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Original article

Effect of taurine supplementation on exercise capacity of patients with heart failure

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KEYWORDS
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Summary
Background: Taurine (2-aminoethanesulfonic acid) is a semi-essential amino acid found in mammalian tissues that is not involved in protein synthesis. The function of taurine is not completely understood. Some studies have demonstrated that taurine supplementation reduces death rate in rabbits with heart failure (HF) and diminishes HF severity in human models of congestive HF. In this study we have evaluated the effect of taurine supplementation on exercise capacity of patients with HF.
Methods: A randomized single-blind placebo-controlled clinical trial was conducted on 29 patients with HF with left ventricular ejection fraction (LVEF) less than 50% who were in functional class II or III according to New York Heart Association classification. A total of 15 patients received taurine supplementation 500 mg three times a day while the remaining 14 patients received placebo for 2 weeks. All patients performed exercise tolerance test before and after taurine and placebo supplementation.

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Results: The mean age of patients was 60.57 ± 6.54 years, they were mostly male (26 of 29), and had mean LVEF of 29.27 ± 6.97%. There were no significant differences in terms of LVEF, body mass index, and also exercise time, metabolic equivalents (METS) and exercise distance before supplementation. Exercise time, METS, and exercise distance increased significantly in patients who received taurine supplement for 2 weeks (p-value < 0.0001 for all), but did not increase significantly in patients who received placebo (p-values 0.379, 0.244, and 0.577 respectively).
Conclusion: Taurine supplementation in patients with HF who are taking standard medical treatment can increase their exercise capacity.

Background

Taurine (2-aminoethanesulfonic acid) is a semi-essential amino acid found in mammalian tissues that is not involved in protein synthesis and is the most abundant free amino acid in the heart, retina, skeletal muscle, brain, and leukocytes [1]. Taurine's function is not understood completely but some cellular osmoregulations are modulated by taurine [2,3]. It has been demonstrated in vitro in various species that low levels of taurine are associated with various pathological lesions, including cardiomyopathy [4].

Taurine has been used in experimental and clinical studies for treating several cardiovascular diseases including hypertension, hypercholesterolemia, atherosclerosis, cardiomyopathy, and congestive heart failure (CHF) [2,5—7].

In experimental CHF in dogs [8] and rabbits [9] increasing taurine levels in heart have been shown, as in left ventricular muscle of patients who had died of CHF [10].

Some studies have demonstrated that taurine supplementation reduces death rate in rabbits with heart failure (HF) [9] and diminishes HF severity in human models of CHF [11].

In this study we have evaluated the effect of taurine supplementation on exercise capacity of patients with HF.

Methods

A randomized single-blind placebo-controlled clinical trial approved by the ethics committee of Shahid Beheshti Medical University was executed in accordance with the Declaration of Helsinki in Loghman Hakim Hospital in Tehran, Iran in 2008. After obtaining their informed consents, 29 patients with HF due to coronary heart disease with left ventricle ejection fraction (LVEF) less than 50% who were in functional class II or III according to New York Heart Association (NYHA) classification were randomized to four groups (Table 1): seven patients who received taurine supplementation (Taurine capsule, Solgar, Leonia, NJ, USA) 500 mg three times a day for 2 weeks and performed exercise tolerance test (ETT) with Bruce protocol before and after taurine supplementation; eight patients received taurine and performed ETT with modified Bruce protocol; and six and eight patients received placebo (starch) and performed ETT with Bruce and modified Bruce protocols, respectively.

Drug history, electrocardiogram characteristics, heart rates (HR) and blood pressures (BP) of patients were recorded before ETT and then a 10-mL blood sample was taken for measuring taurine serum levels by high performance liquid chromatography (HPLC) method. In addition to the usual parameters of ETT, metabolic equivalents (METS) and distances patients had covered were recorded. After 2 weeks of supplementation, all of these parameters were measured again. We used chi-square tests (Fisher's exact test where applicable) for categorical variables and ANOVA and Tukey's tests for quantitative variables to analyze our data. A p-value less than 0.05 was considered statistically significant. SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used for all statistical tests.

Results

The patients had a mean age of 60.57 ± 6.54 (50—65 years) years, were mostly male (26 of 29) and had mean LVEF of 29.27 ± 6.97%. There were no significant differences in terms of LVEF, body mass index (BMI) and also exercise time, METS and exercise distance before supplementation (Table 2). Drug history regarding use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, aspirin, statins, diuretics, and nitrates before and after supplementation was not significantly different between groups with taurine supplement and placebo supplement (p-values were 0.876, 0.483, 0.33 0.483, 0.10, 0.191, and 1, respectively).

Exercise time, METS, and exercise distance in group 1 (taurine — Bruce) increased significantly (p-values were 0.022, 0.043, and 0.012, respectively).

In group 2 (taurine — modified Bruce) also, exercise time, METS, and exercise distance increased significantly (p-values were 0.000, 0.001, and 0.003, respectively).

Exercise time, METS, and exercise distance were increased significantly in all of 15 patients who received taurine supplement (group 1 + group 2) after 2 weeks (p-values < 0.0001 for all).

In group 3 (placebo — Bruce), exercise time, METS, and exercise distance did not increase significantly (p-values were 0.264, 0.057, and 0.099, respectively).

Exercise time and exercise distance did not increase significantly (p-values were 0.155 and 0.071, respectively) in group 4 (placebo — modified Bruce), but METS increased significantly (p-value = 0.029).

All of these parameters did not increase significantly in all of 14 patients (group 3 + group 4) who did not receive taurine supplementation (p-values were 0.379, 0.244, and 0.577) (Table 3).

Discussion

This study shows that taurine supplementation 500 mg three times a day in patients with HF in NYHA class II or III, who were on medical treatment, increased exercise time, METS,

Table 1 Patient randomization groups.

ETT protocol	Taurine supplement		Placebo		Total
	N	Group name	*N*	Group name	
Bruce	7	Taurine – Bruce (G1)	6	Placebo – Bruce (G3)	13
Modified Bruce	8	Taurine – M Bruce (G2)	8	Placebo – M Bruce (G4)	16
Total	15		14		29

ETT, exercise tolerance test.

Table 2 Patients' characteristics before taurine supplementation according to comparison of various groups.

Group Definition	G1 T-B	G3 P-B	*p*-value	G2 T-MB	G4 P-MB	*p*-value	G1 + G2 T-B + MB	G3 + G4 P-B + MB	*p*-value
n	7	6	–	8	8	–	15	14	–
Sex (M)	6	5	–	8	7	–	14	12	–
Age mean (years)	61.7 ± 6.4	60.4 ± 6.95	0.78	60.13 ± 5.36	61.13 ± 8.36	0.13	60.87 ± 5.72	60.26 ± 7.45	0.8
BMI (kg/m^2)	25.2 ± 3.4	22.9 ± 1.20	0.21	24.22 ± 1.05	24.23 ± 1.10	0.93	24.65 ± 2.43	23.65 ± 1.2	0.35
EF (%)	27.8 ± 8.1	31.4 ± 8.1	0.72	29.75 ± 4.97	28.13 ± 7.53	0.59	28.68 ± 6.43	29.66 ± 7.66	0.83
BP1 sys (mmHg)	121.4 ± 16	115.71 ± 11.34	0.36	106.25 ± 10.61	108.75 ± 15.53	0.53	113.33 ± 15.43	112.14 ± 14.23	0.45
BP1 dias (mmHg)	75.7 ± 12.7	68.57 ± 6.90	0.05	66.25 ± 7.44	65.00 ± 9.26	0.54	70.67 ± 10.99	66.43 ± 8.42	0.33
HR rest 1 (/min)	70.29 ± 9.29	70.86 ± 7.75	0.9	69.38 ± 11.76	68.25 ± 10.42	0.84	69.80 ± 10.31	69.47 ± 9.05	0.92
HR max 1 (/min)	124.7 ± 9.5	134.5 ± 32.66	0.83	117.50 ± 22.904	120.0 ± 22.297	0.76	120.87 ± 17.74	126.21 ± 27.08	0.01
Serum taurine 1 (μmol/l)	55.8 ± 19.1	49.0 ± 6.97	0.01	58.875 ± 19.63	44.125 ± 9.19	0.82	57.47 ± 18.7	46.21 ± 8.13	0.00
Ex time 1 (Min)	5.3 ± 2.1	5.485 ± 2.70	0.24	9.2075 ± 2.52	6.92 ± 2.06	0.55	7.32 ± 3.09	6.307 ± 2.37	0.15
METS1	4.991 ± 0.90	5.216 ± 1.13	0.34	7.525 ± 1.82	5.975 ± 1.62	0.51	6.342 ± 1.93	5.650 ± 1.43	0.10
Distance 1 (m)	458.57 ± 209.27	488.166 ± 231.72	0.64	729.0 ± 178.24	516.5 ± 198.93	0.75	602.8 ± 232.71	504.357 ± 205.36	0.9

T, taurine; B, Bruce protocol; P, placebo; MB, modified Bruce protocol; BMI, body mass index; EF, ejection fraction; BP blood pressure; sys, systolic; dias, diastolic; HR, heart rate; Ex, exercise; METS, metabolic equivalents; 1 = before supplementation.

Table 3 Patients' data before and after taurine supplementation.

Group Definition	G1 T-B	G2 T-MB	G1 + G2 T-B + MB	G3 P-B	G4 P-MB	G3 + G4 P-B + MB
n	7	8	15	6	8	14
Sex (M)	6	8	14	5	7	12
Age mean (years)	6.4 ± 61.7	60.13 ± 5.36	60.87 ± 5.72	60.4 ± 6.95	61.13 ± 8.36	60.26 ± 7.45
BMI (kg/m^2)	25.2 ± 3.4	24.22 ± 1.05	24.65 ± 2.43	22.9 ± 1.20	24.23 ± 1.10	23.65 ± 1.2
EF (%)	27.8 ± 8.1	29.75 ± 4.97	28.68 ± 6.43	31.4 ± 8.1	28.13 ± 7.53	29.66 ± 7.66
BP1 rest sys (mmHg)	16 ± 121.4	106.25 ± 10.61	113.33 ± 15.43	115.71 ± 11.34	108.75 ± 15.53	112.14 ± 14.23
BP2 rest systole (mmHg)	107.14 ± 12.54	106.25 ± 9.16	106.67 ± 10.47	123.33 ± 10.3	112.5 ± 8.87	117.14 ± 10.69
p-value	0.08	1.00	0.126	0.286	0.504	0.205
BP1 rest diastole (mmHg)	12.7 ± 75.7	66.25 ± 7.44	70.67 ± 10.99	68.57 ± 6.90	65.00 ± 9.26	66.43 ± 8.42
BP2 rest diastole (mmHg)	68.57 ± 6.90	68.75 ± 8.34	68.67 ± 7.43	76.67 ± 10.32	70.0 ± 5.34	72.86 ± 8.25
p-value	0.182	0.351	0.486	0.042	0.104	0.007
HR max 1 (/min)	124.7 ± 9.5	117.50 ± 22.90	120.87 ± 17.74	134.5 ± 32.66	120.0 ± 22.29	126.21 ± 27.08
HR max 2 (/min)	7.2 ± 125.8	118.13 ± 11.91	121.73 ± 10.45	128.0 ± 27.39	125.75 ± 14.95	126.71 ± 20.25
p-value	0.419	0.932	0.818	0.620	0.488	0.943
Serum taurine level 1 (μmol/l)	55.8 ± 19.1	58.875 ± 19.63	57.47 ± 18.74	49.0 ± 6.97	44.125 ± 9.19	46.21 ± 8.13
Serum taurine level 2 (μmol/l)	29.4 ± 136	140.50 ± 30.12	138.40 ± 28.84	65.83 ± 14.61	61.63 ± 30.29	63.43 ± 24.10
p-value	0.001	0.000	0.000	0.052	0.200	0.036
Ex time 1 (min)	2.1 ± 5.3	9.21 ± 2.52	7.32 ± 3.09	5.48 ± 2.70	6.92 ± 2.06	6.31 ± 2.37
Ex time 2 (min)	2.8 ± 8.7	12.39 ± 2.66	10.09 ± 3.74	4.83 ± 2.30	8.44 ± 3.64	6.89 ± 3.55
p-value	0.022	0.000	0.000	0.264	0.154	0.379
METS 1	4.99 ± 0.90	7.52 ± 1.82	6.34 ± 1.93	5.22 ± 1.13	5.97 ± 1.62	5.65 ± 1.43
METS 2	6.04 ± 1.45	9.75 ± 2.06	8.02 ± 2.58	4.67 ± 1.17	7.11 ± 2.49	6.06 ± 2.33
p-value	0.043	0.001	0.000	0.057	0.029	0.244
Distance 1 (m)	458.57 ± 209.27	729.0 ± 178.24	602.8 ± 232.71	488.166 ± 231.72	516.5 ± 198.93	504.357 ± 205.36
Distance 2 (m)	648.57 ± 278.22	941.125 ± 209.20	804.60 ± 279.07	417.666 ± 191.01	603.87 ± 198.93	524.071 ± 243.67
p-value	0.012	0.003	0.000	0.099	0.071	0.577

T, taurine; B, Bruce protocol; P, placebo; MB, modified Bruce protocol; BMI, body mass index; EF, ejection fraction; BP blood pressure; sys, systolic; dias, diastolic; HR, heart rate; Ex, exercise; METS, metabolic equivalents; 1 = before supplementation; 2 = after supplementation.

and exercise distance. Animal studies demonstrate that taurine supplementation prevents or slows HF development, reduces mortality, and hence improves survival [12—14].

However, in humans, there is paucity of data on assessment of taurine effects on HF. Azuma et al. showed that taurine supplementation with a dose of 2 g BID for 4 or 8 weeks in 24 patients with CHF improved their clinical situations and NYHA functional class [11]. In a double-blind crossover trial on 14 patients with CHF, Azuma et al. demonstrated that taurine supplementation for a 4-week period improved NYHA functional class, pulmonary crackles, and chest film abnormalities in comparison with placebo [15]. In another study Azuma et al. evaluated the effect of oral administration of taurine (3 g/day) and coenzyme Q10 (CoQ10) (30 mg/day) in 17 patients with CHF secondary to ischemic or idiopathic dilated cardiomyopathy with LVEF less than 50% and showed significant improvement in LV systolic function after 6 weeks [16].

The positive effects of taurine on LV function may be due to its regulatory role in intracellular Ca^{2+} homeostasis via its effect on voltage-dependent Ca^{2+} channels, by regulation of Na+ channels, and via Na—Ca exchange and Na(+)-taurine cotransport [17,18]. Hence taurine modulates intracellular Ca^{2+} levels. Taurine also has a potent antioxidant role that may contribute to its potential benefits in patients with HF [19]. The failing myocardium exhibits increased intracellular and mitochondrial calcium, which results in a decrease in myocardial energy production and an increase in oxidative stress [20]. Taurine has many other effects on the cardiovascular system including its beneficial impact on macrovascular endothelial function [21] that may have some speculative role in patients with HF.

To the best of our knowledge, our study is the first clinical trial that specifically assesses the effect of taurine supplementation on exercise capacity of patients with HF and is compatible with other studies that have shown a positive effect of taurine on patients with HF.

Limitations of this study include small size of the sample, single-blind study and lack of repetition of echocardiography after supplementation.

Conclusion

Taurine supplementation in patients with CHF who are taking standard medical treatment can increase their exercise capacity.

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References

[1] Schuller-Levis GB, Park E. Taurine: new implications for an old amino acid. FEMS Microbiol Lett 2003;226:195—202.

[2] Militante JD, Lombardiniab JB. Increased cardiac levels of taurine in cardiomyopathy: the paradoxical benefits of oral taurine treatment. Nutr Res 2001;21:93—102.

[3] McBroom JJ, Welty JD. Effects of taurine on heart calcium in the cardiomyopathic hamster. J Mol Cell Cardiol 1977;9:853—8.

[4] Eby G, Halcomb WW. Elimination of cardiac arrhythmias using oral taurine with L-arginine with case histories: hypothesis for nitric oxide stabilization of the sinus node. Med Hypotheses 2006;67:1200—4.

[5] Militante JD, Lombardini JB. Dietary taurine supplementation: hypolipidemic and antiatherogenic effects. Nutr Res 2004;24:787—801.

[6] Gompf RE. Nutritional and herbal therapies in the treatment of heart disease in cats and dogs. J Am Anim Hosp Assoc 2005;41:355—67.

[7] Militante JD, Lombardini JB. Treatment of hypertension with oral taurine: experimental and clinical studies. Amino Acids 2002;23:381—93.

[8] Peterson MB, Mead RJ, Welty JD. Free amino acids in congestive heart failure. J Mol Cell Cardiol 1973;5:139—47.

[9] Takihara K, Azuma J, Awata N, Ohta H, Hamaguchi T, Sawamura A, Tanaka Y, Kishimoto S, Sperelakis N. Beneficial effect of taurine in rabbits with chronic congestive heart failure. Am Heart J 1986;112:1278—84.

[10] Huxtable R, Bressler R. Taurine concentrations in congestive heart failure. Science 1974;184:1187—8.

[11] Azuma J, Hasegawa H, Sawamura A, Awata N, Ogura K, Harada H, Yamamura Y, Kishimoto S. Therapy of congestive heart failure with orally administered taurine. Clin Ther 1983;5:398—408.

[12] Azuma J, Takihara K, Awata N, Ohta H, Sawamura A, Harada H, Kishimoto S. Beneficial effect of taurine on congestive heart failure induced by chronic aortic regurgitation in rabbits. Res Commun Chem Pathol Pharmacol 1984;45:261—70.

[13] Orlova TR, Elizarova EP, Ryff IM, Fetisova NI, Mit'kina LI. Use of taurine in the treatment of experimental congestive heart failure. Kardiologiia 1991;31:77—80.

[14] Elizarova EP, Orlova TR, Medvedeva NV. Effects on heart membranes after taurine treatment in rabbits with congestive heart failure. Arzneimittelforschung 1993;43:308—12.

[15] Azuma J, Sawamura A, Awata N, Ohta H, Hamaguchi T, Harada H, Takihara K, Hasegawa H, Yamagami T, Ishiyama T, Iwata H, Kishimoto S. Therapeutic effect of taurine in congestive heart failure: a double-blind crossover trial. Clin Cardiol 1985;8:276—82.

[16] Azuma J, Sawamura A, Awata N. Usefulness of taurine in chronic congestive heart failure and its prospective application. Jpn Circ J 1992;56:95—9.

[17] Satoh H, Sperelakis N. Review of some actions of taurine on ion channels of cardiac muscle cells and others. Gen Pharmacol 1998;30:451—63.

[18] Soukoulis V, Dihu JB, Sole M, Anker SD, Cleland J, Fonarow GC, Metra M, Pasini E, Strzelczyk T, Taegtmeyer H, Gheorghiade M. Micronutrient deficiencies an unmet need in heart failure. J Am Coll Cardiol 2009;54:1660—73.

[19] Oudit GY, Trivieri MG, Khaper N, Husain T, Wilson GJ, Liu P, Sole MJ, Backx PH. Taurine supplementation reduces oxidative stress and improves cardiovascular function in an iron-overload murine model. Circulation 2004;109:1877—85.

[20] Allard ML, Jeejeebhoy KN, Sole MJ. The management of conditioned nutritional requirements in heart failure. Heart Fail Rev 2006;11:75—82.

[21] Fennessy FM, Moneley DS, Wang JH, Kelly CJ, Bouchier-Hayes DJ. Taurine and vitamin C modify monocyte and endothelial dysfunction in young smokers. Circulation 2003;107:410—5.