Efficacy of Jollab in the Treatment of Depression: A Randomized Double-Blind Controlled Trial

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Abstract

Background and Aims: One of the most common psychiatric problems is depression. The utilization of traditional medicine, such as Jollab, as a complementary medicine in conjunction with modern medicine is likely to result in a more effective treatment of depression with fewer adverse effects. The current study aimed to evaluate the effectiveness of Jollab, as a Persian medicine in the depression treatment.

Materials and Methods: A randomized, double-blind, placebo-controlled clinical trial was conducted in 50 patients with mild to moderate depression . Patients were randomly divided into two groups, including treatment and placebo groups. The participants received experimental drug (Jollab) or placebo 15 ml three times a day, after meals for one month. After this period, Beck Depression Questionnaire II (BDI II) was completed by two groups, as well as before this period. Post-collection data were analyzed using independent t-test, paired t-test and chi-square test.

Results: Regarding Beck Depression Inventory, the values of both groups were similar before the experiment (p-value=0.320). BDI II score significantly decreased in treament group after treatment (p-value < 0.001), and the score difference between the placebo and treatment groups were statistically significant (p-value< 0.001) at the end of experiment.

Conclusion: Based on the results of the present research work, the Jollab treatment showed more effectiveness than the placebo. As a result, Jollab may be used as a pharmaceutical supplement to treat depression. However, more research is still needed in this subject. Furthermore, since medicinal plants are less expensive for both patients and medical personnel, this treatment strategy may be a viable option.

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1. Introduction

Depression is one of the mental disorders that arises as a result of some complex psycho-neurotic disorders. This disease is associated with persistent sadness, loss of interest, mood disorders, and impaired cognition, which results in distress to the patient, and effectively impairs the patients capability to function, and leads to an unsatisfying family, professional, and social life [1-3].

Based on world health organization (WHO), there are more than 300 million persons who suffer from depression globally [4]. This mental disease affects more women than males [5]. This illness is one of the leading causes of disability worldwide, accounting for a large portion of the global disease burden [6]. It accounts for approximately 35 to 45% of mental health problems in Iran and affects 8 to 20% of the Iranian population [7].

Depression requires comprehensive treatment, including pharmacological treatment [8]. Recently, integrative and complementary medicine was proposed to treat depression, which has fewer side effects compared to modern medicine [9]. Using the traditional medicine remedies as complementary medicines, along with modern medicine can help in finding better disease treatment for chronic diseases, such as depression with fewer side effects [10].

Persian medicine scientists mentioned many antidepressant remedies in Persian textbooks, and one of these remedies is Jollab, a familiar antidepressant syrup in traditional Persian medicine. Jollab is often suggested as an antidepressant and euphoric. Jollab has various impacts on the neural system, cardiovascular system, digestive system, and may also induce drowsiness. Jollab is a beverage that often includes saffron, white saffron, rose water, and water as its main components [11, 12]. Because there are few clinical studies evaluating the effectiveness of Jollab in depressed patients, this randomized clinical trial aimed to evalute the effect of Jollab on depression.

2. Patients and Methods

Study Design and participants

This study was a randomized, double-blinded, placebo-controlled parallel group clinical study which was conducted from June 1st to November 30th, 2021 in the Psychiatric clinic of Rafsnjan, a district in southeastern Iran. This research comprised 52 people, aged between 18- 65 years, who were diagnosed with mild to moderate depression based on the Beck criteria. Every patient had an interview conducted by a psychiatrist, who subsequently verified the diagnosis. The participants were excluded in the case of severe depression, using other traditional medicines, addiction, alcohol dependence, breastfeeding, pregnancy and diabetes mellitus. Besides, subjects were excluded if the case of some other serious psychiatric disorders diagnosis, such as paranoia. This study was approved by Ethics Committee of Rafsanjan Medical University (ethics number: IR.RUMS.REC.1398.204). Written informed consent was obtained from all participants and only the researchers were allowed to access the participants' information.

Randomization and sample size:

Randomization was performed using a computer-generated program and each patient was assigned a random code by an independent research coordinator. The randomization codes

were checked at the conclusion of the trial to confirm that the study's blinding was maintained. The therapy session was intended to last one month. Finally, 52 patients were separated into two groups: the therapy group and the placebo group. Throughout the study period, the psychiatrist did not know the patients' code, and the drug and placebo were completely similar in appearance. After the evaluation of patients by the psychiatrist, the diagnosis and registration of the drug, and placebo was done by another person.

Using a previous study (11) and considering the type I and II errors of 0.05 and 0.2, σ_1 = 6.45 and σ_2 = 9.85, $\mu_1 - \mu_2$ = 7, and attrition= 10% the final sample size was 26 cases in each group using the below formula:

$$n = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2 \left(\sigma_1^2 + \sigma_2^2\right)}{\left(\mu_1 - \mu_2\right)^2}$$

Experimental Medication:

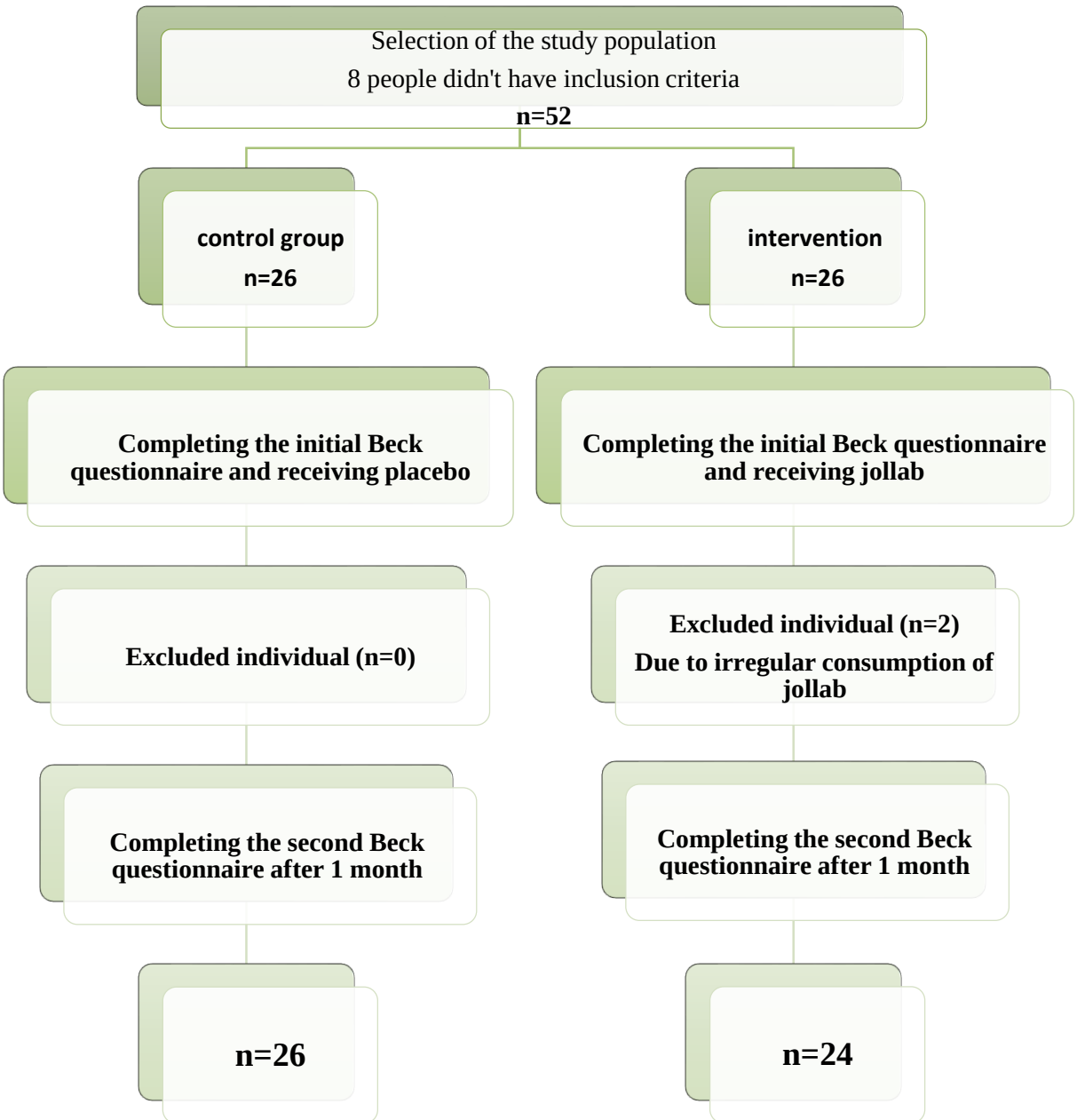
In our study, we used Jollab as a cheerful drink in the traditional Persian medicine texts to study depression. This is a mixed syrup made from water, saffron, rose water and white rock sugar. They were all under the control of Ministry of Health. Rose water is the distillation of rose petals (from the rosacea family) in the production of essential oils. The Qaynat Company produced the saffron stigmas, which were also used to make white rock sugar. This formulation adheres to the guidelines outlined in Ibn Sina's Qanoon. Consequently, the rock sugar was dissolved in rose water under a mild fire.. Then, the saffron was suspended, and soaked in the mixture. The daily dose was 15 mililiters (mls) of prepared syrup, three times a day after meals. The placebo was assigned the same attenuated properties and the use of standard additives, such as food coloring, and rose water was diluted in water at a concentration of 1:10 with the same packaging.

Groups:

Two treatment and placebo groups were considered for this study. The treatment group consumed 45 mls of traditional Iranian syrup (Jollab) daily in three sessions (15 mls of syrup, 20 minutes after breakfast, lunch, and dinner) for one month. Moreover, the placebo group consumed 45 mls of placebo syrup dialy (15 mls of syrup, 20 minutes after each meal) with an appearance similar to syrup during the same period.

Assessments:

Beck Depression Inventory II (BDI II) questionnaire was used to assess the severity of depression as a recognized self-report instrument for evaluating depressive symptoms in the adults [13]. This is a practical and validated questionnaire including 21 items with a total score ranging from 0 to 63 [14, 15]. The score of BDI II ranging from 0-13 (no depression), to 14-19 (mild depression), 20 to 28 (moderate depression), and 29 t0 60 (severe depression). The questionnaire was completed by psychiatrist via an interview with every patient before and after the intervention. The outcomes were defined as an improvement in depression in the event of a decrease in the total score as determined by the Beck Depression Inventory II. Participants were requested to document all adverse effects that occurred during the treatment period. They also could call the first author to report side effects in emergency situations.



Statistical Analysis

The collected data were statistically analyzed by SPSS version 24 software. The results for quantitative data are reported as "standard deviation ± mean", and for the qualitative data as "number (percentage)". The intention to treat (ITT) approach was used for data analysis. The mean of quantitative variables in the two investigated groups was compared using an independent two-sample t-test. Hence, to compare the frequency distribution of qualitative variables in two studied groups, Chi-square test was used. Paired-Samples T Test was used to evaluate the jollab effectivness before and after intervention. Using the Kolmogorov-Smirnov non-parametric test and the skewness and kurtosis indices, the normality of the frequency distribution of the quantitative variables was assessed. No deviation from this assumption was observed (P>0.05). The significance level in the tests was considered 0.05.

3. Results:

The demographic characteristics of subjects is presented in Table 1. There was no statistically significant difference in age between placebo and treatment groups (40.00±2.60 vs 40.33±4.26, P=0.738 respectively). Furthermore, there was no stastically significant difference in education (p-value=0.281), occupation (p-value=0.963), marital status (p-value=0.887), and BMI (p-value=0.113) between placebo and treatment group (Table 1).

Table 1. Demographic and clinical characteristics of patients.

P-value	Groups		Characteristics
	Treatment (n=24)	**Placebo (n=26)**	
0.738		**Age**	
	40.33±4.26	40.00±2.60	mean±SD
0.897		**Gender n(%)**	
	13 (54)	**15 (57)**	**Male**
	11 (46)	**11 (43)**	**Female**
		BDI II score	
0.320	14.50±0.66	13.00±1.02	mean±SD
0.887		**Marital status-n(%)**	
	5 (20.8)	5 (19.2)	Single
	19 (79.2)	21 (80.8)	Married
0.281		**Education-year-n(%)**	
	3 (12.5)	3 (11.5)	No schooling
	6 (25.0)	12 (46.2)	1–5 years of school
	15 (62.5)	11 (42.3)	≥6 years of school
0.963		**Occupation-n(%)**	
	14 (58.3)	15 (57.7)	Employed
	10 (41.7)	11 (42.3)	Unemployed
0.113		**BMI-n(%)**	
	2(8.3)	4(15.4)	under weight
	10(41.7)	4(15.4)	normal
	12(50.0)	18(69.2)	over weight and obese

BDI II: Beck Depression Inventory II, BMI: Body Mass Index

Before the treatment session, BDI II score did not show any statistically significant variation between the placebo and treatment groups (p-value=0.320). The BDI II score in the treatment group was much lower after intervention than it had been before treatment (p-value 0.001). On the other hand, the deprresion score significantly increased (p-value<0.001) in the placebo group compared to before (table 2). There was significant difference in BDI II score between the groups after the intervention (p-value<0.001) (table 2).

Table 2. Comparison of Placebo and Treatment group.

characteristics	Groups							
	Placebo (n=26)			Treatment (n=24)			**P-value betwen groups (Befor)	**P-value betwen groups (After)
	Befor	After	*P-value	Befor	After	*P-value		
BDI II score			<0.001			<0.001	0.320	<0.001
Mean ± SD	13.00±1.02	15.32±1.78		14.50±0.66	12.42±1.69			

*p value derived from Paired-Samples T Test
** p value derived from Independent two-sample t test
BDI II: Beck Depression Inventory II

4. Discussion:

The current clinical trial was designed to assess the effectivness of Jollab as a traditional syrup in treating depression. The B DI II score decreased considerably in the therapy group after intervention, but it rose noticeably in the placebo group. Among the limitations of this research, this might be the result of confusing elements like lifestyle and food, which were not examined in this one. Our results aligned with those of various other studies. Pasalar et al. reported favorable effects of jolab on depressive symtoms and functional dyspepsia in 2020 [16]. Furthermore, there were some other studies evaluating the effects of natural herbs alone or as adjunctive therapy with psychiatric medications on depression which showed favorable effects [17-19]. Akhondzadeh et al. showed a better effect of imipramine in combination with lavandula tincture as a medical herb in treatment of mild to modetare depression rather than imipramine alone in a randomized clinical trial [17].

Rose water was one of the herbs in jolab syrup. Vorious studies reported different healing properties for rose, including antimicrbial, skinprotection and anthiasmathic properties [20,21]. Besides, some other studies have shown antidepressant effects of water rose which was consistent with the findings of the present study [22-24]. They reported that aromatherapy with rose had beneficial effects on depression and anxiety in expectant women who experienced nausea and vomiting in a clinical trial conducted by Afiat in 2022 [22]. Additionally, other studies have demonstrated the beneficial effects of aromatherapy with rose on anxiety and postpartum depression [23, 24]. Saffron was the another medicinal herb in Jollab syrup. The main components of saffron are picrocrocin, crucin and safranal with many medicinal properties [25]. Research showed that this herb can significantly lower depression compared to placebo. Moreover, some other investigations have found that saffron can be as effective as antidepressants [26, 27].

Limitations

One of the limitations of current study was the small sample size, which needed to be enlarged to accomplish better results.Therefore, it is not correct to investigate the effect of this syrup in depressed patients without seeing other significant accompanying factors. In this regard,

the findings should be evaluated more specifically.

5. Conclusion:

The present research was conducted to provide the evidence for the safety and effectiveness of a familiar Persian drink, Jollab, that was used in traditional Iranian medicine for the psychiatric problems. The results indicated that this solution was more effective than a placebo in treating melancholy in patients. Nevertheless, additional research is still required in this field. Furthermore, due to the fact that medicinal plants are cheaper for people and the treatment staff, using this treatment method can be a solution.

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Conflict of interest

The authors declare no conflict of interest.

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