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ORIGINAL ARTICLE

The effect of HMB supplementation on body composition, fitness, hormonal and inflammatory mediators in elite adolescent volleyball players: a prospective randomized, double-blind, placebo-controlled study

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Abstract The use of ergogenic nutritional supplements is becoming inseparable from competitive sports. β-Hydroxy-β-Methylbutyric acid (HMB) has recently been suggested to promote fat-free mass (FFM) and strength gains during resistance training in adults. In this prospective randomized, double-blind, placebo-controlled study, we studied the effect of HMB (3 g/day) supplementation on body composition, muscle strength, anaerobic and aerobic capacity, anabolic/catabolic hormones and inflammatory mediators in elite, national team level adolescent volleyball players (13.5–18 years, 14 males, 14 females, Tanner stage 4–5) during the first 7 weeks of the training season. HMB led to a significant greater increase in FFM by skinfold thickness (56.4 ± 10.2 to 56.3 ± 8.6 vs. 59.3 ± 11.3 to 61.6 ± 11.3 kg in the control and HMB group, respectively, $p < 0.001$). HMB led to a significant greater increase in both dominant and non-dominant knee flexion isokinetic force/FFM, measured at fast (180°/sec) and slow (60°/sec) angle speeds, but had no significant effect on knee extension and elbow flexion and extension. HMB led to a significant greater increase in peak and mean anaerobic power determined by the Wingate anaerobic test (peak power: 15.5 ± 1.6 to 16.2 ± 1.2 vs. 15.4 ± 1.6 to 17.2 ± 1.2 watts/FFM, mean power: 10.6 ± 0.9 to 10.8 ± 1.1 vs. 10.7 ± 0.8 to 11.8 ± 1.0 watts/FFM in control and HMB group, respectively, $p < 0.01$), with no effect on fatigue index. HMB had no significant effect on aerobic fitness or on anabolic (growth hormone, IGF-I, testosterone), catabolic (cortisol) and inflammatory mediators (IL-6 and IL-1 receptor antagonist). HMB supplementation was associated with greater increases in muscle mass, muscle strength and anaerobic properties with no effect on aerobic capacity suggesting some advantage for its use in elite adolescent volleyball players during the initial phases of the training season. These effects were not accompanied by hormonal and inflammatory mediator changes.

Keywords Supplements · Youth · Athletes · Cytokines · Growth

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Introduction

In the highly competitive sports world, where few millimeters or one-hundredth of a second could be the difference between fame and shame in an athlete's career, nutritional supplements are becoming an inseparable part

of sport. Billions of dollars are spent throughout the world on nutritional supplements, or "ergogenic aids". These substances are alleged to enhance performance by increasing exercise training-associated anabolic and reducing catabolic effects, decreasing fatigue, inducing desirable changes in body composition and improving aggression (Nemet et al. 2005).

Protein and amino acids are among the most popular "performance enhancing" supplements. Since amino acids and proteins are essential for the synthesis of structural proteins and are involved in numerous metabolic pathways associated with exercise, it has been suggested that athletes require additional proteins, either in their diet, or as supplements. Although the use of protein supplements in sports is very common, limited clinical data are available on beneficial effects of protein supplementation on exercise performance.

β-Hydroxy-β-methylbutyric acid (HMB) has recently become a popular dietary supplement suggested to promote gains in fat-free mass and strength during resistance training (Nissen et al. 1996). HMB is a bioactive metabolite formed from breakdown of the essential branched amino acid leucine. Leucine and its metabolite ketoisocaproate (KIC) appear to inhibit protein degradation, and this anti-proteolytic effect is believed to be mediated by HMB. HMB exerts its effects through protective, anticatabolic mechanisms and has been shown to directly influence protein synthesis (Slater and Jenkins 2000). Possible mechanisms of action include reduced muscle damage due to stabilization of muscle cell membrane, modulation of protein degradation by inhibition of the ubiquitin–proteosome system, and upregulation of IGF-1 gene expression in the skeletal muscle, and the mTOR signaling pathway leading to protein synthesis (Wilson et al. 2008; Zanchi et al. 2010).

β-Hydroxy-β-methylbutyric acid supplementation has been reported to promote significantly greater gains of fat-free mass and strength in untrained men and women initiating 3–8 weeks of resistance training (Nissen et al. 1996). Recently, a double-blind placebo-controlled study demonstrated that 9 weeks of HMB supplementation in trained men led to increase muscle strength with no change in body composition (Thomson et al. 2009). In addition, several studies also demonstrated beneficial effects for HMB in endurance-type training (Lamboley et al. 2007; Vukovich and Dreifort 2001). Although these findings suggest that HMB supplementation during training may enhance adaptations of trained and untrained individuals, others report no significant effects of HMB supplementation (Hoffman et al. 2004; Kreider et al. 1999). Thus, the available scientific literature on HMB supplementation in humans is still preliminary in nature and should be considered with reservation (Decombaz et al. 2003).

The aim of the present study was to assess the effect of a randomized, double-blind, placebo-controlled supplementation of HMB on body composition, fitness characteristics (strength, anaerobic and aerobic), anabolic (the growth hormone insulin-like growth factor-I axis and testosterone) and catabolic hormones (cortisol), and inflammatory mediators (interleukin-6) in elite, national team level, male and female volleyball players during the initial 7-week phase of the training season. We studied the effect of HMB supplementation during the initial phases of the training season since previous studies suggested better effects of HMB in untrained compared with trained individuals (Rowlands and Thomson 2009). We elected to study adolescent athletes since the use of nutritional supplements becomes common in this population, without scientific evidence of beneficial effect of these substances during a time of physiological, naturally occurring, hormonally mediated, rapid growth, and remarkable increase in muscle mass (Nemet and Eliakim 2007).

We hypothesized that HMB supplementation will lead to a greater increase in fat-free mass, muscle strength, anaerobic and aerobic capacity and will be accompanied by an increase in anabolic hormonal response and reduced catabolic, and inflammatoty response.

Subjects and methods

Twenty-nine (15 males, 14 females) healthy, elite, national team level Israeli junior volleyball players (age range 13.5–18 years, Tanner stage for pubic hair 4–5) participated in the study. All participants played in the Israeli premier junior volleyball league, and were members of the Israeli National Academy for Gifted Athletes and the Israeli national junior volleyball team. The study was performed during the early phase (first 7 weeks) of the volleyball season. The study was approved by the local Institutional Review Board and all parents and participants signed an informed consent prior to participation.

Participants were randomly assigned (using computerized software) by gender and maturity to the HMB (3 g/day) or placebo group. We used a dose of 3 g/day, since previous studies in adults suggested that the use of this dose resulted in the greatest effects on muscle mass and muscle strength [lower doses were found significantly less effective, and higher doses were not significantly more effective (Gallagher et al. 2000)].

The HMB and placebo pills were prepared by the same manufacturer (Supherb, Israel) and packed in exactly the same packages. Players, coaches, and study personnel were blinded to the group assignment. The key of randomization information regarding the type of pill in each pack was opened at the end of the study after the completion of data

collection. To ensure compliance, participants took their pill (HMB or placebo) every day during the morning practice in front of their coaches. None of the participants received any additional medications or food supplements other than HMB or placebo.

Participants from both HMB and placebo-supplemented groups trained together 18–22 h per week. Exercise training involved tactical and technical drills emphasizing volleyball skills and team strategies (about 20% of training), power and speed drills with and without a ball (about 25% of training), and interval sessions (about 25% of training). The interval sessions included repeated hits and digs (e.g. several repetitions of 30–60 s of quick hits over the net with sprinting from the net to the end of the court in between), or short-distance repetitions without the ball (i.e. 120–300 m runs). About 15% of training consisted of endurance-type training (i.e. long-distance cross-country running). The additional 15% of training consisted of resistance training using mainly circuit training with free weights at 65–75% of maximal one repetition (1RM).

All participants attended the Israeli National Academy for the Gifted and lived in the dormitories during the intervention. Both HMB- and placebo-supplemented participants were exposed to the same training and sleep regimens (i.e. 8 h/night), and were all exposed to similar nutritional conditions (i.e. all meals were served at the Wingate institute dining room). All participants, except for one from the HMB group who left the Academy due to familial cause, unrelated to the study, completed their training program and the pre and post intervention evaluation. Therefore, at the completion of the study, there were 14 members in the HMB group and 14 members in the placebo-controlled group.

Pre and post evaluations were performed for all the participants together, at the same time of the day. Standard, calibrated scales and stadiometer were used to determine height and body mass. Skinfold measurement at two sites (triceps and sub-scapular) were used to calculate percent body fat using standard equations (Slaughter et al. 1988). Each measurement was performed in triplicate and the average was taken for analysis. Body fat was also measured using air displacement plethysmography by BOD POD (Bod Pod "gold standard" model, Life Measurement, Inc., Concord, CA).

Fitness assessment

All fitness measurements were performed during the week before and after the intervention. Since volleyball training includes power, strength, anaerobic and aerobic fitness characteristics, all these components were assessed in the present study.

Power assessment

Vertical Jump Test. Vertical jump height was measured by a maximum vertical jump using a free countermovement jump technique (FCMJ). Participants began in an erect standing position, moved into a semi-squat position (90° at the knee joint) before jumping, and touched the wall with extended arms when reaching the maximal height. Three trials were completed with 1-min rest between trials, with the subject using a vigorous double-arm swing as he jumped vertically. The highest FCMJ height achieved was recorded.

Strength assessment

Upper and lower limb strength. Strength was evaluated while participants tried to lift six maximal repetitions (6RM). Upper limb strength was evaluated in a sitting position with the back flat and the arms at mid-chest level. Lower limb strength was evaluated in a sitting position leg press with the seat back slightly angled. We chose 6RM as the preferred testing method because it combines 1RM and 10RM which is often used to asses muscle endurance. Initial weight for the maximal 6RM test was set according to the participants' experience during resistance training. If the participant completed the six repetitions successfully, the weights were raised by 5% for the next trial. Participants received maximum three trials to reach their best performance. Five minutes of rest was allowed between each set to allow complete recovery.

Isokinetic force. An isokinetic dynamometer (Biodex Systems II, Biodex, Shirley, NY, USA) was used to objectively measure muscle strength, based on the validity and reliability of isokinetic devices for this purpose in adults and in children (Molnar and Alexander 1974). The knee and elbow extensors and flexors (dominant and non-dominant) were tested. The dynamometer was fitted separately for the leg and arm evaluations and adjusted individually to align the axis of rotation of the specific joint with the dynamometer's pivoting axis. Following warm-up, which consisted of six contractions at progressive effort, participants were instructed to produce maximal muscular force for both flexion and extension. The subject performed five maximal voluntary contractions at each velocity, and the highest torque was recorded. Verbal encouragement and visual feedback of the torque were provided during the test.

Isokinetic strength was measured at angular velocities of 1.04 rad s^{-1} (60° s^{-1}) and 3.12 rad s^{-1} (180° s^{-1}). The range of motion for the knee was 1.57 rad (90°), starting with the knee flexed at 1.57 rad (90°) and ending in full extension. The range of motion for the elbow was 1.74 rad (100°), starting with the elbow fully extended and ending in flexion.

Anaerobic power

The Wingate Anaerobic Test (*WAnT*). Anaerobic work responses were obtained using a Monark 834 k cycle ergometer (Monark, Stockholm). Seat height was adjusted to each participant's satisfaction and toe clips with straps were used to prevent the feet from slipping off the pedals. During the warm-up, participants pedaled at a constant pace of 60 RPM for 5 min against a light load of 1 kg. This was followed with two run-up practices of 3 s, during which the actual test load was imposed to accustom the participants to the resistance. For the actual test each participant cycled as fast as possible for 30 s against constant resistance of 0.075 kg per each participant's kg body weight. Prior to the test, participants were instructed to pedal as fast as possible throughout the 30-s test period. Participants were verbally encouraged during the test to maintain their maximum pedal rate.

The WAnT measured the peak power output (PP), the mean power output (MP), and the fatigue index (FI). All power output measurements are based on 5-s averages calculated by the WAnT computer software and reported in watts/kg. PP was calculated from the highest 5-s work output. MP was calculated as the mean power output throughout the 30-s of the test. FI was calculated as the percentage of power output drop throughout the test from the maximal power output (Bar-Or 1987).

Aerobic power test

Twenty-minute Shuttle Run Test. The 20-m shuttle run test is a field test that predicts aerobic fitness (VO_2 max) and has been shown to be a reliable and valid indicator (Castro-Pinero et al. 2009) of aerobic power in various populations (St Clair et al. 1998). The test consisted of shuttle running at increasing speeds between two markers placed 20 m apart. A portable compact disk (Sony CFD-V7) dictated the pace of the test by emitting tones at appropriate intervals. The participants were required to be at one of the ends of the 20-m course at the signal. A start speed of 8.5 km/h was maintained for 1 min, and thereafter the speed was increased by 0.5 km/h every minute. The test score achieved was the number of 20-m laps completed before the subject either withdrew voluntarily from the test or failed to arrive within 3 m of the end line on two consecutive tones. VO_2 was derived by the formula $Y = 6.0X - 24.4$, where Y equals the predicted VO_2 max and X equals the maximum speed achieved.

Nutritional assessment

All participants were instructed to keep a 2-day food record and were evaluated for understanding and accuracy by administration of a 24-h recall prior to initiation of the study. Participants kept the 2-day food records (week day and weekend day) at baseline and at the end of the intervention. The food record data were reviewed by the project nutritionists and checked for omissions (for example, to verify if dressing was used on a salad listed as ingested with no dressing) and errors (for example, inappropriate portion size). This approach was validated by Crawford et al. (Crawford et al. 1994) in children and adolescents. All subjects completed the baseline and post intervention food record.

Food records were analyzed using the Israeli Ministry of Health tables. A computer algorithm based on these tables calculates the total caloric intake and the proportion of the total calorie intake derived from protein, fat and carbohydrate, and the amount of calcium and iron intake.

Habitual activity assessment

Habitual physical activity was assessed using a physical activity questionnaire (Godin and Shephard 1985). Each type of activity was scored according to an estimated MET score, and final weighted score was calculated.

Blood sampling and analysis

Early morning, fasting blood samples were collected before and after the intervention. Subjects were instructed to drink two glasses of water (350–400 ml) upon awakening to ensure proper hydration. All female participants had regular menses, and blood samples were collected during the early follicular phase of their menstrual cycle (first five days of the cycle). Blood samples were immediately centrifuged at 3,000 rpm at 4°C for 20 min. The serum was separated and stored at −80°C. All pre and post exercise specimens from each individual were analyzed in the same batch by an experienced technician who was blinded to the group (placebo vs. HMB) and to order of samples (pre vs. post training program).

Growth Hormone. GH serum concentrations were determined by ELISA with the use of the DSL-10-1900 Active kit (Diagnostic System Laboratories, Webster, Texas). Intra-assay CV was 3.3–4.5%, inter-assay CV was 5.5–12.9%, and the sensitivity was 0.03 ng/ml.

Insulin-like Growth Factor-I. IGF-I was extracted from IGF-binding proteins (IGFBPs) using the acid–ethanol extraction method. Serum IGF-I concentrations were determined by a two-site immunoradiometric assay using the DSL-5600 Active kit (Diagnostic System Laboratories, Webster, TX). IGF-I intra-assay CV was 1.5–3.4% and the inter-assay CV was 3.7–8.2%. Assay sensitivity was 0.8 ng/ml.

IGFBP-3. IGFBP-3 serum concentrations were determined by ELISA with the use of the DSL 10-6600 Active

kit (Diagnostic System Laboratories). Intra-assay CV was 7.3–9.6%, inter-assay CV was 8.2–11.4%, and the sensitivity was 0.04 ng/ml.

Lactate. Serum lactate was measured spectrophotometrically (YSI 1500, Yellow Springs, OH). Intra-assay CV was 2.8%, inter-assay CV was 3.5%, and the sensitivity was 0.2 mMl/L.

Cortisol. Serum cortisol levels were determined by a commercial RIA (Diagnostic Products Corporation, Los Angeles, CA). The intra- and inter-assay CV for this assay were 3.2% and 6.8%, respectively.

Testosterone. Testosterone serum concentrations were determined by ELISA with the use of the DSL commercial kit (Diagnostic System Laboratories, Webster, Texas). Intra-assay CV was 4.8–5.3%, inter-assay CV was 2.8–4.9%, and the sensitivity was 0.04 ng/ml.

Inflammatory mediators. Inflammatory mediators were analyzed by ELISA, using the R&D system Quantikine High-Sensitivity commercial kits (R&D system; Minneapolis, MN).

Interleukin-6 (*IL-6*). Intra-assay CV was 3.8–11.1%, inter-assay CV was 7.1–29.5%, and the sensitivity was 0.009 pg/ml.

Interleukin-1 receptor antagonist (*IL-1ra*). Intra-assay CV was 3.1–6.2%, inter-assay CV was 4.4–6.7%, and the sensitivity was 22 pg/ml.

Statistical analyses

Two-sample *t* test was used to compare baseline anthropometric, fitness, and hormonal levels between the HMB and control group participants. Repeated measures ANCOVA was used to assess the effect of HMB administration on body composition, nutrition, fitness, hormonal and inflammatory mediators with time serving as the within group factor and HMB as the between-group factor. Data are presented as mean ± SD. Significance was set at an alpha level of $p \leq 0.05$.

Results

Anthropometric characteristics of the participants are summarized in Table 1. No baseline differences were found between the HMB and placebo group. The effect of HMB compared with placebo supplementation on anthropometric measures of the study participants are shown in Table 2. HMB supplementation resulted in a significantly greater increase of fat-free mass and a significantly greater decrease in percent body fat. There were no significant differences in body weight and BMI changes between groups.

The effect of HMB compared with placebo supplementation on power and strength measurements in the study participants are shown in Tables 3 and 4. Since the intervention led to a significant change in body composition, the results are expressed relative to body mass and fat-free mass. There were no significant baseline differences between the groups in vertical jump height, bench press, and leg press strength. HMB supplementation resulted in a significantly greater strength gain in the 6RM bench press and leg press. HMB supplementation had no effect on vertical jump height.

Isokinetic force of the lower legs was measured at fast (180°/sec) and slow (60°/sec) angle speeds. There were no significant baseline differences between the groups in any of the measurements in both the dominant and non-dominant sides at fast (180°/sec) and slow (60°/sec) angle

Table 1 Baseline anthropometrics of study participants

Variable	Control ($n = 14$)	HMB ($n = 14$)	*p*
Gender (M/F)	7/7	7/7	
Age (yr)	16.2 ± 1.3	16.1 ± 1.3	0.67
Height (cm)	181.9 ± 9.0	185.0 ± 9.6	0.38
Weight (kg)	69.9 ± 11.3	72.3 ± 10.3	0.61
BMI (kg/m^2)	21.1 ± 2.5	21.0 ± 2.1	0.92
BMI percentage (% ile)	52.9 ± 28.2	54.6 ± 20.6	0.85
Fat percentage—Caliper (%)	19.2 ± 6.9	18.1 ± 6.2	0.64
FFM (kg)	56.4 ± 10.2	59.3 ± 11.3	0.48
Fat percentage—BIA (%)	20.4 ± 8.2	18.7 ± 7.3	0.55
Fat percentage—BOD–POD (%)	17.8 ± 9.2	17.4 ± 5.8	0.89
Pubertal stage (tanner)	4.1 ± 0.5	4.4 ± 0.6	0.25

*Tanner	I	II	III	IV	V	I	II	III	IV	V
n of subjects			1	10	3			1	7	6

M male, *F* female, *FFM* fat-free mass

* Tanner: *1* pre, *2* early, *3* mid, *4* late, *5* pubertal

Table 2 The effect of HMB supplementation on anthropometric measures

Variable	Control		HMB		*p*
	Pre	Post	Pre	Post	
Weight (kg)	69.9 ± 11.3	70.5 ± 11.0	72.3 ± 10.3	73.8 ± 10.1	0.16
BMI (kg/m^2)	21.1 ± 2.5	21.4 ± 2.4	21.0 ± 2.1	21.5 ± 2.1	0.32
Fat percent—Caliper (%)	19.2 ± 6.9	19.9 ± 7.6	18.1 ± 6.2	16.9 ± 6.4	0.04*
FFM (kg)	56.4 ± 10.2	56.3 ± 8.6	59.3 ± 11.3	61.6 ± 11.3	0.00*

* $p < 0.05$ for pre versus post between-group difference

Table 3 The effect of HMB supplementation on power and strength measurements

Variable	Control		HMB		*p*
	Pre	Post	Pre	Post	
Vertical jump (m)	2.95 ± 0.24	2.96 ± 0.25	2.97 ± 0.23	3.03 ± 0.22	0.34
Bench press (kg/kg BW)	1.11 ± 0.41	1.19 ± 0.39	1.13 ± 0.39	1.34 ± 0.40	0.00*
Bench press (kg/FFM)	1.36 ± 0.41	1.48 ± 0.40	1.36 ± 0.39	1.59 ± 0.39	0.01*
Leg press (kg/kg BW)	2.57 ± 0.73	2.57 ± 0.67	2.15 ± 0.72	2.81 ± 0.60	0.00*
Leg press (kg/FFM)	2.88 ± 0.82	3.22 ± 0.76	2.61 ± 0.78	3.37 ± 0.56	0.00*

* $p < 0.05$ for pre versus post between-group differences

Table 4 The effect of HMB supplementation on knee flexion isokinetic force

Knee flexion	Control		HMB		*p*
	Pre	Post	Pre	Post	
Non dominant					
N·M/kg BW: @60°/sec	1.45 ± 0.31	1.55 ± 0.23	1.57 ± 0.32	1.77 ± 0.33	0.04*
N·M/FFM: @60°/sec	1.85 ± 0.32	1.99 ± 0.30	1.84 ± 0.25	2.08 ± 0.22	NS
N·M/kg BW: @180°/sec	1.13 ± 0.20	1.25 ± 0.22	1.19 ± 0.21	1.4 ± 0.20	0.10
N·M/FFM: @180°/sec	1.39 ± 0.16	1.62 ± 0.27	1.44 ± 0.22	1.68 ± 0.20	NS
Dominant					
N·M/kg BW: @60°/sec	1.43 ± 0.33	1.54 ± 0.24	1.54 ± 0.22	1.78 ± 0.35	0.06
N·M/FFM: @60°/sec	1.76 ± 0.44	1.9 ± 0.23	1.87 ± 0.25	2.14 ± 0.32	0.04*
N·M/kg BW: @180°/sec	1.21 ± 0.20	1.24 ± 0.21	1.28 ± 0.22	1.48 ± 0.24	0.00*
N·M/FFM: @180°/sec	1.50 ± 0.22	1.55 ± 0.22	1.55 ± 0.20	1.78 ± 0.22	0.01*

* $p < 0.05$ for pre versus post between-group differences

speeds. In the dominant leg, HMB supplementation resulted in a significant greater knee flexion strength relative to body mass and free fat mass at both fast (180°/sec) and slow (60°/sec) angle speeds. In the non-dominant leg, HMB supplementation resulted in significantly greater knee flexion strength relative to body mass and fat-free mass only in the slow angle speed. HMB supplementation had no effect on knee extension in both the dominant and the non-dominant leg. HMB supplementation had no significant effect on the dominant and non-dominant arm elbow flexion and extension at both slow and fast angle speeds.

The effect of HMB supplementation on aerobic and anaerobic capacity in the study participants is shown in Table 5. There were no significant baseline differences between the groups in any of the measurements. HMB supplementation resulted in a significant greater increase in peak and mean anaerobic power relative to body mass and fat-free mass, but had no effect on FI. HMB supplementation had no significant effect on the predicted maximal oxygen consumption of the study participants.

There were no significant differences between the groups in caloric, macronutrient, calcium, and iron intake at baseline or following supplementation. Habitual physical activity was negligible during the intervention in both groups and, therefore, not presented.

The effect of HMB supplementation on anabolic and catabolic hormones, pro and anti-inflammatory mediators is shown in Table 6. There were no significant baseline differences between the groups in any of the measurements. There were no significant differences in the anabolic/catabolic hormonal changes and pro/anti inflammatory mediator changes between the groups.

Discussion

Nutritional supplements are commonly used by athletes to enhance athletic performance. While it is believed that these substances increase the training-associated anabolic adaptations and reduce their catabolic effects, increase

Table 5 The effect of HMB supplementation on aerobic and anaerobic capacity

Variable (watts)	Control		HMB		*p*
	Pre	Post	Pre	Post	
Peak power/kg BW	12.5 ± 1.1	12.9 ± 1.2	12.6 ± 1.7	14.3 ± 1.5	0.00*
Peak power/FFM	15.5 ± 1.6	16.2 ± 1.2	15.4 ± 1.6	17.2 ± 1.2	0.00*
Mean power/kg BW	8.6 ± 1.1	8.7 ± 0.9	8.8 ± 0.1	9.7 ± 1.0	0.00*
Mean power/FFM	10.6 ± 0.9	10.8 ± 1.1	10.7 ± 0.8	11.8 ± 1.0	0.01*
Fatigue index	57.8 ± 5.3	54.2 ± 10.4	60.3 ± 13.4	54.6 ± 9.4	0.8
VO_2max (mL kg^{-1} min^{-1})	42.0 ± 6.6	43.2 ± 6.5	42.0 ± 5.4	44.7 ± 4.6	0.25

*$p < 0.05$ for pre versus post between-group differences

Table 6 The effect of HMB supplementation on anabolic and catabolic hormones and pro and anti-inflammatory mediators

Variable	Control		HMB		*p*
	Pre	Post	Pre	Post	
GH (ng/ml)	1.2 ± 2.0	0.7 ± 1.8	0.7 ± 1.8	1.0 ± 1.5	0.92
IGF-I (ng/ml)	497.9 ± 117.7	482.4 ± 83.7	527.0 ± 99.9	509.1 ± 82.7	0.90
IGFBP-3 (ng/ml)	5,839 ± 710	5,393 ± 1,422	6,287 ± 1,022	5,562 ± 827	0.89
Testosterone (ng/ml)	4.23 ± 2.74	4.62 ± 2.80	3.45 ±1.88	4.10 ± 2.37	0.59
Cortisol (mcg/L)	23.07 ± 9.98	24.90 ± 5.80	25.76 ± 8.19	28.50 ± 7.69	0.38
IL-6 (pg/ml)	1.18 ± 0.56	1.51 ± 2.14	1.18 ± 0.49	1.03 ± 0.21	0.75
IL1ra (pg/ml)	356.1 ± 118.7	324.3 ± 65.3	300.7 ± 81.1	331.4 ± 92.8	0.82

muscle mass, decrease fatigue, and improve aggression, very little scientific evidence supports this notion. In the present study we examined the effect of a prospective, randomized, double-blind, placebo-controlled administration of HMB on body composition, fitness characteristics, anabolic and catabolic hormones, and inflammatory mediators in elite, national team level, male and female volleyball players during the initial phase (7 weeks) of the training season. HMB administration was associated with a significant greater increase in muscle mass, a significant greater increase in muscle strength determined by bench and leg press, and a significant greater isokinetic force of the knee flexors at both slow and fast speed angle speeds. HMB had no significant effect on vertical jump and on isokinetic force of the knee extensors and elbow flexor and extensors. HMB administration led to a significant greater improvement in anaerobic peak and mean power during the WAnT, but had no effect on the FI. HMB supplementation had no effect on predicted aerobic capacity. Finally, the beneficial effects of HMB supplementation were not accompanied by basal changes in anabolic hormones (GH–IGF–I axis and testosterone), catabolic hormones (cortisol), and inflammatory mediators (interleukin-6).

β-Hydroxy-β-methylbutyric acid supplementation was associated with a greater increase in muscle mass, muscle strength, and isokinetic force. Since the intervention led to a significant change in muscle mass, the effects on muscle strength are expressed relative to fat-free mass. HMB supplementation resulted in a significant greater increase in muscle strength determined by bench and leg press and a significant greater isokinetic force of the knee flexors at both slow and fast angle speeds. HMB had no significant effect on isokinetic force of the knee extensors and elbow flexor, and extensors. This suggests that beneficial effects of HMB use were more likely to occur in strength modalities that were frequently practiced during the intervention period, and probably in selected muscle sites (i.e. lower compared with upper extremities, knee flexors compared with knee extensors). HMB had no significant effect on vertical jump, which is very important for volleyball players. The cause for that is not clearly understood; however, it might be related to the fact that vertical jump is significantly affected by both muscle strength and the technical skills of the athlete. This is particularly relevant since the initial training period of the season is characterized mainly by heavy training load and very little technical practice. Thus, we can only speculate that HMB supplementation during training that is more technical and less intense may possibly lead to significant improvements in vertical jump as well.

β-Hydroxy-β-methylbutyric acid supplementation was associated with a significantly greater increase in anaerobic performance indices as indicated by the peak and mean power in the WaNT. These beneficial effects were not accompanied by significant improvement in FI. In contrast to our hypothesis, HMB supplementation was not associated with significant effect on aerobic capacity. Improvement in peak anaerobic power was probably the result of the significant improvement in muscle strength, which may also lead to the improvement in the mean anaerobic power.

The beneficial effect on anaerobic, and not aerobic capacity, is also consistent with the notion that HMB supplementation was more effective in fitness characteristics that were practiced during the intervention period since only 15% of training time was aerobic in nature.

Previous studies suggested that the beneficial effects of HMB supplementation on performance result from anabolic adaptations and reduced catabolic effects. Therefore, we hypothesized that the beneficial effects of HMB supplementation on muscle mass, strength, and anaerobic capacity will be accompanied by an increase in circulating levels of the GH–IGF–I axis hormones and testosterone, and by a decrease of the catabolic hormone cortisol and inflammatory mediators like IL-6. In contrast to our hypothesis, there was no significant difference in any of these measures between the HMB and placebo-controlled groups. Unlike our findings, Kraemer et al. (Kraemer et al. 2009) demonstrated that the HMB beneficial changes in lean body mass, muscle strength, and power were accompanied by increases in resting and exercise-induced testosterone and resting growth hormone concentrations. In addition, they found reduced preexercise cortisol concentrations. These discrepancies may be attributed to several factors such as younger age and maturity in the present study (adolescents vs. young adults), shorter duration of training (7 vs. 12 weeks) and different type of exercise training (Mixed anaerobic and endurance vs. heavy resistance), or the different hormonal assays used. We previously demonstrated in children and adolescents that the initial response to 4–16 weeks of endurance-type exercise training was associated with a decrease in circulating anabolic hormones. These adjustments occurred despite training-induced increases in muscle mass and improvement in fitness (Eliakim et al. 2002; Nemet et al. 2004b), suggesting different *local* tissue, and *systemic* responses to training. These changes occurred even without evidence of negative energy balance or weight loss (Nemet et al. 2004a) and were associated with increases in inflammatory mediators (Eliakim et al. 2005). These observations led to the speculation that the sudden imposition of endurance training program first leads to hormonal adaptations suggestive of a catabolic state, but at some point, an anabolic rebound occurs. Consistent with this hypothesis, longer periods of training (Koziris et al. 1999) and tapering down the training intensity (Eliakim et al. 2002; Nemet et al. 2004b) were indeed associated with increases in circulating anabolic hormones. It is possible that the length of the training intervention in the present study (only 7 weeks) without tapering of the training intensity prevented the detection of circulating hormonal anabolic response or anti-inflammatory adaptation. It is also possible that basal systemic circulating measurements do not reflect daily hormonal signals and local tissue (muscle) anabolic/catabolic or inflammatory responses to HMB supplementation. Local hormonal effects may lead to the changes in muscle mass and strength that were found in our study.

The purpose of the present study was to determine the effect of HMB supplementation in "real-life" conditions of young elite athletes. Therefore, we did not interfere with the original training program of the volleyball players. We were able to control training and sleep regimens since all the study participants attended the Israeli National Academy for Gifted Athletes and lived in dormitories during the intervention, and more importantly were exposed to similar nutritional conditions (all meals were served in the Wingate Institute dining room). As a consequence, there were no significant differences in caloric and relative macronutrient intake, calcium, and iron intake between the HMB and placebo group at the beginning and at the end of the intervention period. Moreover, since training was so demanding and intense during the intervention (18–22 h/week), participants from both the HMB and the control groups were not practically involved in any other physical activity besides actual training.

Fortunately, the dropout rate during the study was also negligible (only one participant from the HMB group left the academy due to reasons unrelated to the study). All these factors lead us to believe that HMB supplementation was indeed the main cause for the significant beneficial effects on muscle mass, muscle strength, and anaerobic capabilities in this group of elite volleyball players during the initial phase of the training season. Possible effects of longer HMB administration, at different stages of the training season, should be further studied.

In summary, we demonstrated that HMB supplementation in elite, male and female adolescent volleyball players was associated with a greater increase in muscle mass, muscle strength, and anaerobic properties with no effect on vertical jump and on aerobic capacity during the initial phases of the training season. These changes were not accompanied by basal circulating hormonal and inflammatory mediators' change. Further studies are needed to determine the effect of HMB supplementation during longer and/or other training periods (e.g. specific training, competition period, etc.) and in different sports types in order to optimize the beneficial effects of HMB supplementation in adolescent athletes.

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