Evaluation of Saffron (Crocus Sativus L) Effects on Anxiety in Hospitalized Patients with Acute Coronary Syndrome

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Abstract

Background: Anxiety is a common psychiatric condition in cardio-vascular diseases. Saffron appears to have a wide range of therapeutic effects on psychiatric conditions and cardio-vascular disorders. The aim of this study was to determine the effect of saffron on anxiety in hospitalized patients with acute coronary syndrome (ACS).

Materials and Methods: In this clinical investigation, we selected 80 patients with ACS from Tohid Medical Center, Sanandaj. Patients were divided randomly into two groups, intervention group (n = 41), and control group (n = 39), based on how they received saffron and placebo every 12 hours for 4 days, respectively. The Spielberger Anxiety Inventory was completed before and after the intervention in both groups.

Results: There was no significant difference between the intervention and control groups regarding the mean scores of the trait and state anxiety before and after the intervention (P > 0.05).

Conclusion: The present study did not corroborate the therapeutic effects of saffron on reducing anxiety in patients with ACS.

Keywords: Acute coronary syndrome, anxiety, crocus sativus L., saffron

INTRODUCTION

Coronary heart disease (CHD) is the leading cause of death in the world. According to the World Health Organization in 2015, CHD took the lives of 8.8 million people worldwide. Acute coronary syndrome (ACS) is a sort of CHD which address to a group of situations that include ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina.[1]

In ACS, more than one-third of the patients experience high levels of anxiety.[2] Watkins' study showed that anxiety is associated with an increased risk of death in patients with CHD, particularly if it is associated with depression.[3] Fear and anxiety increase the respiration rate, blood pressure, cardiac output, cardiac irritability, and the possibility of irregular heart rhythm.[3] Anxiety is associated with development of atherosclerosis too.[4]

Saffron is a Middle-Eastern plant belonging to the lily species, and its dried stigma is known to be the most expensive spice in the world.[5] The favorable profile of saffron in the improvement of mental disorders and cardio-vascular diseases has recently received scientific attention.[6] The benzodiazepine-like effects of saffron on the gamma-aminobutyric acid-receptor complex of benzodiazepines and opioid receptors have been recently demonstrated.[7]

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There is no research regarding the effect of saffron on patients who have medically acute conditions. Therefore, this study is designed to determine the effect of saffron on anxiety in patients with ACS during hospitalization.

MATERIALS AND METHODS

This randomized clinical investigation is undergone on 80 patients with ACS in Tohid Hospital, Sanandaj, Iran, from October 2010 to May 2016.

Patients with ST-segment elevation confirmed by a cardiologist and over 18 years of age were included in this study. Exclusion criteria were allergies to saffron, use of anti-anxiety drugs, history of coagulopathy disorder, INR >2, pregnancy, kidney diseases, and history of psychiatric disorders.

After obtaining informed consent from participants in accordance with the revised Helsinki Declaration of 2013, patients were divided into intervention (n = 41) and control (n = 39) groups using a random number table. The study and placebo capsules were placed in vague, uniform, and uniformly sealed envelopes. Afterward, one of the random codes was assigned to each envelope. The drug was given to the patient every 12 hours for 4 days. The patients, the members of the research team who evaluated the patients, and the statistical consultant were blind to the assigned intervention and control groups.

After preparing the plant from the pharmaceutical market, 120 grams of dried saffron stigma was ground by soaking in three stages with 1800 ml of ethanol, and the extract was diluted. The ethanol extract then evaporated at 35–45°C and filled into the capsules with excipients (powders). 300 mg of bread powder was placed in the placebo and prepared in capsules of the same size and color as the drug capsules. The

demographic information form and Spielberger State-Trait Anxiety Inventory (STAI) questionnaire were used to collect data prior to the intervention. The Spielberger Anxiety Questionnaire comprises two parts, namely, overt anxiety and covert anxiety, each of which contains 20 options. These options were rated on a scale of 1–4 in the range of 20–80; they further divided into three groups: mild anxiety (20–40), moderate anxiety (41–60), and severe anxiety (61–80).

The Spielberger questionnaire was completed on the second and fourth days of hospitalization. Laboratory tests including complete blood cell count, serum electrolytes, and cardiac enzymes, including lactate dehydrogenase, creatinephosphokinase, and troponin, and blood urea nitrogen, creatinine, and coagulation tests were performed every 12 hours. Baseline and daily electro-cardiograms were taken too.

During the intervention, the cardiologist was responsible for deciding whether to continue or discontinue the intervention in the event of drug side effects.

Statics

In this study, considering a 10% drop, 40 people were assigned to each group according to the study of Lopresti *et al.*,[8] 0.05 type error, and 70% test.

Mean and standard deviation are calculated for quantitative and frequency variables and percentage for qualitative variables. Chi-square and analysis of covariance (ANCOVA) tests used to analyze the findings.

RESULTS

Of 90 patients who were randomized to study, 80 completed the investigation and ten cases were excluded [Figure 1].
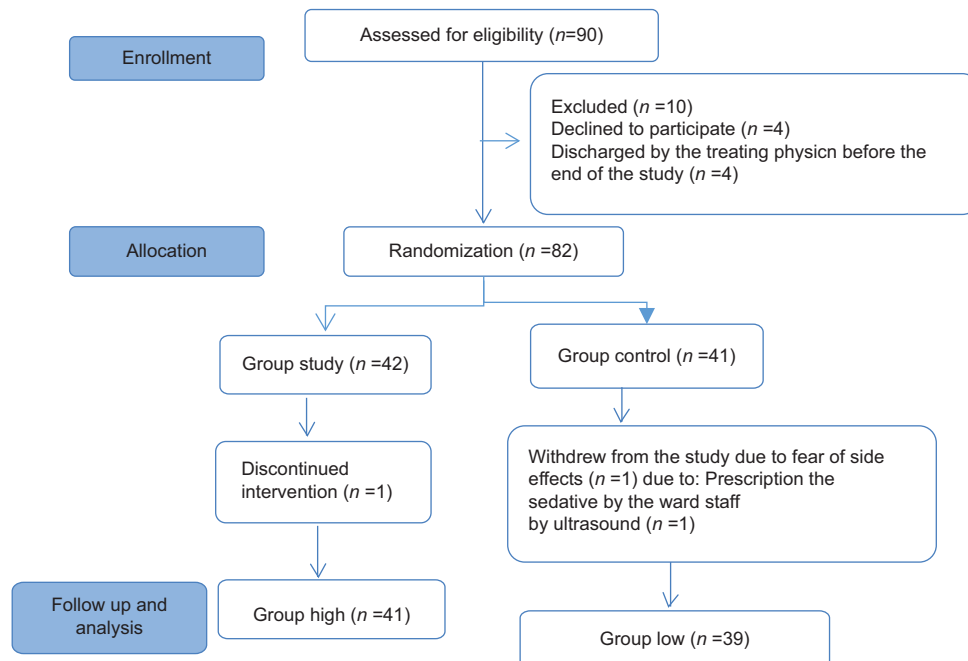

Figure 1: CONSORT flow diagram

According to the results of Chi-square test, the two groups matched in terms of demographic variable [Table 1].

There was no significant difference between the mean of trait anxiety before the intervention on the second day and after 4 days of the study in the two groups (p > 0.05) [Table 2].

There was a significant difference between the mean of state anxiety before the intervention and on the second day (p > 0.05). However, there was no significant difference between the mean of state anxiety on the first and fourth days. In addition, there was no significant difference between the mean of trait anxiety before the intervention with trait anxiety on the second day and the mean of trait anxiety on the second day with the fourth day of the study within the groups [Table 3].

DISCUSSION

Based on the results of this study, saffron had no effect on mean scores of overt and covert anxiety compared with placebo on patients with ACS during hospitalization. This means that our study did not support the hypothesis of saffron anti-anxiety effects in reducing anxiety in patients with the ACS.

Moazen-Zade *et al*.[9] examined the effect of saffron on cognition, anxiety, and depression in 22 patients who underwent on-pump coronary artery bypass graft. They prescribed 15 mg/twice daily saffron for 12 weeks and concluded that they cannot confirm the anti-anxiety effects of saffron.[8] The result of this study is consistent with the results of our study. However, the duration of treatment is not the same.

Mazidi *et al*.[10] studied saffron effects on 60 patients with anxiety and depression and concluded that it has a significant impact on the treatment of anxiety and depression disorder. The differences between our results with the above-mentioned study has two aspects. First, Mazidi *et al*. studied about a chronic disorder instead of a state induced by intervention like our study; second, the duration of intervention was 12 weeks instead of 4 days of our study.[9]

Godarzi *et al*. and Basiri-Moghadam *et al*. compared the effects of saffron with those of diazepam on reduction anxiety before and after urological surgery[11,12]; in their study, saffron did not reduce state anxiety, which is consistent with the results of the present study, whereas its effect on trait anxiety was significant. Differences in findings may be related to the study population. Those studies enrolled only the male population, whereas the present study considered both genders.

Shahdadi *et al*.[13] reported the effect of saffron on reducing anxiety and improving sleep quality in diabetic patients in an out-patient clinic, which is not consistent with the results of the present study. Differences in findings may be because of the differences in sampling method. Hospitalization in coronary care units, invasive procedures such as angiography, and the need for treatments such as percutaneous coronary intervention and coronary artery bypass grafting lead to a high level of anxiety in each patient.[14] This is because human heart is a critical organ, and the dose of saffron used in their study was higher than that of the present study. Because the effect of sedative hypnotics on the central nervous system is dose-dependent,[15] the lethal dose of saffron considered 20.7 grams per day[6]; therefore, the safety margin of saffron is high, making it possible to use higher doses.

Table 1: Cognitive characteristics of study group patients

P	Placebo Group (*n*=39)	Saffron group (*n*=41)	Variable
	frequency	absolute frequency	
Gender			
Female	14 (41/2%)	20 (58/8%)	0/267
Male	25 (54/3%)	21 (47/5%)	
Marital status			
Married	36 (5/7%)	35 (49/3%)	0/483
Single	0.0 (0.0)	0.0 (0.0)	
Spouse has died	3 (3/33%)	6 (6/66%)	
Level of Education			
Illiterate	20 (48/8%)	21 (51/2%)	
Primary	8 (38/1%)	13 (61/9%)	0/486
Third-grade middle school	6 (75%)	2 (25%)	
College education	3 (60%)	2 (40%)	
Job			
Employee	3 (75%)	1 (25%)	0.685
Retired	8 (50%)	8 (50%)	
Freelance	28 (47/5%)	31 (52/5%)	
Jobless	1 (10%)	0.0 (0.0%)	
Hospital history			
Mean±SD	4/15 (3/17)	3/93 (3/27)	0/71

Table 2: Comparison of changes in mean anxiety score between saffron and placebo groups

Variable	Saffron	Placebo	Test statistics	P
State anxiety				
State anxiety before intervention	60.32 (9.012)	61.77 (6.834)	0.809	0.421
State anxiety The second day of the intervention		64.79 (6.354)	0.680	0.498
Fourth day State anxiety	63.68 (8.110)	62.90 (9.936)	0.956	0.342
Trait anxiety	64.85 (8.341)			
Trait anxiety Before intervention		59.44 (9,599)	0.288	0.774
Trait anxiety The second day of the intervention	58.85 (8.449)	58.77 (8.43)	-0.020	0.984
Trait anxiety on the fourth day of the intervention	63.68 (8.11)	58.51 (9.453)	0.349	0. 728

Table 3: Comparison of anxiety at days 2 and 4 in two groups

Variable	Placebo	Saffron	*P*
Score of anxiety before intervention Mean±SD	8.04. ± 57.83	58.12±8.22	0.34
Score of anxiety on the second day Mean±SD	8.11±0.63 68	64.39±7.48	0.42
Score of anxiety on the fourth day Mean±SD	64.53±8.43	63.72±8.21	0.34

The action mechanism of saffron in anxiety and depression in addition to its effect on the GABA receptor complex has been attributed to the modulatory effects of the hypothalamic-pituitary-adrenal axis and the inhibition of the re-absorption of monoamines and serotonin.[4] The therapeutic effects of saffron on neuro-transmitter changes in the brain may be similar to the response to drug therapy in anxiety or slow depression over 2 weeks or more.[6] Accordingly, the short duration of our study compared to most studies, which lasted for at least 6–8 weeks, led to a different outcome.[9,10] In the present study, no significant side effects were observed, except headache, dizziness, and heaviness of the head. There were no severe side effects in the patients.

The long interval between the admission and the assignment of patients by a cardiologist, the relationship between reduced anxiety and decreased symptoms of the disease at the time of admission, and the sampling during the outbreak of coronavirus disease 2019 could be among the causes of increased anxiety and stress in patients.

Conclusion

Based on our study results, acute and short-time (4 days) administration of saffron has no effects on anxiety in hospitalized patients with ACS.

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Conflicts of interest

There are no conflicts of interest.

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