

Does the use of dietary supplements enhance athletes' sport performances? A systematic review and a meta-analysis.

LAURENTI PATRIZIA⁽¹⁾, DE WAURE CHIARA⁽¹⁾, DE MEO CONCETTA^{(1)*}, TERRACCIANO ELISA⁽¹⁾,
DI NARDO FRANCESCO⁽¹⁾, RICCIARDI WALTER⁽¹⁾

ABSTRACT

BACKGROUND: The consumption of dietary supplements has increased in recent years. Despite their widespread use, there is confusion about effects on sport performances. The aim of this study was to investigate association between use of supplements and enhance of athletes' sports performance.

METHODS: A review and a meta-analysis of studies conducted on Dietary Supplements and Sports between 2003 and 2013 were performed. Enhancement on sport performances was considered as outcome. The following aspects related to enhancement were considered: ergogenic effect (EE), time to exhaustion (TTE), muscular endurance (ME), post-exercise recovery (PER) and body mass (BM). With respect to meta-analysis, data on level of post Exercise Glucose (GpE [mg/dL]) and level of post exercise Lactate (LpE [mmol/L]) were considered as indicators of TTE, PER and EE. Similarly, Change in Body Mass (CBM) [kg] was used as indicator of BM.

RESULTS: The most investigated dietary supplements were: Creatine, Carbohydrates, Beta-alanine, Proteins. The qualitative analysis evaluating the effect of supplements on sports listed by the International Olympic Committee has achieved interesting results: supplements didn't show statistically significant effects when compared to placebo in more than 48% of papers.

For the quantitative analysis, 15 studies were considered. The meta-analysis showed that there was no significant effect of Beta-alanine, Creatine and Carbohydrates on LpE and GpE. Furthermore, a non-significant increase in BM was observed in athletes undergoing Creatine compared to placebo.

CONCLUSION: Considering the increasing attention to this topic, it would be interesting to investigate the existing awareness about effectiveness and possible risks of supplements.

Key words: Creatine, Carbohydrate, Beta-alanine, Athletes, Sport performances.

(1) Institute of Public Health, Section of Hygiene, Università Cattolica del Sacro Cuore, Rome 00168, Italy.

CORRESPONDING AUTHOR: Concetta De Meo, Institute of Public Health, Section of Hygiene, Università Cattolica del Sacro Cuore, Rome 00168, Italy. Phone number: +390630154396, fax: +390635001522
Email: concetta.demeo87@gmail.com

DOI: 10.2427/11593

Accepted on December 11, 2015

INTRODUCTION

A dietary supplement is an administered orally product “the purpose of which is to supplement the normal diet and to provide concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination” [1]. The top dietary supplements sold in 2013 were: vitamins (32.2%), botanical and herbs (17.1%) and sports nutrition products (12.7%) [2].

The use of dietary supplements is growing in all developed countries, including Europe, where these products are currently regulated by Directive 2002/46/EC. Also in Europe, the main supplements marketed were those based on vitamins and minerals (50%), followed by supplements containing “other substances” (43%). The European State with the broader market of supplements was Italy, followed by Germany, United Kingdom and France [3].

Apart from the wide consumption, consumers’ conceptions about efficacy, safety and real needs are not clear. In fact, the most common reasons for using dietary supplements are improving or maintaining health and wellness [4].

Fifty percent of the American adult population is a regular supplement user. However, these data could be underestimated because when occasional and seasonal users are taken into consideration the overall prevalence is closer to two thirds of adult population [4]. In the population of athletes, even though there is no complete awareness about efficacy, safety and mechanisms of action, their use is widespread and growing as ergogenic aid to improve athletic performance.

The population of athletes has commonalities and divergences compared to regular users: athletes are primarily young men while regular users are mainly women. Then, regular users typically take their products every day and for long time [4]; on the contrary, athletes tend to use supplements during the season of competitions and there are poor evidence about an intake for consecutive years. Moreover, combination of different products is very common in athletes and uncommon in regular users who usually take only one [4]. Therefore, while regular users take mainly vitamins and/or minerals for example to treat clinical deficiencies of nutrients, athletes use primarily supplements which could enhance their performance such as Amino acids, Creatine and Carbohydrates.

Regarding common aspects, both athletes and non-athletes regular users, compared to non-users, are more likely to adopt positive behaviours such as exercising regularly, avoiding smoking and paying attention to Body Mass Index [4].

The scientific interest on dietary supplements has increased over the past 10 years. In particular, several studies [5-7] have investigated the potential ergogenic value of Beta-alanine, Creatine, Proteins and Carbohydrates supplementation on exercise performance in athletes. The need to collect scientific evidence is growing, with the aim to clarify real benefits, safety and efficacy of dietary supplements on sports performance.

The aim of this study is to perform a systematic review and a meta-analysis of studies in order to investigate the association between their use and sports performance in athletes. In particular, this study focuses on Amino acids, Creatine, Proteins and Carbohydrates, the four supplements mainly used by athletes, and on their effects on performance results.

METHODS

Data sources

We searched PubMed for studies evaluating the effect of dietary supplements on performance of sports belonging to the summer and winter sports lists of the International Olympic Committee. We used the following key words: “dietary supplement” AND: “Swimming”; “Rowing”; “Running”; “Track and Field”; “Canoeing”; “Ice Skating”; “Cross Country”; “Skiing”; “Weightlifting”; “Cycling”; “Jump”; “Launch”; “Calisthenics”; “Archery”; “Skating”; “Sailing”; “Boxing”; “Fencing”; “Wrestling”; “Judo”; “Taekwondo”; “Basketball”; “Badminton”; “Water Polo”; “Decathlon”; “Biathlon”; “Triathlon”; “Heptathlon”; “Pentathlon”; “Curling”; “Hockey”; “Rugby”; “Tennis”; “Football”; “Table Tennis”; “Beach Volley”; “Baseball”; “Handball”; “Volleyball”.

The search was limited to 10 years (from January 1st 2003 to May 31st 2013). The search was restricted using the limits “Humans” and “presence of abstract” and to papers published in English. In addition, we manually screened references of selected articles for additional relevant studies.

Studies selection and quality assessment

Two independent investigators (ET, PL) reviewed the results of the literature search. Every type of study, either observational or experimental, evaluating the effect of dietary supplements on athletic performance of sports belonging to the summer and winter list of the International Olympic Committee, were selected for the qualitative analysis. On the other hand, only clinical trials with available quantitative data were included in the meta-analysis. Studies were excluded if the abstract was not available, or the study was not conducted on humans, or if the dietary supplement, the sport or the study population were not specified. The selection of potential eligible studies was performed on the basis of abstract/title. The full text of potential eligible studies was collected in order to decide upon the inclusion in the review. All disagreements were resolved by consensus.

Two independent investigators (ET, FDN) reviewed all the papers included in the meta-analysis using the Cochrane Collaboration quality assessment tool [8]. The investigators stated whether the risk of bias was “Low”, “High” or “Unclear” for each potential bias. Potential biases investigated were selection bias (random sequence generation and allocation concealment), performance bias, detection bias, attrition bias and reporting bias. Randomization was considered adequate when a study was described as randomized, even if the precise randomization method was not reported. All disagreements were resolved by consensus.

Data synthesis

In order to synthesize data, the four most common supplements were identified: Beta-alanine, Creatine, Proteins and Carbohydrates. Likewise, various “types” of sports activities were identified: aerobic, anaerobic and mixed activities [9]. Activities of medium and long duration in which the oxygen supply is crucial (distance running, walking, road cycling) were classified as aerobic. Anaerobic sports which involve predominantly high intensity exercise of short or very short duration (running velocity, cycling velocity, volleyball) were classified as anaerobic. Most team sports (football, basketball, hockey) were enclosed in mixed activities.

As many studies [7,10-12] have examined

the effects of Beta-alanine, Creatine, Proteins and Carbohydrates on exercise performance, in this study enhancement on sport performances was considered as outcome. In particular, the following aspects related to performance results [6] in athletes were considered: ergogenic effect (EE) (including performance improvements), time to exhaustion (TTE), muscular endurance (ME), post-exercise recovery (PER) and body mass (BM). With respect to meta-analysis, data on level of post Exercise Glucose (GpE [mg/dL]) and level of post Exercise Lactate (LpE [mmol/L]) were considered as indicators of TTE, PER and EE [13,14]. Similarly, Change in Body Mass (CBM) [kg] was used as indicator of BM.

To perform the meta-analysis a fixed effects model was employed. In case of heterogeneity ($I^2 \geq 50\%$) a random effects model was applied. Meta-analyses were carried out if at least three studies were available for combining data and with respect to mean difference with their 95% confidence intervals (95% CI).

Statistical analysis was performed with Review Manager 5.1 software for Windows.

The statistical significance was set at $p = 0.05$.

RESULTS

Study selection

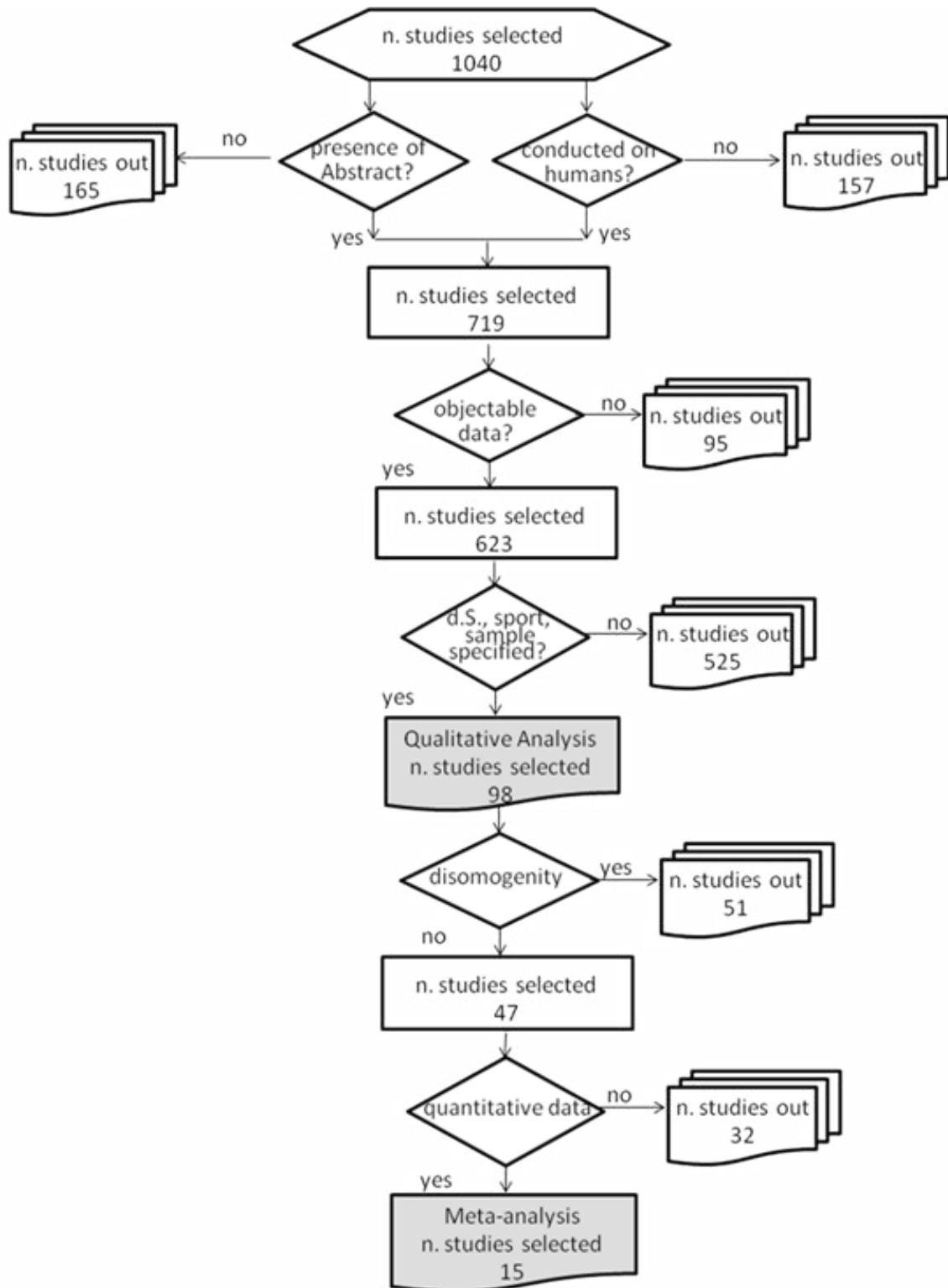
The literature search retrieved 1040 studies but 942 studies were discarded (see Figure 1).

Ninety-eight studies (observational case-control studies and randomized or non-randomized or cross-over clinical trials) were included in the qualitative analysis whereas 15 experimental studies were included in the quantitative analysis [15-29].

As regards the continent in which the study was performed, of the 98 studies included in the qualitative analysis the 37.8% was carried out in Europe, the 26.5% in America, the 15.3% in Australia, the 12.2% in Asia, the 7.1% in Eurasia and the 1.1% in Africa. Considering the specific country of origin of the 98 studies, 15 (15.3%) were carried out in the US, 11 (11.2%) in Australia, 8 (8.2%) in the UK, 6 (6.1%) in Turkey, 6 (6.1%) in Brazil, 5 (5.0%) in Greece, 4 (4.1%) in Canada, 4 (4.1%) in Japan, 4 (4.1%) in New Zealand, 3 (3.1%) in Poland, 3 (3.1%) in Spain, 2 (2.1%) in Austria, 2 (2.1%) in Belgium, 2 (2.1%) in China, 2 (2.1%) in France, 2 (2.1%) in Israel, 2 (2.1%) in Serbia, 1 (1.0%) in Estonia, 1 (1.0%) in Finland, 1

FIGURE 1

FLOW CHART-THE PROCESS FOR SELECTING EVIDENCE



(1.0%) in Hungary, 1 (1.0%) in Iran, 1 (1.0%) in Italy, 1 (1.0%) in Malaysia, 1 (1.0%) in Portugal, 1 (1.0%) in Russia, 1 (1.0%) in Scotland, 1 (1.0%) in South Africa, 1 (1.0%) in Slovakia, 1 (1.0%) in Sweden, 1 (1.0%) in Taiwan, 1 (1.0%) in the Netherlands, 1 (1.0%) in Thailand, 1 (1.0%) in Uruguay and 1 (1.1%) in Yugoslavia.

As regards the continent in which the 15 studies included in meta-analysis were performed, 8 (53.3%) were carried out in America, 6 (40%) in Europe and only one (6.7%) in Asia. In particular, 4 (26.6%) were performed in the US, 2 (13.3%) in Belgium, 2 (13.3%) in Canada, 2 (13.3%) in UK, 1 (6.7%) in Uruguay, 1 (6.7%) in China, 1 (6.7%) in Finland, 1 (6.7%) in the Netherlands and 1 (6.7%) in Brazil.

Regarding the characteristics of the subjects involved, only 93 out of 98 studies included in the qualitative analysis reported the sample size, which varied between 2 and 42 participants with a total sample of 1390 individuals studied.

The mean age of the study population was available only for 62 studies. The weighted average age was 23.3 years and ranged from 13.8 to 54 years.

In 59 studies (60.2%) only males were studied while 12 (12.2%) studies were performed on both males and females. Only 3 (3.1%) studies were carried out on females only. In 24 studies (24.5%) information on gender was not available.

Sample sizes of the 15 clinical trials considered in the meta-analysis varied between 9 and 36 participants, yielding a total sample of 281 individuals. The mean age of the study population was available for 14 studies. The weighted average age was 22.3 years and ranged from 19.3 to 28.7 years. In 10 trials (66.7%) only males were studied while 5 trials (33.3%) were performed on both males and females.

Each study dealt with only one sport. Many sports (90.4%) were studied in less than 8 papers. Only three sports (swimming, cycling and running) were analysed in more than 14 studies. In particular, in the 15 clinical trials included in the meta-analysis, cycling was analysed in 5 studies [16,20-22,28]; swimming in 4 [24-27]; ice-hockey in 2 [19,29]. The others sports were: rowing [15], football [17], rugby [18] and tennis [23]. Finally, there was a total of 35 supplements analysed in all 98 studies: Creatine, Carbohydrate, Beta-alanine, Antioxidant, Alpha-Tocopherol, Sodium bicarbonate, Beta-

hydroxyl-beta-methyl butyrate, Branched-chain amino acid, Caffeine, Egg white protein, Omega-3, Glutamine, Iron, Multi-nutrient supplement, Multivitamin and mineral supplement, Nitrate, Sago, Zinc, Arginine, Cystine/theanine, Galactose, High-dose serotonin-depleting large neutral amino acid, L-carnitine, Low-protein colostrum powder, Lycopene, Probiotic *Lactobacillus fermentum* VRI-003, Protein, *R. rosea* extract, Soy protein, Sports drink containing Proteins and Carbohydrates, Taurine, *tribulus terrestris*, Vitamin A, Vitamin C, Yohimbine. Among these, 44.4% were tested in only one study, 25.6% were analysed from two studies and the remaining 30.0% were analysed in at least three studies.

The dietary supplements mainly tested in the 98 papers were: Creatine involved in 25.5% of the studies [17-19,23-27,29-45]; Amino acids in 23.5% [15,20,22,28,40,46-63] and Carbohydrates in 13.2% [20-22,29,38,64-71].

In the 15 clinical trials included in meta-analysis the supplements tested were: Beta-alanine versus placebo in 3 [15,16,28]; Protein + Carbohydrates versus Carbohydrates in 3 [20-22]; Creatine versus placebo in 9 [17-19,23-27,29]. In particular, Mero et al. [25] examined the effect of the combination of Creatine and sodium bicarbonate supplementation versus placebo.

Data synthesis

The differences in supplements under study have made it difficult to draw conclusions on the effects. Notwithstanding, we have sought to establish whether papers have provided similar results.

No effect of dietary supplements on sport performance was observed in 48% of studies included in the qualitative assessment.

With respect to Carbohydrates, included studies were numerous and aerobic activities were mainly investigated. Study outcomes were very different: 45% of papers testing Carbohydrates did not show relevant results on athletes' performance, while the others have pointed out a positive feedback. In particular, Sousa et al. [71] highlighted how decline in performance was attenuated in athletes receiving Carbohydrates as supplement. De Sousa et al. pointed out how Carbohydrates supplementation improves running performance [67] and recovery during intensive training in runners [66].

Therefore these three studies [66,67,71] reached the same conclusions showing that Carbohydrates reduce decline in performance and improve recovery during intense aerobic training.

Also for Creatine, several papers (44.0%) did not reveal significant effects. Among the papers in which positive common results were identified we can mention: Juhász et al. [36] who highlighted that Creatine enhances dynamic strength and improves performance in consecutive maximal swims in highly trained fin swimmers; Mero et al. [25] which pointed out that Creatine enhances performance in consecutive maximal swims; Chwalbinska-Moneta [33] which emphasized how Creatine improves endurance and anaerobic performance in rowing; Kocak and Karli [37] and Gill et al. [34] who pointed out an ergogenic effect on anaerobic capacity in wrestling and cycling; Anomasiri et al. [30] who highlighted how Creatine enhances physical performance in swimmers; Hoffmann et al. [23] who emphasized how Creatine improves strength in football players; Chilibeck et al. [18] who pointed out how Creatine increase muscular endurance in rugby players.

As pointed out by these studies, the intake of Creatine has an EE on anaerobic capacity improving performance in short duration and high intensity exercise and provides power improvement.

Other studies found an unclear change in performance [39] or no efficacy in improving performance in specific sport such as ice-hockey and tennis [19,27,43].

Quantitative analysis

Table 1 shows the main features of the 15 studies included in meta-analysis.

Three studies [15,16,28] compared Beta-alanine and placebo, while five studies compared Creatine and placebo [19,24-26,29] with respect to LpE.

Three studies compared Proteins plus Carbohydrates Versus Carbohydrates alone in terms of GpE [20-22]. Finally, CBM at the end of the treatment was evaluated in six studies [17,18,23,24,26,27]. Studies generally suffered from a lack of standardization. Table 2 summarizes the results of the quality assessment. Major reasons of concern came from the sample size of the studies which was generally low (mean number of patients enrolled: 18.7). Three clinical trials were not randomized and most studies

did not describe randomization or allocation methods. Moreover, in many cases blinding methods were not properly described and in some studies drop outs were not described.

There were no statistically significant differences in blood concentrations of LpE in subjects treated with Beta-alanine compared to those treated with placebo even though athletes assuming Beta-alanine showed a higher LpE (mean difference: 0.10 mmol/L, 95% CI: -1.14, 1.34; I2: 0%, see figure 2).

With regard to the Creatine, the treatment did not increase LpE concentrations which appeared slightly lower in athletes assuming Creatine (mean difference: - 0.12 mmol/L, 95% CI: - 1.45, 1.20, I2: 94%, see figure 3).

The intake of Carbohydrates alone before exercise was not more effective in maintaining higher levels of GpE than taking supplements composed by Protein and Carbohydrates (mean difference: 9.50 mg/dL, 95% CI: -2.43, 21.43; I2: 72 %, see figure 4).

Finally, treatments based on Creatine were not more effective than placebo in increasing BM (mean difference, 0.40 kg of variation; 95 % CI: - 0.12, 0.93 I2: 99%, see figure 5).

DISCUSSION

This systematic review with meta-analysis has shown an increasing interest of the scientific literature on dietary supplements during the past decade.

However while the number of studies on a specific supplement grows up, methods and outcomes diversify too (single/multiple dose, before/during/after exercise, in combination or not with other supplements). Also the type of sports studied is very different between papers: in fact only three sports (swimming, cycling and running) were analysed in more than 14 studies and the results are not unique. Because the great heterogeneity among studies for athletes'country of origin, duration of intake and type of supplements used, type of sports analyzed, conclusions could be drawn only for few supplements.

With regard to performance data, the 48% of scientific publications analysed have shown no significant improvement or differences compared to placebo. The remaining 52% instead have identified a positive effect on athletic performance.

Regarding Carbohydrates, it has been suggested that taking proper quantities of

SYSTEMATIC REVIEWS AND META- AND POOLED ANALYSES

TABLE 1

STUDIES INCLUDED INTO THE META-ANALYSIS								
AUTHOR	YEAR	SPORT	STUDY DESIGN	INTERVENTION ANALYSED	INDICATORS STUDIED	N	AGE (MEAN)	D.T (DAYS)
BAGUET ET AL. 2010A	2010	Rowing	RCT	Beta-alanine vs. placebo	Lactate post-exercise	18	23.2	49
BAGUET ET AL. 2010B	2010	Cycling	RCT	Beta-alanine vs. placebo	Lactate post-exercise	14	21.9	28
CANCELA ET AL. 2008	2008	Football	RCT	Creatine vs. placebo	Change in body mass	14	19.6	56
CHILIBECK ET AL. 2007	2007	Rugby	RCT	Creatine vs. placebo	Change in body mass	19	27.2	56
CORNISH ET AL. 2006	2006	Basketball	RCT	Creatine vs. placebo	Lactate post-exercise	17	19.3	5
SHI 2005	2005	Ice-Hockey	CT	Creatine vs. placebo	Lactate post-exercise	20	21	8
FERGUSON-STEGALL ET AL. 2010	2010	Cycling	C. O. RCT	Protein +Carbohydrates vs. Carbohydrates	Glucose post-exercise	15	28.7	1
GOH ET AL. 2012	2012	Cycling	C. O. RCT	Protein +Carbohydrates vs. Carbohydrates	Glucose post-exercise	12	25	1
GREER ET AL. 2011	2011	Cycling	C. O. CT	Protein +Carbohydrates vs. Carbohydrates	Glucose post-exercise	9	21.6	1
HOFFMAN ET AL. 2006	2006	Tennis	RCT	Creatine vs. placebo	Change in body mass	33	NA	70
MERO ET AL. 2004	2004	Swimming	C. O. RCT	Creatine+NaHCO ₃ vs. placebo	Lactate post-exercise	16	17.8	6
PEYREBRUNE ET AL. 2005	2005	Swimming	CT	Creatine vs. placebo	Lactate post-exercise	23	20	NA
					Change in body mass	20	25	5
PLUIM ET AL. 2006	2006	Swimming	RCT	Creatine vs. placebo	Change in body mass	36	22.5	34
MENDES ET AL. 2004	2004	Swimming	RCT	Creatine vs. placebo	Lactate post-exercise	18	19.6	6
					Change in body mass	18	20	8
SALE ET AL. 2011	2011	Cycling	RCT	Beta-alanine vs. placebo	Lactate post-exercise	20	25	28

Note: In this table has shown the main features of the 15 studies included in meta-analysis. D.T. (days): Duration of treatment (days); CT: Clinical Trial; RCT: Randomized Clinical Trial; C.O.CT: Crossover Clinical Trial; NA: Data not available

carbohydrates at the right time could improve athletic performance by ensuring adequate energy stores available when necessary. In this study improvements of performance mainly concerned the resistance. In particular, some

studies have found a decrease in the physiological decline of performance in “repetitions” [67,71] or a shortening of the recovery time between intensive exercises [66]. These findings are not univocal in all publications [21,64,68].

TABLE 2

ASSESSMENT OF THE RISK OF BIAS OF THE STUDIES INCLUDED IN THE META-ANALYSIS						
AUTHOR	SB	PB	DB	AB	RB	MAJOR CONCERNS
BAGUET ET AL. 2010A	U	L	U	L	L	Randomization and blinding of the outcome assessment not described.
BAGUET ET AL. 2010B	U	L	U	L	L	Randomization and blinding of the outcome assessment not described.
CANCELA ET AL. 2008	U	L	U	U	L	Randomization and blinding of the outcome assessment not described. Not specified if there were drop outs.
CHILIBECK ET AL. 2007	U	L	U	L	L	Randomization and blinding of the outcome assessment not described.
CORNISH ET AL. 2006	L	L	U	H	L	Blinding of the outcome assessment not described. Drop outs characteristics not described.
SHI 2005	H	H	H	U	L	Not randomized, not blinded. Not specified if there were drop outs.
FERGUSON-STEGALL ET AL. 2010	U	L	U	U	L	Randomization and blinding of the outcome assessment not described. Not specified if there were drop outs.
GOH ET AL. 2012	U	L	U	L	L	Randomization and blinding of the outcome assessment not described.
GREER ET AL. 2011	H	U	H	L	L	Not randomized. Blinding not described. Physicians were not blinded.
HOFFMAN ET AL. 2006	U	U	U	L	L	Randomization and blinding not properly described.
MERO ET AL. 2004	L	L	U	L	L	Blinding of the outcome assessment not described.
PEYREBRUNE ET AL. 2005	H	H	H	L	L	Not randomized, not blinded.
PLUIM ET AL. 2006	U	U	U	L	H	Randomization and blinding not properly described. Not all results were reported.
MENDES ET AL. 2004	U	U	U	L	L	Randomization and blinding not properly described.
SALE ET AL. 2011	U	L	U	L	L	Randomization and blinding of the outcome assessment not described.

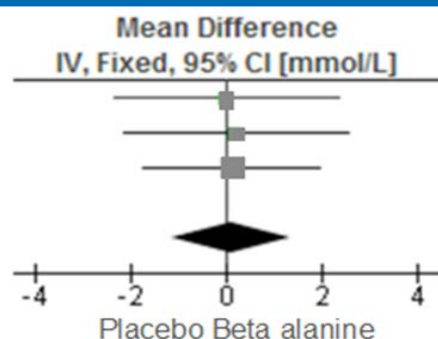
Note: Table 2 summarizes the results of the quality assessment. SB: Selection bias; PB: Performance bias; DB: Detection bias; AB: Attrition bias; RB: Reporting bias; H: High risk of bias; L: Low risk of bias; U: Unclear risk of bias.

Creatine is most commonly used for improving exercise performance and increasing muscle mass in athletes. In this study, results on Creatine are not homogeneous. Some studies in fact have shown no significant effect on performance [19,24,26,43]; instead others have found an increase in strength [23,25,30,33,41]. Among the studies that found positive correlations between intake of Creatine and

sports performance, the outcomes were not the same. For example in some studies the resistance was improved [18,33,36,], in others the explosive strength [23,25,30,35-38,41]. Likewise health effects are different among the analysed papers. In fact some studies have shown an increase in BM [38] although not further specified in terms of body fat, muscle mass or liquid [17,24,35]; others have shown no effects on weight and

FIGURE 2

BLOOD CONCENTRATIONS OF LACTATE [MMOL/L] AT THE END OF EXERCISE. BETA-ALANINE VS. PLACEBO



STUDY OR SUBGROUP	BETA-ALANINE			PLACEBO			MEAN DIFFERENCE IV, RANDOM, 95% CI (mmol/L)
	MEAN (mmol/L)	SD (mmol/L)	TOTAL	MEAN (mmol/L)	SD (mmol/L)	TOTAL	
Baguet et al. 2010a	13	2.5	8	13	2.5	9	0.00 [-2.38, 2.38]
Baguet et al. 2010b	12.2	2.6	7	12	1.8	7	0.20 [-2.14, 2.54]
Sale et al. 2011	12.6	2.2	10	12.5	2	10	0.10 [-1.74, 1.94]
Total (95% CI)			25			26	0.10 [-1.14, 1.34]

Heterogeneity $\text{Chi}^2=0.01$, $\text{df}=2$ ($P=0.99$); $I^2=0\%$

Test for overall effect $Z=0.16$ ($P=0.87$)

body composition [18,43]. Some studies on Creatine have also pointed out an improvement in reduction of the inflammatory response [32] generated by strenuous training. Therefore there are still some uncertainties about exactly who can benefit from Creatine and about its effects and it is not possible to draw firm conclusions for its use.

The main findings of the quantitative analysis showed that: Beta-alanine versus placebo (Figure 2) as well Creatine versus placebo (Figure 3) did not affect LpE; Carbohydrates alone did not have a significant impact on GpE compared to Carbohydrates and Protein together (Figure 4) and BMI was not significantly affected by the assumption of Creatine versus placebo (Figure 5).

Apart from Carbohydrates and Creatine, it has been possible to find further research with common elements in particular with respect to the use of Beta-alanine [16,28,51,52] in aerobic activities and the use of antioxidants [72-76].

A meta-analysis [77] suggests an increase in

ME concerning exercises lasting 60-240 sec or > 240 sec. These findings are partially endorsed [16,51] and partly refuted by other studies [52]. On the basis of other studies it may be also said that Beta-alanine improves TTE and high intensity cycling capacity [28]; decreases fatigue rate during the wingate anaerobic power test [51]; stimulates lean mass accrual in wrestler [52]; increases carnosine content in soleus and gastrocnemius in rowers [15] and enhances performance [15,52].

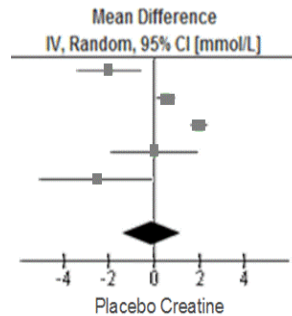
Many of these studies have analysed effects of supplements on exercise in young, healthy, active males or female while we focused on their effects in athletes.

This study has some limitations. Data extracted for the quantitative analyses generally came from studies which enrolled few people and with great heterogeneity. Moreover, there was concern on the quality of these studies, for the possible presence of selection, performance and detection bias.

Another pitfall is the lack of standardization of methods and outcome assessment across studies. Therefore blood chemistry indicators,

FIGURE 3

BLOOD CONCENTRATIONS OF LACTATE [MMOL/L] AT THE END OF EXERCISE. CREATINE VS. PLACEBO



STUDY OR SUBGROUP	CREATINE			PLACEBO			WEIGHT	MEAN DIFFERENCE
	MEAN (mmol/L)	SD (mmol/L)	TOTAL	MEAN (mmol/L)	SD (mmol/L)	TOTAL		IV, RANDOM, 95% CI (mmol/L)
Cornish et al. 2006	19	1.1	9	21	1.7	8	20.0%	-2.00 [-3.39,-0.82]
Shi 2005	10.7	0.2	5	10.2	0.4	5	25.0%	0.50 [0.11,0.89]
Mero et al. 2004	10	0.5	16	8	0.5	16	25.1%	2.00 [1.65,2.35]
Peyrebrune et al. 2005	15	2.1	9	15	2.3	11	16.5%	0.00 [-1.93,1.93]
Mendes et al. 2004	8.9	1.7	9	11.5	3.4	9	13.5%	-2.60 [-5.08,-0.12]
Total (95% CI)			48			49	100%	-0.12 [-1.45,1.20]

Heterogeneity $\tau^2=1.79$; $\chi^2=63.80$, $df=4$ ($P<0.00001$); $I^2=94\%$
 Test for overall effect $Z=0.18$ ($P=0.86$)

methods to execute them, protocols to assess performance and the type of athletes should be standardized, in order to have homogeneous groups for age, weight and body composition. This would allow to better observe differences in pre and post exercise status and in presence or absence of supplementation.

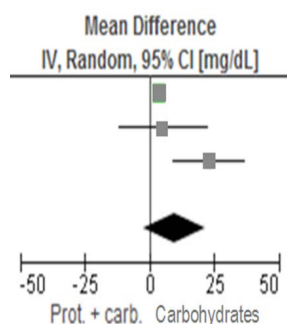
Secondly, we discarded many studies because they did not meet the inclusion criteria, investigating the propensity to consume and not the effectiveness. Notwithstanding, the large number of studies included in this review allowed us to make some conclusions on the impact of supplements on performance.

Considering these data, and the increasing attention to this topic, it would be interesting to

investigate how many and which are the “myths” and the existing awareness about supplements and their effectiveness and possible risks. The danger is that once athletes start using a dietary supplement, they will continue to use always more or with other different supplements, eventually trying something that may not be safe. For this reason, is very important increase knowledge about method of action, safety and potential efficacy, available research, adverse effects and legality of the mainly dietary supplement used in order to ensure choosing and using of supplements safely. Moreover, because the current legal requirements might not be sufficient to ensure the safety and health of dietary supplements users, further research

FIGURE 4

BLOOD GLUCOSE CONCENTRATIONS [MG/DL] AFTER EXERCISE. PROTEIN + CARBOHYDRATE VS. CARBOHYDRATES



STUDY OR SUBGROUP	CARBOHYDRATES			PROTEIN+ CARBOHYDRATES			WEIGHT	MEAN DIFFERENCE
	MEAN (mg/dl)	SD (mg/dl)	TOTAL	MEAN (mg/dl)	SD (mg/dl)	TOTAL		IV, RANDOM, 95% CI (mg/dl)
Ferguson-Stegall et al. 2010	86.5	18	15	82.9	3.6	15	46.6%	3.60 [1.56,5.64]
Goh et al. 2012	107.5	17.5	9	102.3	18.8	9	24.4%	5.20 [-11.58,21.98]
Greer et al. 2011	110.6	17.5	12	88	16.9	12	29.0%	22.60 [8.84,36.36]
Total (95% CI)			36			36	100%	9.50 [-2.43, 21.43]

Heterogeneity $\tau^2=78.49$; $\chi^2=7.18$, $df=2$ ($P=0.03$); $I^2=72\%$
 Test for overall effect $Z=1.56$ ($P=0.12$)

should be promoted. In fact, concerns remain about manufacture, advertising and marketing of these products as well as about their efficacy and safety. There are no provisions under law or regulation that require to disclose the information about the safety and purported or real benefits of their dietary supplement products, with consequent possible risks for users.

For all these reasons, it is very important to identify new research topics, in particular in the efficacy and legal areas, in order to assure from one side that benefits are demonstrated and, on the other side, that safety is guaranteed.

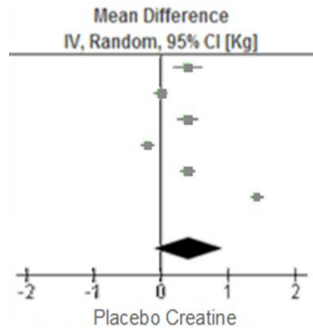
ACKNOWLEDGEMENTS

COMPETING INTERESTS: The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS: The study was designed by PL and ET. FDN and ET participated in the search of the scientific literature, selection and quality assessment of article, data collection and data analysis. FDN and CdW performed the meta-analysis. CDM helped to manage the database and to draft the manuscript. PL drafted discussion and conclusion and WR supervised the work. All authors participated in the study design and in writing of the manuscript. All authors read and approved the final manuscript.

FIGURE 5

CHANGES IN BODY MASS [KG] AT THE END OF TREATMENT. CREATINE VS. PLACEBO



STUDY OR SUBGROUP	CREATINE			PLACEBO			WEIGHT	MEAN DIFFERENCE IV, RANDOM, 95% CI (mg/dL)
	MEAN (Kg)	SD (Kg)	TOTAL	MEAN (Kg)	SD (Kg)	TOTAL		
Cancela et al. 2008	1.4	0.2	7	1	0.2	7	16.4%	0.40 [0.19, 0.61]
Chillbeck et al. 2007	-0.2	0.1	10	-0.2	0.1	9	16.7%	0.00 [-0.09, 0.09]
Hoffman et al., 2006	1	0.1	11	0.6	0.2	11	16.6%	0.40 [0.27, 0.53]
Peyrebrune et al. 2005	-0.2	0.1	9	0	0.1	11	16.7%	-0.20 [-0.29, -0.11]
Pluim et al. 2006	0.9	0.2	24	0.5	0.1	12	16.7%	0.40 [0.30, 0.50]
Mendes et al. 2004	1.34	0.1	9	-0.09	0.1	9	16.7%	1.43 [1.34, 1.52]
Total (95% CI)			70			59	100%	0.40 [-0.12, 0.93]

Heterogeneity $\tau^2=78.49$; $\chi^2=7.18$, $df=2$ ($P=0.03$); $I^2=72\%$
 Test for overall effect $Z=1.56$ ($P=0.12$)

References

[1] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. Official Journal of the European Communities L 183, 2002 P. 0051 - 7.

[2] Garcia-Cazarin ML, Wambogo EA, Regan KS, Davis CD. Dietary Supplements Research Portfolio at the NIH, 2009-2011. J Nutr 2014; 144(4):414-8.

[3] European Communities. Characteristics and perspectives of the market for food supplements containing substances other than vitamins and minerals. Brussels, 5.12.2008 - SEC (2008) 2976.. www.ec.europa.eu/food/ Accessed 14 June 2015

[4] Dickinson A, Makay D. Health habits and other characteristics of dietary supplement users: a review. Nutr J. Feb 2014; 13(1):14.

[5] Cermak NM, van Loon LJ. The use of carbohydrates during exercise as an ergogenic aid. Sports Med 2013; 43(11):1139-55.

[6] Culbertson J.Y, Kreider R.B, Greenwood M, Cooke M. Effects of Beta-Alanine on Muscle Carnosine and Exercise Performance:A Review of the Current

SYSTEMATIC REVIEWS AND META- AND POOLED ANALYSES

- Literature. *Nutrients* 2010; 2(1), 75–98.
- [7] Kreider RB. Effects of creatine supplementation on performance and training adaptations. *Mol Cell Biochem* 2003; 244(1-2):89-94.
- [8] Higgins JPT, Green S. (editors). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.
- [9] Zeppilli P, Palmieri V. *Manuale di medicina dello sport e pronto soccorso*, Roma: Cesi; 2001.
- [10] Hall M, Trojian, TH. Creatine supplementation. *Curr Sports Med Rep* 2013; 12(4):240-4.
- [11] Mesa JL, Ruiz JR, González-Gross MM, Gutiérrez Sáinz A, Castillo Garzón MJ. Oral creatine supplementation and skeletal muscle metabolism in physical exercise. *Sports Med* 2002; 32(14):903-44.
- [12] Ormsbee M.J, Bach C.W, Baur D.A. Pre-Exercise Nutrition: The Role of Macronutrients, Modified Starches and Supplements on Metabolism and Endurance Performance. *Nutrients* 2014; 6(5):1782-808.
- [13] Brooks G.A. Cell-cell and intracellular lactate shuttles. *The Journal of Physiology* 2009; 587(Pt 23), 5591–5600. doi:10.1113/jphysiol.2009.178350
- [14] Robergs RA, Ghiasvand F, Parker D. Biochemistry of exercise-induced metabolic acidosis. *Am J Physiol Regul Integr Comp Physiol* 2004; 287(3):R502-16.
- [15] Baguet A, Bourgois J, Vanhee L, Achten E, Derave W. Important role of muscle carnosine in rowing performance. *J Appl Physiol* 2011; 109(4):1096-101. (a)
- [16] Baguet A, Koppo K, Pottier A, Derave W. Beta-alanine supplementation reduces acidosis but not oxygen uptake response during high-intensity cycling exercise. *Eur J Appl Physiol* 2010; 108(3):495-503. (b)
- [17] Cancela P, Ohanian C, Cuitiño E, Hackney AC. Creatine supplementation does not affect clinical health markers in football players. *Br J Sports Med* 2008; 42(9):731-5.
- [18] Chilibeck PD, Magnus C, Anderson M. Effect of in-season creatine supplementation on body composition and performance in rugby union football players. *Appl Physiol Nutr Metab* 2007; 32(6):1052-7.
- [19] Cornish SM, Chilibeck PD, Burke DG. The effect of creatine monohydrate supplementation on sprint skating in ice-hockey players. *J Sports Med Phys Fitness* 2006; 46(1):90-8.
- [20] Ferguson-Stegall L, McCleave EL, Ding Z, et al. The effect of a low carbohydrate beverage with added protein on cycling endurance performance in trained athletes. *J Strength Cond Res* 2010; 24(10):2577-86.
- [21] Goh Q, Boop CA, Luden ND, Smith AG, Womack CJ, Saunders MJ. Recovery from cycling exercise: effects of carbohydrate and protein beverages. *Nutrients* 2012; 4(7):568-84.
- [22] Greer BK, White JP, Arguello EM, Haymes EM. Branched-chain amino acid supplementation lowers perceived exertion but does not affect performance in untrained males. *J Strength Cond Res* 2011; 25(2):539-44.
- [23] Hoffman J, Ratamess N, Kang J, Mangine G, Faigenbaum A, Stout J. Effect of creatine and beta-alanine supplementation on performance and endocrine responses in strength/power athletes. *Int J Sport Nutr Exerc Metab* 2006; 16(4):430-46.
- [24] Mendes RR, Pires I, Oliveira A, Tirapegui J. Effects of creatine supplementation on the performance and body composition of competitive swimmers. *J Nutr Biochem* 2004; 15(8):473-8.
- [25] Mero AA, Keskinen KL, Malvela MT, Sallinen JM. Combined creatine and sodium bicarbonate supplementation enhances interval swimming. *J Strength Cond Res* 2004; 18(2):306-10.
- [26] Peyrebrune MC, Stokes K, Hall GM, Nevill ME. Effect of creatine supplementation on training for competition in elite swimmers. *Med Sci Sports Exerc* 2005; 37(12):2140-7.
- [27] Plum BM, Ferrauti A, Broekhof F, et al. The effects of creatine supplementation on selected factors of tennis specific training. *Br J Sports Med* 2006; 40(6):507-11.
- [28] Sale C, Saunders B, Hudson Wise JA, Harris RC, Sunderland CD. Effect of -alanine plus sodium bicarbonate on high-intensity cycling capacity. *Med Sci Sports Exerc* 2011; 43(10):1972-8.
- [29] Shi D. Oligosaccharide and creatine supplementation on glucose and urea nitrogen in blood and serum creatine kinase in basketball athletes. *J Huazhong Univ Sci Technolog Med Sci* 2005; 25(5):587-9.
- [30] Anomasiri W, Sanguanrungrasirikul S, Saichandee, P. Low dose creatine supplementation enhances sprint phase of 400 meters swimming performance. *J Med Assoc Thai* 2004; 87 Suppl 2:S228-32.
- [31] Ayoama R, Hiruma E, Sasaki H. Effects of creatine loading on muscular strength and endurance of female softball players. *J Sports Med Phys Fitness* 2003; 43(4):481-7.
- [32] Bassit RA, Curi R, Costa Rosa LF. Creatine supplementation reduces plasma levels of pro-inflammatory cytokines and PGE2 after a half-ironman competition. *Amino Acids* 2008; 35(2):425-31
- [33] Chwalbińska-Moneta J. Effect of creatine supplementation on aerobic performance and anaerobic capacity in elite rowers in the course of endurance training. *Int J Sport Nutr Exerc Metab* 2003; 13(2):173-83.
- [34] Gill ND, Hall RD, Blazevich AJ. Creatine serum is not as effective as creatine powder for improving cycle sprint performance in competitive male team-sport athletes. *J Strength Cond Res* 2004; 18(2):272-5.
- [35] Herda TJ, Beck TW, Ryan ED, et al. Effects of creatine monohydrate and polyethylene glycosylated creatine supplementation on muscular strength, endurance, and power output. *J Strength Cond Res*. 2009; 23(3):818-26.

- [36] Juhász I, Györe I, Csende Z, Rác L, Tihanyi J. Creatine supplementation improves the anaerobic performance of elite junior fin swimmers. *Acta Physiol Hung* 2009; 96(3):325-36.
- [37] Koçak S, Karli U. Effects of high dose oral creatine supplementation on anaerobic capacity of elite wrestlers. *J Sports Med Phys Fitness* 2003; 43(4):488-92.
- [38] Koenig CA, Benardot D, Cody M, Thompson WR. Comparison of creatine monohydrate and carbohydrate supplementation on repeated jump height performance. *J Strength Cond Res* 2008; 22(4):1081-6.
- [39] Lamontagne-Lacasse M, Nadon R, Goulet EDB. Effect of creatine supplementation on jumping performance in elite volleyball players. *Int J Sports Physiol Perform* 2011; 6(4):525-33.
- [40] O'Connor DM, Crowe MJ. Effects of six weeks of beta-hydroxy-beta-methylbutyrate (HMB) and HMB/creatine supplementation on strength, power, and anthropometry of highly trained athletes. *J Strength Cond Res* 2007; 21(2):419-23.
- [41] Ostojic SM. Creatine supplementation in young soccer players. *Int J Sport Nutr Exerc Metab* 2004; 14(1):95-103.
- [42] Schröder H, Terrados N, Tramullas A. Risk assessment of the potential side effects of long-term creatine supplementation in team sport athletes. *Eur J Nutr* 2005; 44(4):255-61.
- [43] Silva AJ, Machado Reis V, Guidetti L, et al. Effect of creatine on swimming velocity, body composition and hydrodynamic variables. *J Sports Med Phys Fitness* 2007; 47(1):58-64.
- [44] Theodorou AS, Havenetidis K, Zanker CL, et al. Effects of acute creatine loading with or without carbohydrate on repeated bouts of maximal swimming in high-performance swimmers. *J Strength Cond Res* 2005; 19(2):265-9.
- [45] Van der Merwe J, Brooks NE, Myburgh KH. Three weeks of creatine monohydrate supplementation affects dihydrotestosterone to testosterone ratio in college-aged rugby players. *Clin J Sport Med* 2009; 19(5):399-404.
- [46] Alghannam AF. Carbohydrate-protein ingestion improves subsequent running capacity towards the end of a football-specific intermittent exercise. *Appl Physiol Nutr Metab* 2011; 36(5):748-57.
- [47] Antonio J, Sanders MS, Kalman D, Woodgate D, Street C. The effects of high-dose glutamine ingestion on weightlifting performance. *J Strength Cond Res* 2002; 16(1):157-60.
- [48] Bassini-Cameron A, Monteiro A, Gomes A, Werneck-de-Castro JP, Cameron L. Glutamine protects against increases in blood ammonia in football players in an exercise intensity-dependent way. *Br J Sports Med* 2008; 42(4):260-6.
- [49] Broad EM, Maughan RJ, Galloway SDR. Effects of exercise intensity and altered substrate availability on cardiovascular and metabolic responses to exercise after oral carnitine supplementation in athletes. *Int J Sport Nutr Exerc Metab* 2011; 21(5):385-97.
- [50] Fahlström M, Fahlström PG, Lorentzon R, Henriksson-Larsén K. Positive short-term subjective effect of sports drink supplementation during recovery. *J Sports Med Phys Fitness* 2006; 46(4):578-84.
- [51] Hoffman J, Ratamess NA, Faigenbaum AD, et al. Short-duration beta-alanine supplementation increases training volume and reduces subjective feelings of fatigue in college football players. *Nutr Res* 2008; 28(1):31-5.
- [52] Kern BD, Robinson TL. Effects of -alanine supplementation on performance and body composition in collegiate wrestlers and football players. *J Strength Cond Res* 2011; 25(7):1804-15.
- [53] Kirby TJ, Triplett NT, Haines TL, Skinner JW, Fairbrother KR, McBride JM. Effect of leucine supplementation on indices of muscle damage following drop jumps and resistance exercise. *Amino Acids* 2012; 42(5):1987-96.
- [54] Laskowski R, Antosiewicz J. Increased adaptability of young judo sportsmen after protein supplementation. *J Sports Med Phys Fitness* 2003; 43(3):342-6.
- [55] Mekata Y, Hayashi N, Masuda Y, Kashimura O, Arai S, Kawano Y. Blood substrates and hormonal responses to increased egg white protein intake prior to a 12,000 m run in heat. *J Nutr Sci Vitaminol* 2008; 54(2):154-62.
- [56] Murakami S, Kurihara S, Koikawa N, et al. Effects of oral supplementation with cystine and theanine on the immune function of athletes in endurance exercise: randomized, double-blind, placebo-controlled trial. *Biosci Biotechnol Biochem* 2009; 73(4):817-21.
- [57] Portal S, Zadik Z, Rabinowitz J, et al. 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. *Eur J Appl Physiol* 2011; 111(9):2261-9.
- [58] Portier H, Chatard JC, Filaire E, Jaunet-Devienne MF, Robert A, Guezennec CY. Effects of branched-chain amino acids supplementation on physiological and psychological performance during an offshore sailing race. *Eur J Appl Physiol* 2008; 104(5):787-94.
- [59] Rutherford JA, Spriet LL, Stellingwerff T. The effect of acute taurine ingestion on endurance performance and metabolism in well-trained cyclists. *Int J Sport Nutr Exerc Metab* 2010; 20(4):322-9.
- [60] Stepto NK, Shipperd BB, Hyman G, McInerney B, Pyne, DB. Effects of high-dose large neutral amino acid supplementation on exercise, motor skill, and mental performance in Australian Rules Football players. *Appl Physiol Nutr Metab* 2011; 36(5):671-81.
- [61] Sureda A, Pons A. Arginine and citrulline supplementation in sports and exercise: ergogenic nutrients? *Med Sport Sci* 2012; 59:18-28.

- [62] Tang FC. Influence of branched-chain amino acid supplementation on urinary protein metabolite concentrations after swimming. *J Am Coll Nutr* 2006; 25(3):188-94.
- [63] Tsai PH, Tang TK, Juang CL, Chen KW, Chi CA, Hsu MC. Effects of arginine supplementation on post-exercise metabolic responses. *Chin J Physiol* 2009; 52(3):136-42.
- [64] Breen L, Tipton KD, Jeukendrup AE. No effect of carbohydrate-protein on cycling performance and indices of recovery. *Med Sci Sports Exerc* 2010; 42(6):1140-8.
- [65] Cox AJ, Pyne DB, Cox GR, Callister R, Gleeson M. Influence of chronic dietary carbohydrate supplementation on plasma cytokine responses to exercise. *Int J Sports Med* 2010; 31(3):207-12.
- [66] De Sousa MV, Madsen K, Fukui R, Santos A, da Silva ME. Carbohydrate supplementation delays DNA damage in elite runners during intensive microcycle training. *Eur J Appl Physiol* 2012; 112(2):493-500.
- [67] De Sousa MV, Madsen K, Simões HG, et al. Effects of carbohydrate supplementation on competitive runners undergoing overload training followed by a session of intermittent exercise. *Eur J Appl Physiol* 2010; 109(3):507-16.
- [68] Ferguson-Stegall L, McCleave EL, Ding Z, et al. Postexercise carbohydrate-protein supplementation improves subsequent exercise performance and intracellular signaling for protein synthesis. *J Strength Cond Res* 2011; 25(5):1210-24.
- [69] McRae KA, Galloway SD. Carbohydrate-electrolyte drink ingestion and skill performance during and after 2 hr of indoor tennis match play. *Int J Sport Nutr Exerc Metab* 2012; 22(1):38-46.
- [70] Richardson KL, Coburn JW, Beam WC, Brown LE. Effects of isocaloric carbohydrate vs. carbohydrate-protein supplements on cycling time to exhaustion. *J Strength Cond Res* 2012; 26(5):1361-5.
- [71] Sousa M, Simões HG, Castro CC, et al. Carbohydrate supplementation increases intramyocellular lipid stores in elite runners. *Metabolism* 2012; 61(8):1189-96.
- [72] Konrad M, Nieman DC, Henson DA, Kennerly KM, Jin F, Wallner-Liebmann SJ. The acute effect of ingesting a quercetin-based supplement on exercise-induced inflammation and immune changes in runners. *Int J Sport Nutr Exerc Metab* 2011; 21(4):338-46.
- [73] Martinovi J, Dopsaj V, Kotur-Stevuljevi J, et al. Oxidative stress biomarker monitoring in elite women volleyball athletes during a 6-week training period. *J Strength Cond Res* 2011; 25(5):1360-7.
- [74] McAnulty SR, Nieman DC, McAnulty LS, Lynch WS, Jin F, Henson DA. Effect of mixed flavonoids, n-3 fatty acids, and vitamin C on oxidative stress and antioxidant capacity before and after intense cycling. *Int J Sport Nutr Exerc Metab* 2011; 21(4):328-37.
- [75] Neubauer O, Reichhold S, Nics L, et al. Antioxidant responses to an acute ultra-endurance exercise: impact on DNA stability and indications for an increased need for nutritive antioxidants in the early recovery phase. *Br J Nutr* 2010; 104(8):1129-38.
- [76] Nishizawa M, Hara T, Miura T, et al. Supplementation with a flavanol-rich lychee fruit extract influences the inflammatory status of young athletes. *Phytother Res* 2011; 25(10):1486-93.
- [77] Hobson RM, Saunders B, Ball G, Harris RC, Sale C. Effects of beta-alanine supplementation on exercise performance: a meta-analysis. *Amino Acids* 2012; 43(1):25-37.

