Research article

Is the pattern of dietary amino acids intake associated with serum lipid profile and blood pressure among individuals with spinal cord injury?

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Objective: The probable effect of dietary amino acids intake pattern on serum lipid profile and blood pressure (BP) have not yet been described among individuals with spinal cord injury (SCI).

Design: Cross-sectional.

Setting: Tertiary rehabilitation center.

Participants: People with SCI referred to Brain and Spinal Cord Injury Research Center between 2011 and 2014.

Outcome measures: Dietary intakes were assessed by recording consumed foods by 24-hour dietary recall interviews using Nutritionist IV 3.5.3 modified for Iranian foods. Partial correlation test with adjustment for age, weight, body mass index, total energy intake, total fat, cholesterol and carbohydrate intake, and injury-related variables was used.

Results: Dietary intake of lysine was positively related to levels of fasting plasma glucose (FPG), triglyceride (TG), systolic blood pressure (SBP) and diastolic blood pressure (DBP) ($P < 0.0001$, 0.046 , 0.002 and 0.009 , respectively). There was a positive significant relationship between the intake of cysteine and levels of TG and SBP as well ($P : 0.027$ and 0.048 , respectively). Higher intakes of threonine and leucine had a negative relationship with TG level ($P : 0.001$ and 0.026 , respectively). Furthermore, tyrosine, threonine and leucine were inversely correlated to blood pressure. Total cholesterol level was only related to intake of threonine and leucine ($P : 0.004$ and 0.012 , respectively). FPG was positively associated with intake of all amino acids except for cysteine, glutamic acid, threonine, leucine and histidine.

Conclusion: In the present study, the pattern of relationships between dietary intake of amino acids and serum lipid profile and BP has been described among people with SCI.

Keywords: Amino acids, Triglyceride, Cholesterol, Spinal cord injury

Introduction

Evidence supports the less cholesterolemic and atherogenic effect of vegetable-derived proteins.^{1,2} The influence of dietary protein intake on development of hypercholesterolemia has been investigated so far.^{1,2} However, it has not yet been fully described which amino acids intake is

related to changes in serum lipid profile. In this regard, Ma *et al.*³ has demonstrated that vegetable protein diet with low Lys:Arg ratio may have a favorable effect on serum total cholesterol and low-density lipoprotein cholesterol (LDL-C). On the other hand, Bel-Serrat *et al.*⁴ showed that the association between amino acids intakes and serum lipid profile is influenced by dietary fat intake and therefore, the relationship between dietary amino acids and serum lipid profile remains insignificant when

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dietary fat are considered. The correlation between protein intake and serum lipids has been mostly investigated among patients with hypercholesterolemia.³ Up to now, there is no study illustrating association between amino acids dietary intake and lipid profile among individuals with spinal cord injury (SCI). Furthermore, adverse effects of SCI on serum lipoprotein profiles have been demonstrated,⁵⁻⁷ which shows that people with SCI have potential susceptibility toward hyperlipidemia and dyslipidemia. Thus, it is clinically essential to identify the dietary components which may contribute to dyslipidemia among individuals with SCI. Identification of these component may help clinicians to plan proper dietary modifications for those who are susceptible to hyperlipidemia. Moreover, classification of patients according to the priority of necessity of dietary interventions can be facilitated.

It has been shown that vegetable proteins have a lower Lysin (Lys) /Arginine (Arg) and methionine (Met)/glycine (Gly) ratio than animal proteins and subsequently, increased total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) has been found among animal models fed with diets with high Lys/Arg ratio.⁸⁻¹⁰ Some studies also have indicated that the sulfur-containing amino acids, such as methionine and cysteine (Cys), are associated with hypercholesterolemia whereas, Gly was hypocholesterolemic.^{11,12} These studies are suggestive of existence of a probable relationship between dietary intakes of amino acids and circulatory level of lipids. However, studies on human subjects are so limited and the correlation between intake of amino acids and serum lipids remain unknown.

Furthermore, the association between dietary intake of amino acids and blood pressure still remains controversial.¹³ Previously, a positive association between histidine and systolic blood pressure (SBP) has been observed in both sexes.¹³ Moreover, higher diastolic blood pressure (DBP) with increased methionine intake has been reported in women.¹³ There are so limited studies which have investigated the relationship between dietary amino acids and blood pressure (BP) and most of these studies have recruited healthy people from general population. Up to now, the effect of dietary intake of amino acids on BP remains unclear among people with SCI.

In the present investigation, we aimed to assess the relationships between dietary intakes of amino acids and serum lipid profile along with blood pressure among individuals with SCI.

Patients and Methods

Study Design and Population

In this observational investigation, the probable correlations between dietary intakes of amino acids and

serum lipid profile have been assessed in individuals with SCI. Participants were people with SCI who were referred to Brain and Spinal Cord Injury Research Center between 2011 and 2014. Individuals with SCI were invited to participate in the investigation based on the following inclusion criteria: traumatic spinal cord injury and post injury duration longer than 1 year. Depression has been shown to occur most frequently during the first year after SCI¹⁴ and therefore we only included those patients in stable phase of SCI with post injury duration longer than one year to avoid the bias effect of depression-induced dietary changes. Exclusion criteria were pregnancy, amputation, non-traumatic SCI etiology, history of other chronic medical conditions (e.g. diabetes, cancer, endocrinology disease, acute infection and etc.) and use of special medications such as glucocorticoid, hormones, thyroid hormones, anticonvulsive drugs, heparin, aluminum containing antacids, lithium, blood glucose reducing agents, atorvastatin, Gemfibrozil (serum lipid reducing medications), omega 3 fatty acids or other nutrients supplements. Patients on special prescribed diets were excluded as well. We also exclude those patients with history of smoking cigarettes, alcoholism and addiction to illegal drugs. Informed consents were obtained from each individual before enrollment. Participation was voluntarily. The protocol of the study was approved by ethics committee of Tehran University of Medical Sciences.

Measurements of dietary components

Dietary intakes were assessed by recording consumed foods by 24-hour dietary recall interviews with participants using Nutritionist IV 3.5.3. (N-Squared Computing, Salem, OR, USA) modified for Iranian foods.¹⁵ This software enables the user to analyze single foods, recipes, meals and complete diets for nutrient values. With this software, the dietary intakes extracted by 24-hour recall interviews can be analyzed for dietary components including protein, energy, fat and carbohydrate.

According to Frankenfield,¹⁶ individuals with SCI require daily protein intake of 1.5–2 gr/kg which is higher than recommended protein intake for healthy subjects. Adequate protein intake is essential to prevent pressure ulcers. In this regard, we defined protein intake ≤ 1.5 gr/kg as 'insufficient intake'. The percentage of individuals with protein intake insufficiency has been estimated. Furthermore, Cox *et al.*¹⁷ reported that people with SCI need daily energy intake of about 23 kcal/kg. The percentage of patients with

inadequate energy intake (below 23 kcal/kg/day) has been estimated in this study as well.

Clinical and Neurological Assessment

The age, sex, and time since injury were indexed in pre-prepared forms. Body weight was measured using a digital wheelchair scale, and body height was obtained measuring the supine length. Body mass index (BMI) was calculated as body weight (in kilograms) divided by height (in meters) squared. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured with appropriate tools as well. Since spinal cord-injured individuals (especially with high injury level) are susceptible to autonomic dysreflexia and may exhibit a broad spectrum of changes in blood pressure, therefore BP has been measured twice (with a time interval of at least 6 hours and maximum 24 hours) and the means of measured values have been entered for analysis.

The level of spinal cord injury was determined by magnetic resonance imaging and was confirmed a neurosurgeon. Completeness was classified as either complete (no preserved sensory or motor function) or incomplete (variable preserved motor function).^{18,19} American Spinal Cord Injury Association Scale (ASIA) was used to classify patients as follows: ASIA-A: complete injury; ASIA-B: incomplete injury with preserved sensory function; ASIA-C: preserved motor function in which more than half of key muscles below the neurological level have a muscle grade < 3; ASIA-D: preserved motor function in which at least half of key muscles below the neurological level have a muscle grade of ≥ 3 .

Laboratory measurements

Anticubital venous blood samples were taken from each patient and were centrifuged at 3000 rpm for 10 minutes at 4°C. Samples were sent to the Endocrinology and Metabolism Research Center (EMRC) laboratory for analysis and plasma concentrations of TC, LDL-C, high-density lipoprotein cholesterol (HDL-C), triglyceride (TG) and FBG were measured using Pars Azmon Kits.

Statistical analysis

All statistical analysis was performed using SPSS software version 21 (IBM Corp., Armonk, NY, USA). Categorical variables were described by numbers and percentages whereas mean $\pm$ standard deviation was used to describe continuous variables. Comparison of means between groups was used by t-test and one way analysis of variance (ANOVA) for data with normal distribution. Normality of distribution was tested with Kolmogorov-Smirnov test in different levels classified

base on sex, plagia (tetraplegia vs. paraplegia) and ASIA score. Results showed that all data were normally distributed except for cholesterol intake and aspartic acid intake. We used Pearson correlation test for those data with normal distribution and Spearman test for data which were not normally distributed. The correlation between continuous variables was assessed by partial correlation test with controlling for injury related confounders (time since injury, injury level, completeness and ASIA score) and demographic characteristics (age, sex and body mass index). $P < 0.05$ was considered statistically significant. Hierarchical multiple regression analysis was also performed to confirm findings detected by partial correlation analysis. In this analysis the first block was the intake of different amino acids and the second block included probable confounders. The dependent variables were serum lipids, FPG and blood pressure. Each of the dependent variables was analyzed separately (one at time). We performed a multicollinearity test to select confounders to be included in subsequent multiple regression models. The collinearity statistics showed high Variance Inflation Factor (VIF) for these variables: weight (VIF: 3.47), BMI (VIF: 3.5), total daily energy intake per kg (VIF: 30.95), carbohydrate (VIF: 13.90) and fat (VIF: 6.5). According to these results the multicollinearity was an issue and in order to avoid it we selected the following variables to be further entered in regression analysis model: Total energy intake (kcal) and BMI. Intake of fat and carbohydrate were components in determining total energy intake, therefore we selected total energy intake (per kcal) as a confounder. Weight was a component determining the BMI, therefore BMI was considered as a confounder. The regression analysis was performed with controlling for these confounders: age, sex, BMI, total energy intake and injury-related variables.

Results

A total of 265 patients with SCI participated in this investigation. The majority of participants were male (n: 217, 81.9%). Most subjects had paraplegia (n: 157, 59.2%). Mean age of participants was 36.25 ± 10.76 years old. Mean weight and BMI were 69.54 ± 13.83 kg and 23.58 ± 4.35 kg/m², respectively. The baseline characteristics of participants along with mean dietary intake of amino acids are summarized in Table 1. The highest intakes of amino acids were observed in essential amino-acids including lysine, valine, leucine, isoleucine, threonine, phenylalanine and methionine (4201.0 ± 1698.8 mg, 3397.94 ± 1307.63 mg, 3325.21 ± 1974.77 mg, 2900.0 ± 1119.8 mg, 1437.5 ± 876.33 mg,

Table 1 Baseline characteristics and mean intake of dietary amino acids among participants with spinal cord injury (n: 265)

Variable		Mean (SD)	Frequency (Percentage)
Age (year)		36.25 (10.76)	-
Sex	Male	-	217 (81.9)
	Female	-	48 (18.1)
Injury Completeness	Complete	-	132 (49.8)
	Incomplete	-	133 (50.2)
Plegia	Quadriplegia	-	108 (40.8)
	Paraplegia	-	157 (59.2)
Weight (kg)		69.54 (13.83)	-
BMI (kg/m ²)		23.58 (4.35)	-
Total energy intake (kcal)		1925.55 (657.17)	-
Carbohydrate intake (gr)		252.16 (99.76)	-
Total Protein intake (gr)		69.64 (25.61)	-
Fat intake (gr)		77.57 (35.10)	-
Cholesterol intake (mg)		239.55 (140.84)	-
Protein intake per kg body weight	≤ 1.5 gr/kg/day	-	230 (86.8)
	> 1.5 gr/kg/day	-	35 (13.2)
Energy intake per kg body weight	≤ 23 kcal/kg/day	-	94 (35.5)
	> 23 kcal/kg/day	-	171 (64.5)
Tryptophan (mg)		667.42 (262)	-
Isoleucine (mg)		2900.0 (1119.8)	-
Lysine (mg)		4201.0 (1698.8)	-
Cysteine (mg)		780.57 (297.17)	-
Tyrosine (mg)		2103.52 (811.13)	-
Arginine (mg)		231.77 (186.44)	-
Alanine (mg)		222.39 (167.70)	-
Glutamic acid (mg)		935.78 (576.87)	-
Threonine (mg)		1437.5 (876.33)	-
Leucine (mg)		3325.21 (1974.77)	-
Methionine (mg)		1366.42 (539.50)	-
Phenylalanine (mg)		2693.14 (1017.50)	-
Valine (mg)		3397.94 (1307.63)	-
Histidine (mg)		1625.93 (658.37)	-
Aspartic acid (mg)		377.58 (154.53)	-

BMI: Body Mass Index, SD: Standard Deviation

2693.14 ± 1017.50 mg and 1366.42 ± 539.50, respectively). The intakes of conditionally non-essential amino acids such as arginine and glutamic acid were lower (231.77 ± 186.44 mg and 935.78 ± 576.87 mg, respectively). The lowest dietary intake was detected by alanine intake, which is a non-essential amino acid (222.39 ± 167.70) (Table 1).

It is recommended that people with SCI consume 1.5–2 g/kg protein daily [16]. In our study the majority of patients had insufficient protein intake. Two hundred and thirty individuals (86.8%) had daily protein intake < 1.5 gr/kg and only 35 patients (13.2%) were consuming protein as recommended. Furthermore, according to Cox *et al.*,¹⁷ patients with SCI require approximately 23 kcal/kg/day. Our study showed that the majority of Iranian patients with SCI are receiving more daily calorie than the recommended amount. One hundred and seventy one (64.5%) had daily calorie intake higher than 23 kcal/kg (Table 1)

To determine the confounders that may influence serum lipid profile, the association between injury-related variables, demographic characteristics and total

intake of energy, carbohydrate and fat, and serum lipid profile was assessed. Our results showed that women had significantly higher HDL-C ($P < 0.0001$) whereas the levels of TG and TC were higher among men (0.015 and 0.002, respectively). People with complete SCI had significantly higher systolic and diastolic blood pressure ($P < 0.0001$ for both). On the other hand, TG was higher among individuals with incomplete injury (0.016). Furthermore, TG and blood pressure (BP) were significantly higher among people with quadriplegia ($P : 0.035$ and $P < 0.0001$ for TG and BP, respectively) whereas higher levels of HDL were detected among individuals with paraplegia ($P : 0.004$). Age was positively related to TC and LDL-C ($P : 0.015$, $r = 0.14$ and $P < 0.0001$, $r = 0.28$, respectively). Similarly, the association between older ages and higher blood pressure was significant ($P < 0.0001$, $r = 0.22$ and $P < 0.0001$, $r = 0.21$ for SBP and DBP, respectively). Weight was positively correlated with TG, TC and LDL-C ($P < 0.0001$ for all, $r = 0.29$, 0.33 and 0.24, respectively). Similarly, higher BMI was associated with higher concentrations of TG, TC and

LDL-C (P : 0.002, r = 0.19 for TG; P < 0.0001, r = 0.31 and 0.26 for TC and LDL-C, respectively). On the other hand, weight and BMI were negatively related to HDL-C (P < 0.0001, r = -0.38 and P : 0.002, r = -0.19) (Table 2).

Higher blood pressure was observed among participants with higher total energy intake (P : 0.002, r = 0.20 and P : 0.001, r = 0.22 for SBP and DBP, respectively). Similarly, higher carbohydrate and cholesterol intake were associated with higher BP (Table 2). On The next step of analysis, the correlation between dietary intake of amino acids and serum lipid profile and BP were assessed with controlling for these confounders (age, weight, sex, completeness of injury, plegia, total intake of energy, fat, carbohydrate and cholesterol).

Higher tryptophan intake was associated with higher FPG and lower SBP (P : 0.014, r = 0.16 and P : 0.030, r = -0.14, respectively). Higher intake of isoleucine was associated to higher levels of FPG, TG and blood pressure (P : 0.007, 0.014, 0.012 and 0.040 for FPG, TG, SBP and DBP, respectively). Similarly, dietary intake of lysine was positively related to levels of FPG, TG, SBP and DBP (P < 0.0001, 0.046, 0.002 and 0.009, respectively). There was a positive significant relationship between the intake of cysteine and levels of TG and SBP as well (P : 0.027, r = 0.14 and P : 0.048, r = 0.13, respectively). Table 3 illustrates the pattern of relationships between amino acids intake and lipid profile. Higher intakes of arginine and alanine were also associated with higher FPG and blood pressure (Table 3). There was no relationship between dietary intake of glutamic acid and serum lipid profile whereas the correlation between intake of glutamic acid and blood pressure was significant (P : 0.007, r = 0.18 and P : 0.006, r = 0.18 for SBP and DBP, respectively). Total cholesterol level was only related to intake of threonine and leucine (P : 0.004, r = -0.19 and P : 0.012, r = -0.16, respectively). Higher intakes of threonine and leucine had a negative relationship with TG level (P : 0.001, r = -0.22 and P : 0.026, r = -0.14, respectively). Furthermore, tyrosine, threonine and leucine had blood pressure reducing effect (Table 3). Threonine was associated with increased level of HDL-C (P : 0.024, r = 0.15). These results are indicative of probable favorable effect of threonine on serum lipids, blood pressure and subsequently, risk of cardiovascular diseases. Methionine and valine were associated with increased FPG and blood pressure (Table 3). Histidine intake was not related to circulatory lipids but it had a blood pressure reducing effect. Similarly, no relationship between

lysine/arginine ratio and serum lipid profile could be detected but higher lysine/arginine ratio was associated with lower blood pressure (P : 0.009, r = -0.17 and P : 0.010, r = -0.17 for SBP and DBP, respectively). FPG was positively associated with intake of all amino acids except for Cysteine, Glutamic acid, Threonine, Leucine and Histidine.

Hierarchical regression analysis showed the similar pattern of dietary amino acids intake on serum lipid profile and blood pressure (Tables 4 and 5). The association between dietary intake of amino acids and FPG was not influenced by age, BMI, total energy intake and injury completeness which is in line with the insignificant effect of these factors on FPG illustrated in Table 2. Similarly, the effect of demographic and injury related-variables on serum lipids and BP in hierarchical regression was consistent with our previous analysis shown in Table 2. Tables 4 and 5 demonstrate the results of hierarchical regression analysis. R^2 for FPG, TG, TC, HDL-C, LDL-C, SBP and DBP were 0.33, 0.48, 0.20, 0.32, 0.16, 0.87 and 0.86, respectively). Adjusted R-squares were 0.25, 0.31, 0.12, 0.27, 0.10, 0.83 and 0.84 for FPG, TG, TC, HDL-C, LDL-C, SBP and DBP, respectively. The results show that the model of regression analysis of amino acids intake pattern is a stronger predictor of blood pressure among patients with SCI.

Discussion

Our results showed an inverse association between dietary intakes of threonine and leucine and TC. Previously, Bel-Serrat *et al.*⁴ investigated showed that dietary intakes of alanine, arginine, asparaginic acid, cysteine, glycine, histidine, lysine, threonine and valine (measured by two non-consecutive 24-h dietary recalls) were inversely associated with TC in women and with TG in men. However, Bel-Serrat *et al.*⁴ demonstrated that these correlations are vanished when dietary intakes of lipids are considered. In our study, we did not present data separately for both sexes but the analysis was performed with adjustment for sex and dietary fat intake. Our results revealed that intakes of isoleucine, lysine, cysteine, tyrosine, alanine, phenylalanine and aspartic acid are related to increased TG level even when analysis is adjusted for fat intake which conflicts with Bel-Serrat *et al.*⁴ report. One reason for this controversy can be traced back in the different recruited study population. Bel-Serrat *et al.*⁴ investigated healthy adolescent whereas we studied people with SCI who are known to be susceptible to metabolic syndrome^{20,21} and dyslipidemia.²²⁻²⁴ To our knowledge, this is the first study illustrating the association between dietary

Table 2 The effect of confounder (injury-related variables, dietary fat and carbohydrate intake) on serum lipid profile and blood pressure among people with spinal cord injury

Variables	FPG	TG	TC	HDL-C	LDL-C	SBP	DBP
Sex	0.36	0.015#	0.002#	<0.0001#	0.64	0.95	0.93
Injury completeness	0.39	0.016^	0.06	0.53	0.69	<0.0001^~	<0.0001^~
Plegia	0.69	0.035¥	0.58	0.004¥	0.56	<0.0001¥	<0.0001¥
Age	0.66	0.38	0.015 (r = 0.14)	0.09	<0.0001 (r = 0.28)	<0.0001 (r = 0.22)	<0.0001 (0.21)
Weight	0.16	<0.0001 (r = 0.29)	<0.0001 (r = 0.33)	<0.0001 (r = -0.38)	<0.0001 (r = 0.24)	0.35	0.32
BMI	0.38	0.002 (r = 0.19)	<0.0001 (r = 0.31)	0.002 (r = -0.19)	<0.0001 (r = 0.26)	0.50	0.56
Total energy intake (kcal)	0.28	0.06	0.88	0.34	0.21	0.002 (r = 0.20)	0.001 (r = 0.22)
Carbohydrate intake	0.25	0.018 (r = 0.14)	0.76	0.10	0.52	0.002 (r = 0.20)	<0.0001 (r = 0.23)
Cholesterol intake	0.06	0.73	0.48	0.053	0.25	<0.0001 (r = 0.27)	<0.0001 (0.26)
Fat intake	0.57	0.97	0.37	0.83	0.023 (r = 0.14)	0.002 (r = 0.20)	0.001 (r = 0.21)

Illustrated numbers indicate P-values which stand for comparison of means with one-way analysis of variance between categorical subgroups or correlation analysis between continuous variables.

BMI: Body Mass Index, DBP: Diastolic blood pressure; FPG: Fasting plasma glucose, HDL-C: High density lipoprotein-cholesterol; LDL-C: Low density lipoprotein-cholesterol; TC: Total cholesterol; TG: triglyceride.

TG and cholesterol were significantly higher among men whereas women had higher levels of HDL-C.

^TG was higher among people with incomplete spinal cord injury.

~Systolic and diastolic blood pressures were higher among people with complete spinal cord injury.

¥ TG and blood pressure were significantly higher among people with quadriplegia whereas higher levels of HDL were detected among paraplegics.

Table 3 The association between dietary amino acids intake and serum lipid profile and blood pressure after adjustment for confounders (age, gender, BMI, injury completeness, plegia type, dietary intake of total energy)

Amino Acid	FPG	TG	TC	HDL-C	LDL-C	SBP	DBP
Tryptophan	0.014* (r = 0.16)	0.10	0.57	0.24	0.82	0.030* (r = -0.14)	0.092
Isoleucine	0.007** (r = 0.17)	0.014* (r = 0.16)	0.77	0.18	0.97	0.012* (r = 0.16)	0.040* (r = 0.13)
Lysine	<0.0001** (r = 0.26)	0.046* (r = 0.13)	0.41	0.26	0.65	0.002** (r = 0.20)	0.009** (r = 0.17)
Cysteine	0.11	0.027* (r = 0.14)	0.66	0.08	0.45	0.048* (r = 0.13)	0.13
Tyrosine	0.003** (r = 0.19)	0.041* (r = 0.13)	0.84	0.23	0.86	<0.0001** (r = -0.23)	0.003** (r = -0.20)
Arginine	0.010* (r = 0.17)	0.07	0.23	0.91	0.70	<0.0001** (r = 0.28)	<0.0001** (r = 0.28)
Alanine	0.008** (r = 0.17)	0.041* (r = 0.13)	0.25	0.72	0.65	<0.0001** (r = 0.30)	<0.0001** (r = 0.31)
Glutamic acid	0.08	0.13	0.28	0.75	0.84	0.007** (r = 0.18)	0.006** (r = 0.18)
Threonine	0.068	0.001** (r = -0.22)	0.004** (r = -0.19)	0.024* (r = 0.15)	0.25	<0.0001** (r = -0.85)	<0.0001** (r = -0.84)
Leucine	0.72	0.026* (r = -0.14)	0.012* (r = -0.16)	0.10	0.32	<0.0001** (r = -0.68)	<0.0001** (r = -0.69)
Methionine	<0.0001** (r = 0.26)	0.07	0.43	0.12	0.77	0.001** (r = 0.22)	0.004** (r = 0.18)
Phenylalanine	0.021* (r = 0.15)	0.024* (r = 0.15)	0.85	0.14	0.73	0.004** (r = 0.19)	0.015* (r = 0.16)
Valine	0.007** (r = 0.17)	0.051	0.92	0.18	0.77	0.003** (r = 0.19)	0.012** (r = 0.16)
Histidine	0.15	0.70	0.95	0.07	0.61	<0.0001** (r = -0.31)	<0.0001** (r = -0.32)
Aspartic acid	0.010* (r = 0.17)	0.045* (r = 0.13)	0.29	0.98	0.50	0.001** (r = 0.22)	0.001** (r = 0.21)
Lysine/Arginine Ratio	0.074	0.50	0.55	0.09	0.07	0.009** (r = -0.17)	0.010* (r = -0.17)

Numbers indicate P-values which stand for partial correlation analysis with controlling for probable confounders.

DBP: Diastolic blood pressure; FPG: Fasting plasma glucose, HDL-C: High density lipoprotein-cholesterol; LDL-C: Low density lipoprotein-cholesterol; TC: Total cholesterol; TG: triglyceride.

* Significance at level of $P < 0.05$.

** Significance at level of $P < 0.01$.

Table 4 Hierarchical regression analysis evaluating the relationships between dietary intake of amino acids and fasting plasma glucose and blood pressure

	Fasting Plasma Glucose						Systolic blood pressure						Diastolic Blood Pressure					
	B	β	t	P	R ²	Adj R ²	B	β	t	P	R ²	Adj R ²	B	β	t	P	R ²	Adj R ²
Step 1	-	-	-	-	0.56	0.41	-	-	-	-	0.88	0.80	-	-	-	-	0.90	0.85
Tryptophan	0.12	0.24	0.35	0.041	-	-	-0.34	-0.23	-1.04	0.032	-	-	-0.05	-0.02	-0.65	0.870	-	-
Isoleucine	0.28	0.60	0.76	0.025	-	-	0.77	0.98	1.08	0.001	-	-	0.62	0.99	1.61	0.021	-	-
Lysine	0.19	0.58	0.98	0.046	-	-	0.20	0.23	0.97	0.033	-	-	0.81	0.64	1.42	0.001	-	-
Cysteine	-0.031	-0.42	-0.82	0.982	-	-	0.13	0.11	0.83	0.042	-	-	-0.09	-0.01	-0.43	0.455	-	-
Tyrosine	0.67	0.75	1.01	0.010	-	-	-0.64	-0.87	-1.23	0.002	-	-	-0.16	-0.68	-0.87	0.003	-	-
Arginine	0.08	0.11	0.73	0.031	-	-	0.32	0.88	1.18	0.005	-	-	0.20	0.33	0.98	0.044	-	-
Alanine	0.20	0.34	0.99	0.034	-	-	0.11	0.42	0.91	0.043	-	-	0.11	0.23	0.76	0.039	-	-
Glutamic acid	-0.011	-0.38	-0.54	0.653	-	-	0.41	0.55	0.73	0.038	-	-	0.43	0.59	0.89	0.008	-	-
Threonine	-0.002	-0.08	-0.66	0.787	-	-	-0.67	-0.98	-1.66	0.008	-	-	-0.41	-0.82	-1.65	0.011	-	-
Leucine	-0.003	-0.19	-0.34	0.478	-	-	-0.75	-1.02	-1.98	0.011	-	-	-0.49	-0.98	-1.73	0.004	-	-
Methionine	0.55	0.86	1.08	0.034	-	-	0.67	0.78	1.07	0.006	-	-	0.70	0.89	1.19	0.032	-	-
Phenylalanine	0.39	0.59	0.97	0.049	-	-	0.02	0.12	0.88	0.039	-	-	0.73	0.93	1.87	0.001	-	-
Valine	0.18	0.02	0.43	0.040	-	-	0.08	0.23	0.67	0.041	-	-	0.47	0.64	1.64	0.028	-	-
Histidine	-0.017	-0.30	-0.90	0.872	-	-	-0.19	-0.79	-0.99	0.048	-	-	-0.39	-0.66	-1.23	0.003	-	-
Aspartic acid	0.27	0.24	0.67	0.019	-	-	0.53	0.65	1.50	0.036	-	-	0.28	0.79	1.03	0.006	-	-
Step 2	-	-	-	-	0.33	0.25	-	-	-	-	0.87	0.83	-	-	-	-	0.86	0.84
Tryptophan	0.24	0.03	0.49	0.034	-	-	-0.13	-0.32	-1.00	0.041	-	-	-0.16	-0.34	-0.64	0.542	-	-
Isoleucine	0.33	0.69	1.02	0.021	-	-	0.56	1.17	1.66	0.004	-	-	0.84	1.19	1.68	0.005	-	-
Lysine	0.56	0.68	0.98	0.047	-	-	0.80	1.54	1.89	0.001	-	-	0.21	0.40	1.34	0.009	-	-
Cysteine	-0.009	-0.21	-0.35	0.761	-	-	0.42	0.55	0.81	0.048	-	-	-0.09	-0.12	-0.40	0.681	-	-
Tyrosine	0.88	0.73	0.83	0.011	-	-	-0.33	-0.99	-1.38	0.001	-	-	-0.13	-0.46	-0.79	0.019	-	-
Arginine	0.08	0.09	0.21	0.027	-	-	0.55	0.77	1.21	0.004	-	-	0.28	0.67	0.92	0.017	-	-
Alanine	0.72	0.22	0.86	0.046	-	-	0.32	0.68	1.38	0.026	-	-	0.31	0.66	0.79	0.040	-	-
Glutamic acid	-0.025	-0.15	-0.33	0.937	-	-	0.18	0.39	1.87	0.041	-	-	0.08	0.21	0.94	0.049	-	-
Threonine	-0.010	-0.02	-0.81	0.990	-	-	-0.74	-1.22	-1.98	0.005	-	-	-0.86	-1.09	-1.73	0.014	-	-
Leucine	-0.017	-0.21	-0.93	0.893	-	-	-0.69	-1.02	-2.02	0.008	-	-	-0.27	-0.58	-1.20	0.034	-	-
Methionine	0.95	0.98	1.09	0.021	-	-	0.17	0.23	0.89	0.023	-	-	0.32	0.40	1.88	0.022	-	-
Phenylalanine	0.23	0.61	0.99	0.042	-	-	0.15	0.25	0.66	0.018	-	-	0.78	0.88	1.50	0.019	-	-
Valine	0.15	0.08	0.25	0.037	-	-	0.09	0.20	0.90	0.038	-	-	0.36	0.76	1.99	0.002	-	-
Histidine	-0.054	-0.35	-0.40	0.601	-	-	-0.14	-0.89	-1.11	0.042	-	-	-0.65	-1.09	-2.31	0.011	-	-
Aspartic acid	0.22	0.26	0.76	0.037	-	-	0.23	0.78	1.31	0.045	-	-	0.90	1.31	1.76	0.008	-	-
Age	0.16	0.17	0.91	0.362	-	-	0.28	0.16	0.27	0.024	-	-	0.17	0.58	2.04	0.042	-	-
Energy Intake	-0.002	-0.049	-0.30	0.761	-	-	0.48	0.43	0.70	0.003	-	-	0.48	0.18	0.91	0.003	-	-
BMI	0.011	0.09	0.74	0.323	-	-	0.53	0.04	1.01	0.06	-	-	0.13	0.05	0.90	0.068	-	-
Completeness*	0.73	0.014	0.18	0.855	-	-	2.85	0.90	1.09	0.002	-	-	0.43	0.21	1.78	0.023	-	-
Plegia type	0.87	0.06	0.96	0.334	-	-	-3.85	-0.77	-2.94	0.004	-	-	0.87	1.20	1.89	0.001	-	-

Adj: Adjusted *Completeness indicates completeness of spinal cord injury.

Table 5 Hierarchical regression analysis evaluating the relationships between dietary intake of amino acids and plasma lipids

	Triglyceride					Total Cholesterol					Low-density lipoprotein					High-density lipoprotein				
	B	β	P	R ²	Adj R ²	B	β	P	R ²	Adj R ²	B	β	P	R ²	Adj R ²	B	β	P	R ²	Adj R ²
Step 1	-	-	-	0.59	0.42	-	-	-	0.26	0.15	-	-	-	0.19	0.09	-	-	-	0.48	0.31
Tryptophan	-0.80	-1.98	0.541	-	-	-0.001	-0.02	0.881	-	-	-0.002	-0.012	0.31	-	-	0.01	0.09	0.16	-	-
Isoleucine	0.98	2.68	0.002	-	-	0.07	0.98	0.083	-	-	0.13	0.65	0.08	-	-	-0.08	-0.19	0.05	-	-
Lysine	0.09	0.13	0.048	-	-	0.21	0.67	0.129	-	-	0.02	0.33	0.05	-	-	-0.001	-0.002	0.89	-	-
Cysteine	0.12	0.78	0.041	-	-	0.45	0.77	0.239	-	-	0.08	0.78	0.16	-	-	-0.09	-0.54	0.32	-	-
Tyrosine	0.02	0.18	0.037	-	-	0.01	0.04	0.768	-	-	0.43	0.68	0.09	-	-	0.18	0.65	0.45	-	-
Arginine	-0.88	-1.67	0.877	-	-	-0.04	-0.07	0.092	-	-	-0.08	-0.09	0.36	-	-	0.000	0.003	0.79	-	-
Alanine	0.87	0.93	0.031	-	-	0.14	0.33	0.190	-	-	0.14	0.32	0.48	-	-	-0.001	-0.09	0.23	-	-
Glutamic acid	0.13	0.19	0.770	-	-	-0.11	-0.16	0.663	-	-	0.06	0.08	0.69	-	-	0.09	0.10	0.38	-	-
Threonine	-0.32	-0.56	0.002	-	-	-0.63	-0.88	0.032	-	-	-0.30	-0.41	0.14	-	-	0.000	0.000	0.001	-	-
Leucine	-0.91	-1.38	0.008	-	-	-0.19	-0.91	0.017	-	-	0.16	0.66	0.98	-	-	0.34	0.67	0.77	-	-
Methionine	-0.80	-1.96	0.145	-	-	-0.08	-0.12	0.68	-	-	-0.10	-0.13	0.67	-	-	-0.18	-0.23	0.19	-	-
Phenylalanine	-0.75	-1.40	0.011	-	-	-0.17	-0.98	0.15	-	-	-0.13	-0.54	0.60	-	-	0.49	0.65	0.48	-	-
Valine	0.36	1.15	0.681	-	-	0.15	0.20	0.09	-	-	-0.001	-0.003	0.05	-	-	-0.23	-0.34	0.11	-	-
Histidine	0.09	1.98	0.237	-	-	0.021	0.38	0.27	-	-	-0.03	-0.16	0.29	-	-	0.20	0.44	0.21	-	-
Aspartic acid	0.97	2.14	0.009	-	-	-0.002	-0.11	0.35	-	-	0.008	0.09	0.44	-	-	-0.11	-0.29	0.69	-	-
Step 2	-	-	-	0.48	0.31	-	-	-	0.20	0.12	-	-	-	0.16	0.10	-	-	-	0.32	0.27
Tryptophan	-0.98	-1.21	0.608	-	-	-0.11	-0.14	0.75	-	-	-0.20	-0.33	0.46	-	-	0.007	0.10	0.81	-	-
Isoleucine	0.99	3.72	<0.0001	-	-	0.34	0.99	0.37	-	-	0.18	0.85	0.43	-	-	-0.33	-0.81	0.45	-	-
Lysine	0.01	0.02	0.031	-	-	0.18	0.57	0.54	-	-	0.16	0.96	0.13	-	-	-0.17	-0.35	0.69	-	-
Cysteine	0.55	0.90	0.043	-	-	0.20	0.29	0.69	-	-	0.18	0.66	0.22	-	-	-0.27	-0.42	0.56	-	-
Tyrosine	0.26	0.33	0.047	-	-	0.23	1.45	0.18	-	-	0.98	2.86	0.70	-	-	0.65	0.75	0.47	-	-
Arginine	-0.03	-1.49	0.275	-	-	-0.54	-0.68	0.33	-	-	-0.06	-0.85	0.21	-	-	0.87	1.05	0.12	-	-
Alanine	0.31	0.61	0.022	-	-	0.60	0.77	0.35	-	-	0.05	0.41	0.60	-	-	-0.83	-0.93	0.24	-	-
Glutamic acid	0.02	0.09	0.543	-	-	-0.003	-0.01	0.94	-	-	0.002	0.10	0.53	-	-	0.001	0.002	0.99	-	-
Threonine	-0.28	-0.37	0.006	-	-	-0.55	-0.63	0.001	-	-	-0.03	-1.29	0.24	-	-	0.90	1.09	0.002	-	-
Leucine	-0.85	-1.19	0.001	-	-	-0.38	-0.41	0.023	-	-	0.98	1.82	0.25	-	-	0.69	1.92	0.22	-	-
Methionine	-0.64	-1.33	0.071	-	-	-0.009	-0.60	0.45	-	-	-0.08	-0.75	0.06	-	-	-0.61	-0.79	0.30	-	-
Phenylalanine	0.62	2.87	0.033	-	-	-0.22	-2.03	0.28	-	-	-0.04	-2.46	0.15	-	-	0.14	0.21	0.90	-	-
Valine	0.50	0.70	0.526	-	-	0.31	0.39	0.74	-	-	-0.001	-0.002	0.99	-	-	-0.52	-0.63	0.58	-	-
Histidine	0.11	0.42	0.518	-	-	0.15	0.24	0.73	-	-	-0.13	-0.60	0.37	-	-	0.37	0.70	0.30	-	-
Aspartic acid	0.23	0.91	0.004	-	-	-0.004	-0.05	0.92	-	-	0.01	0.38	0.45	-	-	-0.009	-0.04	0.93	-	-
Age	0.89	0.57	0.002	-	-	0.38	0.51	0.048	-	-	0.56	0.22	0.001	-	-	0.053	0.054	0.42	-	-
Energy Intake	0.000	-0.006	0.96	-	-	0.021	0.18	0.24	-	-	-0.001	-0.02	0.89	-	-	-0.005	-0.006	0.97	-	-
BMI	2.04	1.17	0.006	-	-	4.34	3.74	<0.0001	-	-	1.10	0.18	0.003	-	-	-0.50	-0.22	0.001	-	-
completeness	3.91	0.38	0.048	-	-	-1.99	-0.06	0.36	-	-	1.21	0.06	0.36	-	-	1.34	0.11	0.10	-	-
Plegia type	-0.61	-0.06	0.044	-	-	-2.73	-0.14	0.43	-	-	-0.70	-0.01	0.83	-	-	1.84	0.92	0.048	-	-

Adj: Adjusted *Completeness indicates completeness of spinal cord injury.

amino acid intake and serum lipid profile and blood pressure among people with SCI.

It has been shown by Nordrum *et al.*²⁵ that cysteine increases digestibility of fat and starch. It can be concluded that the positive association between cysteine intake and TG is through increased digestibility of fat.

Previously, Altorf-van der Kuil *et al.*²⁶ reported that glutamic acid contributed the most to total protein intake, whereas lysine had the highest amount of dietary intake among our study population. Since lysine is an essential amino acid and it can also be found in many dietary sources,^{27,28} its highest dietary intake especially in Asian diets can be justified.

In our study, all of the assessed amino acids were positively related to systolic blood pressure except for tyrosine, threonine, leucine and histidine. In fact tyrosine, threonine, leucine and histidine had blood pressure reducing effect. Previously, higher intakes of tyrosine were related to lower systolic blood pressure²⁶ which is in line with our outcomes. Similar to our results, de Moraes *et al.*¹³ reported an inverse association between tyrosine intake and both SBP and DBP. These evidences, including our study, show that tyrosine may contribute to facilitate blood pressure reduction by dietary modifications. This is the first study that illustrates the blood-reducing effects of tyrosine among people with SCI. In this regard, Sved *et al.*²⁹ observed that the blood pressure reducing effect of tyrosine can be blocked by co-administering other large neutral amino acids that reduce tyrosine's uptake into the brain. It can be concluded that the mechanism through which tyrosine reduces blood pressure is an action functioning in central nervous system.

The reduction of blood pressure induced by tryptophan intake has been demonstrated by Feltkamp *et al.*³⁰ which is consistent with our observations. The mechanism behind this effect can probably be traced in the central serotonergic pathways. The role of 5-Hydroxytryptamine (5-HT; serotonin) in modifying blood pressure has been widely discussed.³¹ Here, we have concluded that dietary intake of tryptophan can be considered by administration of dietary modification in spinal cord-injured individuals with hypertension. de Moraes *et al.*¹³ showed a positive correlation between methionine intake and DBP. Here, we observed that methionine was positively related to both SBP and DBP. On the other hand, the positive association between histidine and SBP which was observed by de Moraes *et al.* was not approved in our investigation. Here we detected an inverse correlation between histidine and both SBP and DBP. One reason for this discrepancy can be non-adjusted analysis for dietary fat intake

in de Moraes study. Another reason can be due to differences in study population since we have investigated people with SCI whereas healthy population has been investigated in de Moraes study.

Amino acids are not only structural functions in proteins, but they also contribute to mediating metabolic pathways.³² There are many investigations that have tried to clarify the effect of dietary amino acids intake on obesity and insulin resistance^{33–35} to determine the impact of amino acid intake and subsequently dietary modification on risk of coronary vascular diseases. However, studies on the influence of amino acids intake on serum lipid profile and blood pressure are so scarce. This is the first study illustrating a pattern of relationships between dietary amino acids and lipid profile and BP among individuals with SCI.

It has been demonstrated that women have higher HDL-C and lower TG compared to men in general population.³⁶ In this study we have detected the same pattern among individuals with SCI. Sex differences of the lipid profile suggests sex as a confounder and further analysis was performed with proper adjustments.

Our study showed that FPG was positively associated with intake of all amino acids except for cysteine, glutamic acid, threonine, leucine and histidine. Previously, the ability of amino acids to increase plasma glucose had been reported by intravenous amino acids injections.³⁷ This study reveals that dietary intake of some kinds of amino acids also has the potential to increase FPG among people with SCI.

This study has also revealed that the majority of Iranian individuals with SCI receive inadequate protein intake. This high prevalence of protein intake insufficiency requires immediate attention since adequate protein intake is essential among people with SCI for prevention of pressure ulcers. Moreover, the majority of individuals were consuming energy more than the amount recommended. Unbalanced protein-energy diets may lead to unfavorable weight gain which is accompanied with increased risk of cardiovascular diseases.³⁸ This study illustrates the necessity for dietary modifications among Iranian individuals with SCI.

The strong power of this paper is the adjustment for various factors that are known to affect serum lipids and blood pressure. However, other risk factors for metabolic syndrome, which can be associated with dyslipidemia such as insulin resistance has not been assessed in the present investigation. One limitation of this study is that Apo lipoproteins have not been measured and further investigations are required to clarify the effect of dietary amino acids intake on Apo

lipoproteins. Another major concern that limits the power of this study is the dietary assessment method. Although 24-hour recall dietary measurements are commonly used, the precise effect of an amino acid on lipid profile and BP should be confirmed in clinical trials with dietary interventions.

Study Limitation

There are some concerns about the accuracy of 24-hour dietary recall so it is reasonable that the findings of this study be confirmed by further investigations with use of more reliable dietary measurement methods and also clinical trial with dietary interventions. The cross-sectional design of the study also cannot fully clarify the cause-effect relationships of the associations under investigation.

Conclusion

In the present study, the pattern of relationships between dietary intake of amino acids and serum lipid profile and blood pressure has been described among people with SCI. This investigation demonstrated that dietary intake of lysine was positively related to levels of fasting plasma glucose (FPG), triglyceride (TG), systolic blood pressure (SBP) and diastolic blood pressure (DBP). There was a positive significant relationship between the intake of cysteine and levels of TG and SBP as well. Higher intakes of threonine and leucine had a negative relationship with TG level. Furthermore, tyrosine, threonine and leucine had blood pressure reducing effect. Total cholesterol level was only related to intake of threonine and leucine. All of the assessed amino acids were positively related to systolic blood pressure except for tyrosine, threonine, leucine and histidine. FPG was positively associated with intake of all amino acids except for Cysteine, Glutamic acid, Threonine, Leucine and Histidine. Our study also showed the dominant insufficient intake of protein among Iranian individuals with SCI.

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Conflict of interest

None declared

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