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Comparison between ibuprofen and paracetamol in primary dysmenorrhea

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Abstract

Background: Primary dysmenorrhea refers to the symptom of painful menstruation in the absence of identifiable pelvic or uterus pathology. Initial presentation usually occurs in adolescence and early adulthood. Medications used to treat primary dysmenorrhea include anti-inflammatory drugs, principally, ibuprofen and paracetamol. So far there has been no comparison of effectiveness and security profile between the two pharmaceutical substances.

Objectives: Purpose of this prospective randomized crossover study was to compare the effectiveness and safety profile between those two pharmaceutical substances.

Methods: In this clinical trial, 100 young women were included. The inclusion criteria was: a) age between 18–25 years old, b) no present or previous pelvic pathology, based on their medical history and an ultrasound examination which was performed in the 3–6th day of their menstrual circle, a month before the clinical trial. Vaginal discharge examination and also Papanicolaou test were held to exclude relevant pathology of the genital system. Participants were assessed and divided in two groups. The duration of the study was two months. The first group received ibuprofen for the first month and paracetamol for the second month while the second group received them vice versa (cross-over trial). Both groups filled in a questionnaire in regard to how they responded to each therapy. In addition, the security profile of the pharmaceutical drugs was compared as also their effect to the characteristics of menstruation and their probable side-effects. All participants filled in a questionnaire before the assignment into groups. For the comparison of the results, the 10% of the women with not painful menstruation, steadily every month, were removed and paired-samples t-test was used.

Results: Ibuprofen has been proven as a safe and more effective therapeutic option than paracetamol in all parameters, when treating women with primary dysmenorrhea. After the administration of analgesics for the two following months, the comparison and statistical analysis of the new questionnaires revealed that, when Ibuprofen was compared to Paracetamol, the analgesic effectiveness was 98,9 and 91,1% respectively. Ibuprofen provided a maximum pain relief in 30 minutes – 53,3% of participants –when Paracetamol demonstrated the maximum pain relief in 60 minutes (64,4%). The pain was decreased “moderate” with

the use of Paracetamol (37,8%) and "totally" with Ibuprofen (58,9%). The duration of analgesia with Ibuprofen was 4–8 hours –73,3% of participants– compared to 1–4 hours with Paracetamol (57,4%). Daily activity has been remarkably improved with the use of Ibuprofen (62%) compared to Paracetamol (only 9%). After the administration of Paracetamol 4% of the women appeared side-effects and none of the women appeared with the use of Ibuprofen. All the above results were statistically significant.

Conclusions: Ibuprofen provides a significantly improved quality of life when compared to Paracetamol and no side effects have been noticed.

Key words: Dysmenorrhea, primary, treatment, ibuprofen, paracetamol

Introduction

Dysmenorrhea refers to the symptom of pain in the hypogastrium and the iliac regions during menstruation and it can be divided in primary and secondary dysmenorrhea.

Primary dysmenorrhea refers to the symptom of painful menstruation in the absence of identifiable pelvic or uterine pathology, firstly presented in adolescence and early adulthood[1]. Regarding pathophysiology, pain occurs due to the increased sensibility of the endometrial receptors to prostaglandins or due to uterine ischaemia, caused by the imbalance of the prostaglandins, as both situations contribute to increase tonicity of the endometrium and uterine contractions[2].

Secondary dysmenorrhea is unusual before the 25th year of age and occurs due to pelvic or uterine pathology. Commonly the causes are endometriosis, adenomyosis, fibroids, ovarian cysts, pelvic inflammatory disease and other[3]. The treatment is based on treating the underlying cause.

Primary dysmenorrhea is usually treated with anti-inflammatory drugs, such as ibuprofen and paracetamol, according to the guidelines of the International Scientific Community. The comparison of the effectiveness, between those two pharmaceutical substances, in adolescents and young adult females is crucial. Aim of this prospective randomized cross-over study was to answer this question.

The protocol of the present study has been approved by the Scientific Director and Ethical Committee of the Postgraduate Master of Science program, at the 2nd Department of Obstetrics and Gynecology, Medical School, National and Kapodistrian University of Athens.

Methods

In this clinical trial, 100 young women were included. The inclusion criteria was: a) age between 18–25 years old, b) no present or previous pelvic pathology, based on their medical history and an ultrasound examination which was performed in the 3–6th day of their menstrual circle, a month before the clinical trial. Women with pelvic pathology, such as endometriosis, ovarian cysts, fibroids, adenomyosis and Mullerian abnormalities were excluded. Vaginal discharge examination and also Papanicolaou test were held to exclude relevant pathology of the genital system. Women with pathologic vaginal discharge, caused by infectious and noninfectious causes were excluded as well as women with ASCUS, AGUS, LSIL and HSIL in their Papanicolaou smear test.

Participants were assessed and divided in two groups. The duration of the study was two months. The first group received ibuprofen for the first month and paracetamol for the second month while the second group received them vice versa (cross-over trial). Both groups filled in a questionnaire in regard to how they responded to each therapy. In addition,

the security profile of the pharmaceutical drugs was compared as also their effect to the characteristics of menstruation and their probable side-effects.

All participants filled in a questionnaire before the assignment into groups. For the comparison of the results, the 10% of the women with not painful menstruation, steadily every month, were removed and paired-samples t-test was used. The analysis of the data was performed with statistical software SPSS Version 24.

Results

Before administration of analgesics, 90% of the participants reported constant dysmenorrhea every month and 10% did not. Regarding the severity of pain, 56% answered that the pain is "intense", 23% "moderate", 12% "mild" and 9% "severe". The everyday activity during the menstrual period is significantly affected in 67%, moderate affected in 32% and rarely affected in 1%. All participants believe that it is important not to feel pain during their menstrual period while 79% of them answered that it is "very important". Additionally, 62% of the women answered that they need painkillers, mean number of 3 pills per day, however they believe that their effectiveness is "poor".

After the administration of analgesics for the two following months, the comparison and statistical analysis of the new questionnaires revealed that, when Ibuprofen was compared to Paracetamol, the analgesic effectiveness was 98,9%(S.D.: +/- 0.29) and 91,1%(S.D.: +/- 0.11) respectively (t=2,39, df= 89, sig.2-tailed=0.019).

Ibuprofen provided a maximum pain relief in 30 minutes – 53,3% of participants(S.D.:+/-0.68) –when Paracetamol demonstrated the maximum pain relief in 60 minutes [64,4%(S.D.:+/-0.5)] (t=7,96, df=80, sig.2-tailed=0.00) [Figure 1].

The pain was decreased "moderate" with the use of Paracetamol [37,8%(S.D.: +/- 1.0)] and "totally" with Ibuprofen [58,9%(S.D.: +/- 0.62)] (t=10,24 df= 89, sig.2-tailed=0.00).

The duration of analgesia with Ibuprofen was 4–8 hours –73,3% of participants(S.D.:+/-0.55)– compared to 1–4 hours with Paracetamol [57,4%(S.D.:+/-0.63)] (t=-11,89 df= 89, sig.2-tailed=0.00) [Figure 2].

Daily activity has been remarkably improved with the use of Ibuprofen [62%(S.D.: +/-0.62)] compared to Paracetamol [only 9%(S.D.: +/-1.26)] (t=-13,61 df= 89, sig.2-tailed=0.00) [Figure 3].

After the administration of Paracetamol 4% of the women(S.D.:+/-0.21) appeared side-effects and none of the women(S.D.: +/-0.0) appeared with the use of Ibuprofen (t=-2,04 df=89, sig.2-tailed=0.045).

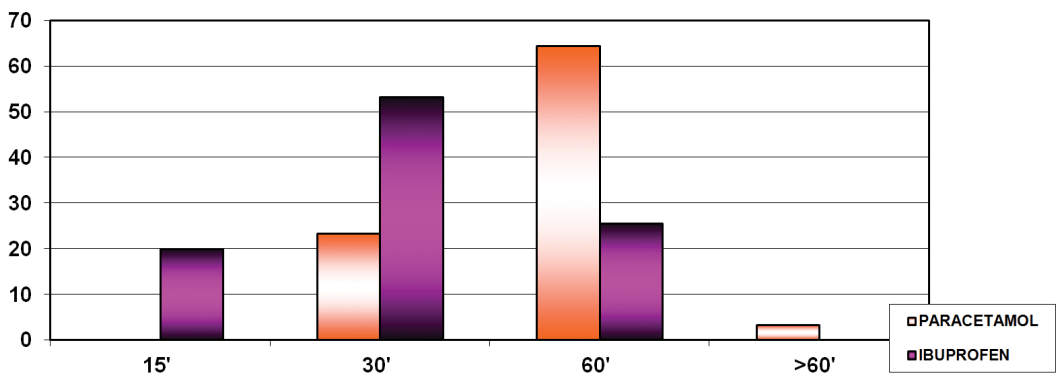

Figure 1. Minutes of maximum pain relief.

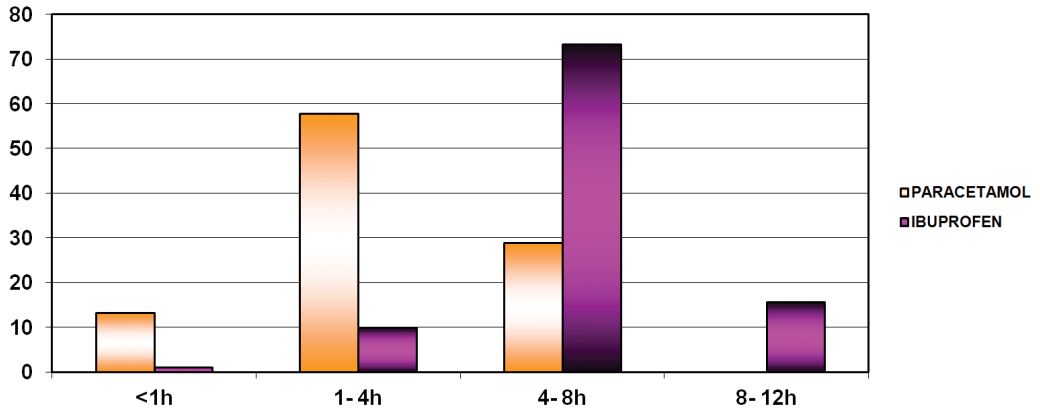

Figure 2. Duration of analgecia.

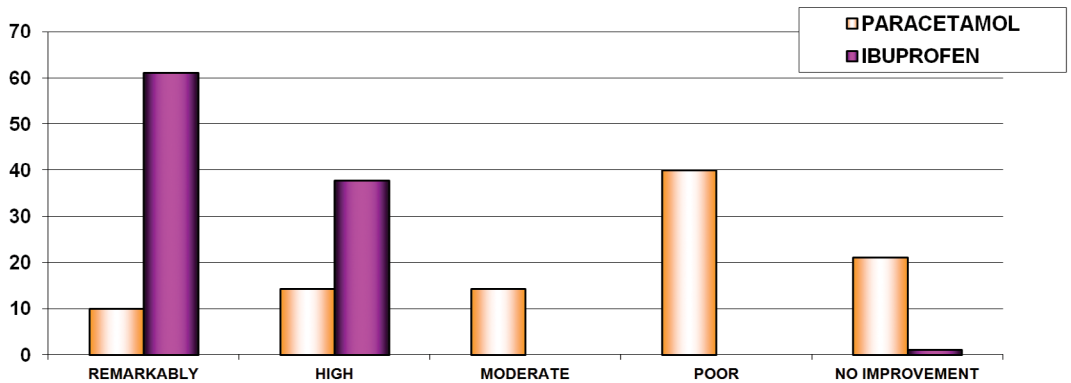

Figure 3. Improvement of daily activity.

All the above results were statistically significant. [Table 1]

Neither the duration of the menstrual circle appear increase for both pharmaceutical drugs –Ibuprofen 97,8%(S.D.: +/-0.62) and Paracetamol 93,3%(S.D.: +/-0.15)(t=-1,64 df= 89, sig.2-tailed=0.105)–, nor the quantity of blood loss appear increase –Ibuprofen 94,4%(S.D.: +/-0.21) and Paracetamol 96,6%(S.D.: +/-0.23)(t=,332 df=89, sig.2-tailed=0.741)–, and there was not statistically significant difference.

Discussion

Primary dysmenorrhea refers to painful menstruation, which appears typically in the first two post-menarcheal years. Menstrual pain may start some days earlier or in the first day of the menstrual cycle and decreases as menstruation proceeds[1]. Dysmenorrhea can appear monthly and sometimes accompanying symptoms as vomiting, fatigue, back pain, headaches, dizziness, and diarrhea, may be present. Sometimes, pain can be reflected in the back or in the inner side of the thighs[2]. Approximately, 25% of women in reproductive age feel pain which is characterized by them as "severe"[4]. Another 20% of women have poor daily activity[5].

Prostaglandins are the main mediators of inflammation. Studies have proven that the plasma and vaginal concentrations of PGE2 and PGF2α, are

Table 1. Pain outcomes among patients that received paracetamol and ibuprofen.

PAIRED SAMPLES TEST									
		PAIRED DIFFERENCES							
		MEAN	STD. DEVIATION	STD. ERROR MEAN	95% CONFIDENCE INTERVAL OF THE DIFFERENCE		T	DF	SIG. (2-TAILED)
					LOWER	UPPER			
Pair 1	1P(Paracetamol). Did the pain relief with the use of the analgesic? - 1I(Ibuprofen). Did the pain relief with the use of Ibuprofen?	0,07778	0,30823	0,03249	0,01322	0,14234	2,394	89	0,019
Pair 2	1P. If yes, how quickly the pain relieved? - 1I. If yes, how quickly the pain relieved?	0,71605	0,80985	0,08998	0,53698	0,89512	7,958	80	0,000
Pair 3	2P. How much did the pain decrease with use of the analgesic? - 2I. How much did the pain decrease with use of the analgesic?	1,32222	1,22546	0,12917	1,06555	1,57889	10,236	89	0,000
Pair 4	3P. How many days was the duration of your menstruation while you were receiving the medication? - 3I. How many days was the duration of your menstruation while you were receiving the medication?	-0,11111	0,64380	0,06786	-0,24595	0,02373	-1,637	89	0,105
Pair 5	4P. How many teaspoons was the blood that you menstruated while you received the medication? - 4I. How many teaspoons was the blood that you menstruated while you received the medication?	0,01111	0,31780	0,03350	-0,05545	0,07767	0,332	89	0,741
Pair 6	5P. Did you have any side effects after administering the medication? - 5I. Did you have any side effects after administering the medication?	-0,04444	0,20723	0,02184	-0,08785	-0,00104	-2,035	89	0,045
Pair 7	6P. How many hours was the duration of analgesia? - 6I. How many hours was the duration of analgesia?	-0,87778	0,70037	0,07383	-1,02447	-0,73109	-11,890	89	0,000
Pair 8	7P. How much was your daily activity improved after the administration of medication?- 7I. How much was your daily activity improved after the administration of medication?	-2,05556	1,43285	0,15104	-2,35566	-1,75545	-13,610	89	0,000

higher during menstruation of women with dysmenorrhea[1]. Pathogenesis is based on the fact that the ratio of vasoconstrictor to vasodilator effect of PGE2 and PGF2α respectively, provoke increased contractions of the myometrium and is subsequent ischemia, both resulting to pain. The relevant risk factors of primary dysmenorrhea are: heredity[6], early puberty[7], anxiety[8], obesity[7], alcohol consumption[9], smoking[9], lack of physical activity.

The first therapeutic option is use of inhibitors of prostaglandin synthesis[10]. These drugs decrease the production of PGF2α, consequently they decrease the stimulation of nerve endings which cause dysmenorrhea. Most drugs of this category are effective. Mefanemic acid[11] and ibuprofen[3] are consider as the most effective and safe. Studies have proved that with appropriate use, the effectiveness of pain relief is approximately 95%.

In our Country, Greece, the mostly used pharmaceutical substances against Dysmenorrhea are ibuprofen and paracetamol.

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID), derivative of propionic acid. It is used as analgesic and antipyretic agent, also for the relief of dysmenorrhea, headaches, migraine, arthritis including rheumatoid arthritis and osteoarthritis. The risk of gastrointestinal bleeding is lower with the use of ibuprofen, compared to aspirin[12].

Paracetamol is a weak inhibitor of prostaglandin synthesis in the central nervous system and has similar analgesic and antipyretic properties with acetylsalicylic acid. With regular use, it can help control the severe pain and decrease the need for stronger analgesic or non-steroidal anti-inflammatory drugs[3].

The comparison between ibuprofen and paracetamol is a challenging topic for research. The most suitable, effective and safe therapeutic option for primary dysmenorrhea is crucial for the quality of life of these women.

A French study, in which 1108 doctors and 8677 women with primary dysmenorrhea participated, with a year duration, extracts the conclusion that gynecologists and pathologists recommend the use of Ibuprofen to relief the pain in primary dysmenorrhea. This study has shown differences in effectiveness of this drug, for some women the pain relief was effective enough and for other was not[1].

Both Ibuprofen and Acetaminophen, reduce the pain which is related with the menstrual circle, but Ibuprofen has more powerful effect, according to an American study which was published in American Journal of Obstetrics and Gynecology[3]. 12 women with primary dysmenorrhea participated in the study, whom was given three different drugs with random succession for three menstrual circles: 1000 mg acetaminophen, 400mg ibuprofen or a placebo four times per day for three days. Ibuprofen and acetaminophen were more effective than the placebo. Ibuprofen had larger duration of analgesia and the women preferred it[3].

A large scale study compared, for their safety, the three most commonly used analgesics (Ibuprofen, Paracetamol, Aspirin). The result was that the tolerance of ibuprofen was equal with paracetamol and better than aspirin. The last one is better to be avoided, because of the increase of bleeding that it can cause[13].

Two recent network meta-analysis[14,15], that studied the efficacy and safety of non-steroidal anti-inflammatory drugs for patients with primary dysmenorrhea have come to a conclusion that ibuprofen is recommended as the optimal over-the-counter analgesic. The first meta analysis[14], had included 72 randomized controlled trials of 5723 patients and 13 drugs and the most recent[15] had 35 trials with 4383 participants. The results of the effectiveness and safety network meta-analysis[15] showed that diclofenac, had the best effectiveness but also the worst safety, compared to naproxen, ibuprofen, aspirin, and ketoprofen. Therefore, they recommend ibuprofen, which was ranked second in terms of effectiveness and safety, to patients with primary dysmenorrhea.

In conclusion, from the results of our trial, the pain was relieved sooner and the duration of analgecia was

larger with the use of Ibuprofen. The everyday activity of the women was more improved with the use of ibuprofen and none of the participated shown any side effects at all. In all the above there is statistically significant superiority of Ibuprofen, which appears to be more effective of the Paracetamol for the primary dysmenorrhea. Concerning the quantity of the blood loss and the duration of the menstrual circle there was no increase with statistically significant difference.

Conflicts of interest

The authors declare no conflicts of interest.

All 100 women have given their informed consent.

The protocol of the present study has been approved by the Scientific Director and Ethical Committee of the Postgraduate Master of Science program, at the 2nd Department of Obstetrics and Gynecology, Medical School, National and Kapodistrian University of Athens.

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