Journal of Pharmaceutical Research International



25(3): 1-7, 2018; Article no.JPRI.45104 ISSN: 2456-9119 (Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Comparative Study on the Effect of *Matricaria chamomile* and *Achillea millefolium* Capsules on Primary Dysmenorrhea Intensity of Dormitory Students of Kurdistan University of Medical Sciences, 2018

Shiva Radfar¹, Roonak Shahoie², Bijan Noori³, Fereshteh Jalilian⁴ and Leila Hashemi Nasab^{5*}

¹Students Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran. ² Clinical Care Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran. ³Department of Biostatistics, Social Determinants of Health Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran.

⁴Pharmaceutical Sciences Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran.

⁵School of Nursing and Midwifery, Kurdistan University of Medical Sciences, Sanandaj, Iran.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2018/v25i330101 <u>Editor(s):</u> (1) Dr. Vijay Ramani, Department of Dermatology, UT Southwestern Medical Center, USA. (2) Dr. Jinyong Peng, Professor, College of Pharmacy, Dalian Medical University, Dalian, China. (3) Dr. Ali Nokhodchi, Professor of Pharmaceutics and Drug Delivery, School of Life Sciences, University of Sussex, UK (1) Dr. Victor Moses, Ahmadu Bello University, Zaria, Nigeria. (2) Tabe Franklin Nyenty, University of Ngaoundere, Cameroon. (3) Franco Mantovan, University of Verona - Bolzano "Claudiana", Italy. Complete Peer review History: <u>http://www.sdiarticle3.com/review-history/45104</u>

> Received 24 August 2018 Accepted 07 November 2018 Published 22 February 2019

Original Research Article

ABSTRACT

Background: Menstrual pain is the most common pain and one of the main causes of referral to a doctor among young women. The aim of this study was to compare the effectiveness of *Achillea millefolium* (Yarrow) and *Matricaria chamomile* plants to treat menstrual pain.

*Corresponding author: E-mail: hasheminasab.I.2014@gmail.com;

Methods: This double-blind randomized controlled trial study was performed on 50 female students of Kurdistan Medical Sciences residing in dormitory in 2018. Individuals were randomly divided into two groups of chmomile and yarrow using sealed envelopes. Twenty for people received 250 mg chamomile capsules every 8 hours and 26 people received 150 mg hydroalcoholic capsules of yarrow every 8 hours during the first three days of menstruation in two menstrual cycles. The data collection tool was a questionnaire and the severity of pain was assessed using visual analogue scale for the pain (VAS).

Results: There was no significant difference between the two groups in terms of pain severity and duration of pain before taking the drug (p > 0.05). The average pain severity in the first menstrual cycle in the two groups decreased significantly (p < 0.05), which was more noticeable in the yarrow group. However, the average pain severity in the yarrow capsule group was lower than that of the chamomile capsule group, but this difference was not statistically significant (p > 0.05).

Conclusion: Both capsules of yarrow and chamomile reduce the severity of pain, but the yarrow capsule, with its long-lasting sedative effect, proved more helpful to reduce the severity of menstrual pain and could be effective in solving one of the issues among women.

Keywords: Menstrual pain; yarrow; chamomile.

1. INTRODUCTION

The term 'initial painful period of menstruation' is used to describe contractions of the uterus during menstruation in the absence of any pelvic and pathologic damage, which occurs at the onset of the first menstrual period or shortly afterwards in ovulation cycles [1]. Menstrual pain is the most common pain among women [2], and affects 80% to 97% of those in fertile life [3]. The prevalence of initial painful menstruation varies according to the World Health Organization (WHO), and is reported to be between 16% and 91% [4], and the prevalence rate has been reported 43.25% in Sanandaj [5]. The results of the studies have shown that menstrual pain causes a change in physical activity, irritability [6], loss of interest in work, adverse mental effects [7], increasing absence from the university, and disturbing social relations [8]. According to the results of the study, painful menstruation has led to a loss of 140 million working hours in the United States [9] and they estimated that the economic loss from one day of absence in japan could be about \$ 4.2 billion [10]. The most common treatments used in this non-steroidal anti-inflammatory are area chemicals and oral contraceptives [11]; but longterm use of steroidal drugs and birth control pills is associated with side effects such as damage to the liver, kidneys, skin, intestines, Gastrointestinal bleeding and myocardial infarction [12,13], depression, loss of libido, and discontinuation of menstrual bleeding [14]. Currently, due to the apparent effects of chemical drug abuse, the willingness of people to use herbs has increased dramatically [15]. Several studies have been conducted on the effects of various medicinal plants such as mint capsules [16], calendula [17], phenylene and vitagnus [18] on painful menstruation. Chamomile and Yarrow are among plants whose effectiveness in the treatment of primary dysmenorrhea has been examined in a number of limited studies [19,20]. According to the researches, there has been no study conducted in order to compare efficacy and complications in treatment of primary dysmenorrhea. Therefore, this study was conducted to compare the effect of chamomile capsule and yarrow capsule on the severity of primary dysmenorrhea among dormitory students of Kurdistan University of Medical Sciences.

2. MATERIALS AND METHODS

This study was a parallel double blind randomized controlled trial. The study population consisted of students residing in Kurdistan University of Medical Sciences dormitories. The sample size using the formula

 $N = \frac{\left(z_{1-\frac{\alpha}{2}+z_{1-\beta}}\right)^2 (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$ was 50 people who were randomly divided into two groups. The criteria for entering the study included: being single, starting a menstruation at the age of 11 to 17, having regular menstruation at intervals of 21 to 35 days, and having a score of 4 to 10 for pain in the menstruation according to the visual analogue scale for the pain and the desire to participate in the study, and exclusion criteria included: unwillingness to continue to participate in the study, not menstruating or abnormal bleeding during the study, epilepsy, coagulation disorder, allergic asthma, digestive diseases, liver, kidney, and uterine problems detected such

as: abnormal bleeding, ovarian cysts, myoma, pelvic tumors, endometriosis, pelvic inflammatory diseases. taking medications such as barbiturates, benzodiazepines, narcotics, antidepressants, triangular anticoagulants, theophylline, hormonal contraceptives and oral contraceptive pills over the past three months, alcohol intake, failure to follow capsule administration instructions and the use of chemical sedatives one hour after taking the herbal medication.

Data were collected using a questionnaire and a visual analogue scale for the pain. The questionnaire included questions about demographic characteristics (age, field of study, educational level, occupation and BMI) and questions about menstrual characteristics (duration, amount of bleeding and severity of menstrual pain). The validity of the questionnaire was determined using content validity method. The reliability of the visual instrument for pain assessment was R=88% in Iran [21].

In order to conduct the study, the researcher selected the volunteers to participate in the study in terms of inclusion and exclusion criteria and obtained written consent. After selecting the samples, the researcher asked the participants to complete the demographic questionnaire, and their weight and height were measured using scales and stadiometer and their body mass index was determined and recorded by the researcher; then individuals learned how to use the visual analogue scale for pain. The visual analogue scale for pain was delivered to the participants one month prior to the onset of the medication intake, and they were asked to record the average of their pain severity in the first three days of the menstrual cycle for a month before treatment. After the end of the month, the predrug questionnaire was delivered to the participants and eligible individuals were assigned to two groups by randomly using sealed envelopes containing the A and B codes. The envelopes named "A" contained chamomile capsules (250 mg made by the Kermanshah Pharmacy Faculty) and envelopes named "B" containing capsules of yarrow (150 mg of hydroalcoholic extract made by the Kermanshah Pharmacy Faculty). Capsules were completely identical in terms of shape, colour, size and aroma, and, except for the pharmacist, neither the researcher nor the participants were aware of the nature of the drug. Each of the participants received two questionnaires on menstruation

questions to complete in two menstrual cycles (using the drug) and how the medications were administered to the participants as follows: Both groups should take one capsule every eight hours during the first three days of menstruation and record their pain score at the end of the first three days of the menstrual cycle and repeat this process in the second cycle of their menstruation. Participants who have been forced to take sedatives for any reason were excluded. The process of completing the questionnaires and taking the medications was regularly reviewed by the researcher in two groups. In case of irregular drug use, lack of willingness to continue cooperation or incorrect completion of questionnaires, the participants were the excluded from the study process. Finally, 26 patients were placed in the group to receive varrow capsules and 24 were placed in the chamomile capsule group. The sampling process began from mid-April 2018 and ended on the first of July. This study was approved by Ethical Committee of Kurdistan University of Medical Sciences (IR.MUK. REC.1396.326) and was registered with the IRCT201712 25038058N1 on IRCT.

For data analysis, Fisher, T-independent and Mann-Whitney tests were used in SPSS version 22. The significance level was considered to be less than 5%.

3. RESULTS

The findings of this study indicate that the average age of the participants was 18-22 years old, and there was no significant difference in the average age of the two groups (p>0.05). Moreover, most of the participants (94%) were students and they were undergraduate (86%), and the two groups did not differ significantly in terms of job status and educational level (p>0.05) (Table 1).

The results of the study showed that there was no significant difference in pain severity (Table 2) and duration of pain (Table 3) before the drug administration between the two groups (p > 0.05). The average of pain severity in the first menstrual cycle of the two groups significantly decreased (p< 0.05), which was more noticeable in the yarrow group. However, the average pain severity in the group receiving yarrow capsule was lower than that of the chamomile capsule; this difference was not statistically significant (p > 0.05) (Table 2).

Group	Chamomile group		Yarrow group	P value
Variable	_			
	Category	Number (%)	Number (%)	
Occupation status	Student	22 (91.67)	25 (96.15)	_
	Student± part-time job	2 (8.33)	1 (3.85)	P > 0.05
	Overall	24 (100)	26 (100)	
Age of students	Age	17 (70.83)	18 (69.23)	P > 0.05
	Overall	24 (100)	26 (100)	
Educational level	Associate's degree	1 (4.17)	1 (3.85)	
	Bachelor's degree	20 (83.33)	23 (88.46)	
	Master's degree	3 (12.50)	2 (7.69)	P > 0.05
	Overall	24 (100)	26 (100)	

Table 1. Frequency distribution of demographic variables in the units under study

 Table 2. Comparing the severity of painful menstruation before and after taking the drug among the participating groups in the study

Group	Chamomile group	Yarrow group	P value
	Mean ±SD	Mean ± SD	
Before taking the drugs	6.46±1.91	6.65±1.92	P >0.05
End of third day of first menstrual cycle	5.29±1.78	4.46±1.53	P <0.05
End of third day of second menstrual cycle	4.33±2.12	3.81±1.06	P >0.05
(rm) P value	P<0001	P<0001	

 Table 3. Comparing the duration of primary dysmenorrhea before and after taking the drugs among the participating groups in the study

Group	Chamomile group	Yarrow group	P value
	Mean± SD	Mean± SD	
Before taking the drug	2.45±0.93	2.73±0.91	P > 0.05
First menstrual cycle	2.54±1.02	2.26±0.77	P > 0.05
Second menstrual cycle	2.54±1.06	1.88±0.81	P < 0.05
(rm) P value	P > 0.05	P<0001	

4. DISCUSSION

The aim of this study was to compare the effect of chamomile capsule and varrow capsule on the severity of primary dysmenorrhea. The results of this study showed that chamomile and varrow capsules were effective in decreasing the severity of primary dysmenorrhea, but the severity of pain reduction was significantly higher in varrow users group, and this decrease was significantly different in both groups of chamomile and yarrow capsules before and after administration drug using repeated measurements. One of the most important findings of the present study, was the significant relationship between the severity of initial painful menstrual period after chamomile and yarrow capsules at the end of the first three days of the first menstrual cycle. The chamomile capsule reduced the severity of pain, which was in line

with the results of the study by Karimian et al. in terms of drug type and method that aimed at the effect of chamomile capsule and mefenamic acid on the rate of menstrual bleeding in Kashan [20]. In the study mentioned above, participants consumed 250 mg chamomile capsule every 8 hours in the first 3 days of menstruation, which is consistent with the present study. In the study by Karimian et al. in addition to menstrual bleeding, the severity of pain was studied. It was also in line with the results of the study by Modarres et al. aimed at the effect of chamomile and mefenamic acid capsules in Tehran [22], indicating that after the end of the first 3 days of menstruation, the severity of pain in the chamomile group decreased significantly. present However, the study showed contradictory results with the study by Sharifi et al. which focused on the analgesic effects of mefenamic Acid and Chamomile on the severity

of pain in the menstrual period [23]. whereby drugs were used every 8 hours on the first three days of menstruation, but after the end of the first 3 days, there was no significant difference between the two groups of chamomile capsules and mefenamic acid. However, chamomile capsule was recommended due to lower complications of herbal medicine. In the study above, both drugs have relieved the same level of pain severity. The reason for the difference between the results of the present study and that of Sharifi et al. might be due to location differences and the types of drugs, considering that a chemical medicine was compared to a herbal, but in the present study, two medicinal herbs were compared and evaluated and, given the fact that Kurdistan province residents believed in herbal medicine, the result of the research could be effective. Moreover, in the present study, the severity of pain decreased after the administration of yarrow capsule, and this was consistent with the results of the study by Jenabi and Fereiduni, which aimed at evaluation of the effect of yarrow on the severity of initial menstrual pain in the Tuiserkan [24]. In the study by Jenabi and Fereiduni, brewed varrow and 4 grams of tea bag were provided to the participants; they received one batch of tea bags brewed for 10 minutes in 300 ml of water every 8 hours during the first 3 days of menstruation. In the present study, 150 mg capsule of varrow was used every 8 hours in the first 3 days of menstruation. In both methods, the same results were observed and the severity of pain decreased. Both chamomile and yarrow can affect the smooth muscles of the uterus and intestine due to the presence of active ingredients in their constituent parts and therefore can reduce the pain of menstrual Chamomile capsule periods. has antiinflammatory and anti-contractile properties due to the presence of flavonoids which are antiinflammatory and analgesic compounds in plants that have a direct effect on the synthesis and reduction of prostaglandins, and consequently can relieve the pain [2]. Essential oils of this plant, especially bisabolol and chamazulene, are responsible for its anti-inflammatory effect [25]. Yarrow capsule inhibits cyclooxygenase enzyme due to presence of flavonoids and alkaloids. therefore. can be effective as an antiprostaglandin in treating the initial painful menstruation; moreover, yarrow causes inhibition of smooth muscle contractions in the intestine by closing calcium channels, as well as anticontractile effects on the smooth muscles of the uterus which can have a very powerful

effect in relieving pain during the menstruation [26].

One other important finding of the present study was that no significant relationship was observed between the severity of initial pain of menstruation and using chamomile and yarrow capsule at the end of the first 3 days of the second menstrual cycle. The results showed that the severity of menstrual pain did not decrease significantly at the end of the first 3 days of the second cycle, which was in line with the following two studies in terms of pain severity before and 3 days after the administration of the drug, the method of work and the species of the plant; the study by Karimian et al. [20]. conducted in the second month of the menstrual cycle and the study by Ebrahimi Varzaneh et al. aimed at the effect of hydroalcoholic yarrow capsule on the severity and duration of dysmenorrhea in Tehran [19]. Despite the use of mefenamic acid in the study, varrow capsule has a significant effect on reducing pain severity, but in the second month there was no significant difference in pain reduction. The reason for the lack of significant correlation was the absence of pain at the time of starting the medication by the participants during the second menstrual cycle, but this was contradictory with the study by Sattarzadeh et al. [27], using another type of varrow to examine the severity of menstrual pain. In this study Achillea *willhemsii* species was used, while in the present study the Achillea millefolium species was used. This variation in the plant species caused the results of the study to be contradictory.

5. CONCLUSION

Yarrow capsule, given the effectiveness on controlling menstrual pain and lack of side effects, can be used as an effective herbal remedy for young women with premenstrual pain and may replace existing chemical drugs.

CONSENT

In order to conduct the study, the researcher selected the volunteers to participate in the study in terms of inclusion and exclusion criteria and obtained written consent.

ETHICAL ISSUE

This study was approved by Ethical Committee of Kurdistan University of Medical Sciences (IR.MUK.REC.1396.326) and in IRCT (IRCT20171225038058N1).

ACKNOWLEDGEMENT

The results of this article are extracted from a dissertation approved by council of Kurdistan University of Medical Sciences (IR.MUK.REC.1396.326). The researcher, herby, appreciated project colleagues, the staff of the Student Research Committee and members of the research council of Kurdistan University of Medical Sciences who approved the project and presented their sincere cooperation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- 1. Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Williams Gynecology; 2018.
- Saei Gharenaz M, Ozgoli G. Effect of medicinal plants in the treatment of primary dysmenorrhea in Iran: A review article. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2015;18(160):14-31. [In Persian]
- Farahani Amiri L, Hasanpoor-Azghdy SB, Kasraei H, Heidari T. Comparison of the effect of honey and mefenamic acid on the severity of pain in women with primary dysmenorrhea. Archives of Gynecology and Obstetrics. 2017;296(2):277-83.
- 4. Ju H, Jones M, Mishra G. The prevalence and risk factors of dysmenorrhea. Epidemiologic Reviews. 2013;36(1):104-13.
- SHahgheibi S, Darvishi N, Usefi Nezhad V, Moghbal N, SHahsavari S. Prevalence of menstrual disorders in 17-18 years old of high school students in Sanandaj. Scientific Journal Kurdistan University. 2005-2006;14:20-44. [In Persian]
- 6. Berkley KJ. Primary dysmenorrhea: An urgent mandate. Pain. 2013;1(1).
- 7. Gebeyehu MB, Mekuria AB, Tefera YG, Andarge DA, Debay YB, Bejiga GS, et al. Prevalence, impact, and management practice of dysmenorrhea among University of Gondar students, Northwestern Ethiopia: A cross- sectional study. International Journal of Reproductive Medicine, 2017:2017:2-8.
- Al-Jefout M, Seham A-F, Jameel H, Randa A-Q, Luscombe G. Dysmenorrhea: Prevalence and impact on guality of life

among young adult Jordanian females. Journal of Pediatric and Adolescent Gynecology. 2015;28(3):173-85.

- 9. Ostrzenski A. Gynecology: Integrating conventional, complementary, and natural alternative therapy. Lippincott Williams & Wilkins; 2002.
- 10. Taketani Y. Research on prophylaxis, diagnostic, and therapy for endometriosis from reproductive health (health on sex and reproduction) standpoint. Health Labour Welfare Ministry Resources. 2000;503-50.
- Zahradnik H-P, Hanjalic-Beck A, Groth K. Nonsteroidal anti-inflammatory drugs and hormonal contraceptives for pain relief from dysmenorrhea: A review. Contraception. 2010;81(3):185-96.
- Scarpignato C. Piroxicam-β-cyclodextrin: A GI safer piroxicam. Current Medicinal CHemistry. 2013;20(19):2415-37.
- 13. Hemati AA, Sistani Karampour N. Effect of ketotifen on inflammation induced by carrageenan in male rats;. 2015. [In Persian]
- Speroff L, Fritz MA. Clinical gynecologic endocrinology and infertility. Lippincott Williams & Wilkins; 2016.
- 15. GHavam M, Jeyhouni Naeeni H, Kiani Salami S. Traditional and indigenous knowledge of the use of medicinal herbs in the city of Naiyne. Native Iranian Knowledge. 2015;4:177-201. [In Persian]
- Masoumi SZ, Asl HR, Poorolajal J, Panah MH, Oliaei SR. Evaluation of mint efficacy regarding dysmenorrhea in comparison with mefenamic acid: A double blinded randomized crossover study. Iranian Journal of Nursing and Midwifery Research. 2017;21(4):363-7.
- Lee H, Choi T-Y, Myung C-S, Lee MS. Herbal medicine Shaofu Zhuyu decoction for primary dysmenorrhea: A systematic review protocol. Systematic Reviews. 2016;5(1):9.
- Zeraati F, Shobeiri F, Nazari M, Araghchian M, Bekhradi R. Comparative evaluation of the efficacy of herbal drugs (Fennelin and Vitagnus) and Mefenamic acid in the treatment of primary dysmenorrhea. Iranian Journal of Nursing and Midwifery Research. 2014;19(6):581.
- 19. Ebrahimi Varzane F, Nahidi F, Mojab F, Hoseingholi MA, Panahi Z. The effect of hydro alcoholic extract of *Achillea millefolium* capsule on duration and severity of primary dysmenorrhea pain.

Journal of Midwifery and Infertility in Iran. 2017;20(3):48-56. [In Persian]

- Karimian Z, Sadat Z, Bahrami N, Kafaie M. Comparison of CHamomile and Mefenamic acid capsules in hemorrhage of menstruation. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2015;18(157):11-7. [In Persian]
- 21. Rezvani A. Correlation between Visual analogue scale and short form of McGill questionnaire in patients with chronic low back pain. Qom University of Medical Sciences Journal. 2012;6(1).
- 22. Modarres M, Mirmohhamad Ali M, Oshrieh Z, Mehran A. Comparison of the effect of Mefenamic Acid and *Matricaria camomilla* capsules on primary dysmenorrhea. Journal of Babol University of Medicine Sciences. 2011;13(3):50-8. [In Persian]
- 23. Sharifi F, Simbar M, Mojab F, Majd HA. Comparison of the effects of *Matricaria chamomila* (Chamomile) extract and Mefenamic acid on the intensity of premenstrual syndrome. Complementary

THerapies in Clinical Practice. 2014;20(1): 81-8.

- 24. Jenabi E, Fereidoony B. Effect of Achillea millefolium on relief of primary dysmenorrhea: A double-blind randomized clinical trial. Journal of Pediatric and Adolescent Gynecology. 2015;28(5):402-4.
- 25. Karamali J. Herbal essences. Tehran. Publisher Atash; 2014.
- Moradi M, Rafieian-Koupaei M, Imani-Rastabi R, Nasiri J, Shahrani M, Rabiei Z, et al. Antispasmodic effects of yarrow (*Achillea millefolium* L.) extract in the isolated ileum of rat. African Journal of Traditional, Complementary and Alternative Medicines. 2013;10(6):499-503.
- Satarzade N, Nazemiye H, Dizajimaleki N, Hashemi M. Effect of Achillea Willhemsii extract on the pain and bleeding of menstruation in students of Tabriz University of Medical Sciences. Tabriz Nursing and Midwifery Journal. 2008;12:4-10. [In Persian]

© 2018 Radfar et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history: The peer review history for this paper can be accessed here: http://www.sdiarticle3.com/review-history/45104