Effect of beta-hydroxy-beta-methylbutyrate supplementation on muscle loss in older adults: A systematic review and meta-analysis

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Abstract

Background: Beta-hydroxy-beta-methylbutyrate (HMB), a metabolite of the branched-chain amino acid leucine, has been investigated as a potential supplement to improve muscle quality; however, whether HMB supplementation has beneficial effects on muscle loss in older adults remains unclear.

Design: Systematic review with meta-analysis.

Setting: PubMed, Medline and EMBASE databases were searched from the earliest possible year to September 2014.

Participants: Individuals aged 65 years and older that reported absolute changes in body composition with use of HMB.

Measures: Two review authors working independently reviewed the trials, and standard mean difference was calculated using a fixed effects model.

Results: A total of seven randomized controlled trials were included, in which 147 older adults received HMB intervention and 140 were assigned to control groups. The meta-analysis showed greater muscle mass gain in the intervention groups compared with the control groups (standard mean difference = 0.352 kg; 95% confidence interval: 0.11, 0.594; Z value = 2.85; P = 0.004). There were no significant fat mass changes between intervention and control groups (standard mean difference = −0.08 kg; 95% confidence interval: −0.32, 0.159; Z value = 0.66; P = 0.511).

Conclusion: Beta-hydroxy-beta-methylbutyrate supplementation contributed to preservation of muscle mass in older adults. HMB supplementation may be useful in the prevention of muscle atrophy induced by bed rest or other factors. Further studies are needed to determine the precise effects of HMB on muscle strength and physical function in older adults.

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4. Discussion ........................................................................................................................................ 173
  4.1. Safety ...................................................................................................................................... 174
  4.2. Limitations .............................................................................................................................. 174
5. Conclusion .................................................................................................................................... 174
Conflicts of interest .......................................................................................................................... 174
Acknowledgement .......................................................................................................................... 174
References ......................................................................................................................................... 174

1. Introduction

Sarcopenia, or loss of muscle mass, is associated with various diseases and with aging, beginning as early as age 40. After age 40, muscle mass declines at a rate of approximately 8% per decade until age 70, after which loss increases at a rate of 15% per decade (Grimby & Saltin, 1983). Loss of muscle mass is an important clinical problem in older adults, and leads to a loss of muscle strength and decreased physical activity, and contributes to multiple adverse consequences, including frailty, disability, morbidity, and mortality (Landi et al., 2013; Malafarina, Uriz-Otano, Iniesta, & Gil-Guerrero, 2012).

Maintenance of muscle mass is dependent on the dynamic equilibrium between protein synthesis and degradation. Multiple strategies have been proposed to reduce muscle loss, including exercise training (Montero-Fernandez & Serra-Rexach, 2013), nutritional supplements (Karelis, Messier, Suppere, Briand, & Rabasa-Lloret, 2015; Malafarina, Uriz-Otano, Iniesta, & Gil-Guerrero, 2013), and hormone replacement (Brioche et al., 2013). Among these, nutritional supplementation is considered an efficient and a safe method. Beta-hydroxy-beta-methylbutyrate (HMB) is a metabolite of the branched-chain amino acid leucine (Nissen & Abumrad, 1997), which has been investigated due to its potential role in improving muscle quality. Multiple studies have explored mechanisms that link HMB to muscle loss; it has been suggested that HMB can enhance protein synthesis via upregulation of anabolic signaling pathways and attenuate proteolysis via downregulation of catabolic signaling pathways (Hasselgren, 2014). Likewise, population surveys and clinical studies suggest that HMB treatment decreased muscle proteolysis (Baier et al., 2009) and muscle damage and increased fat-free mass gain both in young and older adults (Molfino, Gioia, Rossi Fanelli, & Muscaritoli, 2013). Indeed, HMB has been extensively used as an ergogenic aid, especially among bodybuilders and power athletes, who use it to promote exercise performance and skeletal muscle hypertrophy (Wilson et al., 2013a). However, not all studies have found beneficial effects of HMB supplementation. Muscle loss and strength decline are a common comorbid condition in elderly populations, especially in older adults with severe pathological conditions, such as cancer, acquired immunodeficiency syndrome, or chronic disease. Low levels of muscle mass and strength can contribute to disease development and poor responses to treatment. Therefore, it is necessary to establish whether HMB intervention has a beneficial effect on muscle mass in older adults.

We conducted a meta-analysis to evaluate available studies assessing the effect of HMB supplementation on body composition and muscle strength in both healthy older adults and those with pathological conditions. We considered available randomized controlled trials in which HMB was administered either alone or in combination with other compounds.

2. Methods

2.1. Data sources and searches

Pubmed (http://www.ncbi.nlm.nih.gov/pubmed/), Medline (http://www.medline.com/), and Embase (http://www.embase.com/) were used to search for relevant articles from the earliest possible year to September 2014. Search terms used were (HMB or beta-hydroxy-beta-methylbutyrate) and (supplementation, replacement, therapy, treatment, effects or administration) and (muscle strength, grip, muscle loss, muscle mass or sarcopenia) and (aged, aging, older or elderly) and randomized controlled trials. Key words were used in various combinations to maximize search results. The reference lists from articles identified in the computer searches were examined to identify potentially relevant investigations. Manual searches complemented for potential articles. When more information was needed; authors of potential searches were contacted. After removal of duplicated articles; each title and abstract for potential inclusion were screened by two reviewers independently. The inclusion criteria are shown in Table 1. If the article was potentially eligible for inclusion; the full text was examined by two independent reviewers. Six studies were found to fit the criteria (Baier et al., 2009; Deutz et al., 2013; Flakoll et al., 2004; May, Barber, D’Olimpio, Hourihan, & Abumrad, 2002; Stout et al., 2013; Vukovich, Stubbs, & Bohlen, 2001). All studies were randomized placebo-controlled trials.

2.2. Data extraction

Two review authors working independently and in parallel assess the full text of included studies. The following characteristics of each study were extracted: author, year, design, country, sample size, sex, mean age, intervention, HMB dosage (g/d), duration, measurement of muscle strength and measurement of body composition. The primary outcomes of the trials were the absolute changes in body composition, muscle strength and physical performance. The absolute change values from baseline in each group can be calculated from the following formula:

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion criterion</strong></td>
</tr>
<tr>
<td>Study design</td>
</tr>
<tr>
<td>Population of interest</td>
</tr>
<tr>
<td>Intervention</td>
</tr>
<tr>
<td>Duration</td>
</tr>
<tr>
<td>Outcome measurement</td>
</tr>
</tbody>
</table>
\[ m_{t/c} = m_{pre} - m_{end} \]

where \( m_{t/c} \) is the changes from baseline to endpoint of the trial in treatment \( (m_t) \) or control \( (m_c) \) group, \( m_{pre} \) is the mean value of pre-treatment and the \( m_{end} \) is the mean value of the post-treatment in either treatment or control group. Standard deviations (SDs) of the mean difference between baseline and post-treatment in the treatment or control group can be obtained from the formula:

\[
SD_i = \sqrt{\frac{\sum X_i^2 + \sum X_j^2}{N_i} - \left( \frac{\sum X_i + \sum X_j}{N_i} \right)^2}
\]

where \( SD_i \) is the combined standard deviation of changes from baseline to post-treatment in treatment or control group, \( \sum X_i^2 \) is the sum of \( X_i^2 \) in baseline, \( \sum X_j^2 \) is the sum of \( X_j^2 \) in post-treatment and is the sum of sample sized of baseline and post-treatment. The standard mean difference (SMD) between treatment and control group can be calculated from the formula:

\[
SMD = \frac{\text{difference in mean outcome between groups}}{\text{pooled standard deviation}}
\]

The pooled SDs of mean difference between treatment and control group is calculated from following formula:

\[
SD_{\text{pooled}} = \sqrt{\frac{SD_i^2}{n_e} + \frac{SD_c^2}{n_c}}
\]

In studies where the dependent variable was recorded repeatedly, we use the measure that was closest to the termination of intervention to estimate the effect size. Any disagreement in study selection and data collection was adjusted by a third reviewer.

2.3. Assessment of the methodological quality of include studies and risk of bias

The methodological quality of included studies was evaluated using the Cochrane collaboration’s tool which was assessed by two reviewers independently. This is a domain-based evaluation, in which critical assessments are made over seven separate domains: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other source of bias. Using the Cochrane tool, each domain was rated as high, low and unclear risk of bias.

Potential publication bias was represented graphically with funnel plots.

2.4. Data analysis

We used SMD methods to combine study effect size estimates. The random effect models were applied to perform meta-analysis. Heterogeneity of results between studies was determined by \( I^2 \). For \( I^2 \), values from 25% to <50% were considered low heterogeneity, 50% to <75% moderate, and \( \geq 75\% \) highly heterogeneous. Together with \( I^2 \) values, 95% confidence intervals (CI) were calculated for each \( I^2 \) value. Test for overall effect (Z score) was regarded significant at \( P < 0.05 \).

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Fig. 1. Flow diagram of the review progress.
To provide a comparison between outcomes reported by the studies, effect sizes SMD with 95% CI were performed and graphs created by using Stata version 11.0 (Stata-Corp) and Review Manager software 5.0.

3. Results

3.1. Included studies characteristics

Our literature search identified 263 records, 13 of which were reviewed for inclusion. After further exclusions based on our selection criteria, seven provided sufficient information for data extraction and were deemed suitable for final analysis (Fig. 1). In total, these randomized controlled trials (performed in the United States) contributed 287 older adults; 147 received HMB intervention and 140 were assigned to control groups (Table 2).

The mean age ± SD of the participants in these studies varied from 67.1 ± 1.7 to 84.2 ± 1.6. Study sizes ranged from 24 to 104 participants, with duration follow up ranging from 8 weeks to 12 months. The evaluated dosage of HMB ranged from 2 g/d to 3 g/d; in four of the seven studies the dosage was 3 g/d, one study used with a single dosage of 2 g, and one study used dosage dependent on body weight: subjects weighing 68 kg or less were assigned a dosage of 2 g/d, and those subjects weighing >68 kg were assigned a dosage of 3 g/d. In the study conducted by Stout et al. (2013), HMB was supplemented either alone or in combination with resistance training in old adults; since the subjects were different in these two phases, we regarded the two phases as two independent trials. In phase I, HMB was supplemented alone. In phase II, physical exercise was used as a concomitant intervention in addition to HMB supplementation. Three studies supplemented with calcium HMB powder or capsules mixed with flavor agents, two studies used a mixture of HMB, arginine and lysine, and one study participants received a mixture of HMB, arginine and glutamine. The baseline characteristics of these studies also varied. For example, four studies included apparently healthy men and women, one study included only healthy women, and in the study conducted by May et al. (2002) patients with advanced cancer were recruited. Loss rates varied from 3.13% to 67.3%.

3.2. Quality of included studies and risk of bias

Six of seven studies were at a high risk of allocation concealment bias (selection bias), and did not provide enough information for assessment. There was a high risk of attrition bias in two studies with a high dropout rate: in the study conducted by May et al., 15/24 and 18/25 participants withdrew from the treatment and control groups respectively, while in the study performed by Berk et al., 135/226 and 106/220 withdraw from the treatment and control groups respectively. Five studies were at unclear risk of random sequence generation as they did not clearly describe the generation method (Fig. 2).

3.3. Main outcomes

The effects of HMB supplementation on body composition, muscle strength, and physical function for the included studies are shown in Table 3. All the studies reported absolute changes in fat free mass or body lean mass and body fat. In all of the studies reviewed here, measurements of body composition were made using biochemical impedance analyzer or dual X-ray absorptiometry, which have been shown to provide reliable measurements of muscle mass or body fat.

All included studies were examined for heterogeneity; heterogeneity of total lean mass and fat mass was determined to be low ($P = 0.438, I^2 = 0.0\%$), ($P = 0.741, I^2 = 0.0\%$). Accordingly, fixed effect models were applied for further meta-analysis (Fig. 3). Supplementation of HMB alone or in combination with other compounds has a beneficial effect on muscle mass improvement: the meta-analysis of muscle mass outcome showed increased

### Table 2

Descriptive statistics of randomized trials included in the meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample size</th>
<th>Age, mean (SE), sex</th>
<th>Recruitment</th>
<th>Intervention</th>
<th>Dosage (g/d)</th>
<th>Duration (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deutz et al. (2013)</td>
<td>RCT</td>
<td>C:10 D: 2</td>
<td>T: 67.4 (1.4) M/F = 3/8 C: 67.1 (1.7) M/F = 1/7</td>
<td>Healthy older adults performed ten days of bed rest</td>
<td>Sachet contained Ca-HMB</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Baier et al. (2009)</td>
<td>RCT</td>
<td>C:52 D: 12</td>
<td>T: M/F 75.5 (1.4)/75.3 (1.7); C: M/F = 21/19</td>
<td>Apparently healthy older adults</td>
<td>A mixture contained HMB (Ca-HMB), arginine, lysine</td>
<td>Weight ≤68 kg: 2; Weight &gt;68 kg: 3</td>
<td>48</td>
</tr>
<tr>
<td>Vukovich et al. (2001)</td>
<td>RCT</td>
<td>C:17 D: 0</td>
<td>All: 70 (1.0)/M/F = 15/16</td>
<td>Apparently healthy older adults</td>
<td>Ca-HMB</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>May et al. (2002)</td>
<td>RCT</td>
<td>C:25 D: 18</td>
<td>T: 66.0 (2.1)/M/F = 16/9 C: 66.0 (2.3)/M/F = 19/5</td>
<td>Old patients with advanced solid tumors</td>
<td>A mixture contained HMB (Ca-HMB), L-arginine, and L-glutamine</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Flakoll et al. (2004)</td>
<td>RCT</td>
<td>C:23</td>
<td>T: 77.7 (1.5)/M/F = 0/27 C: 75.7 (1.6)/M/F = 0/23</td>
<td>Apparently healthy older women</td>
<td>T: orange drink contained HMB (Ca-HMB), arginine, lysine</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Stout et al. (2013)</td>
<td>RCT</td>
<td>C:9 D: 4</td>
<td>T: 73 (1)/M/F = 13/12 C: 72 (1)/M/F = 14/11</td>
<td>Apparently healthy older adults; age ≤65 year; GRI ≥92; 30.0 BMI &gt;20.0; ambulatory</td>
<td>Phase I: Ca-HMB Phase II: Ca-HMB and RE</td>
<td>3</td>
<td>24</td>
</tr>
</tbody>
</table>

a: SE = standard error; BIA: biochemical impedance analyzer; BMI: body mass index; C: control group; D: drop out subjects; DXA: dual X-ray absorptiometry; GRI: geriatric nutritional risk index; NM: not measured; RCT: randomized control trials; RE: resistance exercise; T: treatment group; Ca-HMB: calcium Beta-hydroxy-beta-methylbutyrate.
muscle gain in the intervention groups than in the control groups (SMD = 0.352 kg; 95% CI: 0.11, 0.594; Z value = 2.85; P = 0.004). This effect seems to be specific for muscle mass and not fat mass, as there were no statistically significant changes in fat mass outcomes between intervention and control groups (SMD = −0.08 kg; 95% CI: −0.32, 0.159; Z value = 0.66; P = 0.511).

Five of the studies measured the effect of HMB on muscle strength, including handgrip strength, leg strength, or knee extensor and flexor strength. Four studies measured the effect of HMB on physical function, including short physical performance battery, get up and go, and 5-item physical performance battery. Due to variation in muscle strength or physical performance measured, these studies were not eligible for meta-analysis (Baier et al., 2009; Deutz et al., 2013; Flakoll et al., 2004; Stout et al., 2013; Vukovich et al., 2001). In the study conducted by Deutz et al., 10 days of bed rest caused a substantial loss of muscle mass in older adults, and HMB treatment prevented muscle mass decline over the bed rest period; however, there was no statistically significant difference between treatment group and control group in strength loss and functionality over the bed rest period. In the study conducted by Baier et al., one year of HMB supplementation (the longest treatment time of included studies) was not associated with any significant improvement in muscle strength and functionality among treatment groups. In the study conducted

![Image](image.png)

**Fig. 2.** Risk of bias of included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Measurement of body composition</th>
<th>Measurement of muscle strength</th>
<th>Muscle strength change, mean (SE), kg (C/T)</th>
<th>Measurement of physical function</th>
<th>Physical function change, mean (SE), (C/T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deutz et al. (2013)</td>
<td>DXA TLM</td>
<td>Isokinetic knee extensor 60°, Nm/s</td>
<td>−12.5 (7.84); 0.67 (6.91)</td>
<td>SPPB GUG, s</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>TFM</td>
<td>Isokinetic knee extensor 180°, Nm/s</td>
<td>−11.0 (8.31); −0.18 (7.07)</td>
<td>S-PPB</td>
<td>−0.43 (0.35); NS</td>
</tr>
<tr>
<td>Baier et al. (2009)</td>
<td>BIA FFM</td>
<td>Leg strength, kg Handgrip, kg</td>
<td>NS</td>
<td>CUG</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>FM</td>
<td></td>
<td></td>
<td>GU</td>
<td>NS</td>
</tr>
<tr>
<td>Vukovich et al. (2001)</td>
<td>DXA FFM</td>
<td>Upper body strength, % Lower body strength, %</td>
<td>14.9 ± 2.9; 14.9 ± 2.0</td>
<td>NM</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>FM</td>
<td>0.1 ± 0.4; 0.3 ± 0.4</td>
<td>18.1 ± 3.4; 21.8 ± 3.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May et al. (2002)</td>
<td>BIA FFM</td>
<td>−1.34 (0.78); 1.12 (0.68) 0.56 (0.95); −0.08 (110)</td>
<td>NM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flakoll et al. (2004)</td>
<td>BIA FFM</td>
<td>Knee extensor, kg Knee flexor, kg Handgrip strength, kg</td>
<td>−0.5 (1.5); 3.0 (1.5) −1.3 (0.7); 0.8 (0.7) −1.1 (0.6); 0.6 (0.6)</td>
<td>GUG, s</td>
<td>−2.3 (0.5); 0.0 (0.3)</td>
</tr>
<tr>
<td></td>
<td>BF</td>
<td>0.0 (0.3); 0.7 (0.3)</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>0.4 (0.6); −0.5 (0.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stout et al. (2013)</td>
<td>DXA TLM</td>
<td>Extensor phase II 180°, Nm/s</td>
<td>−1.2 (2.1); 7.7 (3.5)</td>
<td>GUG, s</td>
<td>0.6 (0.2); −0.5 (0.1)</td>
</tr>
<tr>
<td></td>
<td>TFM</td>
<td>0.2 (0.1); 0.5 (0.1) 0.3 (0.4); 0.6 (0.3)</td>
<td>0.5 (2.5); 14 (1.5)</td>
<td></td>
<td>−0.6 (0.3); −0.7 (0.3)</td>
</tr>
<tr>
<td></td>
<td>Phase II: 0.9 (0.1); 0.7 (0.2) −0.5 (0.3); −0.9 (0.4)</td>
<td>Extensor phase II 180°, Nm/s</td>
<td>0.6 (0.8); 0.02 (0.9) 17.1 (3.8); 9.1 (2.0) 7.0 (5.0); −2.1 (2.2) 11 (3.0); 5.7 (2.5) 3.8 (1.8); −0.1 (1.8) 2.6 (0.6); 2.8 (0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flexor 180°, Nm/s</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Handgrip, kg</td>
<td></td>
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</tr>
</tbody>
</table>

* BF: body fat; BIA: bioelectrical impedance analyzer; DXA: dual X-ray absorptiometry; FFM: fat free mass; FM: fat mass; GUG: get up and go; NM: not measure; NS: not significant; PPB: physical performance battery; SPPB: short physical performance battery; TFM: total fat mass; TLM: total lean mass.

† P < 0.05.

‡ P < 0.01.
by Vukovich et al., subjects were assigned to receive 3 g/d HMB or placebo, and all subjects participated in a series of strength training. After 8 weeks of treatment, though both upper-body strength and lower-body strength were increased, there were no significant differences observed between the HMB and placebo groups. The effect of HMB supplementation in elderly females was examined by Flakoll et al., who found that 2 g/d of calcium HMB supplementation for 12 weeks significantly improved muscle strength (measured by leg extensor force and handgrip strength) and physical function. To investigate the effect of HMB supplementation with and without resistance training in old adults, Stout et al. performed a 24 week study divided into two phases. Phase I consist of two non-exercise groups, and phase II subjects were treated with a combination of HMB or placebo and resistance exercise. After 24 weeks of phase I, HMB significantly improved muscle strength (extensor 180°). Likewise, in phase II, HMB combined with resistance exercise significantly improved muscle strength (extensor 60°, extensor 180°, handgrip) and physical function for both groups (Table 3).

3.4. Sensitivity analyses and publication bias

The I² statistical test was employed to identify heterogeneity, and the results suggested that the heterogeneity of muscle mass and body fat were very low which indicated that those studies were highly homogenous. There was little evidence of funnel plot asymmetry for included studies (Figs. 4 and 5).

4. Discussion

The purpose of this review was to explore the effect of HMB supplementation on changes in body composition, muscle strength, and physical performance in older adults. The majority of studies were of medium to high methodological quality, as assessed using the Cochrane collaboration's tool. This meta-analysis demonstrates that HMB intervention significantly improved the fat free mass in healthy older subjects and in older patients with different pathological conditions. This effect was specific for muscle mass; there were no significant changes in body fat mass compared with the placebo group. While effects on muscle mass were consistent, outcomes for muscle strength and physical performance varied in different reports. Perhaps resistance exercise in combination with HMB treatment is a potent stimulus for muscle improvement. Further studies are needed to investigate the combination of HMB and exercise for improving muscle strength and physical performance.
The effects of HMB on muscle have been explored in many different kinds of studies and indifferent population. A previous meta-analysis carried out by Rowlands and Thomson (2009) has evaluated the effects of HMB supplementation on muscle strength, body composition, and muscle damage in young men and reported that HMB supplementation had no effects on body composition. This study is in contrast with our findings suggesting that HMB has a positive effect on muscle mass in older adults. These different results might indicate that responses to HMB supplementation vary in different population.

HMB is important for muscle development and function. Multiple studies have explored the effects of HMB supplementation on muscle damage and or protein catabolism. Mechanisms underlying the role of HMB in muscle regeneration have also been explored: results indicated that HMB enhances protein synthesis via upregulation of anabolic signaling pathways and attenuate proteolysis via down-regulation of catabolic signaling pathways (Wilkinson et al., 2013). Animal studies have shown that supplemental HMB may enhance protein synthesis in neonatal skeletal muscle by stimulating translation initiation (Wheatley et al., 2014), which may improve survival rates of low-birth-weight infants. In addition, HMB supplementation suppresses apoptotic signaling and the apoptotic index during muscle disuse and during reloading periods after disuse in aged rats (Hao et al., 2011) and improves proliferation of satellite cells in muscles from aged rats in response to a loading stimulus following a period of disuse (Alway, Pereira, Edens, Hao, & Bennett, 2013). Population surveys suggest that HMB can be used to enhance recovery by attenuating exercise induced skeletal muscle damage in trained (Wilson et al., 2013b) and untrained populations (Wilson et al., 2009). In one study included in this analysis conducted by Deutz et al. (2013), results suggest that HMB is an effective nutritional intervention for preservation of muscle mass in healthy older adults confined to bed rest. HMB supplementation has also been reported to positively impact muscle atrophy in several pathological conditions, including cancer, acquired immunodeficiency syndrome, and sepsis (Hasselgren, 2014). Older adults, especially those with pathological conditions, were the main study populations and were limited in physical activities, which accelerates muscle loss. Thus, we hypothesize that HMB supplementation may have an effective role in muscle atrophy induced by bed rest or other conditions.

Based on the meta-analysis, HMB supplementation does not result in a significant change in fat mass. This result is consistent with that of Stout et al. (2013), who demonstrated HMB alone did not cause any fat loss; however, HMB combined with resistance training resulted in a significant loss in fat mass. What’s more, HMB has also been suggested to play a role in the improvement of fatty acid oxidation in muscle cells (Bruckbauer et al., 2012). Together, this results suggest that a combination of HMB and resistance exercise may contribute to the improvement of sarcopenia as well as obesity which impacts metabolic complications and represents a major public health challenge in the elderly (Choi, 2013).

4.1. Safety

Although quantitative safety data of HMB supplementation in humans has not been reported definitively, a number of studies have found no adverse side effects in animals or humans. In fact, the majority of these studies indicate that HMB is safe. The optimal dosage of HMB for muscle improvement is not conclusive: most studies advise taking 3 g of HMB daily for the most benefit. The dosage of HMB provided to the treatment groups ranged between 2 g/d and 3 g/d, but the majority used a dosage of 3 g/d. Consumption of HMB in dosages as high as 100 g/d are used in animal models, and a dosage as high as 6 g/d for 1 month was found to not have any side effects in humans (Fitschen, Wilson, Wilson, & Wilund, 2013). In the study conducted by Baeir et al. (2009), HMB/arginine/lysine supplement in elderly at a dosage of 3 g/d over a year-long period have not found any undesirable changes in blood chemistry, hematology, or urine markers. Currently, the maximal beneficial dosage of HMB is not conclusive; some researchers have recommended that HMB be standardized according to body weight, others suggested that a dosage of 3 g/d may be routinely recommended to maintain or improve muscle mass and function in health and disease. Along with determining an optimal dosage, the long-term safety of HMB supplementation in older adults should be assessed.

4.2. Limitations

The main limitations of this analysis are that only a small number of studies were included and the sample sizes were relatively small. In addition, all of the referred trials had a high rate of withdrawal from treatment. Finally, variation in measurements between studies could have influenced the overall results. A stronger meta-analysis would include uniform measurements of muscle strength.

5. Conclusion

Overall, this meta-analysis indicates that HMB can prevent lean body mass loss in older adults. But the effects of HMB on muscle strength and physical function appears to vary in different populations. Additional well-designed clinical studies are necessary to confirm the effectiveness of HMB in the prevention of loss of muscle strength and physical function.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgement

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