

Effect of a Persian medicine preparation, *Ma'aljobon*, on constipation in patients with hypertension

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Background: Constipation is a common and prevalent digestive problem. Forcing and straining due to constipation may have a negative effect on some parts of the body, including the heart. The aim of the study was to evaluate the effect of *Ma'aljobon* (a kind of whey) on functional constipation in hypertensive patients. **Materials and Methods:** The present double-blind, placebo-controlled randomized clinical trial was a part of the study about the effect of *Ma'aljobon* on stage 1 hypertension, performed in 2017–2018. Hypertensive patients accompanying constipation were included in the study. Patients were randomly divided into two groups: Group A ($n = 19$) received 25 g of *Ma'aljobon* powder and Group B ($n = 22$) received 25 g of maltodextrin powder, twice a day for 6 weeks. The number and quality of defecation during a day were evaluated at baseline and at the end of the study within and between groups. Data were analyzed by SPSS software (version: 17) using Chi-square or Fisher's exact test. $P < 0.05$ was considered as significant level. **Results:** Forty-one patients had inclusion criteria, of whom 34 patients completed the study (19 in Group A and 15 in Group B). The mean \pm standard deviation age of patients was 53.86 ± 8.92 years (range: 34–80 years). Before intervention, there was no significant difference between the two groups with respect to constipation; however, after 6 weeks' treatment, the frequency of constipation was significantly different between groups ($P < 0.001$). At the end of 6th week, constipation in the Group A was improved completely in terms of the number of defecation and stool consistency; but, in the Group B, eight (53.33%) patients still suffered from constipation ($P < 0.001$). No specific complications were reported in both groups. **Conclusion:** *Ma'aljobon* can improve constipation in hypertensive patients without any adverse effect.

Key words: Constipation, hypertension, *Ma'aljobon*, Persian medicine, whey protein

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INTRODUCTION

Constipation is one of the prevalent digestive problems from whose chronic condition, about 15% of the world population suffers.^[1] Over one-seventh of the adult world population complain of chronic constipation. Prevalence of the problem in woman is 2–3 times more than men; and it is more in children compared to adults.^[2,3] Among various producing or aggravating factors of constipation inactivity, unhealthy diet, taking some drugs, particularly opiates, and depressants are mentionable.

An increasing number of constipate patients prefer alternative and complementary treatments because of their worry about different drugs' side effects and deficiency of their long-term effect.^[4] To prevent and treat constipation, the American Digestive Disease Society used to recommend a well-balanced diet consisting of bran grains, fresh fruits and vegetables, and drinking a sufficient amount of fluids; and also physical activity. If these recommendations do not work, the physician might also prescribe laxatives. Bulk-forming laxatives, stimulants, stool softeners, lubricants, and osmotic agents

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are some of the recommended drugs.^[5] Constipation can be a problem associated with systematic complications or neurogenic ones and can be accompanied by the occurrence of hemorrhoid or anal fissure.^[6] Persian medicine (PM) as one of the complementary/alternative medicine (CAM) methods tries to propose simple and useful recommendations for health protection and treatment of diseases.^[7]

PM holds that one of the factors of constipation is increasing dryness of the bowels; thus, moistening foods and drugs treat the problem. Moistening of the bowels can be done through changing the lifestyle and using moistening nutrients and drugs and laxatives.^[8,9] Cheese extract which is called *Ma'aljobon* in Arabic and PM and is a kind of whey protein has wet and cold temperament and is recommended as a moistening food for dry tempered patients in PM.^[8] It is a liquid which is derived down during cheese-producing process through adding either rennet or acid (e.g., citric acid, lactic acid, or acetic acid). *Ma'aljobon* is one of the recommended treatments for the constipation in PM. After observing the existent data, it was found that no studies had been done to assess the remedial effect of *Ma'aljobon*, and the present study is the first one in this respect.

Constipation has been reported to be associated to the occurrence of cardiovascular events. There is also a relation between the management of hypertension and the constipation. Changes to the intestinal microbiota by constipation can rise blood pressure which can trigger some adverse events such as arrhythmia or acute coronary disease.^[10] Regarding that *Ma'aljobon* (a kind of whey) is a kind of nutrient which is administered for treatment of constipation in PM, we compared the effect of *Ma'aljobon* and Maltodextrin (as a placebo) on constipation (number of defecation and stool consistency) in hypertensive patients (Stage 1).

MATERIALS AND METHODS

Type of study

The present double-blind, placebo-controlled randomized clinical trial was part of the study about The effect of *Ma'aljobon* on Stage 1 hypertension, performed in 2017–2018.

Study design

This study was conducted in Birjand Cardiovascular Clinic Center, South Khorasane Province, Iran from October 2017 to March 2018. The study flow diagram (CONSORT) is presented in Figure 1. Patients with hypertension (Stage 1) along with chronic constipation (according to PM definition) were included in the study. According to PM definition, normal defecation frequency is 1–3 times a day, and stool consistency should be like a jam or honey and expel without

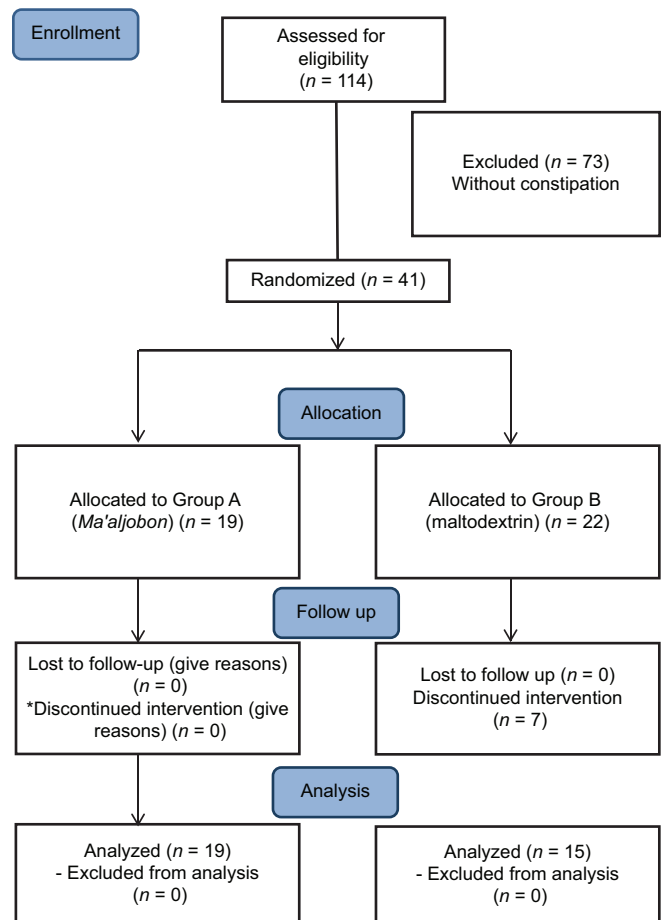


Figure 1: The study flow diagram (CONSORT). *Five patients were not satisfied with the medication's taste, and two did not answer the phone and were excluded

intensive force. Otherwise, the individual is suffering from constipation.^[11,12]

Patients who were under treatment for constipation, those with hypertensive crisis during the study period, and allergy to medication were excluded from the study; also, patients with other cardiovascular, hepatic, and renal diseases; diabetes; malignancies; pregnancy and breastfeeding, drug abuser (e.g., alcohol), and those taking contraceptive, psychiatric drugs, and narcotic drugs were also excluded.

Forty-one cases had inclusion criteria. The patients were divided into two groups: A and B using block randomized method. For random concealment, the number of each case together with the letters A or B was written down on a paper and was put into an entirely closed envelope.

The patients in the intervention group consumed 25g of *Ma'aljobon*, dissolved in 200 cc of warm water, both at fasting time (between 6 A.M. and 7 A.M.) and at 6 P.M. They were advised to walk a little after consumption and avoid sleeping or washing themselves. The cases in the

Group B consumed the same dose of maltodextrin powder in the same way. Since the study was a double-blind one, the same boxes for the two kinds of powder were used and the therapist was also unaware of the type of A or B. The length of the study lasted 6 weeks.

The hematologic factors including fasting blood sugar, lipid profile, liver function test, hematocrit, and platelet count were assessed both in the beginning and the end of the study, as well.

Drug and placebo provision

The drug supply was ordered to Niak Pharmaceutical Company to prepare it, applying the best method of *Ma'aljobon* production, that was described by Mirabzadeh et al.^[13] In this method, *Ma'aljobon* powder was made from 75°C milk by adding vinegar and oxymel to it. *Ma'aljobon* powder is produced by separating the solid by means of filtration or drying in a variety of ways such as spray drying and lyophilization.^[13] The complete process of manufacturing the final product according to the PM sources was as follows:

First of all, 1800 kg cow milk is boiled for 20 min. Then, when its temperature lowers to 75°C, 250 kg of oxymel and 5 kg of vinegar are mixed with the milk so that it is separated. The obtained solution is sprayed at 250 l/h at the input temperature 120°C and output of 50°C through a spray dryer.^[13] Regarding to the sensitivity of proteins to heat a drying freezer machine is used in the company to dry the obtained whey protein.^[14] Finally, each 300 g of it is packed in a polyethylene package.

In our study, maltodextrin powder was used as placebo which is produced through enzymatic hydrolysis of corn starch using α -amylase results in a lighter molecule that is called maltodextrin. The drug and the placebo had the same dose and packages; neither the researcher nor the patients were aware of the type of interventions. Data regarding constipation and other variables were recorded in a data gathering form. Data were analyzed using the Statistical Package for the Social Sciences (SPSS software Version: 17; IBM, NY, USA). The comparison of groups was performed by Chi-square, or Fisher's exact test, and Mann-Whitney U-test. Wilcoxon signed rank test was used for within-group comparisons. $P < 0.05$ was considered as the significant level.

Ethical considerations

This study had gained the Ethical approval and Research Committee of Iran University of Medical Sciences on November 21, 2017 (registration code of IR.IUMS.REC1396.9321309003). It was also registered in Iranian Registry for Clinical Trials under the code of IRCT20140519017756N34.

RESULTS

Forty-one patients had constipation [Figure 1], of whom 34 patients completed the study (19 in Group A: *Ma'aljobon*, 15 in Group B: maltodextrin). The patients aged 34–80 years with the mean and standard deviation of age 53.86 ± 8.92 . Mean age in the two groups did not show a significant difference ($P = 0.073$). There was no statistically significant difference in the number of hypertensive medications between the two groups. Demographic characteristics of patients are presented in Table 1. Results with respect to comparison of different variables within groups during the study period have been shown in Tables 2 and 3.

The changes of lipid profile, liver enzymes, hematocrit, and platelets did not reveal a significant difference within groups during the evaluation time [Table 2].

From 41 constipated patients, five patients were not satisfied with the medication's taste, and two did not follow the protocol and were excluded. 34 patients (19 from the Group A and 15 from the Group B) completed the study. At first, there was no significant difference between the two groups; but, after 6 weeks, the difference regarding the constipation was statistically significant ($P < 0.001$). At the end of 6th week, no one in Group A suffered from constipation; but, in Group B, 8 (53.33%) individuals had still complaint ($P < 0.001$). No specific complications were reported.

DISCUSSION

It was found that a six-week consumption of *Ma'aljobon* improved constipation in patients with constipation and hypertension; this effect was significant in comparison with placebo.

Table 1: Demographic characteristics of hypertensive patients along with constipation in different treatment groups

Variables	Group A (<i>Ma'aljobon</i>) (n=19)	Group B (maltodextrin) (n=15)	P
Age (year), mean±SD	56.7±10.1	50.9±7.6	0.056*
BMI (kg/m ²), mean±SD	27.2±2.6	28.3±1.4	0.37*
Gender, n (%)			
Male	10 (52.6)	0	0.001**
Female	9 (47.4)	15 (100)	
Marital status, n (%)			
Single	2 (10.5)	1 (6.7)	1**
Married	17 (93.3)	14 (93.3)	
Occupational status, n (%)			
Employed	11 (57.8)	6 (40)	0.42***
Unemployed	8 (42.1)	9 (60)	

*Mann-Whitney U-test; **Fisher's exact test; ***Chi-square test. SD=Standard deviation; BMI=Body mass index

Table 2: Comparison of different variables within and between groups at different times

Variable/unit	Groups	Baseline	After 6 th week	P*
Weight (kg)	A	76.12±11.41	75.75±11.56	0.20
	B	67.93±7.63	67.35±7.70	0.28
	P**	0.03	0.01	
FBS	A	102.15±17.91	100.42±14.08	0.57
	B	102.00±9.92	104.26±12.27	0.68
	P	0.6	0.43	
Chol	A	200.52±45.24	191.84±35.38	0.20
	B	180.26±33.77	178.93±39.82	0.79
	P	0.17	0.3	
TG	A	150.26±47.76	146.57±53.83	0.60
	B	150.86±106.23	133.20±81.57	0.15
	P	0.19	0.22	
LDL	A	123.26±37.39	119.78±30.02	0.60
	B	110.40±40.63	100.86±30.29	0.69
	P	0.28	0.13	
HDL	A	42.47±7.35	43.94±10.04	0.27
	B	43.00±9.03	43.00±9.03	0.02
	P	0.97	0.13	
AST	A	23.67±8.83	22.70±11.54	0.32
	B	20.80±6.04	20.33±8.86	0.21
	P	0.41	0.3	
ALT	A	31.04±18.61	29.22±20.16	0.15
	B	19.42±5.79	20.61±10.53	0.60
	P	0.06	0.27	
HCT	A	45.02±4.87	43.28±4.25	0.001
	B	42.82±3.59	42.45±3.74	0.55
	P	0.15	0.81	
PLT	A	251.57±35.80	248.57±42.92	0.98
	B	308.26±80.74	301.53±66.82	0.93
	P	0.02	0.01	

*Wilcoxon signed-rank test; **Mann-Whitney U-test; Data are presented as mean±SD. Group A (*Ma'aljobon*) (n=19); Group B (maltodextrin) (n=15). FBS=Fasting blood sugar (mg/dl); Chol=Cholesterol (mg/dl); TG=Tri glyceride (mg/dl); LDL=Low-density lipoproteins (mg/dl); HDL=High-density lipoproteins (mg/dl); AST=Aspartate aminotransferase (U/L); ALT=Alanine aminotransferase (U/L); HCT=Hematocrit (%); PLT=Platelet (n/ml); SD=Standard deviation

Table 3: Comparison of the frequency of constipation between two groups

	Group A (<i>Ma'aljobon</i>) (n=19)	Group B (maltodextrin) (n=15)	P*
Baseline			
Constipated	19 (100)	15 (100)	0.67
After 6 weeks			
Constipated	0	8 (53.33)	0.001
Unconstipated	19 (100)	7 (46.67)	

*Fisher's exact test data are presented as n (%)

According to PM, *Ma'aljobon* has cold and wet temperament.^[15] Persian physicians believe that *Ma'aljobon* is an outstanding drug since it has got the following peculiarities: it is conveyed to the target organ very soon and prepares the wastes to defecate and also acts as a laxative. It gradually rids the body of viscous wastes, and this purification is done without causing any dryness, but

with moistening and feeding the body.^[15,16] *Ma'aljobon* is both a laxative and a purgative drug. Based on PM, a drug that defecate the waste products from the digestive canal is a laxative. However, a purgative is a drug which conveys waste products from the veins and other body organs to the digestive canal to be emptied.^[17]

As few studies claim, after consumption of probiotics-containing yogurt by people with mean age of 61.8 years, their condition improved, and this was attributed to the improvement in bowels function.^[18] Still more, in other studies conducted in 2007 and 2014, cases with constipation were administered probiotic yogurt which was followed by a decrease in their constipation symptoms.^[19,20] In another study titled "Influence of drinking a probiotic fermented milk beverage containing bifidobacteria on the symptoms of constipation," it was found that consumption of dairy products having or lacking probiotic culture improved constipation condition.^[21] Another study in 2017 evaluated the probiotic effects of Kefir-fermented milk in preventing constipation in 42 individuals with mental and physical disabilities. The participants were administered 2 mg of lyophilized Kefir added to each meal for 12 weeks. As a result, their constipation significantly decreased.^[22] One of the causes of constipation is the dryness of bowels and digestive system,^[12] and according to PM, the moistening property of a drug can be effective in the improvement of constipation.^[20] In 2015, Mehrbani *et al.* assessed the effect of whey and dodder seed extract on 42 patients having atopic dermatitis. Daily use of whey powder (derived from vinegar-produced cheese) dissolved in 400 cc of water had brought about an increase in the elasticity, softness, and moisture of the skin.^[23]

In various articles, the relationship between constipation and cow's milk and allergy to its proteins have been dealt with. Regarding that 80% of the main protein of the milk and cheese is casein^[24-26] and during the process of cheese production this substance settles and it is omitted; then whey protein or *Ma'aljobon* will have an anti-constipation and laxative property.

The quality of the whey produced in different ways is evaluated by means of its main proteins, i.e., alpha-lactalbumin and beta-lactoglobulin.

Another study in 2017 evaluated the probiotic effects of kefir-fermented milk for preventing constipation in 42 persons with mental and physical disabilities. The participants were administered 2 g of lyophilized kefir with each meal for 12 weeks. The intake of kefir significantly reduced constipation.^[22]

Speculations about CAMs producing only a placebo effect still exist. However, similar to other studies that evaluated

the efficacy of herbal preparations in treating functional constipation, a very low placebo effect was observed in this study.^[27]

Study limitations

We did not use the *Ma'aljobon* that is traditionally made through milk coagulation with sour acids in a liquid state, as described in the PM sources. We used its powder form, which was made by Niak factory. We used the powder form, rather than the liquid form, of *Ma'aljobon* as made by Niak factory. This was because of the difficulty and costs associated with storing and distributing liquid *Ma'aljobon* for 6 weeks. Moreover, there was a chance of rancidity since the normal *Ma'aljobon* is prone to rancidity given the over 93% moisture in it. Possibly, if it were possible to use natural, liquid *Ma'aljobon*, it would be more beneficial, but this requires another research.

CONCLUSION

It was found that *Ma'aljobon* was able to improve constipation, significantly. With respect to the availability, low cost, and no side effects of *Ma'aljobon* as a food, it can be an effective modality that can be recommended to the hypertensive patients with constipation along with other common medications. It is recommended to investigate the effect of *Ma'aljobon* as a natural food product in non-hypertensive patients with constipation as well as in hypertensive patients with other stages.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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