Whey protein ingestion and muscle protein anabolism in elderly

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ABSTRACT: Decrease in muscle mass with age makes elderly susceptible to falls, loss of independence and disease. Ingestion of whey protein exerts acute beneficial effects on muscle protein anabolism in elderly. This is probably due to the specific amino acid profile of the whey protein (e.g. essential amino acids), together with its fast absorption and the rate of appearance of its individual amino acids in blood. Further, ingestion of intact whey protein provides a greater anabolic benefit than ingestion of its essential amino acids alone, suggesting that whey protein is more than just a simple source of essential amino acids with respect to providing a stimulus for enhancing muscle protein anabolism in the elderly.

KEYWORDS: Dietary protein, whey protein, skeletal muscle, lean body mass, aging.

INTRODUCTION

Normal aging results in loss of muscle mass, a process that is independent of any disease [1]. Although the rates among individuals may differ, the majority of people start experiencing some loss of muscle mass around the fourth decade of their life [2, 3]. The etiology of this muscle loss is probably multifactorial and the result of several intrinsic (e.g. hormonal status) and extrinsic (e.g. nutritional and physical activity patterns) factors. Whatever the cause may be, loss of contractile proteins and associated skeletal muscle mass can lead to frailty, increased risk of falls and an overall loss of independence in elderly, ultimately making this population more vulnerable to illness [4]. Given that intrinsic factors contributing to muscle protein loss as a result of normal aging are likely less modifiable, extrinsic factors, such as nutrition and physical activity, have gained special attention to reverse or prevent muscle loss. Among nutritional approaches, research has particularly focused on the ingestion of high quality proteins, such as whey, casein as well as soy protein. Absorption and appearance of amino acids from ingested proteins into plasma serves to stimulate and support the synthesis of new proteins in body tissues, including the skeletal muscle. Whey and casein are the major proteins found in milk.

DIETARY PROTEIN INTAKE AND AGING

Skeletal muscle contains more than half of all body’s proteins. In the absence of adequate delivery of amino acids in plasma via protein ingestion, skeletal muscle serves as the primary pool of amino acids to support the synthesis of proteins in other organs as well as metabolic processes such as gluconeogenesis [5]. Dietary protein intake, which has a great impact on regulating normal skeletal muscle protein turnover in humans, decreases in elderly [6, 7], and by itself may be a contributing factor to skeletal muscle protein loss with aging. The current recommendation for protein intake for adults is 0.8 grams protein/kg/day. Whereas some evidence points to the direction that this amount of dietary protein intake, irrespective of age, is probably close to that required by older adults [8], other evidence has argued that this amount may not be adequate for elderly to meet their daily protein requirements [9, 10]. Larger amounts of daily protein intake appear to result in increased whole body protein turnover and amino acid oxidation, in parallel with an increase in net nitrogen balance in elderly [11]. Recent evidence suggests that it may not be the overall daily dietary protein intake, but rather other factors related to the amount, type and timing of protein ingestion that may be more critical in regulating a favourable muscle protein anabolism in elderly.

PROTEIN QUALITY AND MUSCLE PROTEIN ACCUMULATION

In recent years, approaches to enhance skeletal muscle protein accumulation via nutritional means have received particular attention. Among these approaches, ingestion of protein and various amino acid mixtures have been studied extensively in the elderly and as such have largely improved our knowledge with respect to the role of protein/amino acids in enhancing muscle protein accumulation in this population. Muscle protein accumulation can theoretically be achieved by either increasing the rate of protein synthesis, decreasing the rate of protein breakdown, or both. Increased muscle protein accumulation by dietary protein is achieved primarily via stimulation of the muscle protein synthesis following the absorption of the protein-associated amino acids and as a result of the ensuing plasma hyperaminoacidemia [12]. Dietary protein ingestion provides a practical approach to increase the availability of plasma amino acids. Such amino acids serve not only as precursors for protein synthesis but also act as signalling molecules in the initiation process of muscle protein synthesis [13]. Essential amino acids (EAAs), which are amino acids that the body cannot
synthesize, such as the amino acid leucine, are the most important stimuli of these molecular processes. High quality proteins have a large EAAs content. In young individuals, a slow absorbed protein, such as casein, is associated with greater whole body protein accumulation compared to a situation in which there is a rapid absorption and increase in plasma amino acid concentration (14). Contrary to the situation in the young, in the elderly there is greater utilization of amino acids for whole body protein accumulation following ingestion of whey protein, a rapidly digested protein, when compared to the ingestion of casein (15). Although the mechanisms for this greater protein accumulation in elderly following whey versus casein ingestion are not clear, greater whole body protein accretion probably relates to the higher plasma aminoacidemia following the whey ingestion as opposed to the lower, albeit more prolonged, degree of plasma aminoacidemia following the casein ingestion. Also, whey protein appears to have a slightly greater content of the amino acid leucine. It has now become evident that the response of muscle protein synthesis to leucine is either impaired with aging or there is an intrinsic resistance related to protein synthesis in older muscle to the stimulatory effects of plasma amino acids that can be overcome by specifically increasing the plasma concentration of leucine (16).

An important aspect of a high quality protein is that it provides all the EAAs in the amounts that the body needs. EAAs provide the primary stimulus for enhancing muscle protein synthesis. For example, the response of muscle protein synthesis to ingestion of 18 grams of EAAs in elderly is not further enhanced by ingestion of a mixture that contains the same EAAs together with 22 grams of non-essential amino acids (17), suggesting that non-essential amino acids in whey protein may not be necessary for the stimulation of muscle anabolism in elderly. Under the circumstances of that study, it is possible that a maximal response was reached in elderly as a result of the increase in plasma EAAs alone, and based on the fact that the stimulation of muscle protein synthesis by plasma amino acids is a saturable process (18). We sought to determine whether the benefit of whey protein ingestion in elderly is a direct result of the whey’s EAAs content. To test our hypothesis, elderly subjects ingested EAAs at a dose that we have previously documented to result in less than optimal muscle protein accrual in these individuals when compared to young controls (19), and compared this response of muscle protein accrual to that following ingestion of whey protein that contained the exact same amounts of EAAs. Our data, shown in Figure 1, indicate that at that level of EAA ingestion (~7 grams), ingestion of the intact whey protein (15 grams) results in greater accrual of muscle proteins than ingestion of only the EAAs found within the whey (20). Such evidence points to the direction that the whey protein is not just a simple source of EAAs with respect to its effects on muscle protein accumulation. Combining this finding with the fact that whey protein is more easily accessible and a more cost-effective approach to stimulate muscle protein synthesis relative to the EAAs ingestion, whey protein ingestion provides a more practical approach than amino acids ingestion to improve muscle protein anabolism through dietary supplementation in elderly.

A number of studies have shown that older muscle is associated with less than optimal stimulation of proteins synthesis by the plasma amino acids, a response that can be overcome by increasing the plasma availability of the essential amino acid leucine (16, 21). The fact that, compared to other high quality proteins (e.g. casein as well as soy), whey protein has a relatively higher leucine content (14, 22), makes whey a preferable source of dietary protein to enhance muscle protein anabolism, in a circumstance that sufficient amounts of protein are either not ingested or not preferred by the elderly. Also, co-ingestion of whey protein with a meal is known to increase the postprandial plasma amino acid concentrations to a greater extent than those observed after co-ingestion of casein with a meal (23). Further, given other reported benefits of whey protein, such as those in the immune function (24), which declines with age, whey may provide a unique nutritional approach to collectively address detrimental physiological and metabolic consequences of aging.

Amount of ingested whey protein to maximize muscle protein accumulation

It should be indicated that only few studies (11, 25, 26) have evaluated long-term effects of protein/amino acids supplementation on muscle protein anabolism. Based on these findings, the exact amount of either protein or amino acids needed to achieve maximal stimulation of muscle protein anabolism in elderly cannot be exactly determined. However, it is known that when a given amount of dietary protein is spread out over several meals during the day it results in less than optimal whole body protein retention in the elderly as opposed to when that same amount of protein is provided in a single meal (27). This relates probably to the fact that individual small increases in plasma amino acid...
acid concentrations are not sufficient to maximally stimulate muscle protein synthesis in elderly (19). The exact amount of ingested protein that results in maximal muscle protein anabolism may differ among older individuals given the wide continuum of the aging process and that the aging process itself may differ among individuals. It is generally known that muscle protein accumulation in elderly is similar to that in young when 15 grams of EAAs are ingested (28). This amount of EAAs could be extrapolated to ~30 grams of whey protein because whey protein contains ~50 percent of EAAs. According to a different line of evidence from studies in elderly, it appears that muscle protein synthesis does not increase further, and to a considerable degree, with the ingestion of a bolus that contains more than 10 grams of EAAs (29). Further, and given the evidence (Figure 1) that intact whey protein ingestion results in greater muscle protein accrual than ingestion of its EAAs content, the ingested bolus of whey needed to stimulate muscle protein accumulation in elderly similar to that in young is probably less than 30 grams. Overall, the evidence discussed in this paragraph suggests that a bolus ingestion of approximately 20-30 grams of whey protein (i.e. 10-15 grams of EAA) should be able to maximally stimulate muscle protein anabolism during the postprandial period in the elderly.

Timing of ingested whey protein to maximize muscle protein accumulation

In view of the fact that the response of muscle protein anabolism to protein ingestion generally diminishes approximately 4-5 hours postprandially, it would be reasonable to try to maintain this effect by spacing adequate amounts of ingested protein over the course of the day either with the major meals (e.g. morning, noon, evening) or between meals when, for example, protein ingestion is in the form of protein supplements. Such a nutritional approach can retard or possibly reverse the loss of muscle mass observed with aging. Relative to the latter, and based on limited evidence from relevant studies showing improved lean body mass in elderly via increased plasma amino acid concentrations throughout the day by means of amino acids supplements (25, 26), whey protein can provide a similar, in addition to an inexpensive, way to enhance lean body mass. It has been suggested that ingestion of a high quality protein equal to 1.5 grams protein/kg over the course of the day may be a more appropriate amount when compared to current recommendations (i.e. 0.8 grams protein/kg/day) to achieve optimal health outcomes in elderly (30). Most importantly, given the evidence for a ceiling effect in the stimulation of muscle protein anabolism with large increases in plasma amino acid concentrations over a certain period of time (18), and at the same time for a less than optimal response with insufficient increases in plasma amino acid concentrations in elderly (19), it appears that the emphasis for adequate protein intake may need to be placed not only on the overall amount of protein consumed per day but also on the timing of the ingested meal/supplement (e.g. ingestion of an adequate amount of protein ~4-5 hours apart). Spreading the dietary protein out over, for example, 3 times a day may confer the best benefit in terms of muscle protein anabolism, assuming that the amount of whey protein ingested each single time is in the range of 20-30 grams of protein. Ingestion of smaller boluses of protein may results in less than optimal stimulation of muscle protein synthesis as has previously been found (27), and discussed in the previous paragraph. On the other hand, and given that the ingestion of large amounts of protein in older people is still a matter of debate with respect to undesirable physiological/metabolic effects (11, 30), spreading out the amount of protein ingested during the course of the day and at single amounts sufficient to optimize muscle protein anabolism with each ingestion may be important to avoid any potential undesirable effects while at the same time improving muscle protein anabolism in elderly.

CONCLUSIONS

More evidence is needed from experimental and clinical studies to quantify the long-term effects of whey protein ingestion on improving muscle protein accumulation in parallel with improved functional and health outcomes in elderly. Given that the whey protein appears to be a faster and probably a qualitatively better source of amino acids (e.g. leucine) when compared to other proteins, whey may be a preferable dietary source of protein for the up-regulation of muscle protein anabolism in elderly. Overall, current evidence suggests that a bolus ingestion of approximately 20-30 grams of whey protein, when ingested at regular intervals (e.g. between main meals), may provide favourable benefits with respect to improving muscle protein anabolism in elderly.

REFERENCES AND NOTES