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Single Oral Dose Ibuprofen for Pain Relief in Fractional Curettage under Paracervical Block: A Double-Blind Randomized Controlled Trial

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ABSTRACT

Objective To compare the analgesic efficacy of a single oral dose ibuprofen administered prior to fractional curettage under paracervical block with that of placebo in women undergoing fractional curettage.

Design Double-blind, randomized controlled trial.

Setting Gynaecological Out-patient, Department of Obstetrics and Gynaecology, Ramathibodi Hospital.

Intervention The women were randomized to receive either 400 mg ibuprofen (n=70) or placebo(n=70) 30-60 minutes prior to fractional curettage. All women were curetted under paracervical block with 1% lidocaine.

Main outcome measure The intensity of pain during and after the procedure measured by the visual analog score.

Results The intensity of pain in ibuprofen group was not significant difference from the placebo group over the course of the procedure (P>0.05). There were no serious adverse effect from the procedure.

Conclusion Pre-emptive single oral dose ibuprofen for fractional curettage under paracervical block did not relief pain during and after the procedure.

Key words: ibuprofen, paracervical block, visual analog score, fractional curettage

Women with abnormal uterine bleeding usually require endometrial tissue for diagnosis and therapeutics. The way to collect endometrial tissue is by the way of fractional curettage. Because of financial cost, mortality and morbidity associated with general anesthesia, local anesthesia is preferred as it carries less risk if it is administered properly.[1] Out-patient procedure of endometrial curettage is used widely in the developing countries.

The paracervical block has been used for minor gynaecologic procedures since 1925.[2] Lidocaine is the common and safety local anesthetic drug used. It

has rapid onset of action and is inexpensive. Unfortunately, in the earlier study the patients still experience significant pain after the injection of the anesthetic drug, especially during grasping, traction and dilatation of cervix, during curettage and cramps that followed afterwards. Paracervical block with lidocaine does not seem to provide adequate pain relief from uterine contraction during and following curettage.[3,4]

Previous study used ibuprofen, a potent cyclo-oxygenase inhibitor, which has demonstrated a significant analgesic effect in primary dysmenorrhea,[5] in postpartum uterine pain[6] and in the pain associated with curettage.[7] It has antinociceptive effect in visceral pain model[8] and the meta-analysis reviewed support its effectiveness for postoperative pain.[9]

The objective of this study was to compare the analgesic efficacy of a single oral dose ibuprofen 400 mg administered prior to fractional curettage with placebo in women undergoing the procedure.

Materials and Methods

The study was a double-blind, randomized, placebo controlled trial comparing single oral dose ibuprofen with placebo administered prior to fractional curettage under paracervical block. The study was approved by Faculty's Ethical Clearance Committee and signed informed consent was obtained from each volunteer. The procedure was carried out from April 2001 through July 2001.

The women who have hypersensitivity to ibuprofen, lidocaine, blood dyscrasia, gastrointestinal tract bleeding and history of peptic ulcer were excluded.

One hundred and fifty women undergoing fractional curettage were randomly allocated to receive one of the two drugs (computer generated random numbers). The study drugs, ibuprofen 400 mg (Boot Manufacturing, Samutprakan, Thailand) or placebo were prepared in identical containers and labelled with stickers preprinted with computer-generated random numbers. The women were scheduled to receive study drugs between 30 to 60 minutes before the procedure, for the drugs's level could reach peak plasma concentration at the time of curettage and dietary was not restricted. No other premedication was given. The women, the gynaecologist performing the operation and nurse assistance were blinded to the type of drug administered. The women were treated according to the departmental routine. The random-number codes were not broken until data analysis. To using visual analog score for measuring intensity of pain, the women were asked to mark an "X" on a 10-cm line (0 cm = no pain, 10 cm = intolerable pain). Each woman gave four assessments of pain: at immediately after insertion of the speculum, during the curettage, immediately after curettage and 30 minutes after curettage.

Paracervical block injections were made with a 23-gauge spinal needle at 3 and 9 o'clock of cervicovaginal reflection at an estimated depth of 1 cm by marker knot on the needle insertor.[10] Total volumes of 1% lidocaine without adrenaline given to each patient were 20 ml,10 ml each at the two sites, respectively, intermittent aspiration was performed before and during injection to ensure that paracervical blood vessels were not punctured. Oxygen and vasopresssors were always available. Each woman was advised to ask for a lidocaine paracervical block at any time if she wanted more pain relief or wished to leave the study. The repeated injection was limited to 10 ml of 1% lidocaine (Olic Ltd, Ayudthaya, Thailand) so that the total dose of lidocaine did not exceed 300 mg.[11]

The standard procedure of fractional curettage was performed after waiting 2 minutes for the onset of action of lidocaine.[12] The endocervical canal was curetted first, followed by the endometrial cavity. The cervical canal was dilated, if necessary, using Hegar dilator up to 8 mm. diameter. Data recorded included age, marital status, history of previous vaginal deliveries, history of miscarriage, history of curettage, indication for fractional curettage, size of uterus, time from the drug administered to start the procedure, need for cervical dilatation, estimated blood loss, operative time, complications such as uterine perforation and infection, side effects of ibuprofen

such as drowsiness, epigastic pain, lidocaine toxicity and difficulty of the procedure rated by the surgeon (1 = not difficult, 2 = slightly difficult, 3 = moderately difficult, 4 = very difficult).

The sample size was estimated using data from Wiebe's study.[13] We hypothesized that ibuprofen had more analgesic effect than placebo and should reduce pain score by at least 25 percent. Thus 62 women were required in each group to achieve a power of 90% at a type I error of 0.05 (two-tailed test). Data were analysed using the Statistical Package for Social Science 7.5 (SPSS Inc., Chicago,IL). The student *t* test, the Mann-Whitney *U* test, and repeated measures analysis of variance were used to compare continuous variable, and the Chi square test was used to analyse proportion. $P<0.05$ (two-tailed test) was considered significance.

Results

During the study period, 150 women undergoing fractional curettage, ten were excluded because five women in ibuprofen group and three in placebo group took the drug less than 30 minutes before the procedure and two in placebo group had incomplete data. Seventy women were allocated to the ibuprofen group and seventy to the placebo group. No women asked to leave the study but two women in placebo group asked for more lidocaine during the procedure, but it was not statistic significance($P=0.15$) by Chi square test. The groups were similar with respect to age, marital status, history of vaginal deliveries, history of miscarriage, history of curettage, indications for fractional curettage and uterine size by vaginal examination. (Table 1)

Table 1. Characteristics of women undergoing fractional curettage

	Ibuprofen group (n=70)	**placebo group (n=70)**
Age(years)	46±6.3	46±6.5
Married	69(98.6)	66(91.4)
≥1 previous vaginal deliveries	56(80)	49(70)
≥1 previous miscarriage	23(32.9)	23(32.9)
≥1 previous curettages	32(45.7)	31(44.3)
Indications for curettage		
Menometrorrhagia	49(70)	44(62.9)
Postmenopausal bleeding	15(21.4)	17(24.3)
Endometrial hyperplasia	5(7.1)	8(11.4)
Perimenopausal bleeding	1(1.4)	1(1.4)
Uterine size (gestational weeks)		
Normal size – 8 weeks	55(78.5)	55(78.5)
9 weeks – 10 weeks	14(20)	12(17.1)
11 weeks – 14 weeks	1(1.4)	3(4.2)

Data presented as mean±standard deviation or n (%). $P>0.05$ for all comparisons.

There was no difference in the mean of duration of the time taken the drug to the procedure (ibuprofen group:46±17.9 minutes ; placebo group 47±15.8 minutes; P=0.86), operative time(10.6±3.4 versus 10.8±3.8 minutes ; P=0.69). The median difficult level of the procedure was 2 (25^{th} percentile = 2, 75^{th} percentile = 2) in ibuprofen group and 2 (25^{th} percentile = 2, 75^{th} percentile = 2) in placebo group (P=0.39). No different estimated blood loss in both groups. One woman in the ibuprofen group and four in the placebo group needed cervical dilatation before curettage (P=0.17). There was no serious complication from curettage and no adverse effect was found in this study.(Table 2) The visual analog score for both groups were similar over the course of the procedure (P>0.05). (Table 3)

Table 2. Procedure characteristics

	Ibuprofen (n=70)	**Placebo (n=70)**
duration from taking the drug to curetage (min)	46±17.9	47±15.8
operation time (min)	10.6±3.4	10.8±3.8
cervical dilatation	1(1.4)	4(5.7)
asked for lidocaine	0	2(2.9)
difficulty level	2(2,2)	2(2,2)

Data presented as mean±standard deviation, n(%) and median(25^{th}percentile, 75^{th}percentile). P>0.05 for all comparisons.

Table 3. The visual analog score

	Ibuprofen n=70	**placebo n=70**	**P-value**
Pain score			
Speculum insertion	2(2,2)	2(2,3)	0.19
During curettage	3(2,5)	3(2,5)	0.54
Immediate after curettage	2(1,2.5)	2(1,3)	0.15
30 mins post curettage	2(1,2)	2(1,2)	0.75

Data presented as median (25^{th}percentile,75^{th}percentile). P>0.05 for all comparisons.

Discussion

The various procedures used during fractional curettage such as placement of tenaculum, traction of the cervix, and dilatation of the cervical os, as well as curettage itself can cause discomfort. Pain sensation transmits by sensory and sympathetic pathway from the posterolateral aspect of the cervix to the lateral spinothalamic tracts of the spinal cord. Paracervical anesthetics block transmission of pain through sympathetic and parasympathetic sensory fibers before these fibers enter the uterus at the level of the internal cervical os.[10]

Previous study reported that women had moderate to severe pain during the curettage under

paracervical block.[3,4] Many women described the pain during the curettage as being similar to dysmenorrhea, which can be relieved by prostaglandin synthetase inhibitor[14] the evidence suggests that the inhibition effect of prostaglandin synthesis has a concomitant effect on the reduction of intrauterine pressure from uterine contraction leading to the reduction of pain.[5] Ibuprofen, a prostaglandin synthetase inhibitor is inexpensive, has few side effects and is widely prescribed.

Pre-emptive analgesia is based on the idea that analgesia initiated before a nociceptive event will be more effective than analgesia commences afterwards. Prophylactic administration of the drug so that the peak plasma concentration was attained closed to the time of curettage may have contributed to its therapeutic effectiveness.[15] This study was designed to test the analgesic efficacy of preoperatively single oral dose of ibuprofen 400 mg in fractional curettage under paracervical block.

This study design was double-blind, randomized, controlled trial that can minimize difference in factors likely to influence the pain score between the two groups such as age, history of vaginal deliveries, history of miscarriage, history of curettage, indication for curettage, time from the drug administered to start the procedure, size of uterus, need for cervical dilatation, estimated blood loss, operative time and difficulty of the procedure.

We measured the perception of pain at the insertion speculum as a measurement of baseline pain. We hypothesized that pain during the placement of speculum would be positively correlated with the pain at the other time of the procedure.

Pain is always difficult to measure and compare because of its subjective nature and the many factors which influence perception and the reporting of pain. We limited our study to pain assessment and did not address symptom such as anxiety and cramping. However, pain perception is complex and also affected by psychologic factors. We did not study the presence of a supportive person, which also might influence pain perception. Individual physician is also a variable. In our study there were three levels of residents who performed the curettage that may has technical variation which might influence the pain perception and a research assistance introduced women to the study. Fractional curettage is a procedure with a standardized format, so in this study there was no change in the curettage procedure protocols. Thus, the result of this study can be applied to the daily work.

Our data indicated that a single oral dose ibuprofen 400 mg had no advantage over the placebo in decreasing the pain in fractional curettage. No significant difference found across the treatment arms. This study provided placebo for comparison with oral ibuprofen but did not control for placebo effect. We did not measure pain level when no oral tablet was given.

Unlike study by Suprato and Reed,[15] used naproxen sodium for pain relief in suction curettage showed that naproxen sodium women had significant lower pain scores than the placebo group but there was only 46 women in each group. The pain score during curettage in this study were similar in ibuprofen and placebo groups. The failure of ibuprofen, a potent prostaglandin synthetase inhibitor, to relieve pain at the time of the curettage may imply that this pain is not cause mainly by prostaglandin release but from the procedure itself.

The paracervical block used in all women in our study may effectively relieve the pain during fractional curettage already because the women had median of pain score only 3 during the procedure. Thus ibuprofen can not produce a better result. Further research is need to see if there are other medications with better pain relief such as other NSAIDs or anesthetic drugs with sedative effect to use in this procedure and performed the procedure by the same physician to reduced the technical variation.

We conclude that pre-emptive single oral dose ibuprofen for fractional curettage under paracervical block did not relief pain during and after the procedure.

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