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Research Article

Effects of Barberry Capsules on Serum Zinc and Copper in Individuals with Metabolic Syndrome

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Abstract

Aim: In current study, we aimed to investigate the effects of barberry on serum copper (Cu), zinc (Zn) and superoxide dismutase (SOD) levels in subjects with MetS, because of it are the anti-inflammatory and antioxidant properties.

Methods: 106 Subjects were randomly assigned to 2 study groups: 1) A barberry group receiving capsules containing 600 mg barberry daily for 6 weeks (n=53); 2) Control group contained subjects taking one placebo capsule daily (n=53). Atomic absorption was used to measure serum zinc and copper. SOD activity was measured using a pyrogallol indirect spectrophotometric assay.

Results: The results showed that there was no significant difference in changes in serum zinc between the barberry and placebo groups (p=0.620). There were significant differences in changes in serum copper between the 2 study groups (p<0.001). Moreover, there were significant differences in Zn/Cu changes between the barberry and placebo groups (p=0.027). In addition, there were significant differences in changes in serum SOD1 between the study groups (p=0.077).

Conclusion: The results of the current study showed that barberry supplementation (600mg daily) for 6 weeks can increase serum copper and SOD1 levels and decrease the Zn/Cu ratio in patients with MetS.

Keywords: Metabolic syndrome; Barberry; Copper; Zinc; Superoxide dismutase

Abbreviations

Cu: Copper; CHD: Coronary Heart Disease; CVD: Cardiovascular Disease; GSH: Glutathione; GPX: Glutathione Peroxidase; MetS: Metabolic Syndrome; SOD Superoxide Dismutase; Zn: Zinc

Introduction

Metabolic syndrome (MetS) is a condition which characterized by a clustering of several cardiovascular risk factors, which include: central obesity, dyslipidemia, impaired glucose tolerance and hypertension [1]. Excessive intake of dietary calories and insufficient physical activity are two important reasons for the increasing prevalence of MetS in the world. In the United States about 70 million adults are obese and another 70 million are hypertensive. According to recent studies, obese individuals often have other features of MetS, such as dyslipidemia, hypertension and problems in insulin metabolic signaling [2]. Iran has a high prevalence rate of MetS, which affects 33% of the Iranian adult population [3].

MetS is associated with an increased level of oxidative stress. Oxidative stress has a pivotal role in pathophysiology of various diseases, including atherosclerosis and coronary heart disease (CHD) [4]. The activity of antioxidant enzymes such as superoxide dismutase has a crucial protective role in CHD and other chronic disease. The trace elements copper (Cu) and zinc (Zn) are important components of this enzyme. Recent studies have reported that zinc has an important role in the pathophysiology of MetS, by its participation in the regulation of cytokine expression and inflammation suppression. Zinc is also involved in the function of antioxidant enzymes and thereby it can reduce oxidative stress [5]. Intracellular zinc binds to several proteins and exerts an effect known as "protein redox zinc switch". Oxidative stress can remove zinc from its position and then these ions can operate in signaling pathways, change the mitochondrial metabolism and effect on the cell redox situation [6]. Excessive levels of free copper ions can cause lipid oxidation, oxidative stress and the generation of reactive oxygen species and this finally causes some diseases [7].

Some foods derived from the Mediterranean region, such as Barberry, have beneficial effects on disease prevention and possibly their treatment [8].

Barberry has been reported to have anti-diabetic, anti-bacterial and anti-oxidant effects which have been used in medicines since ancient times. Barberry has also been reported to improve the serum cholesterol and triglycerides. Isoquinoline alkaloid, which is present in Barberry, and has been used for treatment of diseases including hyperlipidemia, CHD, diabetes and MetS may partially account for

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these effects [4].

Because of the importance of Zn and Cu to individuals with MetS, as well as the anti-inflammatory and antioxidant properties of barberry we aimed to investigate the effects of barberry on serum Zn and Cu in patients with MetS.

Materials and Methods

The current study was a substudy of our previous double-blind controlled trial on barberry in subjects with MetS which was approved by Mashhad University of Medical Sciences' Ethics Committee [9]. It has been registered in the Iranian Registry of Clinical Trials (IRCT) with a registration number IRCT20110726007117N9. Inclusion and exclusion criteria were explained in detailed previously [9]. A total of 106 patients with MetS based on the International Diabetic Federation Criteria (IDF), who were referred to the Nutrition Clinic, were enrolled in this study.

Subjects were randomly assigned to 2 study groups: Group 1: Barberry group with subjects receiving Barberry capsules of 600 mg for 6 weeks (n=53); Group 2: Control group with subjects taking one Placebo capsule every day (n=53). The barberry and placebo capsules were prepared by Khoosheh Sorkhe Shargh Agro Industrial Company (Tehran, Iran). All subjects received nutritional advice based on American Heart Association guidelines about maintaining an isocaloric diet during the period of the study. A fasting blood sample was collected from all subjects at baseline and 6 weeks after the intervention.

Serum zinc and copper concentrations were determined using Atomic Absorption Spectrophotometer (Varian AA 240 FS model-America) [5,10]. Serum SOD activity was measured using pyrogallol indirect spectrophotometric assay [11].

Statistical analysis

All statistical analysis was undertaken using SPSS version 18 (SPSS Inc. Chicago, IL, USA). Data are presented as mean ± SD for quantitative data or number and percentage for qualitative data. T-test and Chi-square test were used for analysis at baseline and changes after intervention. Paired sample t-test was performed for analysis before and after intervention. All the analyses were two-sided and P values less than or equal to 0.05 were considered significant.

Results

The mean age of the study subjects was 38.96±9.04 and 40.89±9.61 years in the Barberry and Placebo groups, respectively (p>0.05). Female participants comprised 77.36% of the barberry group and 71.7% of the placebo group. There were no significant differences between gender distribution between the barberry and placebo groups, too (p>0.05) (Table 1).

Serum zinc level was 68.7±18.81 (µg/dl) and 78.28±25.21 (µg/dl) in the barberry and placebo groups at baseline, respectively (Table 1). At baseline serum copper level was 79.29±15.62 (µg/dl) in the barberry group and 118.71±10.21 (µg/dl) in the placebo group. Zn/Cu was 0.92±0.34 in the barberry group and 0.66±0.22 (µg/dl) in the placebo group. SOD1 level was 0.75±1.3 (Unit/ml) and 1.43±1.55 (Unit/ml) in the barberry and placebo groups, respectively (Table 1).

As summarized in Table 2, the results showed that the serum zinc level in barberry (p=0.115) and placebo (p=0.132) groups did not changed before and after intervention. Moreover, there was no significant differences in serum Zinc level changes between barberry and placebo groups (p=0.620) (Table 2). Whereas, the serum copper level was significantly increased in barberry group after the intervention (p=0.001), but there were no significant differences between serum copper in placebo group before and after intervention (p=0.056). There were significant differences between changes of copper in barberry and placebo groups (p<0.001) (Table 2).

Table 1: Features of the study groups at baseline.

	Barberry (53) 38.96	Placebo (53)	p
Sex[1]			
Male	12 (22.64%)	15 (28.3%)	0.44
Female	41 (77.36%)	38 (71.7%)	
Age, y[2]	38.96±9.04	40.89±9.61	0.3
Zinc (µg/dl)	68.7±18.81	78.28±25.21	0.067
Copper (µg/dl)	79.29±15.62	118.71±10.21	0.001
Zn/Cu	0.92±0.34	0.66±0.22	0.018
SOD1 (Unit/ml)	0.75±1.3	1.43±1.55	0.001

[1]Q-square
[2]Student t- test
Data presented as Mean±SD or number and percentage.

Zinc to copper ratio decreased in Barberry group after the intervention (p<0.001), but in placebo group it was not significantly changed (p=0.84). Moreover, there were significant differences in Zn/Cu changes between the barberry and placebo groups (p=0.027) (Table 2).

According to the results, superoxide dismutase1 activity has significantly increased in barberry group after the intervention (p=0.024), whereas, in placebo group it was not changed (p=0.49). In addition, there were significant differences in SOD1 changes between the barberry and placebo groups (p=0.077) (Table 2).

Discussion

The result of current study showed that barberry supplementation (600mg daily) has increased serum copper and SOD1 levels and decreased the Zn/Cu ratio in patients with MetS for a period of 6 weeks. To the best of our knowledge, this study is the first one which inquires the effect of barberry supplementation on serum levels of copper, zinc and SOD1 in patients with MetS.

It has been reported that serum Zn/Cu ratio have an important role in pathogenesis of metabolic diseases including diabetes, MetS and CVD [5,10]. Copper is involved in the construction of various enzymes and by this way participated in various interactions such as oxidation and redistribution of the electron chain, and cells protection against free radicals that cause tissue destruction. Copper is the cofactor of SOD1 and according to the result of this study increasing the level of serum Cu increased SOD1 [12].

Previous studies have shown the ability of barberry in preventing the ROS formation in various cells such as macrophages, chelating Fe2+, cleaning free radicals including O2- and OH [4]. According to a study by Ji-Yin Zhou et al., [13], barberry has shown as an agent who exerts protective effect on antioxidant enzymes in the

Table 2: Comparison between trace elements and SOD1 levels in Barberry and Placebo groups.

		Barberry	P-value[1]	Placebo	P-value[1]	P-value (changes)[2]
Zinc (µg/dl)	Before	68.7±18.81	0.115	78.28±25.21	0.132	
	After	64.16±16.49		70.83±23.42		
	Changes	-4.54±19.85		-7.43±31.72		0.62
Copper (µg/dl)	Before	79.29±15.62	0.001	118.71±10.21	0.056	
	After	100.71±29.5		108.88±22.12		
	Changes	21.42±24.62		-9.83±24.43		< 0.001
Zn/Cu	Before	0.92±0.34	< 0.001	0.66±0.22	0.84	
	After	0.75±0.57		0.65±0.57		
	Changes	-0.17±0.36		-0.011±0.35		0.027
SOD1 (Unit/ml)	Before	0.75±1.3	0.024	1.43±1.55	0.49	
	After	1.27±1.19		1.76±1.35		
	Changes	0.52±1.62		1.03±10.64		0.077

[1]Pair t-test has been done.
[2]t-test has been done.
Data presented as Mean±SD.

liver of diabetic rats [13]. Barberry can decrease the concentrations of malondialdehyde and elevate catalase, glutathion peroxidase, superoxide dismutase and glutathion activities in the liver tissue and serum of the rats with diabetes [14]. The difference between Zhou's study and ours was the target groups which were rats and people with MetS, respectively. According to another study by Zilaei et al., PAB levels significantly decreased by using barberry supplementation for six weeks in people with metabolic syndrome [9].

In another study, Cheng et al. revealed that endothelial function can be improved in human vascular endothelium by preventing endothelial microparticles-mediated oxidative stress. The serum levels of malondialdehyde and circulating endothelial microparticles- such as CD31+/CD42- decreased significantly in group which consumed barberry in comparison with the placebo group [15]. In rats with streptozotochin-induced diabetic, using barberry simultaneous with diluting oxidative stress and down-regulating the activity of aldose reductase caused the improvement of renal injury. In this study, taking barberry at a dose of mg/kg/day could increase serum SOD activity and reduce the amount of MDA in diabetic model [16]. According to the study by Farhadi and Gavadifar, using barberry at a dose of 200mg has reduced triglyceride and total cholesterol levels in patients with dyslipidemia [17].

Glutathione (GSH) commonly found in the reduced form in the tissues. GSH has an antioxidant activity in which reacting by superoxide radicals, hydroxyl radicals and singlet oxygen followed by formation of oxidized glutathione and other disulphides. In protecting sulphydryl groups against oxidation GSH is vital [18,19]. In a study by Thirupurasundari et al., an elevation in the levels of hydro-peroxides causes a decrease in the GPX (glutathione peroxidase) level in neoplastic condition but berberine restituted its value in animal treated by drug. GPx catalyses the oxidation of GSH to GSSG and this action elevated by using berberine. If the activity of GPx reduced, lipid hydro-peroxides get stored in cells and this causes a chain reaction in which more unsaturated lipids considered goals for further peroxidative tissue injury [18].

Our finding is consistent with several previous studies [14-18], which have reported barberries' antioxidant effects. Although this is for the first time that the effect of barberry supplementation on serum levels of copper, zinc and SOD1 has been assessed in patients with MetS.

Study Limitation

This study included a small number of patients and the short follow up period. Its outcome should be considered as a pilot study. Further studies should be done in order to determine the exact constituent of barberry that has the greatest antioxidant effect, and the dosage required for optimum effect on the serum level of Cu, Zn and SOD1. A large-scale trial is yet warranted, perhaps followed by some clinical end-point studies.

Conclusion

The result of current study showed for the first time that barberry supplementation (600mg daily) for a period of 6 weeks can increase serum copper and SOD1 levels and decrease the Zn/Cu ratio in patients with MetS.

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Declaration

Conflict of interest: We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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