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The Effect of HMB Supplementation on Cardiovascular Risk Factors after Four Weeks of Resistance Training in Amateur Athletes

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ABSTRACT

Background: Nutritional supplements have been widely used in order to enhance athletic performance and improve health.

Objectives: This study aimed to investigate the effect of Beta-Hydroxy Beta-Methylbutyrate (HMB) supplementation on cardiovascular risk factors after 4 weeks of resistance training in athletes.

Patients and Methods: In this double-blind study, 20 male athletes were selected through simple random sampling, were assigned to supplement and control groups, and participated in resistance training 3 sessions a week for 4 weeks. The supplement group consumed 3 g HMB supplement per day and the control group consumed the placebo (rice flour) in this period. Before and after the test period, blood pressure was measured and fasting blood samples were obtained to determine blood lipids and hematological parameters. After all, paired and unpaired t-test were used to examine within and between group differences, respectively. $P \leq 0.05$ was considered as statistically significant.

Results: After the training period, no significant differences were found between HMB and placebo groups regarding blood lipids, blood pressure, and hematological parameters.

Conclusions: The results of the present study indicated that HMB supplementation was safe and did not result in any adverse effects. Thus, HMB can be used safely by human as an ergogenic aid for exercise training.

►*Implication for health policy/practice/research/medical education:*
HMB supplementation (3 g/d) after 4 weeks of resistance training in amateur athletes caused no change in few cardiovascular risk factors.

1. Background

Nutritional supplements have been widely used in order to enhance athletic performance and improve health (1). In this regard, supplementation with amino acids and proteins has received special attention from the athletes interested in optimizing the adaptations to physical exercise training. In the recent years, there has been an increasing interest in the effects of beta-hydroxy beta- methylbutyrate (HMB) supplementation on skeletal muscles due to its anti-catabolic effects (2-5). HMB is a bioactive metabolite formed from breakdown of the essential branched amino acid, leucine. Leucine and its metabolite, keto-isocaproate (KIC), appear to inhibit protein degradation and this anti-proteolytic effect is believed to be mediated by HMB (6, 7). It has been demonstrated that HMB supplementation, in combination with resistance training program, resulted in increased muscular strength and lean body mass and tended to decrease fat mass (8, 9). Also, it has been suggested that HMB acted as an anti-catabolic agent in reduction of muscle protein breakdown and exercise–induced injury and enhanced recovery from exercise (10). The theory behind HMB supplementation is that HMB provides carbon for cholesterol Synthesis via conversion to b-hydroxy-b-methylglutaryl CoA (HMG-CoA) (11-13). HMG-CoA can be a rate limiting substrate when cholesterol

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synthesis is in great demand, such as during periods of rapid cell growth or membrane repair (14). Thus, HMB may provide the necessary amount of HMG-CoA for cholesterol synthesis and the subsequent membrane production during the periods of high muscular stress. In addition, HMB supplementation has been shown to decrease Low-Density Lipoprotein (LDL) levels in humans (9, 14, 15). However, this finding has not been confirmed by other studies (16-18). On the other hand, it has been reported that HMB may lower Blood Pressure (BP) (18). These effects may partly be attributed to the inclusion of calcium (13). Also, previous studies reported decrease in hematocrit after HMB supplementation (18).

Overall, the data about the influence of HMB supplementation, particularly with resistance training, on cardiovascular risk factors, such as blood lipids, BP, and hematological parameters, are still scarce and inconsistent. Yet, knowing about the effects of HMB supplementation on health factors can be useful for all users and may affect use of this supplement.

2. Objectives

The present study aims to assess the effect of HMB supplementation on cardiovascular risk factors (blood lipids, BP, and hematological parameters) after 4 weeks of resistance training in athletes.

3. Patients and Methods

3.1. Subjects

This double-blind study was conducted on 20 male athletes who were selected through simple random sampling according to Gehan's model. None of the participants had a medical history of digestive and hormonal disorders, hypertension, liver dysfunction, cardiovascular disease, and diabetes. Additionally, they had no regular resistance training in the past 6 months. The participants were provided with complete information about the possible risks and discomforts, and written informed consents for taking part in the study were obtained from all of them. The participants' characteristics have been presented in Table 1.

3.2. Procedures

All the study procedures were in accordance with the Declaration of Helsinki and the study was approved by the faculty Ethics Committee in the University of Guilan. Before initiating the training, all the participants were asked to undergo a clinical evaluation and measurement of weight, height, Body Mass Index (BMI), and body fat. Then, all of them took part in a familiarization session to get familiar with the study procedures and participated in one Repetition Maximum (1RM) strength test. Afterwards, the participants were randomly assigned to supplement and control groups and took part in 4 weeks of resistance training. Blood samples were collected to measure the blood parameters before and after the training period.

All the measurements were performed at the same time of the day for all the participants. Besides, none of the participants received any additional medications or food supplements other than HMB or the placebo. They were also asked to maintain their usual dietary and lifestyle habits and not to perform strenuous physical activities in the study period.

3.3. Anthropometric Measurements

Anthropometric measurements were done in light clothes before and after the training period. Height and weight were measured by an automatic height–weight scale to the nearest 0.1 cm and 0.1 kg, respectively. Besides, BMI was calculated by dividing weight (kg) by the square of the height (m2). To estimate the amount of subcutaneous fat in the body, skinfold thickness was measured (Lafayette Caliper, model 01128, USA) at three sites (chest, abdomen, and quadriceps) in the right side of the body. Each measurement was performed in triplicate and the average was considered for analysis. All the measurements were made in standing position and body fat percent was estimated in accordance with the equation proposed by Jackson and Pollack (19).

3.4. Strength Testing

1RM was assessed prior to and at the end of the second week of training in squat, knee extension, knee flexion, leg press, bench press, lat pull-down, shoulder press, cable biceps curl, and triceps push down exercises. Briefly, the participants performed a warm-up which consisted of slow running, static stretching, and dynamic exercises. Two to three trials separated by 2 - 3 minutes of rest were used to determine the individuals' 1RM for each resistance exercise. In these sessions, a weight that could be lifted maximally to fatigue after 2 - 10 repetitions was used to calculate 1RM according to the formula proposed by Brzycki (14).

3.5. HMB Supplementation and Exercise Protocol

In this double-blind study, the participants were selected through simple random sampling, assigned to supplement or control groups, and trained together for 4 weeks. The supplement group consumed 3 g HMB supplements (GNC Pro Performance®, USA) 3 times a day (a total of 12 capsules), while the control group consumed the placebo (rice flour). It should be noted that both HMB and placebo capsules were identical in size and appearance. Each

Table 1. Characteristics of the Participants (Mean ± SD)

Variables	Control (N = 10)	HMB (N = 10)
Age (y)	22.7 ± 2.9	22.4 ± 3.4
Weight (kg)	73.3 ± 8.1	74.8 ± 7.2
Height (cm)	175.7 ± 5.6	175.9 ± 5.1
BMI (kg/m2)	23.6 ± 1.5	24.1 ± 1.9
Body Fat (%)	15.7 ± 2.3	14.9 ± 3.7

Abbreviations: BMI, body mass index

HMB capsule contained 250 mg Calcium Hydroxymethyl Butyrate Monohydrate (Ca-HMB) and 200 mg Mono-Potassium phosphate (KH2PO4). The previous studies performed on adults suggested that this dose resulted in the greatest effects on muscle mass and muscle strength (11). Also, current evidence has recommended that 1 g of HMB should be consumed 3 times a day (13). Because these suggestions are usually followed by humans, we also decided to apply them in the present study.

Exercise training involved resistance training for 3 sessions per week. The participants performed 2 sets of 9 exercises (squat, knee extension, knee flexion, leg press, bench press, lat pull- down, shoulder press, cable biceps curl, and triceps push down) per session, carrying out 10 repetitions for each set with 80% 1RM in the first 2 weeks and 8 repetitions for each set with 85% 1RM in the last 2 weeks. In addition, 2- and 3- minute rest intervals were considered between the sets and exercises, respectively.

3.6. Blood Sampling and Analysis

Blood samples were taken 1 day before and 3 days after the test period for determining the blood parameters. In doing so, 10 cc blood samples were taken in seated position from the antecubital vein after an overnight fasting. The samples were centrifuged and the serum was frozen and stored at -80°C until analysis.

Lipid profile was considered to examine the levels of total cholesterol, High-Density Lipoproteins (HDL), LDL, and triglycerides. Serum total cholesterol, LDL, HDL, and triglycerides levels were determined through chromatographic enzymatic method using a semiautomatic analyzer (Bayer, Model RA-50, INDIA). Also, the quantities of Red Blood Cells (RBC), Hemoglobin (Hb), Hematocrit (Hct), Mean Corpuscular Volume (MCV), and Mean Corpuscular Hemoglobin (MCH) were determined using an auto counter machine (SYSMEX-Cellcounter, JAPAN).

3.7. Blood Pressure Measurements

Before blood sampling and after a 5-min rest in the seated position, BP was measured for three times using a standard mercury sphygmomanometer (ALPK2, Japan) by the same experienced observer, taking the first and the fifth phases of Korotkoff sounds as Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP), respectively. Then, the mean of the three measurements was recorded as the subjects' BP. In case the pretest values for SBP and DBP were greater than 139 and 89 mmHg, respectively, the participants were excluded from the study.

3.8. Statistical Analysis

All the data were analyzed using the SPSS statistical software (V. 16.0) and expressed as mean ± SD and. Paired and unpaired t-test were used to assess within and between groups differences, respectively. Besides, $P \leq 0.05$ was considered as statistically significant.

4. Results

At baseline, no significant differences were found between the HMB and placebo groups regarding the participants' anthropometric characteristics (Table 1). Pre- and post-training values of blood lipids, BP, and hematological parameters of HMB and control groups have been presented in Table 2. Accordingly, no significant differences were observed between the two groups regarding the baseline values of blood lipids, BP, and hematological parameters. After the training period, a significant decrease was observed in both groups concerning total cholesterol (P = 0.002, P = 0.008), LDL (P = 0.002, P = 0.002), and triglycerides (P = 0.004, P = 0.004). However, HDL level significantly increased in the HMB group (P = 0.024).

The results indicated no significant change in SBP in the study groups. Nevertheless, DBP significantly decreased (P = 0.014) in the HMB group, but remained unchanged in the control group. Regarding the hematological parameters, no significant changes were observed in the two groups with respect to RBC, Hb, Hct, MCV, and MCH. Also, no significant differences were found between the two groups regarding the changes in blood lipids, BP, and hematological parameters.

5. Discussion

The present study aimed to examine the effect of HMB

Table 2. Blood Lipids, Blood Pressure, and Hematological Parameters before and after the Training

Variables	Control (N = 10)			HMB (N = 10)		
	Pre	Post	Delta	Pre	Post	Delta
Serum lipids Chol (mg/dL)	168.8 ± 20.5	160.7 ± 16.8 *	-8.1 ± 7.6	164.3 ± 23.1	151.7 ± 21.6 *	-12.6 ± 9.1
HDL (mg/dL)	45.1 ± 9.1	46.9 ± 10.0	1.8 ± 2.8	44.7 ± 13.7	47.1 ± 15.0 *	2.40 ± 2.7
LDL (mg/dL)	146.1 ± 8.3	138.8 ± 8.6 *	-7.30 ± 5.3	145.90 ± 14.6	136.40 ± 11.80 *	-9.50 ± 7.1
TG (mg/dL)	132.7 ± 31.9	126.0 ± 29.9 *	-6.70 ± 5.5	120.8 ± 29.1	111.2 ± 28.7 *	-9.6 ± 7.8
Blood Pressure SBP (mm-Hg)	123.8 ± 4.1	121.4 ± 3.6	-2.4 ± 3.9	123.1 ± 4.4	121.5 ± 3.8	-1.6 ± 4.3
DBP (mm-Hg)	81.8 ± 4.6	80.4 ± 2.5	-1.4 ± 3.4	83.6 ± 3.5	80.3 ± 2.5 *	-3.3 ± 3.4
Hematology RBC (milion/µL)	5.3 ± 0.3	5.3 ± 0.4	-0.04 ± 0.2	5.3 ± 0.3	5.4 ± 0.3	0.04 ± 0.2
Hb (g/dL)	15.6 ± 0.8	15.9 ± 0.6	0.3 ± 0.8	15.9 ± 0.7	15.5 ± 0.7	-0.4 ± 0.8
Hct (%)	46.7 ± 2.1	47.0 ± 1.1	0.3 ± 2.3	47.1 ± 1.8	46.4 ± 1.7	-0.6 ± 1.7
MCV (fl)	87.7 ± 6.9	88.9 ± 5.1	1.2 ± 4.7	88.5 ± 5.1	86.5 ± 6.7	-1.9 ± 4.1
MCH (pg)	29.4 ± 2.7	30.1 ± 2.2	0.7 ± 1.8	30.3 ± 2.4	30.1 ± 4.3	-0.2 ± 3.6

Abbreviations: Delta, post-pre values; Chol, total cholesterol; TG, triglycerides

Values are expressed as mean ± SD; * Significant difference compared to pre-training values ($P \leq 0.05$).

supplementation on cardiovascular risk factors (blood lipids, BP, and hematological parameters) after 4 weeks of resistance training in athletes. The study results showed that HMB supplementation compared to the placebo did not result in any significant changes in blood lipids, BP, and hematological parameters after 4 weeks of resistance training.

It has been suggested that HMB supplementation alters cholesterol synthesis via conversion to HMG-CoA (11-13). It has also been reported that b-hydroxy-b-methylglutaric acid inhibited liver cholesterol synthesis (20). Thus, the changes in cholesterol synthesis could elicit an alteration in blood cholesterol levels. Some studies have demonstrated that HMB supplementation lowered LDL levels in humans (9, 14, 15). For instance, Coelho and Carvalho reported that HMB supplementation resulted in a significant decrease in LDL levels in the individuals with hypercholesterolemia (15). Our findings revealed beneficial changes in blood lipids in both groups, but these changes were greater in the HMB group. However, no significant differences were found between the two groups concerning blood lipids. Therefore, the beneficial changes in lipid profile can be attributed to taking part in resistance training (21, 22). These findings were consistent with those of the previous studies, indicating that HMB supplementation had no significant effects on blood lipids (16-18). In a study conducted by Gallagher et al. (11), different doses of HMB (0, 3, and 6 g) caused no significant changes in lipid profiles during 8 weeks of resistance training in untrained men. Moreover, Nissen et al. (18) analyzed the safety data from nine studies in which humans received 3 g of HMB per day for 3 to 8 weeks. The studies included both male and female, young and elderly, and exercising and non-exercising participants. The results indicated that HMB supplementation led to a net decrease in total cholesterol (5.8%) and a decrease in LDL level (7.3%). However, HMB did not significantly change LDL levels in the subjects with normal cholesterol levels (< 200 mg/dL), suggesting that HMB may be more effective in lowering LDL levels in case of high cholesterol levels.

The differences among the studies conducted on the issue might be attributed to their experimental design (e.g., dietary controls, quantity and intensity of training, subjects' health status, and duration of experiments), methods (e.g., supplement formulations and blood variables assessment methods), and/or statistical analysis procedures.

In the present study, HMB supplementation had no additional effects apart from resistance training on SBP and DBP after 4 weeks of resistance training. To the best of our knowledge, the study by Nissen et al. (14) is the only one performed on BP after HMB supplementation. These researchers verified that HMB supplementation for 3 - 8 weeks resulted in a significant decrease in SBP (4.4 mmHg) but no change in DBP. The discrepancy in the results might be due to more calcium intake (400 mg/d) with Ca-HMB supplement in the study by Nissen et al. Test duration, employing elderly subjects, and subjects with SBP > 130 mm-Hg by Nissen et al. could have also affected the results (23).

Considering hematology, the results of our study showed that HMB supplementation had no significant effects on RBC, Hb, Hct, MCV, and MCH. A previous research also revealed that receiving HMB for 3 - 8 weeks caused no significant changes in RBC, Hb, MCV, and MCH, but significantly decreased Hct (18). Differences in duration of supplementation may account for this difference. Yet, the exact reasons of this difference are not well known.

The results of the present study about the effects of HMB supplementation were consistent with those of the previous studies (5, 18, 24), indicating that HMB supplementation had no any adverse effects on the above-mentioned cardiovascular risk factors.

In the current study, all the examined variables were within the normal limits and no differences were observed between the HMB and placebo groups regarding any of the variables. Thus, HMB supplementation (3 g/d) caused no changes in few cardiovascular risk factors after 4 weeks of resistance training in athletes. Yet, further studies are necessary to be conducted on the issue.

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Authors' Contribution

Hamid Arazi: Study design, statistical analysis, interpretation, and writing the manuscript; Hadi Rohani: Data collection and writing the manuscript; Ahmad Ghiasi: Data collection and writing the manuscript; Maryam Davaran: Data collection and support

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