Original Research Article

Effect of saffron oral capsule on anxiety and quality of sleep of diabetic patients in a tertiary healthcare facility in southeastern Iran: A quasi-experimental study

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Abstract

Purpose: To determine the effect of oral capsule of saffron (a herbal medicine) on anxiety and quality of sleep of diabetic patients of a tertiary healthcare facility in Zabol, Iran in 2016.
Methods: This was a quasi-experimental study on 50 diabetics of Zabol who met the inclusion criteria. Participants were randomly split into two groups (control and test). Anxiety and quality of sleep were evaluated by Spielberger Anxiety Inventory and Pittsburgh Sleep Quality Index (PSQI). Participants in the intervention group received a daily (between 12 noon and 2 pm) intake of 300 mg saffron capsule after lunch while those in the control group received a placebo daily for a similar duration. After a week, anxiety and sleep quality were assessed.
Results: A significant difference in anxiety and quality of sleep prior to and after saffron oral capsule intake (p = 0.001) was observed. In the control group, anxiety and quality of sleep did not show any significant difference before and after intervention (p = 0.001).
Conclusion: The results show that saffron capsule intake is effective in reducing anxiety and improving the quality of sleep among diabetic patients. Further studies are required to enhance saffron capsule formulation.

Keywords: Anxiety, Blood glucose, Sleep, Diabetes mellitus

INTRODUCTION

Quality of sleep and anxiety are the most important mental disorders in diabetic patients. More than 80 and 14 % of diabetics suffer from low quality of sleep and anxiety disorders respectively [1]. More than 6 % of adult population is affected by diabetes in developing countries. Today, there are over 230 million diabetics worldwide. The prevalence of diabetes is estimated to be 3 - 5 % and more than 90 % of diabetes is Type II [2]. In addition to some complications such as retinopathy, nephropathy, and neuropathy, diabetes creates many psychological and behavioral complications which widely affects the quality of life of the patients.

Sleep is a highly dynamic and organized biological process considered an important part of life. The quantity of sleep is associated with the quality of social interaction. Disturbed sleep is considered an important sickness at every stage of life. Sleep is one of basic human needs which is essential to maintain energy, appearance, and physical well-being. Sleep also reduces anxiety and stress. Chemical Drugs as the first line treatment of mental disorders in

diabetics contribute with different complications [3]. Interest in natural therapies has increased greatly today in many countries. Different evidences showed saffron have preventive and therapeutic role in diabetic patients [4,5]. Considering the limitations of studies concerning the effect of saffron on anxiety and quality of sleep in human's samples and prevalence of sleep disorder and anxiety in diabetics.

EXPERIMENTAL

This study was approved by the ethics committee of Zabol University of Medical Sciences (no. ID 1394-21-2) and complied with EMEA guidelines [6]. This quasi-experimental study included 50 patients referred to diabetic clinic teaching hospital during the period between January and March 2016 in Zabol city, southeast of Iran. Sample size selected as the sample using the Cochran formula, reliability coefficient of 95 % and accuracy of 0.07. The inclusion criteria were oral intake of drug, lack of cognitive disorders, willingness to participate in the study, age 20-60, minimum one-year diabetes, being literate, lack of drug intake which are effective in anxiety, no stressful event during the past year.

Data were collected in Zabol Diabetes Center. A 10-minute face-to-face briefing was done for each of the participant in the center. Informed consent was taken for participating in the study. The participants were randomized in to two groups (intervention (25) and control (25). Demographic questionnaires were completed by the patients. First, anxiety and the quality of sleep were evaluated using research tools. Then, the intervention group was requested for daily intake of saffron oral capsule which contains 300 mg saffron for a week. The capsules were administered between 12 noon and 2 pm, after lunch, once daily [7]. In the control group, placebo capsules, instead of saffron capsules, were taken for a week. A text message was sent to the participants by the researcher in order to remind. After a week, the researcher forwarded the questionnaires to the participants and patients filled them out.

The patients were trained on activity participation in study by following instructions includes: little use of foods that affect anxiety and quality of sleep of participants. They were instructed to avoid such foods. We trained family members for confirmation that participants are following all the instructions.
Data were collected using a questionnaire with three sections: 1. Demographic Questionnaire; 2. Spielberger Anxiety Inventory [8]; 3. Pittsburgh Sleep Quality Questionnaire [9]. Demographic questionnaire covers age, gender, duration of diabetes, marital status and education level. Spielberger Anxiety Inventory (SAI) has 20 items. The 20 items were scored on a one-to-four scale, ranging between 20 and 80. The subjects were split into three groups: Mild Anxiety (20 – 40), Medium Anxiety (41-60), and Severe Anxiety (61-80). Pittsburgh Sleep Quality Index evaluates the quality of sleep (subjective from the patient's perspective) and nocturnal and adequate sleep. The items were scored on a 4-option scale (no, once a week, twice a week, and three time a week). The questionnaire also investigated sleep latency of longer than 30 min, hypnotic drug intake, and night wakening due to frequent urination, shortness of breath, feeling cold and hot and wakening due to pain. The scores were converted into percentage. In order to determine the severity of sleep disorder, the scores were split into the following categories: 0-25: no sleep disorder; 26-50 mild sleep disorder; 51-75: medium sleep disorder; 76-100: severe sleep disorder. The reliability and validity for the two questionnaires (PSQI and SAI) were validated in Iran [10].

Statistical analysis

The Statistical Package for Social Sciences (SPSS version. 22.0 for windows (SPSS Inc., Chicago, IL, USA) was used to analyze the data. The categorical variables were compared using unpaired Student's t-test and ANOVA. Confidence interval of 95 % and $p < 0.05$ was considered significant.

RESULTS

Most participants were male (56 %), married (96 %) and had a master degree (30 %). On average, the duration of diabetes was 6 years. Mean age was 37 ± 2.1 (years). Prior to intervention, 30 patients (60 %) (20 in Experimental group and 10 in control group) suffered from relatively severe anxiety. Twenty patients (40%) (5 in intervention group and 15 in control group) suffered from severe anxiety. The mean score of anxiety was 63.3 in experimental group showing relatively severe or severe anxiety. In control group, the mean score of anxiety was 60 to 74 (mean: 68). The mean scores were between 60 and 74, indicating the fact that the patients in control group had moderate or severe anxiety.

After the intervention, the mean score of anxiety was 25.8 in experimental group, showing mild anxiety. The anxiety scores were between 20 and 37, indicating moderate to low anxiety. The mean score of anxiety was 56.4 in control group

Table 1: Mean scores of anxiety prior to and after intervention in experiment and control

Group		Mean score	Score range	*P*-value
Saffron	Prior to Intervention	**63.3**	**60-74**	
	After Intervention	**25.8**	**20-37**	0.001
Control	Prior to Intervention	63.4	**60-74**	
	After Intervention	56.4	**45-62**	0.067

Table 2: Quality of sleep in both groups before and after intervention

Group		Saffron		Control	
Stage		*Prior to Intervention*	*After Intervention*	*Prior to Intervention*	*After Intervention*
No sleep	N	0	19	0	0
disorder (0)	%	0	38	0	0
Mild sleep	N	2	6	2	1
disorder (1)	%	4	12	4	2
Medium sleep	N	14	0	9	8
disorder (2)	%	28	0	18	16
Severe sleep	N	9	0	14	16
disorder (3)	%	18	0	28	32
P-value		*0.002*		*0.091*	

after a week, showing relatively severe anxiety and the scores ranged between 45 and 62, indicating moderate to high anxiety. In general, a significant difference was found prior to and after intervention concerning anxiety using unpaired Student's t test (*p* = 0.001). However, no significant difference was found in control group prior to and after placebo (Table 1). No significant difference was found concerning anxiety in both groups before intervention (p = 0.067) using unpaired independent sample t-test.

Prior to intervention, 46 %(23) of patients had severe sleep disorder, 46 %(23) had medium sleep disorder, and 8 %(4) had mild sleep disorder in all participants. After intervention, 19 patients (38%) had no sleep disorder and 6 patients (12%) had mild sleep disorder in the experiment group. In the control group after intervention, a patient (2%) had mild sleep disorder, 8 (16%) had medium sleep disorder, and 16 (32%) had severe sleep disorder. Comparing the quality of sleep in both groups before and after intervention using paired sample t-test showed that a significant difference was found between the quality of sleep in intervention group before and after saffron oral capsule intake (p=0.002). No significant difference was found concerning the quality of sleep in control group prior to and after intervention (p=0.091) (Table 2).

Anxiety and quality of sleep were compared in control (56.4±11.4) and experimental groups (25.8±4.6) after intervention using paired sample t-test (Table 3). The results showed that a significant difference was found concerning anxiety in both groups after intervention (*p*=0.001). A significant difference was also

found in terms of quality of sleep in both groups (*p*=0.01), showing that saffron oral capsule improved the quality of sleep of diabetics.

Table 3: Quality of sleep in control and saffron groups after intervention

Sleep disorder	Saffron *No (%)*	Control *No (%)*
No sleep disorder	19(38)	0(0)
Mild sleep disorder	6(12)	1(2)
Medium sleep disorder	0(0)	8(16)
Severe sleep disorder	0(0)	16(32)

P = 0.001

DISCUSSION

The results of study showed a significant effect of Saffron on quality of sleep and anxiety in diabetic patients. In traditional medicine, saffron is used as antispasmodic, sedative, digestive, anti-flatulence, diaphoretic, expectorant, sexual stimulant, increase of appetite, depression, renal colic, anti-inflammatory, analgesic. However, extensive review of scientific literature did not reveal adequate research on the effect of saffron capsules or its other products on anxiety and sleep quality in diabetic patients.

Most of the researches on saffron efficacy have been conducted using animal models; therefore, further studies with diabetic patient's subjects are necessary. Miladjerdi *et al* found that saffron reduced anxiety and increased sleep time in mice which are consistent with the findings of the present study [11]. Hosseinzadeh reported anxiolytic and hypnotic effects of saffron on anxiety and insomnia in mice [12]. Different studies in human subjects shown that saffron

reduced sleep disorders in postmenopausal women [13], anxiety in pregnant women [14], during the active phase of labor in pregnant woman [15].

Potential candidates for the treatment of anxiety disorders and schizophrenia, anxiety and fatigue during the first stage of labor [16]. The results of these studies are consistent with present study. Anxiety is one of the factors closely associated with pain, and pain is also one of the causes of anxiety in patients [17]. Considering these facts, it could be concluded that pain relief is significantly effective in reducing anxiety. Analgesic effects of saffron have been identified in different studies [7,18]. The results were consistent with the present study, proving the effect of saffron on reducing the anxiety of human subjects. The effects of saffron on anxiety and the quality of sleep of diabetics are likely to be associated with the Crocin and safranal of saffron [19]. Crocin is a water-soluble compound and safranal is a fat-soluble one, acting by two different mechanisms. Crocin is likely to be effective in dopaminergic system and norepinephrine reuptake inhibition and safranal in serotonergic system. Saffron has similar activity to diazepam. Similar to diazepam as a benzodiazepine, it has anxiolytic, analgesic, and sleeping effects [20].

Limitations of the study

This study had some limitations: (1) Small sample size. (2) Lack of prior research studies on the topic. (3) Any subject who did not observe the communication arrangements were replaced by another subject.

CONCLUSION

The findings of the study that oral saffron capsules significantly reduces anxiety and improves quality of sleep of diabetic patients. Thus, saffron may be useful as a useful adjuvant therapy for the management of anxiety and sleep disorders but further clinical studies, including its safety and interaction with other medications, are required.

DECLARATIONS

Acknowledgement

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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