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Research Paper

Effect of Barberry Treatment on Blood Pressure in Patients with Metabolic Syndrome

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ABSTRACT

The aim of present study was to investigate the effect of barberry on indices of adiposity, blood pressure and glucose tolerance in patients with metabolic syndrome. Subjects with metabolic syndrome, 18-65 years of age (n=106, 79 female and 27 male) were randomised to receiving three capsules of dried barberry or three capsules of placebo for 6 weeks. All participants were given dietary advice of the American Heart Association guidelines for a 6-weeks period of the study. Anthropometric measurements, blood pressure and fasting blood glucose (FBG) were determined in patients before (week 0) and after (week 6) intervention. Barberry treatment was associated with a reduced body mass index (BMI) but there was no significant difference between the case and control groups. Furthermore there were no significant effects on other anthropometric measurements. FBG was significantly lower in both groups after treatment but there was no significant difference between groups. However barberry treatment was associated with a significant reduction in systolic and diastolic blood pressure in comparison to control group. Results of the present study suggested that barberry supplementation in patients with metabolic syndrome can improve some cardiovascular risk factors.

Key words: Barberry; Metabolic syndrome; Anthropometric measurements.

INTRODUCTION

The metabolic syndrome is a clustering of several cardiovascular risk factors that include central adiposity, impaired glucose tolerance, dyslipidaemia and hypertension. It has been defined using several different criteria (Cameron et al., 2004; Grundy, 2008) and studies show that individuals with the metabolic syndrome have an increased risk of developing diabetes mellitus and atherosclerotic cardiovascular disease (CVD) compared to those without (Nesto, 2003; Gale, 2008). Metabolic syndrome has a high prevalence in developed countries. Thus, the diagnosis and treatment of metabolic syndrome can be important for prevention of CVD.

Several medicinal plants have been reported to improve some of the parameters of metabolic syndrome, including dyslipidemia and hypertension.

Barberry (*Berberis vulgaris*) has also been reported to have some beneficial effects. It contains berberine, an isoquinoline alkaloid found in an array of other plants, and has been used in Indian and Chinese medicines as an antimicrobial, stomachic, bitter tonic and in the treatment of oriental sores. Ebrahimi-Mamaghani., et al (Ebrahimi-Mamaghani et al., 2009) studied the effect of barberry on some of the component features of metabolic syndrome, and have reported that barberry treatment had no significant effects on BMI, total cholesterol, triglycerides and glucose concentrations, whereas LDL-cholesterol concentration and total/HDL cholesterol ratio were significantly decreased and HDL-cholesterol concentration increased.

Berberis vulgaris has been used in various conditions including hypertension and arrhythmia. Some beneficial cardiovascular effects of berberine (an active constituent of Berberis vulgaris) include preventing ischemia induced ventricular tachyarrhythmia, improving cardiac contractility and lowering peripheral vascular resistance and blood pressure (Imanshahidi and Hosseinzadeh, 2008; Cicero and Ertek, 2009), and the pharmacological investigations of berberine have been reported by some investigators previously (Kulkarni et al., 2010). Farhadi., and colleagues (Farhadi, et al., 2010) found that barberry treatment at a dose of 200 mg dried extract significantly reduced blood pressure in patients with moderate hypertension.

We have investigated the effect of barberry on indexes of adiposity, FBG and blood pressure, in patients with metabolic syndrome, because of the limited data in regard to the benefits of barberry on cardiovascular risk factors in this group of individuals who are at high risk of cardiovascular disease.

MATERIALS AND METHODS

Study design: This was a randomized, double-blind, placebo-controlled clinical trial over 6-weeks. The investigation was conducted in the nutrition clinic of Qhaem Hospital, Mashhad, Iran. A flowchart of the study design is in Fig. 1. A total of 106 subjects with metabolic syndrome (defined by the International Diabetic Federation (IDF) Criteria 2005) were recruited from patients attending the Nutrition Clinic of Qhaem Hospital; they were 18-65 years old, and did not have diabetes. They were selected sequentially and then randomised to one of two groups based on computerized randomization; there were 53 individuals in each group. Information sheets were provided to each subject. Inclusion criteria were an age of 18-65 years and the criteria for metabolic syndrome used for determining inclusion were the IDF criteria. Exclusion criteria included known systemic diseases, pregnant and lactating women, and consumption of the lipid-lowering drugs, anti-hypertensive and anti-diabetic drugs. All patients provided written informed consent and the protocol satisfied Mashhad University of Medical Sciences Ethics Committee with the letter no.87480 in 2009.

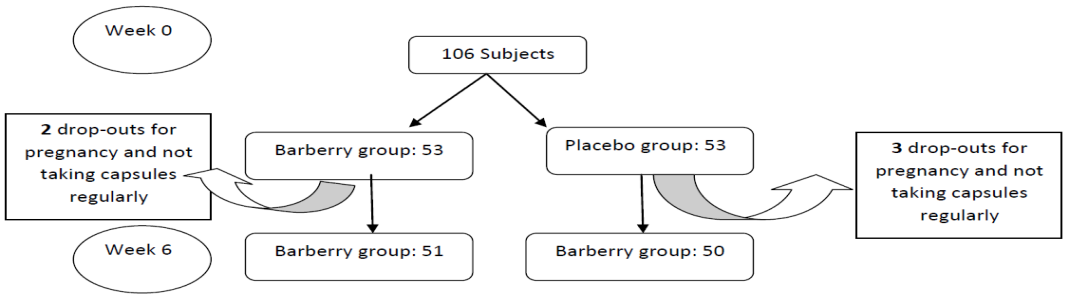

Figure- 1: Flow chart of the study design.

All participants were given dietary advice of the AHA (American Heart Association) guidelines for the 6-weeks period of the study. Compliance was

monitored at a three-weekly visit, assessing compliance by counting capsules; those subjects who did not take their capsules regularly or were intolerant to the medication were excluded from the study.

Blood pressure, FBG and anthropometric measurements were determined in all patients at baseline (week 0) and the end of study (week 6). Blood samples were collected in the morning after a 12hour fasting from subjects. Haemolysed samples were excluded from analysis. After separation, aliquots of serum were frozen at −80°C until analysis. We collected information on their socio-demographic status, occupation, smoking behaviour, medical history and medication for all subjects.

We used a spectrophotometric method (Biotecnica instruments, Italy BT3000. WWW.biotecnica.it) for measuring FBG. We measured the height using the standard method. Other anthropometric parameters were measured with BIA (Bio Impedance Analyzer) and blood pressure was measured in the standard method.

Barberry capsule preparation: Barberry juice was obtained from Ghaen, Khorasan, Iran. It was formulated as a capsule containing 200mg of dried barberry. Placebo capsules were matched for size, shape and volume of content and manufactured by the same company. The barberry capsules which were used in this study contained lactose, starch and the aqueous and ethanol extract of barberry and the placebo capsules contained lactose, starch and permitted food colour.

Statistical analysis: All statistical analyses were performed using SPSS statistical software package. Data were presented as Mean±S.D. and median and inter-quartile range in both groups. Data were assessed for normality by using the Klomogrov-Smirnov test. Paired sample T test and independent sample T test for normally distributed data and Wilcoxon and Mann-Whitney tests for non-normally distributed data were used to data analysis. $P<0.05$ was considered as statistically significant.

RESULTS

***Baseline characteristics of barberry and placebo groups*:** Table 1 shows the comparison of the baseline characteristics between two groups. Data showed that there were no significant differences between two groups in regard to baseline characteristics *(P*>0.05, Table 1). There were no significant differences between two groups in regard to educational level, marriage status and the economic status (*P*=0.08, 0.53 and 0.6 respectively) (data not shown).

Table -1: **Comparison of the baseline characteristics between case and control groups.**

	Case Group	Control Group		P-value
Number	53	53		-------
Gender	**Women (n)**	41	38	0.44
	Men (n)	12	15	
Smokers	**(%)**	11.3	9.4	
	Number	6	5	0.96
Age (year) (Mean ±SD)	38.96± 9.04	40.89 ± 9.61		0.30
BMI (kg/m^2) (Mean ±SD)	31.54± 3.92	32.37± 5.01		0.35
PBF (%) (Mean±SD)	63.61±6.10	36.21±8.30		0.78
Percentage of trunk fat (%) (Mean±SD)	34.40 ±5.40	34.63 ±6.38		0.84
Median FBG (IQR) (mg/dl)	99 (95-111)	103 (95-111)		0.62
SBP(mm hg) Mean±SD	127.01 ±13.91	127.88 ±13.02		0.74
DBP(mm hg) Mean±SD	81.86 ±8.88	79.80 ±7.55		0.21

- BMI: Body Mass Index. PBF: Percentage of Body Fat, FBG, fasting blood glucose; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure. Values are expressed as mean ±SD, median ±inter-quartile range (IQR) or number and percent.
- Mann-Whitney and independent sample T test were used to compare non-parametric and parametric variables between two groups, respectively.
- Data showed that there was no significant difference between the two groups in regard to baseline characteristics.
- None of our subjects had diabetes or consumed other prescription drugs.

Effect of barberry on FBG, anthropometric measurements and blood pressure: BMI (kg/m^2) decreased significantly in the case (Barberry) group (P<0.0001) but in the control group this reduction did not reach statistical significance (P=0.06) and the results showed that there was no significant difference between two groups in regard to BMI (P=0.98). In regard to PBF (percentage of body fat) and percentage of trunk fat, there were no significant differences before and after intervention in either the case or control groups, nor between groups. For blood pressure, both SBP (systolic blood pressure) and DBP (diastolic blood pressure) decreased significantly only in the case group (P <0.001 for each parameter) (P=0.03 and <0.001 respectively for SBP and DBP). For FBG, the results showed that in both groups FBG decreased significantly during the intervention period (but there was no significant difference between groups (P=0.54, Table 2).

Table- 2: Effect of barberry on obesity indexes, FBG and blood pressure.

Parameters	Groups						Mann-Whitney test
	Case Group			Control Group			
	Week 0	Week 6	P-value	Week 0	Week 6	P-value	
Median FBG concentration (IQR)	99 (95-111)	93 (86-103)	0.02	103 (95-111)	95 (84-108)	0.01	0.54
BMI (kg/m2)	31.54± 3.92	30.11±3.73	0.000	32.37± 5.01	31.03±4.94	0.06	0.98
PBF (%)	36.61±6.10	36.31±5.98	0.48	36.21±8.30	36.27±8.19	0.87	0.45
Percentage of trunk fat (%)	34.40 ±5.40	34.27±5.54	0.78	34.63 ±6.38	34.14±7.16	0.20	0.75
SBP(mm hg)	127.01 ±13.91	118.45±10.25	<0.001	127.88±13.02	124.74±19.51	0.17	0.03
DBP(mm hg)	81.86 ±8.88	75.78±6.43	<0.001	79.80 ±7.55	79.20±7.58	0.12	<0.001

- BMI: Body Mass Index. PBF: Percentage of Body Fat, FBG, fasting blood glucose; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure
- Values are expressed as median ±inter-quartile range in regard to FBG and mean±SD in regard to other parameters. Mann-Whitney and Wilcoxon tests were used to compare the FBG between groups and before and after intervention in each group, respectively. Data showed that FBG decreased significantly in both groups but there was no significant difference between groups. Paired T test and independent sample T test were used for compare the anthropometric measurements before and after study and between groups respectively. Data showed that barberry decreased significantly BMI, but there was no significant difference between two groups in regard to anthropometric measurements. Barberry treatment decreased significantly SPB and DBP in comparison to control group. FBG decreased significantly during the study in both group but there was no significant difference between groups.
- P-value is within group comparison; Median FBG concentration (IQR) expressed as mg/dl while BMI; PBF; SBP; DBP and percentage of trunk fat were expressed as Mean±S.D.

DISCUSSION

The results of present study indicated that barberry supplementation for 6 weeks in patients with metabolic syndrome did not have a significant effect on anthropometric measurements and FBG but were associated with a significant reduction in SBP and DBP (6.7% and 7.4% respectively).

The effect of decreased BMI in barberry group may be in part being due to the effect of dietary advice provided to all participants. (Ebrahimi-Mamaghani et al., 2009) in their study showed that barberry treatment for 8 weeks in patients with type 2 diabetes had no significant effects on BMI. In this study no dietary advice was given.

Our results of blood pressure support the work of Fatehi et al., (2005). In their study on hypertensive rats, they showed that beberine lead to a significant reduction in the blood pressure. Farhadi and Shahghasemi (2010) also found that barberry supplementation in hypertensive patients decreased significantly blood pressure. About the mechanism of barberry on blood pressure it is reported that barberry may

induce the production the nitric oxide and thus vasodilatation (Cicero and Ertek 2009).

Ebrahimi-Mamaghani et al., (2009) suggested that there was no significant effect of barberry on FBG. However, Yin et al., (2002) showed that beberine has a glucose lowering effect and this may be due to decreased the activity of beta-glycosidase and disacaridase. Our study showed that in both groups there was a significant decrease in FBG during the intervention period, which may be in part being due to the effect of dietary advice, but there was no significant difference between two groups.

CONCLUSION

Results of the present study suggested that barberry supplementation in patients with metabolic syndrome can improve blood pressure but had no significant effect on FBG and anthropometric measurement, above the effects of dietary advice.

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Conflict of interest: None declared.

REFERENCES

Cameron A.J., Shaw J.E., Zimmet P.Z., (2004): The metabolic syndrome: prevalence in worldwide populations. *Endocrinology and metabolism clinics of North Am.*, 33(2):351.

Cicero A.F., Ertek S., (2009): Berberine: metabolic and cardiovascular effects in preclinical and clinical trials. *Nutr Diet Suppl*., 1(2):1-10.

Ebrahimi-Mamaghani M., S. Arefhosseini Golzarand, Aliasgarzadeh Vahed-Jabbary, (2009): Long-term effects of processed Berberis vulgaris on some metabolic syndrome components. *Iranian Journal of Endocrinology and Metabolism*, 11(1): Pe41-Pe47.

Farhadi A., Shahghasemi H., (2010): Effect of aqueous extract barberry fruit with seeds on blood pressure in patients with hypertension. *J. of Food Sci. and Technology*, (3): 37-43.

Fatehi Hassanabad Z., Jafarzadeh M., Tarhini A., Fatehi M., (2005): The antihypertensive and vasodilator effects of aqueous extract from Berberis vulgaris fruit on hypertensive rats. *Phytotherapy Research*, 19(3): 222-225.

Gale E. A. (2008): Should we dump the metabolic syndrome?: Yes. *Bmj*., 336 (7645): 640-640.

Grundy S.M., (2008): Metabolic syndrome pandemic. *Arteriosclerosis, thrombosis, and vascular biology*., 28(4): 629-636.

Imanshahidi M., Hosseinzadeh H., (2008): Pharmacological and therapeutic effects of Berberis vulgaris and its active constituent, berberine. *Phytotherapy Research*, 22(8): 999-1012.

Kulkarni S., Dhir A., (2010): Berberine: a plant alkaloid with therapeutic potential for central nervous system disorders.*Phytotherapy Research*., 24(3): 317-324.

NestoR.W., (2003): The relation of insulin resistance syndromes to risk of cardiovascular disease. *Reviews in cardiovascular medicine*., 4: S11.

Yin J., Hu R., Chen M., Tang J., Li F., Yang Y., Chen J., (2002): Effects of berberine on glucose metabolism in vitro.*Metabolism*., 51(11): 1439-1443.

