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Effect of Melissa officinalis capsule on the mental health of female adolescents with premenstrual syndrome: a clinical trial study

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Abstract:
Introduction: In spite of its importance, the psychological health requirements of adolescents are ignored; due to the occurrence of mental disorders in this age group and also public interest in the use of supplementary and alternative treatments such as herbal drugs for mental disorders, this study was carried out aimed at examining the impact of the Melissa officinalis capsule on the psychological health of female adolescents.

Methodology: In this randomized clinical trial study, 100 female adolescents were assigned to two groups of either drug and placebo groups. The data collection tool includes demographic information recording note and General Health Standard Questionnaire (GHQ). Intervention has been done in the menstrual cycle during 3 successive months and patients received two 600 mg drug daily in the intervention group, and the control group received placebo. After the intervention, the scores of the participants’ psychological health were measured in both groups and data were analyzed through independent t-test using SPSS software version 16.

Results: The study results showed that psychosomatic symptoms score (p < 0.001), anxiety and sleeping disorder (p < 0.001), and social function disorder (p = 0.021) in the experiment group was significantly less than that of the placebo group.

Conclusion: Based on the findings of this study, Melissa officinalis can decrease psychosomatic symptoms, sleeping disorder and anxiety, depression and disorder in social function in female adolescents.

Keywords: adolescents, Melissa officinalis, premenstrual syndrome

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Introduction

Children and adolescents amount to almost one third of the population of the world and roughly 90% of them live in low and average income countries, regions where they even make up 50% of the population. Psychological health needs of children and adolescents are neglected in spite of their importance, especially in low and average income countries [1]. Psychological health is a part of health based on the World Health Organization (WHO) guidelines [2].

In all societies, a fairly large number of diseases among the youth consist of psychological health issues. Psychological health is strongly related to other healthcare and developmental issues of the youth. Attention to psychological health of the youth for using their potentials and contributing to the development of society is of high importance. A lot of psychological disorders begin at the ages of 12 to 24 years [3]. Psychological health disorders affect 10–20% of the world’s children [1].

Prevalence of mental disorders varies from 8% in the Netherlands to 57% in US. At least one in every four or five adolescents suffers from at least one mental disorder [3]. One of the causes of lack of health for adolescents is psycho-neurological disorder which makes up 15 to 30% of daily adjusted years (DALY) [4]. In spite of a lot emphasis on enhancing the health and preventing diseases, in these groups there is big gap between needs and resources [1]. And a lot of their psychological health needs have failed to be satisfied [3]. On the other hand,
one of the problems which causes problems for women in the reproductive age is premenstrual syndrome (PMS) which imposes a heavy cost on individuals and society [5]: it starts with psychological symptoms such as difficulty concentrating, anger, personal conflicts, anxiety, stress, depression, despair and self-criticism [6]. A study has found a relationship of 22.9% between intense PMS and psychological disorders [7]. Therefore, one can acknowledge the necessity of attention to adolescent psychological health, especially in girls with PMS.

On the other hand, during the past decade, the increase in public attention to complementary and alternative medicine (CAM) and use of herbal medicine have increased [8], [9], and the ratio of referral to traditional medicine experts for psychological issues is comparable with that to ordinary primary care centers. According to Simon et al.’s studies, 10% of American adults have reported that in the past year they have used CAM for psychological disorders, especially depression and anxiety. Studies have also paid more attention to the use of CAM for general and psychological health [9]. In some countries such as Australia, the use of antidepressant drugs is not recommended for people under 18 [10]. There is a wide range of traditional treatments and according to WHO reports, in some of Asian and African countries traditional drugs serve as the primary method of health care for 90% of people [11]. This growing tendency toward the use of medical herbs among people implies the necessity of familiarity of experts with the implications of some drugs which are used more commonly among people [12]. One of the traditional drugs which was used more than 2000 years ago, for curing mental disorders is Melissa officinalis [13], [14], [15]; for a long time this drug has been used as a mild sedative, to induce sleep and as an anti-anxiety medication [8], [13], [14], [15]. In recent years, some studies on the impact of this drug on anxiety, depression, cognition, restless sleep and sleeping disorders have been done [14], [15], [16], [17], [18], and its positive effect on these dimensions has been shown and no side effect has been reported. However, the majority of studies have stressed on the necessity of further studies in this regard. Based on Yoo et al.’s study, “Melissa officinalis leaf extract can decrease corticosterone levels in serum and GABA-T levels in the DG homogenates, and increases cell proliferation, neuroblast differentiation and integration into granule cells through serum corticosterone levels reduction and enhancing GABA levels in the mouse DG” [19]. This herb’s neuroprotective effect against conditions such as ischemic brain injury and ecstasy induced neurotoxicity and apoptosis has been proven [20], [21]. So we chose M. officinalis. Therefore, due to the necessity of further studies in this regard, lack of studies on the effect of this drug on the PMS female adolescents’ mental health, and considering the various dimensions of psychological health including psychosomatic, anxiety, sleeping disorders, social function disorder and depression in Iran, we carried out a study aimed at examining the effect of M. officinalis capsule on the mental health of high school girls with PMS; in the case of a positive effect, one would be able to recommend it as a low cost and safe drug for enhancing this age group’s psychological health.

Method

This study is a randomized controlled double blind clinical trial which was carried out in Shiraz (Iran) high schools between December 2013 and June 2014. The adolescents’ and their parents’ consent was taken and the study was confirmed by the university ethics committee No. 92-6805. The study was registered in the Iran Clinical Trial Registry International Center with code IRCT2014060717998N1. At first, after the confirmation of the Council of Complementary Education of Shiraz University of Medical Sciences and with supervision of education organization, 800 female students were selected randomly through the clustered multiple stage sampling method; among them 100 students with PMS were selected via the premenstrual symptom screening test (PSST) and assigned randomly into two groups of experiment and control, each consisting of 50 students. Inclusion criteria in the study were willingness to participate in the study, student studying, at one of the last three years of high school, selected from four districts of Shiraz Education, affliction with PMS, not currently using any kind of herbal or chemical drug during the study period, and lack of affliction with any mental diseases. Exclusion criteria included a tendency of the individual or their parents to quit the study, occurrence of a stressful event or stress for dolescent or her family during the recent 3 months and during the study period, and use of any other drug during the study.

Capsules containing M. officinalis essence in the form of 600 mg capsules were prepared by a specialized pharmacist in the Shiraz University of Medical Sciences’ medical faculty pharmaceutical group. The dose of the drug was two capsules daily from the first day through to the end of the menstrual period and for three cycles. The researcher contacted at least 3 or 4 times with the study units, talked to the patients for their guidance, and explained the care points and method of taking the drug. In the placebo group, the prepared capsules containing starch were delivered to the control group. The packs of drug and placebo were prepared by a pharmacist blinded to the study and in a confidential manner and the drugs were coded and the codes remained confidential until data analysis. The shape of capsules and drug and placebo packs was exactly the same and their content was unknown to the researcher and the patients. Those who dispensed the drug and the bio-
statistical expert were also unaware of the drug assignment. After finishing the intervention, a questionnaire on demographic information and general health questionnaire were completed to examine the psychological health of the studied population.

The General Health Questionnaire with 29 questions was devised by Goldberg (1972) and consists of four scales (depression, anxiety and sleeping disorder, disorder in social function and somatoform symptoms). Every scale has seven questions. Questions 1 to 7 are related to the somatoform symptoms scale, 8 to 14 to anxiety, 15 to 21 to social function disorder and 22 to 28 to the depression scale. In this study, the Likert scoring method which is scored from lack of symptoms to strong symptoms from 0 to 3 was used [22]. The Farsi version of this questionnaire translated by Ebrahimi et al. was used with sensitivity and specificity of 86.5% and 82%, respectively [23].

Another questionnaire used in this study for screening patients was the PMS screening questionnaire. It includes two parts: symptoms and the impact of symptoms in people’s lives. It includes 19 questions with two parts. The first part includes 14 affective, physical and behavioral symptoms and the second part which measures the impacts of symptoms on people’s lives includes five questions. For each question, four criteria are mentioned, namely not at all, slightly, average and strong which are scored from zero to 3. For diagnosing the average or intense PMS, there is a need to apply the following three conditions:

1. Among options 1 to 4, at least one is average to intense.
2. In addition to prior cases, of options 1 to 14, at least four cases are average or strong.
3. In the section on the impact of symptoms (last five options), one case should be average or intense.

The minimum score was 0 and the maximum was 57. Score 0 to 19 represents slightly, 20 to 38 average and 39 to 57 severe. In this study, people with a score of 20 and greater were included in study.

In some countries such as the US, Japan, Germany, Thailand and Canada, this questionnaire is used [24], [25]. In Iran, the validity and reliability of this questionnaire were established in 2013 by Hariri et al. using 925 female students. In the reliability test of this inventory, the Cronbach’s Alpha was calculated as 0.93. For studying the validity of questionnaire, two apparent and content methods were used. CVR content validity ratio values and content validity index (CVI) were 0.7 and 0.8, respectively, which suggest the high validity of the questionnaire. According to the pilot study results, changes were made in the translation of the questionnaire [26].

After collecting the data using descriptive statistical methods and the independent t-test were analyzed using SPSS software version 16 (SPSS Inc. Chicago, USA) for data analyzing.

Results

Based on the chi-square test, both groups were studied in terms of demographic variables such as age, educational level and they were homogeneous with respect to each other and no significant difference was found between them (Table 1). The mean age of the intervention group was 16.2 ± 1.06 and in the control group it was 16.38 ± 0.66 (p-value = 0.325).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention group</th>
<th>Control group</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>14–16 y/o</td>
<td>22 (44%)</td>
<td>30 (60%)</td>
<td>0.427</td>
</tr>
<tr>
<td>16–18 y/o</td>
<td>26 (56%)</td>
<td>20 (40%)</td>
<td>0.833</td>
</tr>
<tr>
<td>Grade1</td>
<td>14 (28%)</td>
<td>10 (20%)</td>
<td></td>
</tr>
<tr>
<td>Grade2</td>
<td>15 (30%)</td>
<td>13 (26%)</td>
<td></td>
</tr>
<tr>
<td>Grade3</td>
<td>13 (26%)</td>
<td>14 (28%)</td>
<td></td>
</tr>
<tr>
<td>Preparatory</td>
<td>8 (16%)</td>
<td>13 (26%)</td>
<td></td>
</tr>
</tbody>
</table>

Data of this study showed after the intervention, mean scores of general health including physical complaints, anxiety and sleeping disorder, social functions disorders and depression in the intervention group are less than the control group. Based on independent t-test after the intervention, there was a significant difference in the mean score of the components of the questionnaire on general health including physical complaints (p
< 0.001), anxiety and sleeping disorder (p < 0.001), social functions disorders (p = 0.021) and depression (p = 0.001) between the experiment and control groups (Table 2).

Table 2: Comparison of mental health dimension mean score between intervention and control groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention group</th>
<th>Control group</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychosomatic symptom</td>
<td>6.9 ± 3.52</td>
<td>11.04 ± 3.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety and sleep disturbance</td>
<td>8.72 ± 4.69</td>
<td>10.04 ± 6.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Social function disturbance</td>
<td>8.54 ± 3.81</td>
<td>9.46 ± 3.67</td>
<td>0.021</td>
</tr>
<tr>
<td>Depression</td>
<td>10.72 ± 3.69</td>
<td>12.5 ± 4.47</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Discussion

In this study, the mean scores of psychosomatic symptoms, anxiety and sleeping disorder, depression and social functions disorder were significantly lower in the intervention group than in the control group; this suggests the M. officinalis capsule's positive effect on the intervention group when compared with the control group.

Most of the studies done on M. officinalis have examined the effect of this plant on some disorders such as anxiety, sleeping disorder, depression and cognitive disorders [13, 15]. Based on studies, the extract of the leaves of M. officinalis has some effects on slight anxiety [13]; also, based on Kennedy et al.'s study [14] on 25 young people and Scholey’s study, M. officinalis can cause moderation of people’s affective and cognitive performance [15], [28]. In another study, Kennedy has also proved its anti-anxiety effect on 24 healthy people. Dempfél’s study also showed the anxiety reducing effect of M. officinalis sap [29]. Moreover, double blind studies have shown the significant double blind impact of M. officinalis on self-rated calmness in various dosages from 200 to 1600 mg [30], which is consistent with the result of the present study.

Krebs has also pointed out in his study that the aromatherapy through M. officinalis leads to a decrease in anxiety and depression [17].

On the other hand, M. officinalis tea has been used traditionally as a sleep-inducing sedative by people [12], [13]. Based on studies, this drug in a dose of 1 to 4.5 mg can serve as a moderate sedative [8]. In some studies such as that of Mulleret al. [31], the effect of this plant in conjunction with other plants such as valerian has been examined and its effect on restlessness and insomnia in children younger than 12 has been confirmed without reporting any side effect; also, the effect of this drug either alone or in conjunction with valerian has been reported as similar to the effect of benzodiazepine and triazolam, while it does not cause side effects such as drowsiness [13]. Cerny in his study has also mentioned the similar effect of M. officinalis and triazolam on the sleep parameters [32]. Taavoni et al.'s study also showed the effect of herbal supplements of M. officinalis on the quality of sleep in postmenopausal women.

Julian et al. in their study with the aim of reviewing the effect of M. officinalis sap on people with anxiety and sleeping disorders has shown the full remission from anxiety in 70% of samples (14/20), thorough recovery from insomnia in 85% of samples (17/20) and recovery from both morbidities in 70% of them (14/20) [34].

As to the effect of this plant on depression, in addition to Kennedy et al. [15] which has been discussed earlier, Heidari et al. have shown the effect of a daily dosage of 1500 mg of the drug on the decrease in depression of patients after coronary artery bypass graft coronary artery bypass grafting (CABG) surgery surgery [34]. Besides, another article reported that M. officinalis capsules were effective in reducing the severity of physical and psychological symptoms of PMS [35].

Animal studies have also shown that in mice the hydro-alcoholic sap of M. officinalis has a sedative effect [13]. Studies on mice also showed that M. officinalis is also a strong inhibitor of GABA-T and MAO, and it leads to lowering the level of cortisol; they discussed the potential effect of this plant as a sedative [8], [36], [37], [38], and also posited that M. officinalis can serve as an alternative drug for psychological disorders. Also, its anti-anxiety and antidepressant effect has been proved in various studies [39], [40], [41], the main mechanism is intervening in serotonin function.

Based on studies, the main cause of PMS is unknown; however, the reduction in the level of serotonin is considered as one of the causes of this syndrome and it is deemed as one of the psychological symptoms related to it. Serotonin plays a role in expressing irritability, anger and occurrence of depression symptoms and the
amount of severe tendency toward a certain food. Estrogen increases the amount of receptors of serotonin and increases sensitivity to the serotonin agonist. In this paper, one uses *M. officinalis* as it has a mechanism similar to serotonin. Similarly, with its effect on GABA neurotransmitters and the increase of MAO level and decrease of cortisol, *M. officinalis* can positively influence one’s psychological health, including those with PMS [42], [43], [44].

Regarding the effect of *M. officinalis* on social function, Ballard’s study reported the effect of aromatherapy using *M. officinalis* sap on the decrease in social stress and increase in organized activities in patients with severe dementia [45]. However, no other study on the effect of this plant on social functions has been found.

Therefore, the above-mentioned studies have proved the effect of this drug on psycho-neurological system and they have results consistent with this paper. In this paper, no side effect has been reported for *M. officinalis* which is consistent with studies conducted in this respect [15], [27], [46]. Of the limitations of this study, the lack of a mean score of psychological health before the intervention in the experiment and control groups and lack of studies regarding psychological symptoms and social functions can be mentioned. Further studies in these areas are recommended.

**Conclusion**

Use of *M. officinalis* capsule in a daily dose of 1200 mg for 7 days a month can give rise to recovery of adolescents’ psychological health. Considering the risk of dependence on psychotherapeutic drugs and *M. officinalis* not having any obvious side effects, this drug can be used as a method for enhancing the psychological health and treatment of problems such as anxiety, depression and insomnia in adolescents.

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**References**


