MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2019; 25: 157-164
DOI: 10.12659/MSM.911711

Received: 2018.06.19
Accepted: 2018.09.20
Published: 2019.01.06

Comparison of the Effects of Piroxicam and Diclofenac Sodium as Treatments for Primary Dysmenorrhea

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1 Mehpare Camlibel
ABCDEFG 2 Bulent Erdur
BCEG 2 Atakan Yilmaz
BEG 2 Mert Ozen
BG 2 Aykut Uyanik

1 Department of Emergency Medicine, Alanya State Hospital, Antalya, Turkey
2 Department of Emergency Medicine, Pamukkale University, Medical Faculty, Denizli, Turkey

This article was presented at the 2nd Intercontinental Emergency Medicine Congress & 2nd International Critical Care and Emergency Medicine Congres, Antalya, Turkey, Apr 16–19, 2015

Corresponding Author: Bulent Erdur, e-mail: bulenterdur@hotmail.com

Source of support: This research was supported by a grant from Pamukkale University, Faculty of Medicine Research Fund

Background: NSAIDs are the most common agents used in dysmenorrhea treatment. They reduce menstrual pain by reducing uterine pressure and PGF2alpha levels in the menstrual fluid. The aim of this study was to compare the effects of piroxicam and diclofenac sodium as treatments for primary dysmenorrhea.

Material/Methods: The study was conducted using a randomized and double-blind method. Patients with Visual Analogue Scale (VAS) scores greater than 5 were accepted into the study. The patients who were suitable for inclusion were randomized into 2 groups and received either intramuscular piroxicam or diclofenac sodium. The patients' pain levels were measured at baseline and at 15, 30, 45, and 60 min. A VAS of 10 cm, a numeric scale, a verbal scale, and additional symptoms, as well as pain relapse after 24 hours and required analgesics, were recorded.

Results: The study included 400 patients. Overall, 200 patients (50%) were in the proxicam group, and 200 patients were in the diclofenac sodium group. The average decrease on the VAS after piroxicam or diclofenac administration was measured as 7.9±1.8 cm and 7.9±1.7 cm (median ± standard deviation), respectively. The pain-reducing efficiency of all the treatments was compared using the Mann-Whitney U test (p=0.929). Rescue medication was needed for 25 patients in the proxicam group (p=0.014). Overall, 30 patients in the proxicam group and 41 patients in the proxicam group needed analgesics again in the 24-hour period after treatment (p=0.150).

Conclusions: At the end of our study, it was observed that there was no difference in the results of primary dysmenorrhea treatment with 20 mg piroxicam or 75 mg diclofenac sodium.

MeSH Keywords: Diclofenac • Dysmenorrhea • Emergency Service, Hospital • Piroxicam

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/911711

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

Dysmenorrhea is a common gynecological problem consisting of painful cramps accompanying menstruation. Dysmenorrhea affects more than 50% of women who menstruate. Nevertheless, there are many publications that indicate that 90% of women between the ages of 18 and 45 years have dysmenorrhea [1]. Dysmenorrhea is one of the most frequent reasons for emergency admissions. Research has shown that women with dysmenorrhea have high levels of prostaglandin hormones, which are known to cause cramping abdominal pain. Non-steroidal anti-inflammatory drugs (NSAIDs) produce an analgesic effect by blocking prostaglandin production. Therefore, NSAIDs are generally used for dysmenorrhea treatment [2]. Generally, tablet forms of the medications are used in studies that have focused on NSAID usage for dysmenorrhea treatment [3–5]. However, we have observed that parenteral treatment for patients who are admitted to emergency units complaining of strong pain is more comfortable, fast, and effective.

Dysmenorrhea is classified into 2 categories: primary and secondary. Primary dysmenorrhea is defined as menstrual pain occurring without macroscopic pelvic pathology [1]. The current findings show that primary dysmenorrhea pathogenesis is related to PGF2, which is a vasoconstrictor and potent myometrial stimulant that is located in the secretory endometrium. NSAIDs decrease symptoms by inhibiting cyclooxygenase enzymes, depressing the production of cyclic endoperoxides and decreasing prostaglandin levels in menstrual fluid [6]. Taking NSAIDs at an adequate and frequent level can successfully reduce pain [2]. A meta-analysis that included 73 randomized controlled studies determined that NSAIDs are more effective for reducing pain than paracetamol or placebo for the treatment of primary dysmenorrhea. Nevertheless, it was determined that there was not enough evidence to determine which NSAIDs were more effective and reliable for primary dysmenorrhea treatment.

Piroxicam is an anti-inflammatory agent that has analgesic and antipyretic effects. It works by making cyclooxygenase enzymes reverse their inhibition functions, including inhibition of prostaglandin prostanoid synthesis [7]. The increase in endometrial prostaglandins in primary dysmenorrhea causes uterus ischemia and uterus hyper-contraction, which produce pain [4]. Piroxicam, which is the main inhibitor of prostaglandin synthesis, decreases uterus hyper-contractions and is very effective for primary dysmenorrhea treatment [8].

Diclofenac sodium is a type of phenylacetic acid. It has fast and strong anti-inflammatory, antirheumatic, analgesic, and antipyretic effects. These effects include inhibition of prostaglandin synthesis, and it has been shown that the medication is effective for primary dysmenorrhea treatment [9].

In the present study, we compared the analgesic effects of 1 dose of intramuscular piroxicam and diclofenac sodium in patients who were admitted to the emergency unit with complaints of primary dysmenorrhea.

Material and Methods

Study design and setting

Our study included patients who arrived in an emergency unit complaining of dysmenorrhea. We aimed to compare the efficiencies and effectiveness of intramuscular diclofenac sodium and piroxicam. The study is a prospective cohort study that was randomized, double-blinded, and controlled.

Our study was conducted in the Emergency Unit at the Hospital of Medicine Faculty of Pamukkale University (Turkey) during 14 months from 22 May 2013 to 31 July 2014 after approval by the Ministry of Health of the Turkish Republic's Clinical Research Branch of Medication and Pharmaceutics Directorate (approval was granted on 22.05.2013 and the case number was 55126).

The trial was registered in the database of federal clinical trials (clinicaltrials.gov identifier NCT02253446).

Selection of participants

The study took place at the Adult Emergency Department of the Medical Faculty Hospital of Pamukkale University (Turkey) (tertiary referral; ED annual census 78 000).

After informed consent for participation was given by patients who were complaining of dysmenorrhea and came to the emergency unit, the participants who met the inclusion criteria were enrolled in the study and randomized. Participants who did not meet the inclusion criteria were not included in the study. The inclusion and exclusion criteria were determined before the study began.

Inclusion criteria of the study

- Age between 18 and 45 years
- Diagnosed with primary dysmenorrhea
- A VAS score greater than 5

Those with diagnosis of dysmenorrhea not evaluated with a physical or gynecological examination were included as long as no clinical indications of pelvic pathology were reported.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Patients were excluded if they had the following conditions

- Serious liver, kidney, or heart failure
- Women with secondary dysmenorrhea (with identified pathology from a physical examination)
- Asthma, nasal polyps, angioedema, or urticaria reactions to aspirin or other NSAIDs
- Women with irregular/infrequent menstrual cycles (outside of the typical range of 21–35 days cycle)
- Active peptic ulcers, bleeding or perforations
- History of upper gastrointestinal disease
- Diagnosed with phenylketonuria
- Serious cardiovascular failure
- Pregnant or lactating
- Diagnosed with asthma
- Taken an analgesic in the last 4 hours
- Using contraceptive methods and being at reproductive ages. Using digoxin, lithium, furosemide, and other diuretics or anticoagulants with acetylsalicylic acid or coumadin groups
- Peritoneal irritation symptoms and acute abdomen suspicions upon physical examination.

Study protocol

The groups were determined as follows:
First group: 200 patients, Piroxicam 20 mg (Felden® ampul – Pfizer-France) intramuscular (IM)
Second group: 200 patients, diclofenac sodium 75 mg (Miyadren® ampul-Yavuz Medications – İstanbul) intramuscular (IM)

Medications were applied according to a randomization scheme with 5-cm injectors for an intramuscular injection and were covered by plaster to maintain the randomization. The patients, physicians, and nurses were blinded to study. The patients were observed for 60 minutes in the emergency unit, and 45 minutes into that period, the patients received intramuscular tramadol HCL (100 mg-Contramal® ampul-Abdi İbrahim-İstanbul) as a rescue medication for the patients who had a Visual Analogue Scale (VAS) score higher than 5 points.

Study population

The researcher and/or instructor who observed the study for 24 hours was determined ahead of time. The information about patients and the data were collected with questionnaire forms. In the first part of the questionnaire forms, demographic data were collected from the patients, including whether they took medication 4 hours prior to admission, telephone numbers, and other vital information. All of the patients' detailed physical examinations were performed by emergency doctors. After the history and physical examination, the patients with a diagnosis of appendicitis, ovarian torsion, ovarian cyst rupture and acute abdomen were removed from the study. Patients who were not approved for the study were removed from the study because they required advanced diagnosis and treatment.

Measurements

A VAS from 0 to 10 cm was used to evaluate the level of pain. Before and during treatment, the VAS chart was filled out by the patients without looking at their past marks. In addition to VAS scores, the verbal and numeric scales of dysmenorrhea were assessed. The patients' case numbers, age, sex, information about the health professionals who provided treatment, date, and time of treatment application were collected in a single form.

During monitorization of SpO2, blood pressure and pulse were automatically collected, and throughout the process all other medications were recorded. The patients' body temperature was measured from the arm pit with a Nimo® device. Oxygen saturation and blood pressure was measured with a Nihon Kohden® BSM-2301K device.

The pain scores were evaluated and recorded at 0, 15, 30, 45, and 60 minutes after the medication was given. During the same time points, heart rate (bpm), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), breath rate (breaths per minute), and body temperature (ºC) were measured and recorded. Additional symptoms were recorded on the study form. Treatment was applied for additional symptoms when needed. After patients were discharged from the hospital, researchers reached the patients by phone 24 hours later and asked if they had dysmenorrhea that required an analgesic.

All the data were saved to the study form.

Data analysis

The data were analyzed with SPSS *17.0 Windows* (*SPSS İnc, Chicago, IL, USA*). Defining characteristics are presented as the average and percentage distribution. Averages are given as "average±standard deviation". Power analysis indicated that a minimum of 200 people was needed for each group. The groups were compared with a chi-square test and *t* test based on the analysis method. For the statistical analysis of repeating data (VAS, pain scores, arterial blood pressure, pulse, breath rates, and body temperature), the data were compared with a repeated-measures ANOVA. Statistical significance was considered to be $p<0.05$ for all analyses.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

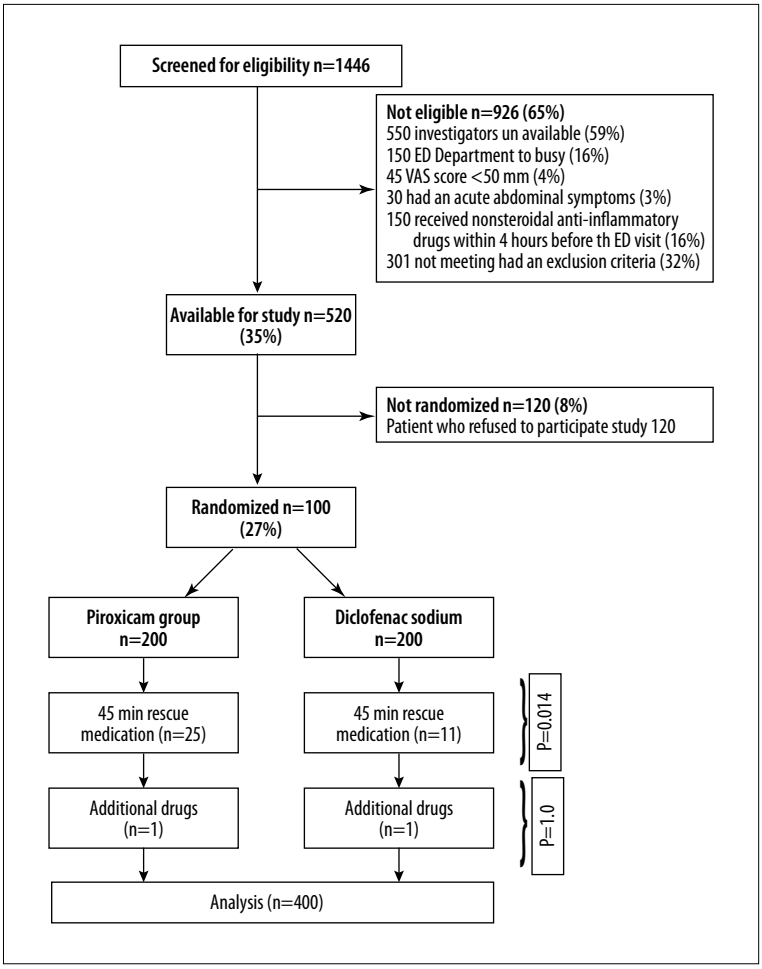

Figure 1. CONSORT diagram.

Results

Overall, 1446 patients with complaints of dysmenorrhea were admitted to the Emergency Unit of Pamukkale University Medicine Faculty throughout the study period from 05.22.2013 to 07.31.2014. Of those patients, 400 (27%) were patients who were approved to be part of the study, and those individuals were divided into 2 groups. There were 200 patients in the piroxicam group and 200 in the diclofenac sodium group. The Consolidated Standards of Reporting Trials (CONSORT) patient flow diagram is shown (Figure 1). The vitals and baseline characteristics of patients are given (Table 1, Figure 2).

The initial dysmenorrhea VAS score of the piroxicam and diclofenac sodium group was 8.6 cm (95% CI 7.4 to 9.8 cm), and 8.5 cm (95% CI 7.3 to 9.7 cm), respectively. The score of the piroxicam and diclofenac sodium group declined by 0.7 cm (95% CI –0.8 to 2.2 cm) and 0.6 cm (95% CI -0.7 to 1.9 cm) at the 60-minute time point, respectively. The overall repeated-measures ANOVA test (P=0.326) did not detect a difference in analgesic efficacy between the 2 treatments.

A decrease was detected in the numeric rating scale and verbal rating scale of the 2 groups over time. There were no significant differences between the groups (Figure 3). The overall repeated-measures ANOVA test for the numeric rating scale (P=0.188) and verbal rating scale (P=0.704) did not detect a difference in analgesic efficacy between the 2 treatments.

Rescue medication was given to 25 (12.5%) patients in the piroxicam group, and diclofenac sodium was given to 11 patients (5.5%). The differences between the groups were statistically significant (p=0.014) (Figure 3)

It was observed that 2 patients (1.0%) in each piroxicam and diclofenac sodium group experienced adverse effects (i.e., epigastric pain) from the medications (Figure 3). Additional medication was given to 1 patient (0.5%) in each group who complained of sickness during the one-hour study (p=1.00) (Table 2).

The patients were classified by their dysmenorrhea grade level according to their dysmenorrhea pain, which was ranked from 0 to 3 (Grade 0: 0 patients. Menstruation is not painful, daily activities not affected; Grade 1: 5 patients. Menstruation is

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 1. Baseline characteristics.

	Medication		p Value
	Piroksikam n (%)	Diklofenac sodium n (%)	
Patients	200	200	
Age (mean ±SD)	21.34±3.11	21.54±3.09	0.520**
Weight (mean ±SD	55.43±7.6	53.60±6.20	0.013*
Systolic blood pressure (mean ±SD)	118.4±11.3	118.6±12.00	0.811*
Diastolic blood pressure (mean ±SD)	69.6±10.1	72.2±9.8	0.009*
Pulse rate (mean ±SD)	84.6±16.1	80.8±12.0	0.008*
Body temperature (mean ±SD)'	35.9±0.5	35.8±0.5	0.360*
Respiratory rate (mean ±SD)	19.6±4.2	19.0±3.9	0.177*

* p value was obtained from *t* test; ** p value was obtained from Pearson chi-square test.

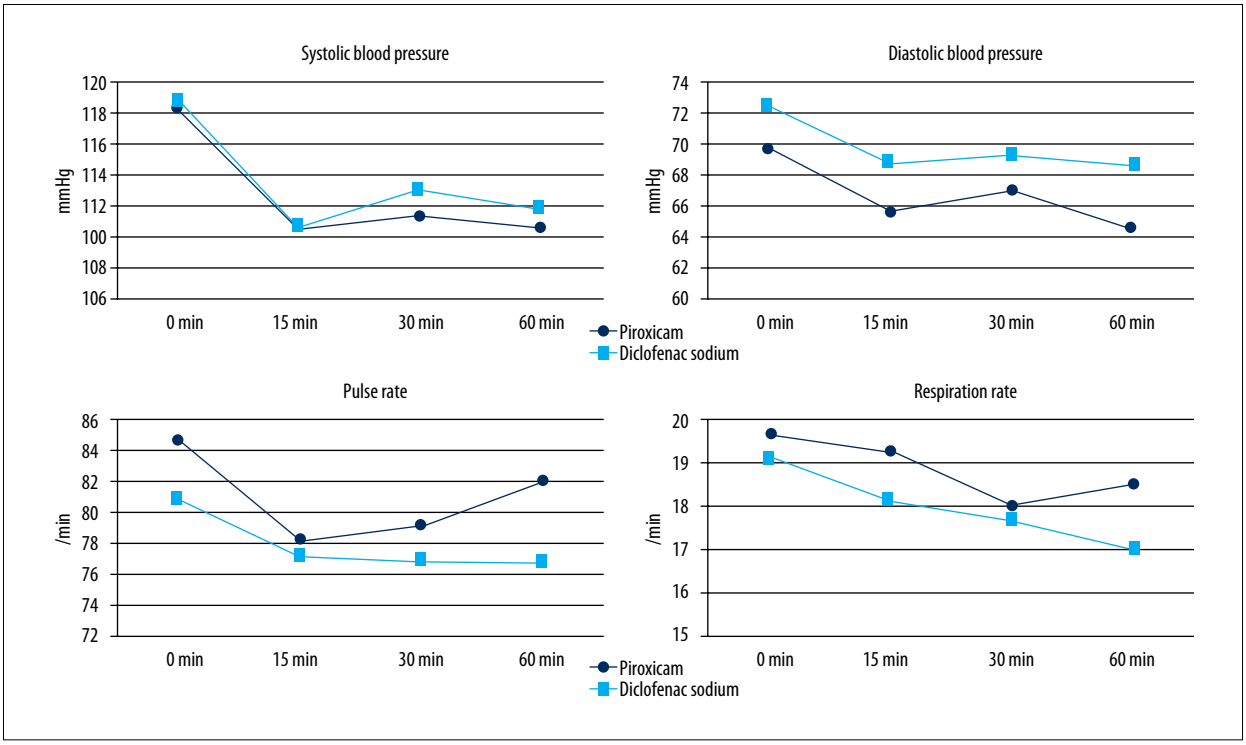

Figure 2. Vital signs graphic.

painful, rarely need analgesic (1.3%); Grade 2: 137 patients. Daily activities are affected, analgesic needed (34.3%); Grade 3: 258 patients. Daily activities distinctly affected (64.5%)). Most of the patients (n=258, 64.5%) were admitted to the hospital when they reached Grade 3.

The patients were called and questioned 24 h after treatment about whether they had pain that required analgesics. Overall, 30 patients from the piroxicam group (15%) and 41 patients from the diclofenac sodium group (20.5%) had repeated pain (p=0.150) (Figure 3).

Discussion

This study aimed to compare the treatment efficiencies of 20 mg intramuscular piroxicam or 75 mg diclofenac sodium for 400 patients who were admitted to the emergency unit complaining of dysmenorrhea. We determined there were no differences between the 2 active ingredients for the efficiency of dysmenorrhea treatment (p_{VAS}=0.326).

We found that the decrease in pain was statistically significant for the VAS, numeric scale and verbal scales when we assessed

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

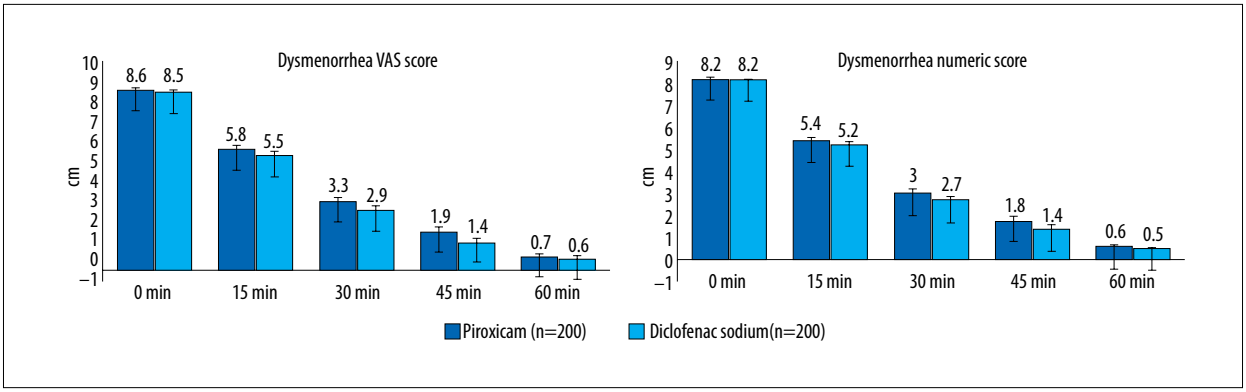

Figure 3. VAS-num with St err.

Table 2. Pain response after treatment. rates of rescue drugs use additional drugs and overall satisfaction.

	Piroxicam n (%)	Diclofenac sodium n (%)	P value
VAS Score mean ±SD			
VAS_0	8.6±1.2	8.5±1.2	
VAS_{15}	5.8±2.1	5.5±2.2	
VAS_{30}	3.3±2.8	2.9±2.6	0.326*
VAS_{45}	1.9±2.5	1.4±2.2	
VAS_{60}	0.7±1.5	0.6±1.3	
Numeric Score mean ±SD			
Numeric $Score_0$	8.2±1.4	8.2±1.4	
Numeric $Score_{15}$	5.4±2.0	5.2±2.1	
Numeric $Score_{30}$	3.0±2.6	2.7±2.4	0.188*
Numeric $Score_{45}$	1.8±2.5	1.4±2.1	
Numeric $Score_{60}$	0.6±1.4	0.5±1.2	
Rescue medication (30 min hydrotalcite) n (%)	25 (12.5)	11 (5.5)	0.014**
Adverse effect (Epigastric pain)	2	2	1**
Additional drugs (metoclopramide)	1	1	1**
Recurrent pain	30 (15)	41 (20.5)	0.150**

* p value was obtained by from repeated ANOVA; ** p value was obtained from Pearson Chi-square test. VAS_{15}, VAS_{30},VAS_{45}, VAS_{60} indicate VAS score at 15, 30, 45, and 60 minutes after treatment, respectively.

both groups (p<0.001). In addition to this analysis, we determined that the rescue medication was used more often in the piroxicam group than in the diclofenac sodium group. The difference in the need for rescue medication between the groups was statistically significant (p=0.014). However, there were no statistically significant differences between the groups in terms of the repeat rate of pain in the first 24 hours.

According to our literature research, our study is the first prospective, randomized, controlled study that has shown the efficiency of NSAID parenteral treatment for primary dysmenorrhea.

Many women do not seek medical support for dysmenorrhea treatment. Most women use NSAIDs and other analgesics or heat treatment in their own homes [10].

When the literature was searched, we found that medication studies for outpatients typically included oral treatment [2–4]. In addition to those studies, clinical research was carried out

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

with various treatment strategies, such as heat treatment, acupuncture, and herbal treatment methods [11,12].

According to our literature survey, there were no medication investigations of intramuscular NSAIDs for treating dysmenorrhea. In this sense, our study is a preliminary survey. It is agreed that gradation according to the intensity of dysmenorrhea pain and the limitation of daily activities assists in producing effective treatments [10].

The patients who were included in our study were compared according to dysmenorrhea score. The daily activities of 258 patients (64.5%) were remarkably restricted, and they determined that they could not achieve enough symptom relief from the self-administration of analgesics at home. It was determined that the daily activities of 137 patients (34.3%) were somewhat restricted, and they felt the need to use analgesics and gained relief from symptoms after taking analgesics.

It was thought that the patients who were included in our study needed to have parenteral treatment to reduce their pain rapidly and help them return to their daily activities because they could not function normally. To the best of our knowledge, there are not enough well-designed studies in the literature on the parenteral treatment of dysmenorrhea.

NSAIDs are the most common treatment in clinics for both primary and secondary dysmenorrhea. They can reduce PGF2 levels in menstrual fluid and reduce uterus pressure [6,13,14].

Although some NSAIDs (especially fenametes) are known to be effective for dysmenorrhea treatment and are commonly used, there is generally not enough evidence to support those claims [15]. Moreover, no well-designed prospective studies were carried out.

Selective COX-2 inhibitors are effective for reducing menstrual pain. According to selectivity, gastrointestinal symptoms are rarer with COX-1 inhibitors. Although some research has recommended the use of oral COX inhibitors, there are limited surveys about oral COX-2 inhibitors for dysmenorrhea treatment in the literature [16].

According to more recent research, it is understood that COX-2 inhibitors are not superior to non-selective NSAIDs [2,14].

Our study was consistent with the literature in terms of the lack of difference in treatment efficiencies between intramuscular 20 mg piroxicam and 75 mg diclofenac sodium.

There was no difference in treatment efficiencies between the patients who received intramuscular 20 mg piroxicam or intramuscular 75 mg diclofenac sodium for complaints of dysmenorrhea in the emergency unit (p=0.326).

The results were similar to the studies of Mello et al. and Letzel et al. [3,4].

Mello et al. compared the effectiveness of using 500 mg mefenamic acid tablets 3 times a day, meloxicam 7.5 mg tablets once a day and 15 mg meloxicam tablets once a day for patients complaining of primary dysmenorrhea, and they also investigated the safety and efficiency of these treatments [3]. The 10 cm VAS was used as an evaluation scale and at the beginning of their study, and the patients who had a VAS score greater than 3.5 were accepted. At the end of the study, which consisted of 3 treatment groups, there was no difference in the general evaluation pattern of the experimental groups.

Letzel et al. investigated the efficacy and safety of aceclofenac 100 mg tablet against placebo and naproxen 500 mg tablets given orally [4]. The evaluation of pain was carried out with a 10-point VAS scale. The patients who had a VAS score higher than 6 were accepted to the study. The VAS scores were recorded 0.5, 1, 1.5, 2, 4, 6, and 8 hours after patients took medication. The patients took rescue medication after 2 hours when needed. Consequently, it is determined that aceclofenac and naproxen were statistically effective compared to placebo for reducing the pain. Moreover, there was not a statistically significant difference between aceclofenac and naproxen with respect to pain scores.

However, those medications are not for emergency treatment, and the studies were performed for long-term follow-up with oral forms of the medication. More studies originating from emergency units are needed to understand the contribution of NSAIDs to dysmenorrhea treatment.

More rescue medication was needed for the piroxicam group ($p<0.001$) in our study. Letzel et al. did not find a significant difference in their comparison, which involved 2 active medication groups, regarding the need for rescue medication [4]. It is thought that there were differences between our study and their study because of treatment duration (our study was 45 minutes and their study was 2 hours).

During our study, the side effects of medications were observed in 4 cases (i.e., epigastric pain). During the study by Letzel et al., headaches occurred in 12 cases and stomach ache in 4 cases, which suggests that the parenteral forms of NSAIDs had fewer adverse effects than their oral forms. However, there is no evidence to support that claim. The usage of parenteral NSAIDs for primary dysmenorrhea treatment and their clinical use are worthy of additional research.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

In our study, 30 patients in the piroxicam group and 41 patients in the diclofenac sodium group needed repeated analgesics for pain after a 24-hour treatment period (p=0.150). Because of this study conducted in emergency unit, these patients were followed up during 24 hours. We believe that while the plasma elimination half-life of piroxicam is 50 hours and is 2–3 hours for diclofenac sodium, which resulted in differences in pain and may explain the need for repeated analgesic treatment [7,8].

Conclusions

At the end of our study, we found out that there was no difference in the analgesic efficacy between 1 dose of intramuscular 20 mg piroxicam and intramuscular 75 mg diclofenac sodium for treatment of primary dysmenorrhea. Both medications treated dysmenorrhea efficiently in the emergency unit.

Nevertheless, it was observed that the piroxicam group needed more rescue medication than the diclofenac sodium group. During the 24-hour period after treatment, 30 patients in the piroxicam group and 41 patients in the diclofenac sodium group had pain that needed repeat treatment with rescue analgesic therapy, but the difference between the groups was not statistically significant.

Conflict of interest

None.

References:

1. Jamieson DJ, Steege JF: The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices. Obstet Gynecol, 1996; 87(1): 55–58
2. Marjoribanks J, Ayeleke RO, Farquhar C et al: Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. Cochrane Database Syst Rev, 2015; 30(7): CD001751
3. Mello N, Baracat E, Tomaz G et al: Double-blind study to evaluate efficacy and safety of meloxicam 7.5 mg and 15 mg versus mefenamic acid 1500 mg in the treatment of primary dysmenorrhea. Acta Obstet Gynecol Scand, 2004; 83: 667–73
4. Letzel H, Me'gard Y, Lamarca R et al: The efficacy and safety of aceclofenac versus placebo and naproxen in women with primary dysmenorrhoea. Eur J Obstet Gynecol Reprod Biol, 2006; 129(2): 162–68
5. Iacovides S, Fiona C, Avidon I: The 24-h progression of menstrual pain in women with primary dysmenorrhea when given diclofenac potassium: A randomized, double-blinded, placebo-controlled crossover study. Arch Gynecol Obstet, 2014; 289(5): 993–1002
6. Dawood MY, Khan-Dawood FS: Clinical efficacy and differential inhibition of menstrual fluid prostaglandin F2alpha in a randomized, double-blind, crossover treatment with placebo, acetaminophen, and ibuprofen in primary dysmenorrhea. Am J Obstet Gynecol, 2007; 196(1): 35.e1–5
7. Marjoribanks J, Proctor M, Farquar C et al: Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. Cochrane Database Syst Rev, 2010; 20(1): CD001751
8. Available from: URL: *https://www.practo.com/medicine-info/piroxicam-40-mg-injection-29752*
9. Available from: URL: *https://www.practo.com/medicine-info/diclofenac-sodium-75-mg-injection-3481*
10. Calis KA: Dysmenorrhea. *http://emedicine.medscape.com/article/253812-overview*
11. Smith CA, Armour M, Zhu X et al: Acupuncture for dysmenorrhoea. Cochrane Database Syst Rev, 2016; 18(4): CD007854
12. Lee H, Choi TY, Myung CS et al: Herbal medicine (Shaofu Zhuyu decoction) for treating primary dysmenorrhea: A systematic review of randomized clinical trials. Maturitas, 2016; 86: 64–73
13. Milsom I, Andersch B, Sundell G: The effect of flurbiprofen and naproxen sodium on intra-uterine pressure and menstrual pain in patients with primary dysmenorrhea. Acta Obstet Gynecol Scand, 1988; 67(8): 711–16
14. Chan WY, Fuchs F, Powell AM: Effects of naproxen sodium on menstrual prostaglandins and primary dysmenorrhea. Obstet Gynecol, 1983; 61(3): 285–91
15. Zhang WY, Li Wan, Po A: Efficacy of minor analgesics in primary dysmenorrhoea: A systematic review. Br J Obstet Gynaecol, 1998; 105(7): 780–89
16. Morrison BW, Daniels SE, Kotey P et al: Rofecoxib, a specific cyclooxygenase-2 inhibitor, in primary dysmenorrhea: A randomized controlled trial. Obstet Gynecol, 1999; 94(4): 504–8

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]