

The effect of turmeric on primary dysmenorrhea: Prospective case-control study

Erhan Okuyan¹, Emre Günakan², Halit Atac¹, Yusuf Çakmak¹

¹Department of Obstetrics and Gynecology,
Batman Education and Research Hospital,
Batman, Turkey

²Department of Perinatology, Baskent University,
School of Medicine, Ankara, Turkey

ORCID ID of the author(s)

EO: 0000-0001-9636-9539
EG: 0000-0001-8854-8190
HA: 0000-0001-6685-7208
YÇ: 0000-0003-3128-247X

Corresponding Author

Erhan Okuyan
Department of Obstetrics and Gynecology,
Batman Maternity and Child Health Hospital,
Batman, Turkey
E-mail: dreo06@hotmail.com

Ethics Committee Approval

This study was approved by Batman Maternity
and Child Health Hospital review board (Number:
2020-7)

ClinicalTrials.gov Identifier: NCT04183556
All procedures in this study involving human
participants were performed in accordance with
the 1964 Helsinki Declaration and its later
amendments.

Conflict of Interest

No conflict of interest was declared by the
authors.

Financial Disclosure

The authors declared that this study has received
no financial support.

Published

2021 July 29

Copyright © 2021 The Author(s)

Published by JOSAM

This is an open access article distributed under the terms of the Creative
Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC
BY-NC-ND 4.0) where it is permissible to download, share, remix,
transform, and buildup the work provided it is properly cited. The work
cannot be used commercially without permission from the journal.



Abstract

Background/Aim: Turmeric is an ancient spice and is still a part of dietary traditions, especially in Asian populations. It has been linked to anti-inflammatory effects; thus, it may be effective in dysmenorrhea which occurs due to inflammatory events. The use of turmeric in the treatment of dysmenorrhea is unclear. We aimed to compare the effectiveness of turmeric when included in dysmenorrhea treatment.

Methods: Nulliparous patients with primary dysmenorrhea (PD) who met the inclusion criteria were included in our prospective case-control study. After the diagnosis of PD was confirmed by the clinician, patients were asked to choose one of the covered papers that wrote group 1 (Control, n=75) and group 2 (Case, n=75), after which they received their related treatment from the doctor in another examination room. Naproxen (750 mg/day) was prescribed to all patients, and 1 g/day turmeric powder was added to the treatment protocol of Group 2 patients as a food supplement to be consumed *peroral* during menstrual bleeding. The turmeric supplements were given to the patients by the assisting nurse. The two groups were asked to score their pain with a visual analog scale (VAS) before and after the treatment, which were comparatively analyzed. All patients signed informed consent forms before the study began.

Results: The two groups were similar in terms of age (22.7 years vs. 23.5 years, $p=0.408$). The overall median pain score of the study population before the treatment was 9.17 (range: 5-10), which decreased to 2.81 (range: 1-5) after the treatment, with a Z-score of -10.64. The decrease in VAS scores was significant in both groups ($P=0.001$ for both). The percentage of VAS score decrease (61.7% vs 76.8%) and the absolute score decrease (5.6 vs 7.0) were significantly higher in Group 2 compared to Group 1 ($P=0.001$, for both).

Conclusion: Turmeric may have a role in PD treatment. Naproxen is an effective agent in PD treatment and concomitant use with turmeric improves pain scores. Further controlled randomized studies investigating turmeric use in PD treatment and its mechanism of action may contribute to the literature.

Keywords: Naproxen, Primary dysmenorrhea, Turmeric, Visual analog scale

Introduction

Primary dysmenorrhea (PD) has a cyclic pattern and occurs in the hypogastric region during the menstrual period. It is frequent and the severity of complaints varies on a patient basis. The pain usually begins a few hours before menstruation and lasts for about 2 or 3 days [1]. The diagnosis is confirmed by excluding the other disorders in the differential diagnosis.

Most women underestimate dysmenorrhea or consider it a part of menstruation; thus, women who need or require treatment visit the gynecologists. The incidence of dysmenorrhea ranges between 45-95% [2].

The well-accepted theory in the pathophysiology of dysmenorrhea is the prostaglandin (PG) theory. At the beginning of menstruation, PGE2 and PGF2 are released from endometrial sloughing, resulting in an inflammatory process, dysrhythmic uterine contractions, decreased blood flow, and ischemia [3]. Higher levels of endometrial prostaglandins and good response to non-steroidal anti-inflammatory drugs (NSAID) which inhibit prostaglandin synthesis through inhibiting cyclooxygenase (COX) enzymes support this theory [4,5], on which the treatment of PD was predominantly formed.

Naproxen, an NSAID that inhibits both Cox 1 and 2 enzymes, is one of the first-line treatment options in primary dysmenorrhea treatment [6, 7].

Turmeric is derived from *Curcuma longa* and includes curcuminoids such as curcumin, demethoxycurcumin, and bisdemethoxycurcumin. It is a member of some regional diets as a spice and has been used as a drug since ancient times in numerous Asian cultures. The estimated dietary intake of turmeric is approximately 2.5 g/day [8]. Various studies regarding the safe dosage of turmeric suggest that it can be consumed up to 12 g/day [9]. Its anti-inflammatory effects by inhibiting enzymes such as Cox, 5-lipoxygenase, cytosolic phospholipase A2 were demonstrated in many studies [10-12].

Considering this information, we thought that turmeric may have a positive effect on PD treatment and conducted this original research.

Materials and methods

This study was approved by Batman Maternity and Child Health Hospital review board (Number: 2020-7), ClinicalTrials.gov ID: NCT04183556) and conducted per the Declaration of Helsinki. A total of 149 patients were included and evaluated in two groups as Group 1, which received naproxen treatment only, and Group 2, which received naproxen + turmeric (1gr/day turmeric in powder form as a dietary supplement) treatment. Nulliparous patients with PD who met the following inclusion criteria were included in the study: Being between 15-45 years of age, and nulliparous, having regular menstrual cycles, BMI<25 kg/m², no systemic diseases, no history of suspected endometriosis, adenomyosis, gynecologic anatomical disorders or abnormalities, gynecologic discharge or pelvic inflammatory disease, no history of drug use, naproxen, or turmeric allergy, and not smoking or consuming alcohol.

After the diagnosis of PD was confirmed by the clinician, patients were asked to choose one of the covered

papers that wrote group 1 and group 2, after which they received their related treatment from the doctor in another examination room. Naproxen (750 mg/day) was prescribed to all patients, and 1 g/day turmeric powder was added to the treatment protocol of Group 2 patients as a food supplement to be consumed peroral during menstrual bleeding. The turmeric supplements were given to the patients by the assisting nurse. The two groups were asked to score their pain with a visual analog scale (VAS) before and after the treatment, which were comparatively analyzed. All patients signed informed consent forms before the study began.

Both groups included 75 patients at the end of recruitment, then, one patient in Group 2 decided to leave the study. Finally, groups 1 and 2 included 75 and 74 patients, respectively. None of the patients experienced any side effects or hypersensitivity.

Statistical analysis

Statistical analysis of the data was performed using the SPSS v.15.0 (Statistical Package for Social Sciences, Chicago, IL, USA) package software. Descriptive analyses were conducted. The Wilcoxon and independent samples T-test were used to compare the groups. *P*-value <0.05 was considered statistically significant.

Results

This study included 149 patients with 75 in Group 1 and 74 in Group 2. The two groups were similar in terms of age (mean ages: 22.7 vs. 23.5, *p*=0.408). The median VAS pain score of the study population was 9.17 (range: 5-10). Before the treatment, the VAS scores were similar between the groups; however, the mean score of Group 2 was significantly lower than that of Group 1 after the treatment (3.47 vs 2.14, *P*=0.001) (Table 1).

Table 1: Evaluation of pain scores before and after treatment

	VAS Score	<i>P</i> -value
Before treatment		
Study population	9.17 (1.0)	
Group 1	9.12 (0.9)	0.568
Group 2	9.22 (1.0)	
After treatment		
Study population	2.8 (1.1)	
Group 1	3.47 (9.77)	<0.001
Group 2	2.14 (0.88)	

The mean VAS score of the entire study population significantly decreased from 9.17 to 2.81 (range: 1-5) with a Z-score of -10.64 following treatment (*P*=0.001). The decrease in VAS scores was significant in both groups (*P*=0.001 for both); however, the percentage of VAS score decrease (61.7% vs 76.8%), and the absolute score decrease (5.6 vs 7.0) were significantly higher in Group 2 (*P*=0.001 for both) (Table 2).

Table 2: Evaluation of the decrease in VAS scores

	Group 1	Group 2	<i>P</i> -value
VAS Z-score	-7.58	-7.53	
VAS score change rate	61.7%	76.8%	<0.001
VAS score change in numbers	5.6	7.0	<0.001

Discussion

We evaluated the effect of turmeric in a group of patients with PD and found significant results. The strengths of our study include its strict selection criteria and homogenous patient characteristics. Patients in both groups benefited from treatment, as indicated by the significantly lowered VAS scores after treatment. The VAS scores of Group 2 decreased

significantly more than those of Group 1, showing that turmeric may improve the success of PD treatment.

Dysmenorrhea is a frequent disorder that is usually considered a normal part of women's lives. When present, it decreases the quality of life significantly [13]. Most women do not seek treatment. While some do not want drug therapy, others turn to alternative therapies. Thus, one can estimate that it has a much higher frequency than expected.

The history of dysmenorrhea treatment dates to early ages when plants or plant-derived foods were used in traditional medicine. Numerous studies were conducted on paramedical dysmenorrhea treatment. Ginger, German chamomile, cinnamon, Damask rose, dill, fennel, fenugreek, or guava are some examples of plant-derived supplements researched for the treatment of dysmenorrhea [14, 15].

Turmeric is an ancient spice and is still a part of dietary traditions, especially in Asian populations [8]. It was linked to antioxidant, and anti-inflammatory effects [16, 17]. The inflammatory process underlying the PD pathophysiology, and the afore-mentioned effects of turmeric constituted the core of our study. We aimed to evaluate whether the addition of turmeric to standard treatment improved dysmenorrhea treatment outcomes.

NSAIDs are the well-accepted first-line treatment in PD [18]. Naproxen, an NSAID, reversibly inhibits both Cox-1 and Cox-2 enzymes, thus preventing PG synthesis. It is an effective agent in dysmenorrhea treatment [19]. Although the decrease in survey scores differed on a patient basis, patients in both groups benefited from the treatment as expected and stated lower pain scores after treatment. This result resembled those in the literature about the effectiveness of Naproxen and NSAIDs in dysmenorrhea. The patients in Group 2 had significantly lower VAS pain scores compared to Group 1, which indicates that turmeric use improved the PD treatment. This may be due to the anti-inflammatory and antioxidant effects of turmeric. An unknown pattern of analgesia may also be playing a role in this process. Another point is that turmeric is a familiar supplement that is frequently used in regional diets. This also may have caused a placebo effect on the self-evaluation of patients.

Overall, patients with PD benefited from turmeric treatment. This is important because turmeric is a common dietary supplement with a wide safety window, and limited negative effects [20]. It may play a role in PD treatment as an added or alternative option in selected patient groups such as those who do not prefer or have not benefited from drug therapy.

Conclusion

Turmeric is a widely used dietary supplement that may play a role in PD treatment. Naproxen is an effective agent against PD and its concomitant use with turmeric improves pain scores. Further controlled randomized studies investigating turmeric use in PD treatment and its mechanism of action may contribute to the literature.

References

- Chen CX, Kwekkeboom KL, Ward SE. Self-report pain and symptom measures for primary dysmenorrhoea: a critical review. *Eur J Pain*. 2015 Mar;19(3):377-91. doi: 10.1002/ejp.556. PMID: 25059384.
- Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. *Hum Reprod Update*. 2015 Nov-Dec;21(6):762-78. doi: 10.1093/humupd/dmv039. Epub 2015 Sep 7. PMID: 26346058
- Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. *Obstet Gynecol*. 2006 Aug;108(2):428-41. doi: 10.1097/01.AOG.0000230214.26638.0c. PMID: 16880317.
- Lundström V, Gréen K. Endogenous levels of prostaglandin F2alpha and its main metabolites in plasma and endometrium of normal and dysmenorrhoeic women. *Am J Obstet Gynecol*. 1978 Mar 15;130(6):640-6. doi: 10.1016/0002-9378(78)90320-4. PMID: 637076.
- Marjoribanks J, Ayeleke RO, Farquhar C, Proctor M. Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. *Cochrane Database Syst Rev*. 2015 Jul 30;2015(7):CD001751. doi: 10.1002/14651858.CD001751.pub3. PMID: 26224322; PMCID: PMC6953236.
- Brutzkus JC, Shahrokhi M, Varacallo M. Naproxen. 2021 May 19. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. PMID: 30247840.
- Carrarelli P, Funghi L, Bruni S, Luisi S, Arcuri F, Petraglia F. Naproxen sodium decreases prostaglandins secretion from cultured human endometrial stromal cells modulating metabolizing enzymes mRNA expression. *Gynecol Endocrinol*. 2016;32(4):319-22. doi: 10.3109/09513590.2015.1115973. Epub 2015 Dec 3. PMID: 26634864.
- Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of tumeric (*Curcuma longa*). *J Altern Complement Med*. 2003 Feb;9(1):161-8. doi: 10.1089/107555303321223035. PMID: 12676044.
- Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. *AAPS J*. 2013 Jan;15(1):195-218. doi: 10.1208/s12248-012-9432-8. Epub 2012 Nov 10. PMID: 23143785; PMCID: PMC3535097.
- Goel A, Boland CR, Chauhan DP. Specific inhibition of cyclooxygenase-2 (COX-2) expression by dietary curcumin in HT-29 human colon cancer cells. *Cancer Lett*. 2001 Oct 30;172(2):111-8. doi: 10.1016/s0304-3835(01)00655-3. PMID: 11566484.
- Ramsewak RS, DeWitt DL, Nair MG. Cytotoxicity, antioxidant and anti-inflammatory activities of curcumins I-III from *Curcuma longa*. *Phytochemistry*. 2000 Jul;7(4):303-8. doi: 10.1016/S0944-7113(00)80048-3. PMID: 10969724.
- Aggarwal BB, Deb L, Prasad S. Curcumin differs from tetrahydrocurcumin for molecular targets, signaling pathways and cellular responses. *Molecules*. 2014 Dec 24;20(1):185-205. doi: 10.3390/molecules20010185. PMID: 25547723; PMCID: PMC6272158.
- French L. Dysmenorrhea. *Am Fam Physician*. 2005 Jan 15;71(2):285-91. PMID: 15686299.
- Jenabi E. The effect of ginger for relieving of primary dysmenorrhoea. *J Pak Med Assoc*. 2013 Jan;63(1):8-10. PMID: 23865123.
- Pattanittum P, Kunyanone N, Brown J, Sangkomkamhang US, Barnes J, Seyfoddin V, et al. Dietary supplements for dysmenorrhoea. *Cochrane Database Syst Rev*. 2016 Mar 22;3(3):CD002124. doi: 10.1002/14651858.CD002124.pub2. PMID: 27000311; PMCID: PMC7387104.
- Daveray A, Agrawal SK. Curcumin alleviates oxidative stress and mitochondrial dysfunction in astrocytes. *Neuroscience*. 2016 Oct 1;333:92-103. doi: 10.1016/j.neuroscience.2016.07.012. Epub 2016 Jul 14. PMID: 27423629.
- Funk JL, Oyarzo JN, Frye JB, Chen G, Lantz RC, Jolad SD, et al, Timmermann BN. Turmeric extracts containing curcuminoids prevent experimental rheumatoid arthritis. *J Nat Prod*. 2006 Mar;69(3):351-5. doi: 10.1021/np050327j. PMID: 16562833; PMCID: PMC2533857.
- Roger P Smith, MD Andrew M Kaunitz, MD. Dysmenorrhea in adult women: Treatment. UpToDate Inc. <https://www.uptodate.com> (Accessed on May 05, 2020).
- Daniels SE, Paredes-Diaz A, An R, Centofanti R, Tajaddini A. Significant, long-lasting pain relief in primary dysmenorrhea with low-dose naproxen sodium compared with acetaminophen: a double-blind, randomized, single-dose, crossover study. *Curr Med Res Opin*. 2019 Dec;35(12):2139-2147. doi: 10.1080/03007995.2019.1654987. Epub 2019 Aug 28. PMID: 31397597.
- FKAI. Health Secret of Turmeric (Kunyit). 2011. Jakarta: PT. Elex Media Computindo.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.