Original Article

Complementary/alternative medicine Section

Comparison of Effect of *Lavandula officinalis* and Venlafaxine in Treating Depression: A Double Blind Clinical Trial

MASOUD NIKFARJAM[1], REZA RAKHSHAN[2], HOURIVASH GHADERI[3]

ABSTRACT

Introduction: Major depressive disorder is a chronic disease which may be associated with other mental illnesses. *Lavandula officinalis* and venlafaxine, herbal and chemical drugs respectively, are used to treat depression. Despite pharmacotherapy, major depressive disorder has a complicated pattern of resistance and recurrence.

Aim: The aim of this study was to determine the effect of *L. officinalis* and venlafaxine in treating depression.

Materials and Methods: For this study, 120 patients referred to the psychiatry clinic of the Shahrekord University of Medical Sciences, Shahrekord, Iran, were randomly selected. The participants were randomly assigned to three groups: venlafaxine (Control Group), venlafaxine + *L. officinalis* (*L. officinalis* Group), and venlafaxine + placebo (Placebo Group). All the patients underwent treatment for six weeks. Depression test was administered to the three groups at different time intervals before the treatment, four weeks after the treatment and at completion of the treatment. The data were analysed by SPSS version17.0.

Results: Depression scores of all the groups decreased over time (p=0.001). The depression scores were significantly different between the control and *L. officinalis* groups (p=0.004), and the control and placebo groups (p=0.002), but were not significantly different between the *L. officinalis* and placebo groups (p=0.95).

Conclusion: Adding *L. officinalis* or a placebo is equally effective in decreasing mean depression score and venlafaxine obviously decreased this score.

Keywords: Antidepressant, Depressive disorder, Medicinal plant

INTRODUCTION

Health Organization has projected that approximately 350 million people of all ages are suffering from depression. Most of these people are women [1]. Major Depressive Disorder (MDD) is a chronic disease which may be associated with other mental diseases and has a complicated pattern of resistance and recurrence [2,3]. For this reason, this disease disturbs the function and efficiency of affected people and therefore represents a major economic burden on health care systems [4]. Also, chronic diseases adversely affect the quality of life of the patient [5-9]. In addition to many complications and problems, suicide is one of the most dangerous outcomes of this disease [10].

Worldwide, depression is a prevalent mental disease and a major cause of disability. The treatment for depression is based mainly on the use of antidepressants and pharmacotherapy [11]. Most psychiatrists begin the treatment with a Serotonin-Specific Reuptake Inhibitor (SSRI). Pharmacotherapies include bupropion (a noradrenergic, dopaminergic drug with properties similar to those of stimulants), the SSRIs, norepinephrine (venlafaxine and duloxetine), nefazodone (a drug with serotoninergic properties), and tricyclics [12].

Among these drugs, venlafaxine is a relatively new drug which is different from other antidepressants. Venlafaxine is likely to have no or fewer complications, especially cholinergic, than other antidepressants or be more effective than the SSRIs in treating depression [13,14]. Headache, sleeplessness, nausea, dry mouth, dyspepsia, diarrhea, weakness, dizziness, constipation and decreased libido are the cardiogenic complications and convulsion is one of the side effects of venlafaxine [12,15,16].

Despite the progress achieved in pharmacotherapy, the symptoms remain to recover in a large proportion of people with depression, who undergo treatment with these drugs [17]. It is argued that antidepressants exert inhibitory effects and fail to treat the disease [18]. Therefore, it is necessary to find a useful therapeutic approach for the patients.

Using medicinal plants to treat mental disorders and chronic diseases has recently become widespread [19-21]. *Lavandula officinalis* is a medicinal plant that is used to treat depression. *L. officinalis* is a plant of family Lamiaceae [22] and has long been used as antibacterial, antifungal and antidepressant. *L. officinalis* oil is sedative and is used to treat wound burns and stings [22]. *L. officinalis* flower has therapeutic uses. *L. officinalis* contains flavonoid components that affect benzodiazepine receptors [23]. The existence of certain components, such as linalool and linalyl acetate and the flavonoid, such as luteolin in Lavandula Vera, raises the possibility that *L. officinalis* may be effective on central nervous system. The linalool in *L. officinalis* causes increase in noradrenalin and dopamine and therefore helps to exert antidepressant effect [24]. Inhaling the odour of linalool, a significant component of *L. officinalis*, has sedative effects on both humans and animals [25].

The essential oil of *L. officinalis* contains monoterpenes (1-3%). The most important components are linalyl acetate (30%-55%), linalool (20%-35%), beta-ocimene, cineol, camphor, sesquiterpene, caryophyllene oxide, tannin, rosmarinic acid derivatives, coumarine and flavonoids [26].

Antidepressants may not be welcomed because of inducing several side effects in some people [27]; moreover, there are debates over the immunity and the side effects of the medicinal plants that are used to treat mental diseases [28]. Venlafaxine is a drug of choice to treat depression. To date, little research has been conducted on venlafaxine and no study has been conducted to compare the effects of venlafaxine with *L. officinalis* in depression. Therefore, it

is necessary to find a useful therapeutic approach for the patients. This clinical trial was conducted to compare the therapeutic effects of venlafaxine and *L. officinalis* in people suffering from MDD.

MATERIALS AND METHODS

The study was a double-blind clinical trial and was conducted in 2015. The Ethics Committee of the Shahrekord University of Medical Sciences approved the protocol of the study (approval no. 25-94 and IRCT201604116480N13). Study population consisted of the patients with mild to moderate MDD who were referred to the psychiatry clinic. The diagnosis was made by a structured clinical interview conducted by a psychiatrist according to the DSM-5 criteria [29, 30]. The patients with a score of at least 17 on Hamilton Depression Rating Scale were diagnosed with depression and included in the study.

Withdrawal from the study or being under routine treatments for depression, allergy to *L. officinalis*, history of using antidepressants, *L. officinalis*, or any medicinal plants with antidepressant effects, psychosis, underlying diseases and substance abuse were considered for exclusion. From the people with inclusion criteria who provided written consent to participate in the study, 120 people were selected. Sampling was done gradually and purposively. After the research purpose was explained to the people, they were assigned to three groups by simple randomization. For single blinding purpose we administered placebo to one of the study groups.

The patients were divided into three groups: Venlafaxine (Control Group), venlafaxine + *L. officinalis* (*L. officinalis* Group), and venlafaxine + placebo (Placebo Group). Control Group was administered with a routine treatment for depression, 37.5 mg venlafaxine, placebo group with 37.5 mg venlafaxine and peppermint (in a 1.5 gm tea bag placed in a cup of boiling water for 10-15 minutes and then taken with candy every 12 hours) (according to German pharmacopoeia), and case group with 37.5 g venlafaxine and *L. officinalis* (in a 1.5 g tea bag placed in a cup of boiling water for 10-15 minutes and then taken with candy every 12 hours) (according to German pharmacopoiea).

The enrollment of the people and administration of the treatments were conducted within six months. The questionnaire of depression was administered to all the patients prior to the treatments and then at three and six weeks after initiation of the treatments depending on the day of referral.

The participants were followed up by the psychiatrist during the study. The psychiatrist examined them for side effects, depression symptoms, and the risk of suicide and recorded the relevant data. If the risk of suicide was diagnosed at any stage of treatment, they were immediately referred to the psychiatrist for treatment. The data were gathered through interview, the questionnaires of demographic characteristics, side effects and the Hamilton Depression Rating Scale. For ethical considerations, a form enlisting the side effects was provided to all the participants to record potential side effects.

Concurrent validity yielded moderate to high correlation coefficients, 0.55-0.96 and r=72 mdn, with clinical rating of psychiatric patients. The corresponding correlation coefficient was obtained 0.73 with the Hamilton Depression Rating Scale [31].

The scores 17-24 were considered mild depression, 25-30 moderate depression, and the total scores above 31 severe depression [32,33]. The data were analysed by descriptive statistics, chi-square, and t-test was used. Data analysis was conducted by SPSS version 17.0.

RESULTS

The data on the age, gender, education level, and place of residence were compared among the groups. The mean (standard deviation) age of the patients was 36.7±2.09, 38.2±2.32 and 34.9±2.16 in control, case and placebo respectively. There was no significant difference among three groups (p=0.55). The chi-square results indicated that the three groups were matched on age, gender, education level, and the place of residence (p>0.05) [Table/Fig-1].

The depression scores of the groups were measured at the three points of time. The repeated measures ANOVA indicated that the depression indices of the groups decreased over time (p≤0.001).

Groups Variables	Scale	Control Group	Case Group	Placebo group	p-value
Sex					
Male	No (%)	22 (55)	20 (50)	19 (47.5)	0.79
Female		18 (45)	20 (50)	21 (52.5)	
Education level					
Diploma and under	No. (%)	26 (65)	19 (47.5)	15 (37.5)	0.06
Associate Degree		9 (22.5)	16 (40)	22 (55)	
Bachelor's degree		4 (10)	3 (7.5)	1 (2.5)	
MSc and higher		1 (2.5)	2 (5)	2 (5)	
Place of residence					
Urban	No. (%)	27 (67.5)	27 (67.5)	23 (57.5)	0.56
Rural		13 (32.5)	13 (32.5)	17 (42.5)	

[Table/Fig-1]: Mean (Standard deviation) of demographic characteristics in the control, *L. officinalis* and placebo groups.
*chi square test used

The depression scores were significantly different between the control and *L. officinalis* groups (p=0.004), and the control and placebo groups (p=0.002), but were not significantly different between the *L. officinalis* and placebo groups (p=0.95). The depression scores of the groups were significantly different at different points of time [Table/Fig-2].

DISCUSSION

This study was conducted to determine the effects of venlafaxine and *L. officinalis* in treating people with depression at three points of time.

In this study, the depression indices in Venlafaxine Group obviously decreased (from 1.04±0.01 at the baseline to 0.71±0.01 in the six weeks after treatment) while in *L. officinalis* and placebo groups, no significant difference in decreased depression scores at different intervals was seen (p>0.05).

Also, a double-blind clinical trial to investigate the effects of *L. officinalis* tincture and imipramine in treating mild to moderate depression, found that the effect of the *L. officinalis* effect was lesser than the imipramine effect. However, combined imipramine and *L. officinalis* tincture was more effective than the imipramine alone [32]. Relevantly, another study using the Hamilton Depression Rating Scale to measure the depression severity, demonstrated that the mean depression indices of the case group, administered with citalopram and *L. officinalis*, declined more notably than the control group, administered with citalopram alone, after eight weeks [33]. A study reported that L. officinalis cream could relieve anxiety, stress, and depression of pregnant women [34].

Animal studies have confirmed the antidepressant effects of *L. officinalis*. Kageyama A et al., found that the *L. officinalis* extract, administered at three points of time, caused decrease in the mice's

Point of time	Groups	Mean±SD	p-value
Before treatment	Control	1.04±0.01	0.99
	Placebo	1.04±0.01	
	Control	1.04±0.01	0.99
	L. officinalis *	1.04±0.01	
	Placebo	1.04±0.01	0.98
	L. officinalis	1.04±0.01	
Three weeks after treatment	Control	0.91±0.01	0.04
	Placebo	0.97±0.01	
	Control	0.91±0.01	0.26
	L. officinalis *	0.95±0.01	
	Placebo	0.97±0.01	0.66
	L. officinalis	0.95±0.01	
Six weeks after treatment	Control	0.71±0.01	<0.001
	Placebo	0.90±0.01	
	Control	0.71±0.01	<0.001
	L. officinalis *	0.90±0.01	
	Placebo	0.90±0.01	0.97
	L. officinalis	0.90±0.01	

[Table/Fig-2]: Mean (standard deviation) scores of depression in the control, *L. officinalis* and placebo groups.
t-test used.

physical inactivity. This finding was comparable to the imipramine effect. Linalool, an effective aromatic component of *L. officinalis*, was removed during preparation. Rosmarinic acid and apigenin glycosides of *L. officinalis*, which were studied in Kageyama A et al., study, have similar effects to antidepressants [35].

Seol GH et al., study on the laboratory rats reported consistent findings [36] with the present study. Studies indicated that methanolic and aqueous extract of *L. officinalis*, exert sedative and hypnotic effects on Central Nervous System (CNS) and therefore can prevent psychological problems [37,38]. This effect could induce through decreasing amount of cortisol and increasing amount of serotonin [39]; However, high concentration (0.1 mg/ml) of *L. officinalis*, oil induced a neurotoxicity effect [40]. Many of the plant based products have several components at different therapeutic concentrations, which affect controlling their quality and dose of administration [41]. Depressions may be influenced by many factors and the duration of follow up of case group is likely to confound the findings.

The findings demonstrated that the depression indices of the three studied groups, control, *L. officinalis* and placebo declined over time. However, certain drugs and multiple drug therapy can have better effects on the treatment course in some patients [42]. Cipriani A et al., study found that citalopram had better effects than venlafaxine and the herbal drugs, such as hypericum, in treating MDD [43].

Depression may be associated with other mental illnesses and no consideration of such classification was a limitation of the present study. Because depression is a chronic disease and the effect duration of different drugs may vary, future studies are recommended to adopt a longer duration for administration of the drugs under study. Moreover, to obtain higher quality findings, future studies should examine the efficacy of a single drug or multiple drugs in a pilot study and then assign the patients into treatments of interest in main study. Toxicity is an important issue about the medicinal plants.

LIMITATION

Other mental illnesses concomitant with depression was one of the limitations of this study.

CONCLUSION

Adding *L. officinalis* or a placebo is equally effective in decreasing mean depression score. In contrast, in Venlafaxine Group the decrease in mean depression score was more marked compared to the other groups.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Psychiatry, Islamic Medicine Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran.
2. General Practitioner, Student Research Committee, Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, I.R. Iran.
3. Assistant Professor, Department of Psychiatry, Modeling in Health Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Hourivash Ghaderi,
Assistant Professor, Department of Psychiatry, Modeling in Health Research Center,
Shahrekord University of Medical Sciences, Shahrekord, Iran.
E-mail: ghaderi.houri@gmail.com

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