Eur J Nutr 38:263–270 (1999)

ORIGINAL CONTRIBUTION

P.C. Colombani
R. Bitzi
P. Frey-Rindova
W. Frey
M. Arnold
W. Langhans
C. Wenk

Chronic arginine aspartate supplementation in runners reduces total plasma amino acid level at rest and during a marathon run

Received: 29 December 1998
Accepted: 26 November 1999

P.C. Colombani (✉) · R. Bitzi
P. Frey-Rindova · C. Wenk
Swiss Federal Institute of Technology Zurich
INW Nutrition Biology
ETH Zentrum
CH-8092 Zurich, Switzerland
Tel.: ++41 1 6 32 11 28
Fax: ++41 1 6 32 46 35
E-mail: paolo.colombani@inw.agrl.ethz.ch

W. Frey
Department of Sports Medicine
Schulthess Hospital
Lenghalde 2
CH-8008 Zurich, Switzerland

M. Arnold · W. Langhans
Swiss Federal Institute of Technology Zurich
INW Physiology
ETH Zentrum
CH-8092 Zurich, Switzerland

Summary *Background:* Athletes consume arginine and/or aspartate as potential nutritional ergogenics. Their metabolic effects are controversial and there is some evidence that ingestion of large doses of single amino acids can adversely affect the nitrogen balance or induce an amino acid imbalance. Nevertheless, the general metabolic influence of an arginine aspartate supplementation during a prolonged exercise bout has not yet been investigated.

Aim of the study: The aim of this study was, therefore, to investigate the general metabolic impact of a chronic supplementation with arginine aspartate in endurance-trained athletes at rest and during a marathon run.

Methods: Fourteen endurance-trained runners participated in this field study which was carried out according to a double-blind crossover design. 15 g of arginine aspartate or a carbohydrate-based placebo were supplemented daily for 14 days before a marathon run. Blood samples for analysis of metabolites and hormones were collected shortly before the run, after 31 km, at the end of the run, and after a recovery period of two hours. Additionally, the respiratory exchange ratio was determined during the run.

Results: The plasma level of carbohydrate (glucose, lactate, pyruvate) and fat metabolites (fatty acids, glycerol, ß-hydroxybutyrate), cortisol, insulin, ammonia, lactate dehydrogenase, and creatine kinase as well as the respiratory exchange ratio were unaffected by the supplementation. In contrast, the plasma level of somatotropic hormone, glucagon, urea, and arginine were significantly increased, and the level of most of the remaining plasma amino acids as well as their sum was significantly reduced.

Conclusions: There was no obvious metabolic benefit derived from the chronic supplementation with arginine aspartate. And since furthermore the consequences of a reduction of the total plasma amino acid level are not known, the practice of using single amino acid supplements as potential ergogenics should be critically reevaluated.

Key words Ergogenics – amino acids – exercise – arginine aspartate

European Journal of Nutrition, Vol. 38, Number 6 (1999)

Introduction

Different amino acids are assumed to exert ergogenic effects in exercising athletes (9). Observations of the metabolic effects of such supplementations are controversial. Studies with exercising rats reported a dramatic increase in endurance capacity of 40 % (11) as well as a myofibrillar degeneration and disruption of mitochondrial membranes after supplementation with aspartate, asparagine, and carnitine (12). An increase in endurance capacity in humans was also documented in an early report on potassium-magnesium aspartate supplementation (1). But, on the other hand, no performance or metabolic effects were observed in a later study using the same supplement (15). Recent findings suggest that arginine supplementation enhances the exercise-induced blood flow and vasodilatation in patients with angina pectoris or heart failure (23, 10, 19). However, these people have a reduced peripheral blood flow compared to healthy people. A review of the literature concerning arginine and/or aspartate supplementations reveals that in most studies no ergogenic effects were observed with healthy, exercising people. Nonetheless, and in spite of the fact that their general metabolic impact has not been investigated in exercising people up to now, their consumption is widespread in many sport categories.

Ingestion of single amino acid supplements can also exert some negative metabolic effects (8). The addition of lysine to a balanced amino acid mixture for total parenteral nutrition worsened, for example, a negative nitrogen balance over a ten-day period in patients (7). Further, the oxidation of supplemented amino acids could increase the concentration of free plasma ammonia (14) which might to promote fatigue in exercising people (3). A change in the proportion of dietary amino acids (i.e., supplementing single or few amino acids, or protein lacking single amino acids) can also cause an amino acid imbalance in animals (5), but in none of the studies on arginine and/or aspartate supplementation in humans was the plasma amino acid response investigated.

Since preliminary unpublished results of our laboratory suggested that after long-term arginine aspartate supplementation most plasma amino acids were slightly reduced, with the exception of arginine, and since the general metabolic impact of such a supplementation is not known, the influence of a two-week-long arginine aspartate supplementation was investigated on the metabolism before and during a marathon run in endurance-trained athletes.

Material and methods

Subjects

Twenty endurance-trained male athletes agreed to participate in this study after having been informed about purpose and possible risks. They were chosen on the self-estimated capacity to finish two marathon runs within five weeks and with a maximal running time of four hours for one marathon. Five athletes did not complete both marathon runs because of injury or illness, and the results of one athlete were excluded from the evaluation because of his abnormal plasma levels of several metabolites. The characteristics of the remaining 14 athletes (mean and 95 % confidence interval of the mean) were: age 37 years (33–42), body mass 72 kg (67–77), running exercise in a regular week 51 km (39–62), running exercise in an intense week 72 km (47–97).

Study design

The study was carried out according to a double-blind crossover design and lasted five weeks. It consisted of a two-week-long supplementation period, a wash-out period of one week, and a second two-week-long supplementation period. The athletes performed a non-competitive marathon run at the end of each supplementation period. Half of the athletes ingested the placebo during the first supplementation period and half of them during the second supplementation period. The athletes were allocated at random to the sequences of the treatment and they followed their habitual eating and training patterns during the whole study. During the supplementation period, the athletes ingested daily 15 g of L-arginine-L-aspartate (Dynamisan® Forte, kindly provided by Sandoz-Wander Pharma, Berne, Switzerland) or placebo in addition to their habitual diet. Although the recommended daily intake of the supplement is 5 g in addition to the regular diet, it is common among athletes to ingest the double or triple dose. The supplement for one supplementation period was provided to the athletes in 14 prepackaged doses as a powder which had to be dissolved in 500 mL of water before ingestion. Half of the supplement was ingested on an empty stomach in the morning and the rest one hour before bedtime. The last dose of each supplementation period was ingested completely on the morning of the marathon run. The placebo consisted of maltodextrine (9 g), saccharose (6 g), and flavoring substances to match the sensory properties of the supplement.

The subjects were advised to eat qualitatively the same carbohydrate-rich meals for dinner the day before the run and for breakfast on the running day on both occasions. Caffeine, alcohol, and dairy products were not allowed starting from the evening before the running day until the end of the two-hour recovery period. No physical activity was allowed the day prior to the run.

Ambient temperature during the runs ranged between -2 °C and 6 °C and relative humidity was between 60 % and 90 %. The athletes were forced to drink 150 mL of sweetened tea (90 g carbohydrates per liter) every five kilometers during the run. Additionally, they were allowed to drink water ad libitum, but food intake was not permitted. Only water intake was allowed during the two-hour recovery period after the run.

Respiratory exchange ratio and blood sampling

The respiratory exchange ratio (RER) was determined on a treadmill (1.5 % grade) before the start, after 31 km, and at the end of the run using a half-open system (Oxycon Sigma, Mijnhardt BV, Bunnik, Netherlands). Blood samples (24 mL) for metabolite and hormone analyses were collected from the antecubital vein into lithium heparin or EDTA fluoride Vacutainer® tubes (Becton Dickinson Vacutainer System, Rutherford New Jersey, USA) whilst the subjects were in a lying position at the following time points: 30 min to one hour before the run at rest (T1), after 31 km (T2), after the run (T3), and two hours after the run (T4). For glucagon analysis 500 KIU*) Aprotinin® (Böhringer Mannheim GmbH, Mannheim, Germany) were added to a glass tube containing 1 mL blood which was immediately centrifuged for 10 min at 4 °C and 2000x g, and the plasma was stored in a glass tube at -20 °C. The remaining blood was also centrifuged and the plasma was stored without additive under the same conditions except for the plasma for ammonia and amino acid analysis. Plasma for ammonia analysis was kept at 0 °C and analyzed within two hours. 1 mL plasma for amino acid analysis was mixed with 1 mL of a deproteinisation solution containing 50 mg sulphosalycilic acid and nor-leucine as internal standard, allowed to stand for one hour in ice water, and centrifuged for 10 min at 4 °C and 1000x g. The supernatant was then stored at -75 °C.

Biochemical analyses

Free amino acids and taurine were analyzed by high performance liquid chromatography with post-column derivatisation with ninhydrin on a LKB 4151 Alpha Plus system equipped for physiological sample analysis (Pharmacia LKB, Bromma, Sweden). Plasma sampled according to the method described in the previous paragraph was centrifuged for 10 min at 4 °C and 1000x g. The supernatant was adjusted to a pH of 2.2 with lithium hydroxide (0.3 $mol \cdot L^{-1}$) and filtered through a 0.2 μm filter membrane before analysis. Commercially available buffers used during the analysis were formulated on a lithium basis covering a pH range from 2.20 to 3.55 and a lithium ion concentration from 0.20 to 1.65 $mol \cdot L^{-1}$, respectively, and were purchased from the manufacturer of the analytical system. Chromatograms were evaluated by comparison of an external standard containing a mixture of commercially available amino acids including the internal standard nor-leucine and taurine (Sigma Diagnostics, St. Louis MO, USA). The reliable detection limit of the assay system is 10 $\mu mol \cdot L^{-1}$.

Plasma metabolites were analyzed enzymatically at 37 °C on a Cobas-Mira analyzer (Roche, Basel, Switzerland). The following commercially available kits were used: fatty acids, Wako Chemicals GmbH, Neuss, Germany; β-hydroxybutyrate, Sigma Diagnostics, St. Louis MO, USA; glucose, lactate, pyruvate, glycerol, urea, ammonia, creatine kinase, lactate dehydrogenase, Roche, Basel, Switzerland.

Hormones were analyzed using commercially available radioimmunoassay kits (insulin: Kabi Pharmacia Diagnostics, Uppsala, Sweden; cortisol, somatotropic hormone (STH), and glucagon: Diagnostic Products Corporation, Los Angeles, USA). Plasma osmolality was measured by means of freezing-point reduction with an osmometer (Multiosmette, Precision System Inc., Natick MA, USA).

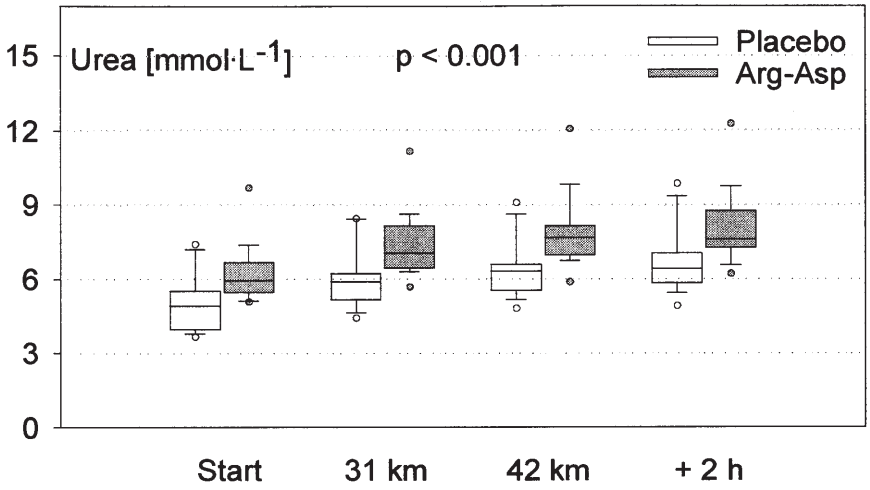
Statistical analyses

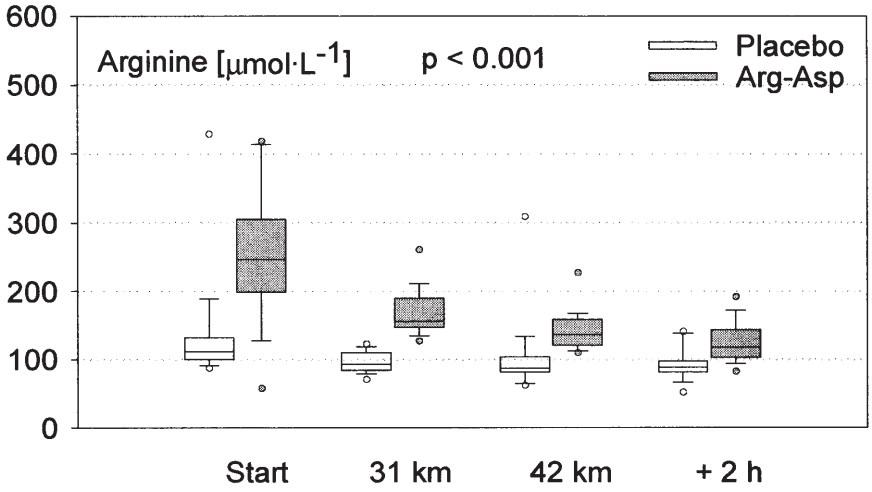
All statistical analyses were performed with the Statistica/W™ software (Statsoft™ Inc., Tulsa OK, USA). An ANOVA with two repeated factors (treatment and time) was used to detect treatment differences. Paired samples were analyzed with the T-test for dependent samples. The level of significance was set at $p < 0.05$. Data in text and tables are presented as mean and 95 % confidence interval of the mean. Box and whisker plots were preferred to line plots with standard deviation to better visualize the distribution of the data.

Results

Aspartate and glutamate were not included in the results of the plasma amino acids, since their plasma level was mostly below the reliable level of 10 $\mu mol \cdot L^{-1}$. Due to capacity problems, the RER from four athletes was not measured before the start. The RER data from only ten athletes were, therefore, included in the results.

The mean running time was 194 min (181–206) and 196 min (185–207) with the placebo and supplement treatment, respectively, and not significantly different. Carbohydrate and fat metabolites in plasma as well as plasma osmolality, ammonia, lactate dehydrogenase, creatine kinase, and the RER were unaffected by the treatment (Table 1). In contrast, the plasma level of urea, arginine, and ornithine (Fig. 1) was significantly increased with the supplement treatment. The level of 13 of the 15 other analyzed amino acids as well as the sum of the analyzed plasma amino acids was, however, significantly reduced with the supplement treatment (Table 2). The reduction of the total plasma amino acids was in an order of





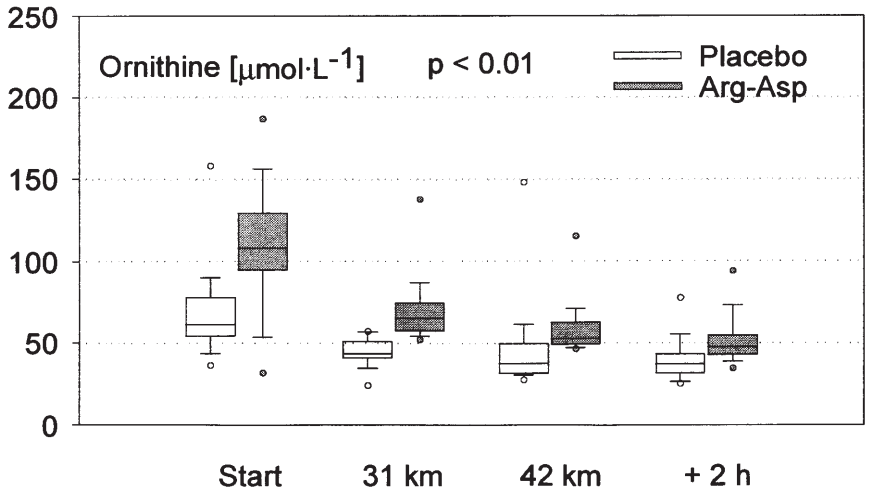


Fig. 1 Time course of circulating urea, arginine, and ornithine of the arginine aspartate (=Arg-Asp) and placebo treatment, respectively. The line within the box marks the median, the boundaries of the box indicate the 25th and 75th percentile. Whiskers above and below the box represent the 90th and 10th percentiles. Data points beyond the whiskers are plotted separately. The gray and transparent boxes represent data of the arginine aspartate and placebo treatment, respectively, and the p-value shows the level of significance of the factor "treatment" of the ANOVA for two repeated factors.

100 to 200 μmol·L^{-1} despite an increase in the arginine concentration of about 30 to 120 μmol·L^{-1}.

The plasma level of the hormones insulin and cortisol was similar in both treatments, whereas plasma glucagon and STH were significantly increased as a consequence of the supplement treatment (Table 3).

Discussion

The general metabolic effect of a two-week-long supplementation with arginine aspartate was investigated during an endurance exercise bout. For the first time the total plasma amino acid response to such a supplementation is reported. Despite a marked increase of circulating plasma arginine, the sum of the analyzed plasma amino acids was significantly reduced with the supplement treatment.

It is obviously not possible to conclude from the present results if and to which extent the observed reduction of the sum of the analyzed plasma amino acids affects the amino acid metabolism. However, an excessive supply with several grams of single amino acids, as is the case when supplementing single amino acids or peptides, can cause a large disproportion of the amino acid content of the regular diet. In different animals, such an amino acid imbalance causes depression of food intake and decreases weight gain (6, 18), but no information is available about amino acid imbalances and its effects in healthy humans. This issue was discussed in a recent review article about high protein intakes (8).

The last dose of the supplement was ingested only a few hours before the run. It can, therefore, not be differentiated if the observed metabolic effects were a consequence of this single dose or of the chronic supplementation. Nevertheless, since the ureagenesis rate is also controlled by substrate availability (17) and the urea cycle enzymes have half-lives of 3 to 9 days (17), it is likely that the chronic supplementation was at least partially responsible for the observed effects.

The supplementation increased both the plasma level of urea and ornithine, two direct products of the arginine metabolism. The systemic increase in circulating arginine also caused an increase in the level of STH and glucagon.

Table 1 Time course of plasma metabolites, osmolality, and respiratory exchange ratio of the arginine aspartate (=Arg-Asp) and placebo treatment, respectively

Parameter	Treatment	T1	T2	T3	T4	p-value
Glucose	Placebo	4.8 (4.3-5.4)	6.7 (6.2-7.2)	6.0 (5.5-6.5)	5.5 (5.1-5.9)	0.64
mmol·L^{-1}	Arg-Asp	5.3 (4.7-5.8)	6.6 (6.2-7.0)	6.0 (5.7-6.2)	5.5 (5.1-5.8)	
Lactate	Placebo	1.6 (1.4-1.8)	2.6 (1.9-3.2)	2.2 (1.6-2.8)	1.7 (1.4-2.0)	0.43
mmol·L^{-1}	Arg-Asp	1.6 (1.4-1.8)	2.4 (2.1-2.7)	2.2 (1.9-2.5)	1.6 (1.4-1.7)	
Pyruvate	Placebo	97 (87-109)	160 (126-193)	135 (110-160)	116 (76-156)	0.19
μmol·L^{-1}	Arg-Asp	91 (78-105)	134 (112-156)	133 (114-151)	101 (80-122)	
Fatty acids	Placebo	0.2 (0.1-0.2)	1.5 (1.3-1.8)	1.9 (1.6-2.1)	1.6 (1.3-2.0)	0.50
mmol·L^{-1}	Arg-Asp	0.2 (0.1-0.2)	1.6 (1.3-1.9)	2.0 (1.7-2.3)	1.7 (1.3-2.0)	
Glycerol	Placebo	67 (55-79)	567 (531-604)	715 (646-786)	247 (198-296)	0.99
μmol·L^{-1}	Arg-Asp	65 (56-76)	579 (509-648)	719 (634-802)	234 (190-277)	
β-Hdroxybutyrate	Placebo	17 (5-29)	93 (56-129)	187 (110-264)	687 (433-941)	0.39
μmol·L^{-1}	Arg-Asp	20 (8-32)	92 (43-142)	197 (122-272)	818 (541-1095)	
Ammonia	Placebo	15 (10-20)	72 (53-92)	84 (56-111)	12 (8-17)	0.51
μmol·L^{-1}	Arg-Asp	9 (5-12)	75 (56-95)	77 (56-98)	9 (6-13)	
Osmolality	Placebo	287 (284-290)	296 (293-299)	295 (292-298)	286 (282-290)	0.40
mmol·kg^{-1}	Arg-Asp	290 (289-292)	296 (294-298)	294 (292-297)	288 (285-292)	
Lactate dehydrogenase	Placebo	6.2 (5.3-7.1)	8.7 (7.6-9.8)	10.6 (8.8-12.5)	9.4 (7.9-10.9)	0.94
μkat·L^{-1}	Arg-Asp	6.4 (5.7-7.1)	8.6 (7.5-9.8)	10.7 (9.4-11.9)	9.3 (8.4-10.3)	
Creatine kinase	Placebo	2.7 (2.0-3.3)	4.8 (3.9-5.7)	6.4 (5.4-7.3)	7.8 (6.5-9.2)	0.42
μkat·L^{-1}	Arg-Asp	2.7 (2.1-3.4)	5.1 (4.2-6.0)	6.7 (5.4-8.0)	8.6 (6.6-10.5)	
Respiratory exchange ratio	Placebo	1.00 (0.96-1.03)	0.90 (0.85-0.95)	0.84 (0.82-0.86)	-	0.16
	Arg-Asp	0.98 (0.95-1.01)	0.88 (0.85-0.91)	0.84 (0.82-0.86)		

Data are presented as mean and 95 % confidence interval. T1 = before marathon, T2 = after 31 km, T3 = end of marathon, T4 = two hours after the run. P-value = level of significance of the factor “treatment” of the ANOVA for two repeated factors

Table 2 Time course of plasma amino acids and taurine level of the arginine aspartate (=Arg-Asp) and placebo treatment, respectively

Parameter	Treatment	T1	T2	T3	T4	p-value
Alanine	Placebo	688 (623-753)	536 (450-622)	390 (316-464)	363 (300-426)	< 0.05
	Arg-Asp	639 (540-739)	526 (457-595)	377 (329-425)	315 (280-351)	
Asparagine	Placebo	61 (51-70)	46 (36-55)	42 (36-47)	38 (34-46)	< 0.05
	Arg-Asp	49 (41-57)	42 (38-46)	37 (34-41)	34 (31-37)	
Cysteine	Placebo	56 (53-59)	65 (60-71)	68 (62-74)	64 (59-68)	0.06
	Arg-Asp	54 (51-57)	64 (60-68)	63 (60-66)	63 (58-67)	
Glycine	Placebo	313 (276-350)	255 (225-285)	220 (197-242)	194 (177-211)	< 0.001
	Arg-Asp	251 (220-281)	218 (201-235)	191 (172-210)	161 (150-173)	
Glutamine	Placebo	783 (724-841)	698 (642-755)	620 (558-683)	600 (545-656)	< 0.001
	Arg-Asp	705 (628-783)	652 (607-696)	565 (518-612)	529 (490-568)	
Histidine	Placebo	99 (94-105)	91 (84-98)	82 (76-89)	79 (73-85)	< 0.05
	Arg-Asp	94 (86-103)	87 (82-91)	77 (73-82)	74 (71-77)	
Isoleucine	Placebo	65 (58-72)	58 (53-64)	54 (49-59)	61 (56-66)	< 0.01
	Arg-Asp	57 (50-63)	58 (48-60)	49 (46-52)	58 (53-64)	
Leucine	Placebo	135 (124-146)	123 (114-132)	113 (105-122)	121 (111-131)	< 0.01
	Arg-Asp	120 (107-133)	117 (107-127)	103 (97-109)	120 (109-131)	
Lysine	Placebo	142 (128-157)	130 (116-143)	118 (105-132)	116 (106-126)	< 0.001
	Arg-Asp	122 (110-135)	107 (98-117)	95 (87-104)	96 (90-102)	
Methionine	Placebo	29 (26-31)	32 (29-35)	27 (24-31)	24 (22-26)	< 0.01
	Arg-Asp	24 (21-26)	29 (27-32)	25 (24-27)	20 (18-21)	
Phenylalanine	Placebo	70 (65-75)	77 (71-84)	74 (69-80)	71 (69-76)	< 0.05
	Arg-Asp	63 (60-66)	76 (71-80)	73 (69-77)	69 (66-72)	
Serine	Placebo	129 (113-145)	104 (87-121)	93 (81-104)	88 (79-97)	< 0.001
	Arg-Asp	102 (88-116)	92 (84-101)	75 (67-83)	73 (66-80)	
Threonine	Placebo	150 (129-171)	126 (108-145)	111 (97-126)	106 (96-116)	< 0.001
	Arg-Asp	113 (97-129)	102 (93-111)	85 (78-92)	84 (77-91)	
Tyrosine	Placebo	86 (80-91)	102 (95-110)	97 (90-104)	87 (81-93)	< 0.001
	Arg-Asp	75 (69-82)	96 (88-103)	92 (87-97)	78 (74-83)	
Valine	Placebo	228 (212-244)	212 (197-227)	201 (187-214)	196 (184-204)	0.12
	Arg-Asp	216 (194-238)	207 (190-224)	186 (175-198)	195 (180-209)	
Sum of analyzed amino acids	Placebo	3170 (2967-3374)	2753 (2519-2986)	2413 (2202-2625)	2302 (2133-2472)	< 0.05
	Arg-Asp	2938 (2624-3251)	2636 (2474-2798)	2237 (2112-2363)	2095 (2000-2190)	
Taurine	Placebo	49 (42-55)	69 (58-80)	71 (60-82)	56 (51-62)	0.75
	Arg-Asp	56 (41-71)	70 (61-80)	67 (58-76)	56 (49-64)	

All values are presented in $\mu mol \cdot L^{-1}$. For further explanations see footnote to Table 1

Arginine is a potent stimulator of glucagon secretion at rest as well as during exercise (22). Glucagon in turn stimulates gluconeogenesis in the liver by increasing the uptake of gluconeogenetic precursors into the liver. This could explain the reduction of the plasma level of some, but not all, amino acids. An increased plasma glucagon level promotes the hepatic glucose output and should consequently enhance the glucose availability to the muscles. However, this did not impact on the measured plasma carbohydrate and fat metabolites as well as on insulin and the RER since they were unaffected by the supplementation.

The increase in the plasma STH level with the arginine aspartate supplementation was particularly clear after 31 km (+ 40 %). The levels were, however, very similar with both treatments before the start and two hours after the run although circulating arginine was markedly elevated at these time points. An explanation for this is not evi-

Table 3 Time course of plasma hormone levels of the arginine aspartate (=Arg-Asp) and placebo treatment, respectively

Parameter	Treatment	T1	T2	T3	T4	p-value
Insulin	Placebo	12.4 (9.5-15.3)	6.8 (4.6-9.0)	4.4 (3.3-5.5)	5.0 (3.8-6.2)	0.63
$\mu Um \cdot L^{-1}$	Arg-Asp	11.5 (7.9-15.1)	6.2 (4.4-8.1)	4.4 (3.5-5.4)	4.8 (4.0-5.5)	
Glucagon	Placebo	106 (88-124)	140 (126-154)	179 (150-209)	126 (105-148)	< 0.05
$ng \cdot L^{-1}$	Arg-Asp	122 (107-137)	154 (132-176)	185 (160-209)	145 (122-169)	
STH	Placebo	1.3 (0.2-2.4)	5.5 (4.0-7.0)	9.8 (7.7-11.9)	1.7 (1.1-2.3)	< 0.05
$\mu U \cdot mL^{-1}$	Arg-Asp	1.4 (0.2-2.5)	7.7 (5.9-9.5)	10.6 (8.1-13.0)	2.0 (1.2-2.8)	
Cortisol	Placebo	459 (375-544)	817 (708-926)	1045 (927-1164)	772 (641-903)	0.27
$nmol \cdot L^{-1}$	Arg-Asp	466 (392-541)	850 (723-977)	1101 (994-1208)	839 (696-981)	

For explanations see footnote to Table 1

dent. Exercise itself is a very potent stimulator of STH secretion (21). Intense exercise induces a peak STH serum level that is nearly three times the level observed after an arginine infusion of 0.5 $g \cdot kg^{-1}$ body mass in humans (21). The combination of exercise with the ingestion of a nutritive STH stimulator in our study elevated the exercise STH level more than exercise alone. Although the mechanism of an exercise-induced STH increase is not exactly known (13), there are some ideas about its metabolic effects. STH stimulates lipolysis in adipose tissue and reduces protein and glucose metabolism by shifting the oxidative metabolism towards fatty acid utilization (13). This could theoretically spare glycogen. But, nevertheless, we did not observe any shift in RER or circulating carbohydrate and fat metabolites. The significantly higher STH level with the arginine aspartate treatment might, therefore, not be physiologically relevant concerning fat and carbohydrate metabolism.

Another theoretically positive aspect of an STH increase during exercise is its possible effect on the immediate recovery period after the exercise session. STH could promote protein synthesis and reduce protein breakdown by its anabolic properties (2), but this is speculative and we did not measure protein turnover in this field study.

It should be mentioned that the STH increase with the arginine aspartate supplementation was individually variable. Some athletes had a strongly increased circulating STH level during the latter stage of the marathon, while others had very similar STH level with both treatments (results not shown). This is in line with a very recent observation that an oral intake of arginine at rest induced a strong increase of circulating STH in the subsequent four hours in some subjects, but nearly no change of the baseline STH level was observed in other subjects (16).

The running time with both treatments was almost identical. The observed metabolic changes with the supplementation treatment had, therefore, no measurable ergogenic effect. This is in contrast to a previous study in which an improvement of the endurance capacity was found after a three-week-long supplementation with 3 g of arginine aspartate (20). Unfortunately, no crossover design was applied in that study. The improvement of the endurance capacity could, therefore, have been caused by the regular exercise which was probably continued during the supplementation period. This is underlined by the observed metabolic changes during an endurance exercise test performed after the supplementation (lower lactate and urea level, more constant glucose and insulin level compared to the same test before the supplementation).

An effect of arginine aspartate on the exercise-induced hyperammonemia has been described previously (4). After a ten-day-long supplementation with 20 g of arginine aspartate a slightly, but significantly reduced increase in the plasma ammonia level was observed after 15 min of a cycle ergometer exercise at 80 % VO_2 max, but not at 30 and 45 min of the exercise test. The authors considered this difference too small to be due to a consistent biological effect. In our study, we did not observe a treatment effect on the plasma ammonia level.

For the first time we have reported the general metabolic impact and plasma amino acid response of an arginine aspartate supplementation during an endurance exercise bout. Since there was no obvious metabolic benefit derived from the supplementation, and since it is not known how the observed reduction of the plasma amino acids affects the amino acid metabolism, the practice of using single amino acid supplements as potential ergogenics should be critically reevaluated.

Acknowledgment We thank Anthony Moses for the analyses of the metabolites.

References

1. Ahlborg B, Ekelund LG, Nilsson CC (1968) Effect of potassium-magnesium-aspartate on the capacity for prolonged exercise in man. Acta Physiol Scand 74: 238–245
2. Aron DC, Findling JW, Tyrell JB (1997) Hypothalamus and Pituitary. In: Greenspan FS, Strewler GJ (eds) Basic and Clinical Endocrinology. Prentice-Hall International, London, pp 95–156
3. Banister EW, Cameron BJ (1990) Exercise-induced hyperammonemia: peripheral and central effects. Int J Sports Med 11 Suppl 2: S129–S142
4. Denis C, Dormois D, Linossier MT, Eychenne JL, Hauseux P, Lacour JR (1991) Effect of arginine aspartate on the exercise-induced hyperammoniemia in humans: a two periods cross-over trial. Arch Int Physiol Biochim Biophys 99: 123–127
5. Harper AE (1964) Amino acid toxicities and imbalances. In: Munro HN, Allison JB (eds) Mammalian protein metabolism (Volume II). Academic Press, New York, pp 87–134
6. Harper AE, Rogers QR (1965) Amino acid imbalance. Proc Nutr Soc 24: 173–190
7. Heinrichs W, Fauth U, Seufert W, Halmagyi M (1987) Auswirkung einer durch L-Lysin ausgelösten Aminosäuren-Imbalanz auf die Stickstoffbilanz bei vollständig parenteral ernährten Patienten. Infusionsther Klin Ernahr 14: 252–255
8. Jackson AA (1999) Limits of adaptation to high dietary protein intakes. Eur J Clin Nutr 53 Suppl 1: S44–S52
9. Kreider RB, Miriel V, Bertun E (1993) Amino acid supplementation and exercise performance. Analysis of the proposed ergogenic value. Sports Med 16: 190–209
10. Kubota T, Imaizumi T, Oyama J, Ando S, Takeshita A (1997) L-arginine increases exercise-induced vasodilation of the forearm in patients with heart failure. Jpn Circ J 61: 471–480
11. Lancha AH, Recco MB, Abdalla DSP, Curi R (1995) Effect of aspartate, asparagine, and carnitine supplementation in the diet on metabolism of skeletal muscle during a moderate exercise. Physiol Behav 57: 367–371
12. Lancha AH, Santos MF, Palanch AC, Curi R (1997) Supplementation of aspartate, asparagine and carnitine in the diet causes marked changes in the ultrastructure of soleus muscle. J Submicr Cytol Path 29: 405–408
13. Macintyre JG (1987) Growth hormone and athletes. Sports Med 4: 129–142
14. MacLean DA, Graham TE, Saltin B (1996) Stimulation of muscle ammonia production during exercise following branched chain amino acid supplementation in humans. J Physiol Lon 493: 902–922
15. Maughan RJ, Sadler DJ (1983) The effects of oral administration of salts of aspartic acid on the metabolic response to prolonged exhausting exercise in man. Int J Sports Med 4: 119–123
16. Moore TA, Switzer BR, McMurray RG, Hall JE (1998) Growth hormone response to oral arginine supplementation. Med Sci Sports Exerc 30: S18 (abstract)
17. Morris SMJ (1992) Regulation of enzymes of urea and arginine synthesis. Annu Rev Nutr 12: 81–101
18. (1988) Amino acid imbalance in the pig. Nutr Rev 46: 360–363
19. Rector TS, Bank AJ, Mullen KA, Tschumperlin LK, Sih R, Pillai K, Kubo SH (1996) Randomized, double-blind, placebo-controlled study of supplemental oral L-arginine in patients with heart failure. Circulation 93: 2135–2141
20. Schmid P, Gleispach H, Wolf W, Pessenhofer H, Schwaberger G (1980) Leistungsbeeinflussung und Stoffwechselveränderungen während Langzeitbelastung unter Argininaspartat. Leistungssport 10: 486–495
21. Sutton J, Lazarus L (1976) Growth hormone in exercise: comparison of physiological and pharmacological stimuli. J Appl Physiol 41: 523–527
22. Trabelsi F, Lavoie JM (1996) Arginine induced pancreatic hormone secretion during exercise in rats. J Appl Physiol 81: 2528–2533
23. Tuttle JL, Potteiger JA, Evans BW, Ozmun JC (1995) Effect of acute potassium-magnesium aspartate supplementation on ammonia concentrations during and after resistance training. Int J Sport Nutr 5: 102–109