, which are absorbed, primarily by the liver, within 10 minutes, from where they are sent throughout the body. Amino acids can also be reabsorbed by the kidneys through the proximal tubular epithelium and returned to the blood [8]. The human body has a high capacity to oxidize amino acids and dietary proteins to form water-soluble metabolites, including ammonia, sulfate, and homocysteine. Intestinal bacteria also participate in the final process of digestion, producing metabolites such as short-chain fatty acids, p-cresol, skatole, and sulfide from amino acids. Finally, the kidneys are also responsible for the excretion of urea, ammonia, and sulfate from this digestion process [9]. Adverse effects of high protein intake include intestinal discomfort, hyperaminoacidemia, hyperammonemia, hyperinsulinemia, dehydration, irritability, nausea, diarrhea, liver and kidney damage, fatigue, headache, seizures, and a high risk of cardiovascular disease or even death. These problems can be aggravated by low carbohydrate intake, due to the overload on the liver and kidneys in producing large amounts of glucose from amino acids, in addition to their role in eliminating excess ammonia and urea [9].

Nutritional supplements can be defined as substances added to the diet to supplement, fill nutritional deficiencies, or improve physical performance [10]. Currently, they can be easily found in many direct-to-consumer or e-commerce outlets, in various presentations such as capsules, powder, gel, liquid, shakes, and bars, generating a market worth billions of dollars annually worldwide [11]. Among the different types currently available, protein supplements stand out, being consumed by individuals of all ages, especially adolescents and young males, with the main purpose of building a muscular body and defining it as a standard of aesthetics and health [12, 13]. Although they are widely publicized (marketing strategies, recommendations from health professionals and/or digital influencers) as products that help the body meet certain nutritional needs in specific situations and in body remodeling processes when associated with physical activity, protein supplements should be consumed with caution, carefully indicated and under the supervision of qualified professionals, as they can cause adverse effects and complications in approximately 9% of consumers due to the amounts of protein ingested daily and, eventually, the products associated with them, such as caffeine, sugar and preservatives, among others [11, 14, 15].

One of the most widely consumed protein supplements today is whey protein (WP), consisting of a group of globular proteins isolated from cow's milk whey—beta-lactoglobulin (65%), alpha-lactalbumin (25%), and serum albumin (8%)—with vitamins and calcium minerals. WP has proven biological benefits, including synergistic anti-inflammatory, antimicrobial, and protective effects [16], which have earned it great popularity. WP also has effects on improving muscle mass and body weight control [17], provided its consumption is properly controlled and supervised. WP can be found in three main forms, each prepared with different processing methods and compositions. Concentrated WP is produced by ultrafiltration of whey to remove water, lactose, and some minerals, maintaining a protein content of 70% to 80% protein by weight, and also containing lactose (4% to 8%) and fat (4% to 6%). The second form is WP isolate, which undergoes an additional filtration process to remove more lactose, fat, and impurities, raising its protein content to 90% to 95% and is most commonly used in high-protein supplements and clinical nutrition. WP hydrolysate is the third processed form of whey in which enzymatic hydrolysis is used to break down WP into smaller peptides and amino acids [16].

Effects of excess protein on different organs and systems

Due to the current widespread popularity of protein supplements and their increasing consumption, often without proper guidance or control, it is important to highlight the harm that excessive protein intake can cause to the body, which receives amounts that exceed daily requirements and can lead to metabolic overload in various organs and systems [6, 15, 18]. Excess protein combined with low water intake can lead to dehydration. Furthermore, excessive consumption without reducing fat or carbohydrate intake contributes to increased energy intake and, consequently, to the development of overweight and obesity [19]. On the other hand, ghrelin, a peptide that stimulates appetite, decreases after protein consumption, contributing to feelings of fullness, which is interpreted by many as an effect that can lead to weight control [11].

Kidney

Kidneys are the main structures involved in the excretion of the end products of protein digestion and can undergo several changes resulting from this activity. During the protein digestion process, an amine group leaves the amino acid molecule to form an ammonia molecule and a ketoacid molecule, with the ammonia being converted to urea and excreted in urine. Excess protein leads to decreased renal function due to the increased workload on the kidneys, causing increased renal blood flow and glomerular

hyperfiltration [11, 15], often leading to glomerular injury due to increased intraglomerular pressure and flow, which can cause progressive glomerular damage, proteinuria, and sclerosis in kidneys with preexisting damage [6, 11, 20, 21]. Excess protein also leads to a large amount of acid in body fluids, which causes the kidneys to excrete this excess acid, which in turn directly inhibits the renal reabsorption of calcium and urinary sodium, leading to hypercalciuria, which is a risk factor for the development of kidney stones composed of calcium oxalate, which can be aggravated by low water intake [6, 11, 15, 19, 20]. Furthermore, the high acid load increases the risk of developing diabetic nephropathy and glomerulonephritis [6].

Gastrointestinal Tract

Excess protein can significantly interfere with the composition and function of the gut microbiota, causing amino acid fermentation in the colon, cramping, and diarrhea [11, 18, 20]. This fermentation process results in the production of potentially harmful metabolites such as amines, phenols, sulfides, and ammonia, which can have detrimental health effects. Compounds such as hydrogen sulfide, p-cresol, and phenols are associated with inflammation, increased intestinal permeability, and diseases such as irritable bowel syndrome and colon cancer [9, 11, 19, 20]. High concentrations of amino acids stimulate the release of anorectic hormones that have effects on satiety. The presence of these amino acids in the intestinal lumen also stimulates the secretion of cholecystokinin, which, among other metabolic functions, promotes satiety and suppresses appetite [22]. Excess protein can also lead to liver function disorders due to increased nitrogen metabolism and the production of urea and uric acid [15, 16], which can be verified by increased bilirubin, albumin and transaminases in the bloodstream [15].

Cardiovascular System

Increased protein consumption may be associated with a higher risk of high blood pressure since, when stimulated by a high protein load, immune system cells can release free radicals, such as cytokines and other vasoactive factors, causing an increase in blood pressure [6, 23]. Furthermore, it is known that animal proteins are associated with increased LDL (low-density lipoprotein) cholesterol, chronic inflammation, and oxidative stress, which may be risk factors for cardiovascular disease. The possibility that excess protein may precipitate the progression of coronary artery disease in patients with associated risk factors has also been suggested [15]. Leucine, an aminoacid found in various protein supplements, stimulates insulin production, affecting vasodilation and vasoconstriction through its impact on nitric oxide production and bioavailability [11]. Elevated plasma homocysteine levels decrease nitric oxide bioavailability in endothelial cells, which can cause vascular dysfunction [9].

Endocrine System

Due to their compositional characteristics, some protein supplements may be rapidly digested and absorbed, causing a rapid and significant increase in amino acid and insulin levels in the blood, potentially desensitizing insulin receptors and contributing to the development of insulin resistance [17]. Therefore, a possible undesirable effect of excessive protein consumption is an increased risk of prediabetes and type 2 diabetes [19, 20, 24] due to the potential for insulin resistance caused by the inotropic effect of protein [25]. Leucine, an amino acid found in several protein supplements, stimulates insulin production, affecting vasodilation and vasoconstriction through its impact on nitric oxide production and bioavailability [11]. The enzyme glutamate dehydrogenase, present in the cells of the islets of Langerhans and acinar cells, is activated by several amino acids leading to increased activity of the Krebs cycle and oxygen consumption, resulting in increased insulin production [11].

Bones and Muscles

Excessive protein intake and low water intake are risk factors for kidney stone formation due to increased renal acid excretion, primarily in the form of sulfates and phosphates generated during digestion. However, this high amount of acid can be partially buffered by bone, which, in an attempt to create a buffering effect, releases calcium, which is then excreted by the kidneys. Protein-induced hypercalciuria can lead to the formation of calcium oxalate kidney stones [6, 15, 19, 20] and negatively affect bones due to decreased bone mineral density and an increased risk of fractures [15, 20, 25, 26]. Excess protein can lead to increased muscle protein synthesis and increased muscle mass, associated with loss of body fat. However, this high amount of protein is associated with increased resting metabolic activity and thermogenesis, as the body requires more energy to metabolize protein [6].

Skin

Research has shown that chronic protein supplementation can increase the occurrence of acne in athletes, particularly related to the consumption of whey protein, which contains insulin-like growth factor-1, associated with the promotion of cell growth and division, sebum production, and increased estrogen levels. This may explain the increase in acne [11, 18, 27] and, eventually, hair loss [16].

Emotional

Excess protein can reduce brain serotonin production due to tryptophan's increased competition with branched-chain amino acids (valine, leucine, and isoleucine) and aromatic amino acids (tyrosine and phenylalanine), which may be responsible for stress, irritability, depression, and anxiety [18, 28, 29]. Furthermore, the level of aggression and anger can be observed in individuals who ingest high amounts of protein [11, 30].

Conclusion

The consumption of protein supplements has increased significantly in recent years worldwide, due to the wide range of products available and the promotion of their effects on the body, particularly related to physical activity and body appearance. Due to the undesirable effects that excess protein can have on the body, especially among adolescents still in a phase of physical and emotional growth and development, it is essential that guidance be provided on the risks and benefits of this practice, as well as the importance of monitoring.

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