The Effects of Beta-Alanine Supplementation on Performance: A Systematic Review of the Literature

Jairus J. Quesnele, Michelle A. Laframboise, Jessica J. Wong, Peter Kim, and Greg D. Wells

Purpose: To critically review the methodological quality and synthesize information from systematic reviews and high quality studies on the effects of beta alanine (BA) on exercise and athletic performance. Methods: A search strategy was developed in accordance with the standards for the reporting of scientific literature via systematic reviews. Five databases were thoroughly searched from inception to November 2012. Inclusion criteria were English language, human studies, used BA to increase exercise or athletic performance, systematic reviews or randomized controlled trials and were published in a peer-reviewed journal. Included studies were systematically graded for their methodological quality by rotating pairs of reviewers and the results were qualitatively synthesized. Results: One systematic review and 19 randomized trials were included in this review. There is one systematic review with several methodological weaknesses that limit the confidence in its results. There are moderate to high quality studies that appear to support that BA may increase power output and working capacity, decrease the feeling of fatigue and exhaustion, and have of positive effect on body composition and carnosine content. The reporting of side effects from BA supplementation in the athletic population was generally under-reported. Conclusions: There appears to be some evidence from this review that supplementation with BA may increase athletic performance. However, there is insufficient evidence examining the safety of BA supplementation and its side effects. It is therefore recommended to err on the side of caution in using BA as an ergogenic aid until there is sufficient evidence confirming its safety.

Keywords: athletic, exercise, ergogenic, aerobic, anaerobic

Muscular fatigue is a multifactorial phenomenon occurring with high-intensity exercise that is not completely understood (Artioli et al., 2010; Derave et al., 2010). However, it has been established that acute high intensity anaerobic physical activity results in a decrease in adenosine triphosphate (ATP) molecules, creatine phosphate stores, and glycolytic substrates that are needed for energy metabolism in the muscle cell. High intensity exercise can also lead to an increase in intracellular metabolites such as adenosine diphosphate, inorganic phosphate, hydrogen ions, and lactate (Artioli et al., 2010). This breakdown of energy stores and increase in intracellular metabolites may be among the causative factors that lead to muscle fatigue during short-term high-intensity exercise (Allen et al., 1995; Derave et al., 2010). Early fatigue is of significant importance to the athlete as it may impair performance through decreased force generation and muscular capacity.

Some athletes have considered using beta alanine (BA) supplementation to augment fatigue threshold and improve performance. BA, a precursor of carnosine, has been shown to increase intracellular levels of carnosine (Harris et al., 2006; Derave et al., 2007; Baguet et al., 2010a, 2010b) and reduce acidosis during high-intensity exercise. This indicates that carnosine may act as a physiologically meaningful physiochemical buffer (Baguet et al., 2010b). In normal conditions, rate of BA production is relatively low and serum BA concentration is undetectable. If there is an increase in BA to a detectable level in the bloodstream, there may also be a subsequent increase in carnosine in the muscle. This increase has been considered as enhancing blood buffering capacity and decreasing neuromuscular fatigue (Artioli et al., 2010; Harris et al., 2006; Kern & Robinson, 2011; Stout et al., 2007). Thus, the rationale of supplementing with BA as an ergogenic aid has often been described to increase athletic performance (Allen et al., 1995; Artioli et al., 2010; Derave et al., 2007, 2010; Harris et al., 2006; Hill et al., 2007; Hobson et al., 2012; Stout et al., 2007).

Currently there are several randomized controlled trials (RCTs) and reviews published that examine the effects of BA supplementation on exercise performance. However, a well-controlled critical assessment of the literature examining the effects of beta alanine on exercise performance is needed. The purpose of this systematic review is to critically review the methodological quality of the literature on BA and its effects on exercise performance.
or athletic performance and to qualitatively synthesize information from systematic reviews and high quality studies. The aim is to inform others on the effectiveness and safety of BA supplementation for enhancing exercise performance using the best available evidence.

Method

Search Strategy

A search strategy was developed in accordance with the standards for the reporting of scientific literature via systematic reviews. The STARLITE (STAndards for Reporting LITErature searches) proposal and mnemonic was used to outline the characteristics of the search, demonstrate sound search methodology, and support the consensus for standards for reporting literature searches. Five electronic databases were searched (MEDLINE, CINAHL, SPORTDiscus, Rehabilitation & Sports Medicine Source and the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library)) from inception until November 2012. The search strategy combined terms relevant to beta alanine supplementation for exercise performance, including subject headings specific to each database and free text words.

Study Selection

Only systematic reviews with or without meta-analysis and RCTs were included in this review because they theoretically provide the highest level of evidence for this research question (Merlin, Weston, & Tooher, 2009). Selection criteria for all relevant articles were as follows: 1) English language; 2) Human studies; 3) Beta alanine supplementation used to increase exercise or athletic performance (performance included measures of power, strength, endurance, fatigue, metabolic measures and sport specific measures); 4) Systematic review with or without meta-analysis or randomized controlled trial (RCT; with no supplementation group); and 5) Published in a peer-reviewed journal.

Studies that examined the effects of multiple performance enhancing substances or supplements were excluded if they did not perform a stratified analysis for the beta alanine supplement only. Literature reviews that used narrative and/or nonsystematic methods were excluded.

One author (JQ) screened titles and abstracts of identified citations and retrieved the full text publication of articles that were judged potentially eligible. A second author (ML) independently reviewed all relevant studies and determined the eligibility of the studies by reviewing the methods section of the potentially eligible studies. Studies were deemed eligible if they pertained to beta alanine supplementation for athletic performance. Any disagreements were resolved by discussion to reach consensus.

Data Collection and Analysis

Rotating pairs of reviewers independently performed a critical review for potential sources of bias in study methodology. Relevant systematic reviews were critically appraised using Assessing the Methodological Quality of Systematic Reviews (AMSTAR) checklist for systematic reviews (Shea et al., 2007; Table 1). Systematic reviews were critically reviewed to determine if they had important methodological weakness limiting confidence in their results. Presence of fatal flaws (i.e., inadequate search strategy, inadequate critical appraisal or inadequate consideration of scientific quality when formulating recommendations) was judged to render the review scientifically inadmissible. Systematic reviews deemed scientifically admissible (i.e., without any fatal flaws) were to be included in the qualitative synthesis.

RCTs were critically appraised using the Physiotherapy Evidence Database (PEDro) rating scale for RCTs. The PEDro scale was used to assess the internal validity of the eligible trials. Minor modifications were made to two criteria on the instrument: 1) “therapists” were changed to “administrator of supplement/placebo” when assessing blinding; and 2) “prognostic indicators” was expanded to include the health, functional and training status of subjects when assessing similarity at baseline. The PEDro criteria has demonstrated fair to good reliability for rating quality of RCTs (Maher, Sherrington, Herbert, Moseley, & Elkins, 2003). Studies were reviewed and scored on the a priori criteria used to rank research to determine the quality of each publication.

A grading system was used to grade the strength of the evidence from RCTs. Studies with a score of 7 and above were deemed as high quality according to the PEDro scale. Studies scoring 5 or 6 were considered to be moderate quality and those studies scoring less than 5 were deemed as poor quality. In an effort to simplify the interpretation of the results, the authors used the aforementioned descriptive terms of quality assessment. Similar descriptive classifications of the PEDro scale have been previously used in other reviews (Silva et al., 2012; Teasell et al., 2007).

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement will be used for reporting this systematic review (Moher et al., 2009). Individual RCT demographics including inclusion and exclusion criteria, cointerventions, primary outcome, gender, age of participants, and duration of treatment dose for each group are summarized in Table 2.

Results

Search Results

Figure 1 outlined the search process and flow of this review. One systematic review (Hobson et al., 2012; Table 1) and nineteen RCTs were included (Table 2). The search combining MeSH, search terms and limiters yielded 77 studies, which included 25 duplicates. Fifty-two articles’ titles and abstracts were screened for eligibility. There were 38 potentially relevant trials that were retrieved in full text. Nineteen of these full text articles were deemed ineligible: three studies had inadequate randomization
(Kendrick et al., 2008; Sale et al., 2011; Sweeney, Wright, Brice, & Doberstein, 2010) and two failed to stratify for BA supplementation (Hoffman et al., 2006; Spradley et al., 2012). Twelve were nonsystematic or narrative reviews (Artioli et al., 2010; Campbell et al., 2010; Castell et al., 2010; Culbertson et al., 2010; Deldicque & Francaux, 2008; Derave et al., 2010; Hoffman et al., 2012; Sale et al., 2010; Stellingwerff et al., 2007; Stout, 2005; Tipton et al., 2007; Wilson et al., 2010), one was a thesis (Jagim, 2010), and one was a medical grand rounds (Messinger-Rapport, 2010). No unpublished preliminary studies were included in this review.

Methodological Quality of Systematic Reviews

One systematic review (Hobson et al., 2012) was relevant for critical appraisal. Table 1 depicts the AMSTAR rating of the included systematic review. The systematic review had several methodological weaknesses: 1) no critical appraisal of relevant studies to assess risk of bias (fatal flaw); 2) no consideration of scientific quality when formulating recommendations (fatal flaw); 3) inadequate consideration for study similarities when pooling results; and 4) inadequate assessment of publication bias. This systematic review was deemed scientifically inadmissible as per a priori criteria and was not included in our analysis.

Characteristics of RCTs

The sample sizes in the included studies ranged from 8 to 55. Details of the studies’ characteristics and interventions are provided in Table 2. All studies reported mean ages ranging from 18.4 to 85.3 and participants were overwhelmingly male. There were two studies which exclusively included female participants (Stout et al., 2007; Walter et al., 2010), three studies that included 17–20 female subjects (Chung et al., 2012; Smith-Ryan et al., 2012; Stout et al., 2008) and another study which included one female participant (Baguet et al., 2010a). The participants ranged from elite level athletics to recreational level and the elderly. Rowers were studied in one trial (Baguet et al., 2010a), football players and wrestlers in two trials (Hoffman et al., 2008a; Kern & Robinson, 2011), track-and-field athletes in one trial...
Table 1  AMSTAR Ratings of Systematic Reviews

<table>
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<tr>
<th>AMSTAR Criteria</th>
<th>Hobson et al., 2012</th>
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<tr>
<td>1. Was a priori design provided?</td>
<td>Yes</td>
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<td>2. Was there duplicate study selection and data extraction?</td>
<td>Yes</td>
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<td>3. Was a comprehensive literature search performed?</td>
<td>Yes</td>
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<tr>
<td>4. Was the status of publication (i.e., gray literature) used as an inclusion criterion?</td>
<td>No</td>
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<tr>
<td>5. Was a list of studies (included and excluded) provided?</td>
<td>Yes</td>
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<tr>
<td>6. Were the characteristics of the included studies provided?</td>
<td>Yes</td>
</tr>
<tr>
<td>7. Was the scientific quality of the included studies assessed and documented?</td>
<td>No</td>
</tr>
<tr>
<td>8. Was the scientific quality of the included studies used appropriately in formulating conclusions?</td>
<td>No</td>
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<td>9. Were the methods used to combine the findings of studies appropriate?</td>
<td>No</td>
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<td>10. Was the likelihood of publication bias assessed?</td>
<td>No</td>
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<td>11. Was the conflict of interest included?</td>
<td>Yes</td>
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<td>TOTAL</td>
<td>6/11</td>
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</table>

Methodological quality of RCTs

Table 3 depicts the quality score of each of the included studies. The PEDro criteria was used to adequately evaluate the internal validity and statistical rigor of all 19 RCTs and allowed for greater objectivity in the results. All RCTs reviewed scored moderate to high, with scores of 5 or higher. Four studies scored 6, six studies scored 7 and eight studies scored 8 out of 10, while Stout et al. (2006) was the only study to score 5. A total of 14 studies had a methodological quality score of 7 or more. Only two trials reported allocation concealment. Only six trials reported adequate baseline comparability (Baguet et al., 2010a; Chung et al., 2012; del Favero et al., 2012; Jordan et al., 2010; Van Thiemen et al., 2009; Walter et al., 2010), whereas eight studies did not report adequate follow-up (Chung et al., 2012; Hoffman et al., 2008a; Kern & Robinson, 2011; Smith et al., 2009a; Stout et al., 2006, 2007, 2008; Zoeller et al., 2007).

Almost all of the trials did not report blinding of the assessor; however, Baguet et al. (2010b), Stout et al. (2007), and Zoeller et al. (2007) did. Many of the studies included stated that the trial was double blinded in the methodology but did not explicitly state whether the assessor was blinded or if the clinician administering the treatment was blinded. All other categories within the PEDro criteria were well described and reflect the high scores given.

Treatment Dose

All of the studies reported the dosage of BA; however, there was large variability in the amount of BA given per dose, total grams per day, and duration of supplementation. The total BA per day ranged from 2.0 g per day to 6.4 g per day. Many of the studies used an incremental dosage strategy, whereby there were smaller dosages given early in the intervention period and larger dosages given late in the intervention period. The intervention period ranged from 4 weeks to 13 weeks. The BA supplement was commonly given as either a capsule or powder form. However, there were several studies that used BA supplements containing other potential ergogenic aids. Specific brands of BA supplements were used which include N-Acetylcysteine, alpha-lipoic acid, and vitamin E within the supplement itself and thus may represent potential cointerventions. Both Jordan et al. (2010) and Kern and Robinson (2011) reported using BA supplements which contained the aforementioned other ingredients, albeit, in relatively small amounts. Furthermore, more than half of the studies used a generic brand name BA supplement and explicit reporting about the ingredients contained within this BA supplement was not well documented. In addition, the BA supplement prescribed in many of the trials also contained dextrose or a sugar derivative, which may also have contributed to the studies’ results (Smith et al., 2009a, 2009b; Stout et al., 2006; Walter et al., 2010;
<table>
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<tr>
<th>First author, year</th>
<th>N, sex, sport</th>
<th>Mean age (range or ± SD)</th>
<th>Group(s)</th>
<th>Beta-Alanine dose</th>
<th>Outcome Measure</th>
<th>Training; Testing protocol</th>
<th>Follow-up</th>
<th>Other Intervention</th>
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<tr>
<td>Baguet et al., 2010a</td>
<td>17 male and 1 female, elite rowers</td>
<td>23.2 (± 4.4)</td>
<td>1. BA grp</td>
<td>5.0 g/day (7 wks)</td>
<td>muscle carnosine content, LT, sprint time</td>
<td>rowing training; 2000 m ergometer test</td>
<td>7 weeks</td>
<td>rowing training</td>
</tr>
<tr>
<td>Baguet et al., 2010b</td>
<td>14 male, physical education students</td>
<td>21.9 (± 1.5)</td>
<td>1. BA grp</td>
<td>4.8 g/day (4 wks)</td>
<td>VT, VO₂peak, pH, LT, bicarbonate, base excess</td>
<td>NR; 6 min cycling exercise</td>
<td>4 weeks</td>
<td>normal physical activity</td>
</tr>
<tr>
<td>Chung et al., 2012</td>
<td>34 male, 26 female, elite/sub-elite swimmers</td>
<td>BA 22.6 (± 2.8)</td>
<td>1. BA grp</td>
<td>4.8 g/day (10 weeks)</td>
<td>Swim performance, pH, bicarbonate, lactate</td>
<td>none; incremental test on treadmill, time-stands, timed-up-and-go tests</td>
<td>10 weeks</td>
<td>none</td>
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<td>del Favero et al., 2012</td>
<td>8 males, 10 females, physically inactive adults</td>
<td>BA 65 (± 4)</td>
<td>1. BA grp</td>
<td>3.2 g/day (12 weeks)</td>
<td>muscle carnosine, physical capacity tests, muscle function tests, QALY, blood and urinary tests</td>
<td>none; incremental test on treadmill, time-stands, timed-up-and-go tests</td>
<td>12 weeks</td>
<td>dextrose</td>
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<tr>
<td>Derave et al., 2007</td>
<td>15 male, track-and-field</td>
<td>18.4 (± 1.5)</td>
<td>1. BA grp</td>
<td>2.4 g/day (d 1–4) 3.6 g/day (d 5–9) 4.8 g/day (d 10–4wk)</td>
<td>calf muscle carnosine content, sprint time</td>
<td>isokinetic and isotonic dynamometer testing, 400m sprint cycle capacity test</td>
<td>4 weeks</td>
<td>track-and-field training</td>
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<tr>
<td>Hill et al., 2007</td>
<td>25 male, physically active</td>
<td>BL 25.4 (± 2.1) PL 29.2 (± 6.9)</td>
<td>1. BA grp</td>
<td>4.0 g/day (wk 1) 4.8 g/day (wk 2) 5.6 g/day (wk 3) 6.4 g/day (wk 4–10)</td>
<td>TWD, maximum power, muscle biopsies, carnosine content</td>
<td>cycle capacity test</td>
<td>10 weeks</td>
<td>maintained similar physical activity</td>
</tr>
<tr>
<td>Hoffman et al., 2008</td>
<td>8 male, experienced resistance-trained</td>
<td>19.7 (± 1.7)</td>
<td>1. BA grp</td>
<td>4.8 g/day (two 4 week sessions)</td>
<td>growth hormone, testosterone, cortisol</td>
<td>1RM, 6 sets of 12 reps squats at 70% 1RM</td>
<td>12 weeks</td>
<td>resistance training program</td>
</tr>
<tr>
<td>Hoffman et al., 2008</td>
<td>26 male, college football</td>
<td>19.7 (± 1.6)</td>
<td>1. BA grp</td>
<td>3× 1.5 g/day (3wks before season + 9 days preseason</td>
<td>power and total work, sprint time, questionnaires-intensity, soreness</td>
<td>resistance training; wingate, 3 line drills</td>
<td>30 days</td>
<td>practice training</td>
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<td>Jordan et al., 2010</td>
<td>17 male, recreationally active</td>
<td>24.9 (± 5.1)</td>
<td>1. BA grp</td>
<td>6.0 g/day (28 days)</td>
<td>%HRmax, %VO₂max, OBLA, VO₂max, Body mass</td>
<td>incremental treadmill running protocol</td>
<td>28 days</td>
<td>600 mg N-Acetylcysteine, 2.7 mg alpha-lipoic acid, 45 IU Vitamin E</td>
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<tr>
<td>First author, year</td>
<td>N, sex, sport</td>
<td>Mean age (range or ± SD)</td>
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<tr>
<td>Kern et al., 2011</td>
<td>37 male college football (FB), wrestler (WR)</td>
<td>FB (18.6 ± 1.5), WR (19.9 ± 1.9)</td>
<td>1. BA grp</td>
<td>2× 2.0 g/day (wk 1–8)</td>
<td>300 yd shuttle time, 90 °FAH time</td>
<td>HIIT, FAH and shuttle time</td>
<td>8 weeks</td>
<td>resistance training and practice, N-Acetyl L-Cysteine, Alpha-Lipoic Acid</td>
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<tr>
<td>Smith et al., 2009</td>
<td>46 male, recreationally active</td>
<td>22.2 (± 3.3)</td>
<td>1. BA grp</td>
<td>1.5 g 4×/day (wk 1–3)</td>
<td>EMG&lt;sub&gt;FT&lt;/sub&gt;, EEA,</td>
<td>HIIT 4 × 2 min bouts on cycle ergometer</td>
<td>6 weeks</td>
<td>dextrose</td>
</tr>
<tr>
<td>Smith et al., 2009</td>
<td>46 male, recreationally active</td>
<td>22.2 (± 2.7)</td>
<td>1. BA grp</td>
<td>1.5 g 4×/day (0–21), 3.0 g 2×/day (22–42)</td>
<td>VO&lt;sub&gt;2peak&lt;/sub&gt;, VO&lt;sub&gt;2max&lt;/sub&gt;, VT, TWD, body mass</td>
<td>HIIT, cycle ergometer</td>
<td>6 weeks</td>
<td>dextrose, HIIT</td>
</tr>
<tr>
<td>Smith-Ryan et al., 2012</td>
<td>50 (26 men, 24 women) recreationally active</td>
<td>men: 22.0 (± 2.7); women: 21.7 (± 2.1)</td>
<td>1. BA grp</td>
<td>2× 800 mg 3×/day (0–28)</td>
<td>high-intensity running performance, peak velocity</td>
<td>a graded exercise test on a treadmill</td>
<td>28 days</td>
<td>none</td>
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<tr>
<td>Stout et al., 2007</td>
<td>22 female</td>
<td>27.4 (±6.1)</td>
<td>1. BA grp</td>
<td>3.2 g/day (wk 1) 6.4 g/day (wk 2–4)</td>
<td>PWC&lt;sub&gt;FT&lt;/sub&gt;, VT, VO&lt;sub&gt;2max&lt;/sub&gt;, TTE, body mass</td>
<td>incremental cycle ergometry</td>
<td>28 days</td>
<td>none</td>
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<td>Stout et al., 2006</td>
<td>51 male</td>
<td>24.5 (± 5.3)</td>
<td>1. Placebo grp</td>
<td>1.6 g 4×/day, for 6 days, then 2×/day for 22 days</td>
<td>PWC&lt;sub&gt;FT&lt;/sub&gt;</td>
<td>continuous incremental cycle ergometry</td>
<td>28 days</td>
<td>dextrose</td>
</tr>
<tr>
<td>Stout et al., 2008</td>
<td>26 elderly (9 males, 17 females)</td>
<td>BA 72.1 (± 10.6); PL 73.4 (± 11.9)</td>
<td>1. BA grp</td>
<td>2.4 g/day (90 days)</td>
<td>PWC&lt;sub&gt;FT&lt;/sub&gt;</td>
<td>discontinuous cycle ergometry</td>
<td>90 days</td>
<td>none</td>
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<td>Van Thienen et al., 2009</td>
<td>17 male, mod-well trained cyclists</td>
<td>24.9 (18–30)</td>
<td>1. BA grp</td>
<td>2.0 g/day (wk 1–2); 3.0 g/day (wk 3–4); 4.0 g/day (wk 5–8)</td>
<td>Power, LT, pH values</td>
<td>simulated bike race-ergometer</td>
<td>8 weeks</td>
<td>none</td>
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<td>Walter et al., 2010</td>
<td>44 female, recreationally active</td>
<td>21.8 (NR)</td>
<td>1. BA grp</td>
<td>1.5 g 4×/day (0–4wk), 1.5 g 2×/day (5–8)</td>
<td>VO&lt;sub&gt;2peak&lt;/sub&gt;, VTw, body composition</td>
<td>HIIT, cycle ergometer</td>
<td>8 weeks</td>
<td>dextrose</td>
</tr>
<tr>
<td>Zoeller et al., 2007</td>
<td>55 male</td>
<td>24.5 (±5.3)</td>
<td>1. Placebo grp</td>
<td>1.6 g 6×/day, for 6 days, then 2×/day for 22 days</td>
<td>VO&lt;sub&gt;2peak&lt;/sub&gt;, VT, LT, TTE</td>
<td>cycle ergometer</td>
<td>4 weeks</td>
<td>dextrose</td>
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NR: not reported; BA: beta alanine; VO<sub>2</sub>: oxygen utilization; VT: ventilatory threshold, VTw: workload at which VT occurred; PWC<sub>FT</sub>: physical working capacity at fatigue threshold; TWD: total work done; LT: lactate threshold, TTE: time to exhaustion; Cr: creatine; HIIT: high intensity interval training; EMG<sub>FT</sub>: electromyographic fatigue threshold; EEA: efficiency of electrical activity; FAH: flexed arm hang; QALY: Quality of Life.
<table>
<thead>
<tr>
<th>PEDro Scale Items</th>
<th>Baguet et al., 2010a</th>
<th>Baguet et al., 2010b</th>
<th>Chung et al., 2012</th>
<th>del Favero et al., 2012</th>
<th>Derave et al., 2007</th>
<th>Hill et al., 2007</th>
<th>Hoffman et al., 2008</th>
<th>Hoffman et al., 2008</th>
<th>Jordan et al., 2010</th>
<th>Kern &amp; Robinson, 2011</th>
<th>Smith et al., 2009a</th>
<th>Smith et al., 2009b</th>
<th>Smith-Ryan et al., 2012</th>
<th>Stout et al., 2006</th>
<th>Stout et al., 2007</th>
<th>Stout et al., 2008</th>
<th>Van Thiemen et al., 2009</th>
<th>Walter et al., 2010</th>
<th>Zoeller et al., 2007</th>
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<tr>
<td>1. random allocation</td>
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<td>2. concealed allocation</td>
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*Note: Each satisfied item contributes 1 point to the total PEDro score (range 0–10 points)*
Zoeller et al., 2007). It was also very common among the included studies to have had an exercise training program prescribed or maintained during the intervention period.

Outcome Measures

There were a variety of outcomes used to assess athletic and exercise performance. Largely the outcome measures used depended on whether the study examined aerobic or anaerobic fitness. There were concrete measures of fitness and athletic performance which included specific time trials, VO2max, ventilator threshold (VT), lactate threshold (LT), power output and less concrete or indirect measures of performance such as muscle carnosine levels and body composition. In addition, several studies included rates of perceived exertion, fatigue and time to exhaustion as other measures of cardiorespiratory fitness (Smith et al., 2009b; Stout et al., 2007; Zoeller et al., 2007). For the purposes of this review the outcomes were grouped into four general categories: endurance and aerobic measures, strength, anaerobic measures and workload, sport specific measures, and metabolic and other measures.

The Effect of Beta-Alanine Supplementation on Aerobic Oxidative Metabolism

The effect of beta alanine on aerobic fitness and capacity were assessed in nine studies (Baguet et al., 2010; Baguet et al., 2010b; Jordan et al., 2010; Kern & Robinson, 2011; Smith et al., 2009b; Stout et al., 2007; Van Thienen et al., 2009; Walter et al., 2010; Zoeller et al., 2007). The most common measures of endurance and aerobic capacity included, but were not limited to, VO2, VT, LT, and other measures of acidosis and cardiorespiratory fitness. Of the six studies which examined the effects of BA on VO2, (Baguet, Koppo, et al., 2010; Jordan et al., 2010; Smith et al., 2009a; Stout et al., 2007; Walter et al., 2010; Zoeller et al., 2007) only Smith et al. (2009b) found significant increases in VO2peak and VO2te for the BA group compared with placebo after a second three-week supplementation period. Walter et al. (2010) found significant increases in VO2peak during each training session in both the BA and placebo groups at 4 and 8 weeks but they did not find any change for the control group. Three studies (Baguet et al., 2010b; Stout et al., 2007; Zoeller et al., 2007) found no significant differences in VO2 measures. For both groups Baguet, Koppo, et al. (2010) found no significant differences in submaximal VO2 throughout exercise before or after supplementation. Stout et al. (2007) found no significant differences in maximal oxygen consumption, VO2max, between BA and PL and Zoeller et al. (2007) also found no significant differences in VO2peak between BA and PL. Interestingly, Jordan et al. (2010) found a reduction in aerobic capacity as evidenced by a decrease in VO2max values in the BA group compared with no change in the placebo group.

Six studies examined the effects of BA on ventilation (VE) and VT (Baguet et al., 2010b; Smith et al., 2009b; Smith-Ryan et al., 2012; Stout et al., 2007; Walter et al., 2010; Zoeller et al., 2007). Stout et al. (2007) demonstrated increases in VT by 13.9% in the BA group versus no change observed in the placebo group. Smith, Walter et al. (2009) observed no significant differences among the improvements in VT between groups. There were nonsignificant improvements from pre to mid VT for both the placebo and BA groups (Smith, Walter, et al., 2009). There were no significant changes between BA and placebo in studies by Zoeller et al. (2007), Smith-Ryan et al. (2012) and Baguet, Koppo, et al. (2010) for VT. However, the lack of effect in the Smith-Ryan et al. (2012) study could be attributed to the large rest time (15 min) that may have allowed the metabolites to disperse between running bouts.

There were eight studies which examined measures of blood lactate measures following treatment inventions with BA (Baguet et al., 2010a, 2010b; Chung et al., 2012; Jordan et al., 2010; Kern & Robinson, 2011; Smith-Ryan et al., 2012; Van Thienen et al., 2009; Zoeller et al., 2007). Both Jordan et al. (2010) and Kern and Robinson (2011) demonstrated improvements in lactate measures following BA supplementation. In studies that measured blood lactate parameters during predominantly aerobic exercise, mixed results were observed. Jordan et al., 2010 demonstrated that the onset of blood lactate accumulation occurred at a higher % of heart rate and % of VO2max in the BA group compared with the placebo group following 28 days of BA supplementation. However, there were no significant changes in maximal lactate measures as reported by Baguet et al. (2010a) following a 2000 m rowing trial which lasted approximately 6 min and 30 s or Baguet et al. (2010b) 6-min cycling trial. Further, no significant differences between BA or placebo groups were noted in the Van Thienen et al. (2009), Zoeller et al. (2007) or Smith-Ryan et al. (2012) papers. In a study that evaluated lactate measures on exercise more associated with anaerobic capacity Kern and Robinson (2011) found no change between BA and placebo in both football players and wrestlers following a 300-yard shuttle or flexed-arm-hang time. Conversely, Chung et al. did not report substantial effects of BA supplementation on pre- versus postswimming race blood pH or bicarbonate levels despite most competitive swimming races relying significantly on anaerobic energy metabolism (Chung et al., 2012).

The Effect of Beta-Alanine on Strength, Anaerobic Capacity and Workload

The most common measures of strength and anaerobic capacity included, but were not limited to, power output, torque, physical working capacity at fatigue threshold (PWC170), total work done (TWD), power output at LT, and sprint time trials. Eight trials examined the effects of BA supplementation on power and TWD and one study examined the effects of BA supplementation on knee torque. Hill et al. (2007) examined 4 weeks of BA supplementation in physically active men on power output. They found a significant increase in total work.
done (TWD) by 13% with a further 3.2% increase at the 10-week point whereas TWD remained unchanged at 4 and 10 weeks in the control group. In addition, in the Hoffman, Ratamess, Ross, et al. (2008) study, there was greater mean power in the BA group versus placebo following 4 weeks for supplementation. In another trial by Hoffman et al. (2008a), 26 football players were administered either BA or placebo and were tested using anaerobic line drills and a Wingate test. Their results indicated no significant difference between mean and peak power or total work. In a study conducted by Smith et al. (2009b) there were also significant differences in TWD after 3 weeks of training and supplementing in the BA and placebo groups, however, there was no significant difference between groups. The physical working capacity at fatigue threshold was examined in three studies which demonstrated a 12.6–28.6% increase for BA versus no changes in the placebo group indicating that BA delays onset of neuromuscular fatigue at submaximum workloads (Stout et al., 2006; Stout et al., 2007; Stout et al., 2008). Walter et al. (2010) observed increases in workload at which VT occurred (VTw) for all groups at weeks four and eight. In addition, Van Thienen et al. (2009) found similar mean power output between placebo and BA, however, during the final sprint after the time trial, BA on average significantly increased both peak power output by 11.4% and mean power output by 5.0% during a 30 s sprint compared with placebo. Smith-Ryan et al. (2012) found no significant treatments effects on anaerobic running capacity and critical sprint velocity after subjects performed a series of runs while using BA.

The Effect of Beta-Alanine on Sport Specific Measures

Three studies reported time trials as indicators of performance enhancement with the treatment intervention. Baguet, Bourgois et al. (2010) examined rowing time trials and muscle carnosine content with BA supplementation and demonstrated nonsignificant improvements (p = .07) in BA group by 2.7 s (+4.8s) compared with placebo. Hoffman, Ratamess, Faigenbaum, et al. (2008) examined training volume and fatigue rates in line drills, intense cycling and resistance exercises and there were no differences in fatigue rate in line drills but a trend (p = .07) was observed for a lower fatigue rate for BA in the bench press exercise and a trend for greater training volume for all resistance exercise sessions. Derave et al. (2007) also studied 400-m sprint times as a measure of performance and did not find significant differences in the BA group. Chung et al. (2012) found greater improvement in training performance after eight weeks, though this effect was not maintained after 10 weeks.

The Effect of Beta-Alanine on Metabolic and Other Measures

Changes to body composition was reported in seven trials (Hill et al., 2007; Jordan et al., 2010; Kern & Robinson, 2011; Smith et al., 2009b; Stout et al., 2007; Van Thienen et al., 2009; Walter et al., 2010). Measures of body composition and lean mass included skin-caliper method, physician scales, or air displacement plethysmography. There were no changes in body composition reported in three trials (Hill et al., 2007; Stout et al., 2007; Van Thienen et al., 2009) while four trials revealed changes in body composition, with increasing lean mass most common in the BA group compared with the placebo group (Jordan et al., 2010; Kern & Robinson, 2011; Smith et al., 2009b; Walter et al., 2010). In another study, Hoffman et al. (2008b) examined the hormonal response to BA supplementation measuring growth hormone, testosterone and cortisol concentrations and found no significant differences between the BA and placebo groups. In addition, muscle carnosine content was examined in three studies using proton magnetic resonance spectroscopy and one study using muscle biopsy HPLC method following supplementation regimes of BA (Baguet et al., 2010a; Del Favero et al. (2012) Derave et al., 2007; Hill et al., 2007). Baguet et al. (2010a) demonstrated significant (p = .042) positive correlations (r = .498) between muscle carnosine concentrations and incremental rowing speeds and performance on a 2000 m simulated race. Derave et al. (2007) demonstrated BA supplementation significantly increased muscle carnosine concentrations in the soleus (+47%) and gastrocnemius (+37%) compared with placebo. del Favero et al. (2012) also found a significant increase in muscle carnosine content in the BA group (+85.4%) compared with placebo (+7.2%). Hill et al. (2007) also demonstrated increases in muscle carnosine following BA supplementation at four weeks (+58.8%) and at 10 weeks (80.1%).

Eight studies included feelings of fatigue and time to exhaustion as a measure of cardiorespiratory fitness. Five studies reported the time to exhaustion (del Favero et al., 2012; Smith et al., 2009b; Smith-Ryan et al., 2012; Stout et al., 2007; Zoeller et al., 2007). del Favero et al., (2012) had time to exhaustion (TTE) as a measure of exercise tolerance (using the difference between ventilatory anaerobic threshold and VO2peak set at 75%) and found TTE significantly improved in the BA group versus placebo group. One other study defined time to exhaustion by the time (in seconds) that the subject could maintain a cadence rate of 60 rpm and was only defined within the VO2 (Smith, Walter, et al., 2009). The two other studies did not define time to exhaustion but it was measured during a graded exercise protocol and reported in seconds (Stout et al., 2007; Zoeller et al., 2007). Stout et al. (2007) found a 2.5% increase (improvement) in time to exhaustion during maximal cycling ergometry performance versus no changes in the placebo group. Smith-Ryan et al. (2012) found no TTE effects that were evident for bouts at 90–110% PV lasting 1.95–5.06 min. In addition, Zoeller et al. (2007) found no significant differences between BA and placebo for TTE following 28 days of supplementation on cycle ergometry testing. Three studies also reported on fatigue following the exercise protocols. Derave et al. (2007) reported fatigue
as measured by exhaustive dynamic knee contractions but did not define what constituted fatigue. While Hoffman, Ratamess, Faigenbaum, et al. (2008) defined rate of fatigue as the drop in power from peak power to lowest power and sprint times (best time/worst time). Subjects were also asked to rate their feelings of fatigue using a 7-point scale. Jordan et al. (2010) assessed overall body rating of perceived exertion using a 6–20 numeric scale. Two studies (Derave et al., 2007; Hoffman, Ratamess, Faigenbaum, et al., 2008) indicated a significantly lower subjective fatigue level for BA compared with placebo.

Adverse Events

Adverse events were generally poorly reported. Seven of the nineteen studies reported on adverse events following BA supplementation. Derave et al. (2007), del Favero et al. (2012) and Van Thienen et al. (2009) reported no adverse events, while other studies reported mild paresthesia and/or infrequent mild transient symptoms such as tingling in hands and fingers (Chung et al., 2012; Hill et al., 2007; Jordan et al., 2010; Smith-Ryan et al., 2012).

Discussion

As the popularity of BA supplementation increases, the need for high quality reviews on the topic is paramount. There is currently one systematic review with meta-analysis on this topic (Hobson et al., 2012); however, the review did not evaluate the methodological quality of the included studies when formulating their results, leading to low confidence in their findings. Previous literature has demonstrated that combining findings from studies without considering their methodological quality can lead to bias (Egger et al., 2002; Schultz et al., 1995). In light of this, this body of literature is lacking a critical assessment of studies to draw appropriate conclusions on BA. Our critical assessment of methodological quality and synthesis of information from high quality studies addresses this important knowledge gap to guide the use of BA for performance.

Overall, nine studies examined the effect of beta alanine on endurance and aerobic capacity. Only one high quality trial, Smith, Walter, et al. (2009), found significant increases in VO2peak and VO2tte favoring the BA group compared with placebo. Another study of high methodological quality, Walter et al. (2010), found significant increases in VO2peak for both the BA and PL groups but did not find any differences between BA and PL. The findings of these studies suggest a potential treatment effect of the exercise program used during the study period rather than the BA supplementation. Furthermore, in a high quality study, Jordan et al. (2010) found a decrease in VO2max in the BA group compared with PL group. Overall, there is one moderate and two high quality studies yielding inconsistent results for the effect of beta alanine on VO2. It appears that BA alone does not affect VO2peak, but may improve it when combined with exercise training. Simply put, it appears that BA may augment the training induced effect on VO2peak.

Likewise, there are high methodological studies yielding inconsistent evidence for the effect of beta alanine on ventilation and ventilatory threshold (Baguet et al., 2010b; Smith et al., 2009b; Stout et al., 2007; Walter et al., 2010; Zoeller et al., 2007). Significant improvements in lactate measures following BA supplementation were also noted in two moderate to high quality studies (Jordan et al., 2010; Kern & Robinson, 2011). While no significant changes in lactate measures between BA and PL groups were noted in six other high quality trials (Baguet, Bourgois, et al., 2010; Baguet, Koppo, et al., 2010; Chung et al., 2012; Smith-Ryan et al., 2012; Van Thienen et al., 2009; Zoeller et al., 2007), thus there is also inconsistent evidence demonstrating an improvement in lactate measures following BA supplementation. Based on inconsistent results across the included studies, the overall conclusion regarding the effect of beta alanine on endurance and aerobic capacity is inconclusive.

Ten studies examined the effects of BA on strength, anaerobic capacity and workload. In one moderate quality trial (Hoffman, Ratamess, Faigenbaum, et al., 2008) and two high quality trials (Hoffman et al., 2008a; Van Thienen et al., 2009) there were significant increases in TWD and mean power for the BA group compared with placebo. In another high quality study (Smith et al., 2009b) there were significant differences in TWD between BA and PL groups, however, there were no significant between group differences. Whereas another moderate quality trial examining power and TWD (Hoffman et al., 2008a) and a high quality trial (Smith-Ryan et al., 2012) examining critical velocity and anaerobic capacity found no significant differences between placebo or BA groups. Physical working capacity and fatigue threshold were examined in three moderate-to-high quality trials (Stout et al., 2006, 2007, 2008). These three studies demonstrated an increase in fatigue threshold for BA versus placebo group indicating that BA may delay the onset of neuromuscular fatigue. Overall, there is moderate to high quality evidence to suggest that BA supplementation may increase TWD, power output, physical working capacity, and fatigue threshold.

The effect of beta alanine on sport specific measures was examined in several trials. In one high quality study, 2000-m rowing time trials improved in the BA group compared with placebo, with the placebo group demonstrating decreases in rowing time trials compared with baseline following a 7 week intervention period (Baguet, Bourgois, et al., 2010). Greater improvement in training performance after 4 weeks was found in another high quality trial, though this effect was not maintained after 10 weeks and should be considered in light of substantial baseline differences between the two groups (Chung et al., 2012). While another high quality trial demonstrated no significant differences in 400 sprint times between BA and PL groups (Derave et al., 2007). Overall, three high quality studies examining time trials yielded inconsistent results for the treatment effect of BA compared...
with placebo on rowing, swimming and running sprint times.

There were also many studies which aimed to identify other treatment effects of BA supplementation on athletes. Factors such as fatigue rates and exhaustion were found to improve in four moderate-to-high quality trials for the BA group compared with placebo (del Favero et al., 2012; Derave et al., 2007; Hoffman et al., 2008a; Stout et al., 2007). Among seven trials, which included body composition as a part of their analysis, four moderate-to-high quality trials revealed changes in body composition, with increasing lean mass being the most common in the BA group compared with placebo (Jordan et al., 2010; Kern & Robinson, 2011; Smith et al., 2009b; Walter et al., 2010). These studies indicate an association of BA supplementation having a positive effect on body composition; however, it is difficult to ascertain whether this effect is due to other factors such as exercising training effect. Muscle content was examined in four high quality studies which demonstrated increased muscle carnosine concentrations in the BA supplementation group with subsequent performance enhancement compared with the placebo group (Baguet et al., 2010a; del Favero et al., 2012; Derave et al., 2007; Hill et al., 2007).

The dosage strategies used within the studies varied considerably. In general, an incremental dosage strategy was most often used. Smaller dosages were given early in the intervention period and larger dosages given later. Employing an incremental strategy of BA ranging from 3.0 to 6.0 g per day may be beneficial; however, there were large discrepancies between the studies in terms of frequency, duration, and amount of BA used. Based on this heterogeneity, interpreting the results for optimal dosage strategy is difficult and thus specific recommendations in this review cannot be made.

Our systematic review found that beta alanine provided improvements in many performance domains and exercise measures. However, there were many inconsistencies within our included studies for endurance and aerobic measures and sport specific measures. Thus, caution should be applied when conferring the widespread treatment effects of BA on exercise performance as a whole. As reported by Hobson et al. (2012), and also demonstrated in our review, is the lack of reporting of adverse events in the BA supplementation trials. Only three trials reported that there were no adverse events observed (del Favero et al., 2012; Derave et al., 2007; Van Thienen et al., 2009) while four studies reported that the adverse events were mild and transient in nature, which included paresthesias (Chung et al., 2012; Hill et al., 2007; Jordan et al., 2010, Smith-Ryan et al. 2012).

The under-reporting of BA supplementation adverse events within the included studies is problematic. There may have been side effects experienced that were of mild nature and thus not reported by the subjects if not explicitly asked. Further, because of the under-reporting of adverse events the possibility of those subjects who were lost to follow-up having left the study because of an adverse event is possible. The under-reporting of adverse events in the included studies makes conclusions pertaining to side effects and adverse events with BA supplementation in this population largely unknown. Recent work by Harris et al. 2006 and Décombaz, Beaumont, Vuichoud, Bouisset, & Stellingwerff, 2012 help to elucidate the potential adverse effects of BA supplementation. Harris et al. (2006) did not find any adverse effects, except for mild flushing in 4 participants receiving BA and one receiving the placebo, of a frequently used supplementation protocol (4 weeks, 4 doses of 800mg/day), on blood biochemical and hematological markers. Further, Decombez et al. (2012) thoroughly investigated the sensory side-effects of acute ingestion of both pure and slow-release beta-alanine (1.6g). Their findings also indicate that when the suggested doses and time are respected, beta-alanine supplementation seems to be safe.

**Limitations**

This review has some possible limitations including those within the included RCTs themselves. Although the PEDro scales takes into consideration many critical methodological factors such as randomization, blinding, and follow-up, it can be argued that the scale removes analytical subjectivity, and thus may over-estimate the actual quality of the study. It may also be argued that in ergogenic supplement trials, the PEDro scale may not be ideal to adequately account for methodological issues unique to these types of trials. These methodological issues include, compliance with supplement dosing strategy, dietary reporting of participants or specific detail regarding training status of the participant, which also contribute as limitations to our review. Although the authors did not find any critical flaws within the 19 included RCTs there were some general concerns. First, very few studies reported adequate baseline comparability on the most important prognostic indicators or reported adequate allocation concealment. There were also many studies with inadequate follow-up or reporting of follow-up. Furthermore, all studies did include placebo as a control group; however, few studies included an additional control group, which did not receive the exercise protocol. Thus, the distinction between the treatment effects of exercise training on performance cannot be clearly made and presents itself as a major limitation to the studies included in this review. There appears to be a positive mechanistic correlation between BA supplementation, an increase in muscle carnosine content and enhanced performance. Ideally muscle carnosine would have been studied in all studies to determine efficacy for performance enhancement; however, only four trials directly measured this effect in our review and thus serves as a limitation to the review. In addition, reporting adequate baseline comparability and evaluating the potential treatment effects of other potentially active ingredients, such as Alpha-Lipoic-Acid and Vitamin E was not well accounted for, as such, the possibility remains that these other active ingredients may have contributed to the
results of the studies and thus serve as confounders in our review. Another limitation was that the sample sizes of most studies were quite small and thus potentially represents underpowered results. These methodological limitations increase the risk of bias and thus make interpretation of studies results difficult.

The primary limitation among the included studies was the lack of homogeneity of the study designs. There were large differences in study samples, dose strategies, exercise interventions, outcome measures, and treatment protocols making it difficult to draw firm conclusions regarding the effect of BA on performance. Another possible limitation in this review is the language bias as we only permitted articles published in the English language. Furthermore, only randomized trials were included in this review, which excludes potential results regarding the effectiveness of BA from nonrandomized but well-controlled cohort studies. The sample was overwhelmingly male and thus interpretation of the results regarding the effect of beta alanine on both genders is limited.

Research Priorities

Future research should be directed to delineate the optimal dose strategy for subgroups of athletes including gender differences and body type. Future research should also aim to further examine the generalizability of BA on different age groups including adolescents and children as well as the older athletes. The safety profile of BA appears to be satisfactory; however, there were insufficient studies that measured adverse events and thus true representation of the safety of BA supplementation in the athletic population cannot be determined. Safety and analysis of adverse events should be included in future work as a specific aim to help substantiate and protect the public who may use this supplement. Further, this review was not able to precisely establish the effects of pure BA on performance, as some studies included other potentially active ingredients and/or additives in relatively small amounts to their beta alanine supplements. In addition, more than half of the studies used a generic brand name BA supplement and did not explicitly state whether this supplement had potentially active ingredients within the BA formula. This is a limitation of the included studies and future studies should consider removing active ingredients from the beta alanine supplements or including similar ingredients into the placebo. This would allow for the effects of pure beta alanine to be better assessed.

Future research should emphasize high methodological rigor to minimize sources of bias and increase our confidence in the results. In RCTs, this emphasis should be placed on adequate baseline comparability, reporting of allocation concealment, adequate follow-up and sample sizes that reach statistical power. Future systematic reviews in this area should conduct appropriate critical appraisal of relevant studies and consider scientific quality when formulating recommendations. This ensures that conclusions are based on studies of low risks of bias and adequate scientific validity only.

Conclusion

Team doctors, therapists, and healthcare professionals need to raise their awareness of the use of beta alanine as an ergogenic substance. Currently, there appears to be some evidence from this review that supplementation with BA may increase athletic performance. Specifically, there appears to be moderate to high quality that BA supplementation may increase TWD and power output. There is also moderate to high quality evidence indicating that BA supplementation may decrease subjective feelings of fatigue and perceived exhaustion. Moderate to high quality research also indicates a positive effect of BA on body composition and muscle carnosine content.

Given these findings, there may be a beneficial role of implementing BA supplementation among select athletes who are closely followed by team doctors or health care professionals. There are currently no long-term trials examining the extended use of BA supplementation in athletic populations. Therefore, one should err on the side of caution in using BA as an ergogenic aid until there is sufficient evidence confirming its safety.

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References


