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Research paper

The efficacy of lemon balm (*Melissa officinalis* L.) alone and combined with lemon balm—*Nepeta menthoides* on premenstrual syndrome and quality of life among students: A randomized controlled trial

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ABSTRACT

The purpose of this study was to assess the efficacy of *Melissa officinalis*, both alone and in combination with *Nepeta menthoides*, on premenstrual syndrome (PMS) and associated quality of life.

A total of 93 female students from Tabriz University of Medical Sciences, Iran, were included in the study. The participants completed the Daily Record of Severity of Problems questionnaire for two consecutive menstrual cycles to establish the presence and severity of PMS symptoms. Participants were then randomly divided into three groups, two intervention groups and one placebo, with each group containing 31 subjects. The intervention groups received either a 500 mg capsule of *M. officinalis* or a capsule containing a combination of 250 mg of *M. officinalis* and 250 mg of *Nepeta menthoides*, whilst the placebo group received a 500 mg capsule of starch powder. Capsules were taken twice daily during the luteal phase of two consecutive menstrual cycles.

The decrease in the mean scores of PMS symptoms in the first [adjusted difference: −55.5 (95% confidence interval, −96.8 to −14.1)] and second [−57.3 (−99.9 to −14.7)] month after intervention in the lemon balm group was significantly greater than that in the placebo group. There was, however, no statistically significant difference between the *M. officinalis*/*N. menthoides* and placebo groups after intervention. In addition, the mean scores of the physical and psychological aspects of quality of life in the *M. officinalis* and *M. officinalis*/*N. menthoides* groups were significantly greater than those of the placebo group at the end of the second month of treatment. The results of this study suggest that *M. officinalis* can reduce the severity of symptoms in women with PMS.

1. Introduction

Premenstrual syndrome (PMS) is a common condition affecting women of reproductive age (Halbreich et al., 2003). It is characterised by a range of physical, psychological and behavioural symptoms that recur during the luteal phase of the menstrual cycle and are relieved by the onset of menses or during the course of the menstrual period. The most common symptoms of PMS are bloating, breast tenderness, fatigue, joint pain, irritability and mood swings (Braverman, 2007). Approximately 50–80% of women experience moderate to severe symptoms of PMS. Very severe symptoms of PMS, which cause daily disability, are categorised as premenstrual dysphoric disorder (PMDD) (Halbreich et al., 2003). Women with PMS report a reduction in their marital satisfaction and quality of life (Halbreich et al., 2003; Braverman, 2007). The exact aetiology of PMS remains unclear, but neurotransmitters and sex steroids are thought to play a role in the development and manifestation of symptoms (Shulman, 2010).

Some herbal medicines have been proposed for the treatment of PMS; however, the Cochrane review on the efficacy of Chinese herbal medicines on this syndrome concluded that there was 'insufficient evidence to support the use of Chinese herbal

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medicine for PMS' and that 'further, well controlled trials are needed'(Jing et al., 2009).

Lemon balm scientifically known as *Melissa officinalis* belongs to the Lamiaceae family. Lemon balm has anxiolytic and antidepressant effects (Taiwo et al., 2012), and has also been shown to improve sleep quality (Cernya and Schmid, 1999), cognitive and behavioural functions (Kennedy et al., 2003), and dysmenorrhea (Kalvandi et al., 2014). Another herb that has a history of traditional use in the treatment of premenstrual symptoms is *Nepeta menthoides*. This herb also belongs to the Lamiaceae family and is known as "Stoechas" in the Azerbaijan region of Iran. *N. menthoides* has been used as a sedative (Bozorgmehr et al., 2012) and an antispasmodic agent (Dinesh-Bisht et al., 2010).

According to a 2013 World Health Organization (WHO) report, because of their effectiveness, low risk, and accessibility, there is an increasing trend in the use of traditional medicines in most countries (World Health Organization, 2013). This study aimed to assess the efficacy of two such herbal medicines, *M. officinalis* and *N. menthoides* on the severity of PMS symptoms and associated quality of life in a group of Iranian students.

2. Materials and methods

2.1. Study design, participants, and setting

This study was a triple-blind randomized controlled trial. The Research Ethics Committee of Tabriz University of Medical Sciences approved the study protocol. It was also registered at the Iranian registry of clinical trials (code: IRCT2014031710324N17).

Students were recruited from governmental and non-governmental dormitories of Tabriz University of Medical Sciences, Iran. Students were briefed on the research project's procedures and all those interested and eligible were invited to participate in the study. The inclusion criteria for participation were that the students were aged 18 years and older, have a regular (21–35 day) menstrual cycle, a normal body mass index (18.5–25 kg/m^2) and experience PMS symptoms during the luteal phase of the menstrual cycle. Students with a medical history of epilepsy, gastrointestinal, cardiovascular, renal or endocrine disease were excluded from the trial. Other exclusion criteria were: the use of any antidepressants, vitamins, herbal or hormonal medications within the last three months; the consumption of any alcohol, tobacco, or hookah (shisha); and the experience of any major stressful event within the past six months.

In order to rule out depression unrelated to PMS, volunteers were asked to complete the Beck Depression Inventory. Having obtained written informed consent, this questionnaire was completed by all participants from the end of the menstrual bleed to the early luteal phase of the cycle. Individuals with total scores <14 were considered non-depressed and anyone with a score >14 was excluded from the study.

Volunteers then, over the course of two consecutive menstrual cycles, completed the Daily Record of Severity of Problems (DRSP) questionnaire. Those classed by the DRSP as having moderate to severe symptoms of PMS and who had not consumed any self-administered medication over these two cycles, were recruited into the study. Socio-demographic and quality of life questionnaires were completed by the participants.

Sample size was calculated using G*POWER and based on the data obtained in the study by Delaram and colleagues on the severity of symptoms in students with PMS (Delaram et al., 2011). Taking into account the mean pre-intervention scores (m1 = 104.3, sd1 = 19.5), and an anticipated 15% reduction in the post-intervention mean score (m2 = 85.5, sd2 = 19.5), $\alpha = 0.05$ and $\beta = 0.2$ were determined for 28 students per group. 31 students were finally allocated to each group, which would allow for a sample loss of 10%.

2.2. Intervention

The capsules were prepared by the Yashil Sahand Darou Pharmacy Co., East Azerbaijan region, Iran. Leaves of *M. officinalis* and flowering tops of *N. menthoides* were collected from the northwest hillsides of Sahand mountain -Kandovan- in the Azerbaijan region of Iran. The plants were identified by the company's expert pharmacist and voucher specimens deposited in their herbarium. The *M. officinalis* leaves and flowering tops of *N. menthoides* were dried at room temperature, ground to a powder and then filled into capsules using an automatic capsule filling machine.

The combined *M. officinalis—N. menthoides* capsules (500 mg) contained 250 mg of the dried, powdered leaf of *M. officinalis* and 250 mg of the dried, powdered flowering tops of *N.menthoides* from the Azerbaijan region. The *M. officinalis* capsules contained 500 mg of the dried, powdered leaf and the placebo capsules contained 500 mg powdered starch. The capsules were identical in appearance.

2.3. Random allocation and follow-up

The subjects were divided into three groups (two intervention and one control) using a computer generated block randomization method.

The capsules were placed inside closed opaque pockets that were numbered sequentially. Two packets, each containing one month's supply of 28 capsules were delivered to the subjects. Each participant was instructed to take two capsules a day from seven days after the end of the menstrual bleed until the onset of the next menstrual cycle, and to complete the DRSP chart for the duration of treatment. For the purpose of concealment, the allocation sequence and preparation of the pockets were carried out by an individual who was not involved in the study, but who had access to the data on participant cycle lengths from the baseline DRSP charts, and was therefore able to ensure that women with cycle lengths longer than 28 days were adequately supplied with two additional pockets of 14 capsules.

Subjects also completed the quality of life questionnaire after the intervention. Compliance was monitored via telephone contact and the completion of a drug consumption checklist. Both participants and the researcher were blind to the intervention throughout the study.

2.4. Data collection tools

Data was collected via the socio-demographic and quality of life questionnaires, as well as the DRSP chart and drug consumption checklist.

2.4.1. Daily record of severity of problems (DRSP)

DRSP is a prospective questionnaire that includes thirty symptoms of PMS based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria. These symptoms are grouped into five major clusters: physical (flatulence, acne, mouth ulcers, nausea, back and abdominal pain, muscle and joint pain, constipation); retention (weight gain and swelling of extremities); anxiety symptoms (emotional swings, irritability, anger, tension or anxiety, and difficulty concentrating); depression (depression, hopelessness, forgetfulness, crying, confusion, mood disorders, change in sleep, seclusion, and decreased interest in daily activities); emotional agitation (headache, perspiration, hot