Comparison Between Lornoxicam and Paracetamol for Pain Management after Dilation and Curettage for Abortion

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ABSTRACT: **Background:** Management of postoperative pain has become a growing concern, even for minor gynecological procedures. Proper postoperative pain management has been shown to lead to earlier mobilization, shortened hospital stay, and increased patient satisfaction. The optimal means of reducing the pain of pregnancy termination has not yet been determined.

Objectives: To compare the efficiency in pain management of two drugs, lornoxicam and paracetamol, given intravenously postoperatively to women who underwent abortion with dilation and curettage.

Methods: The cohort comprised 80 women scheduled for dilation and curettage for pregnancy termination at 6–12 gestational weeks. The anesthesiologist gave 1000 mg paracetamol or 20 mg lornoxicam soon after starting the procedure, according to a randomization table. The medical staff and the patients were blinded to the drug that was administered. Pain levels were evaluated by a 10 cm visual analogue scale (VAS) at 15, 30, 60, 90, and 120 minutes following arrival at the postoperative care unit.

Results: Mean levels of pain decreased from 60 minutes postoperative until the end of recording, reaching minimum levels at 120 minutes: 0.8 ± 0.19 and 1.5 ± 0.28, for lornoxicam and paracetamol, respectively. The differences between the groups were statistically significant ($P < 0.05$ from 60 minutes after the procedure until the time of discharge.

Conclusions: Compared to women who received paracetamol, women who received lornoxicam after dilation and curettage for termination of pregnancy reported lower levels of pain, from 30 minutes postoperative until the time of discharge following the procedure.

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KEY WORDS: lornoxicam, paracetamol, dilation and curettage, non-steroidal anti-inflammatory drug (NSAID), pain

Management of postoperative pain has become a growing concern, even for minor gynecological procedures. Physicians need to ensure that patients are comfortable and safe, with the lowest level of pain possible. Furthermore, proper postoperative pain management has been shown to lead to earlier mobilization, shortened hospital stay, and increased patient satisfaction.

Dilation and curettage is currently the most common method for early pregnancy termination in the first trimester [1]. This procedure involves mechanical dilation of the cervix and mechanical curettage of the uterus, followed by the evacuation of intrauterine contents. Patients are discharged on the same day as the procedure. Nonetheless, moderate to severe pain may result [2], which may prompt administration of an analgesia during or following the procedure [3,4]. Administration of a non-steroidal anti-inflammatory drug (NSAID) such as ketorolac, intravenously or intramuscularly, considerably reduces the need for narcotic consumption during the recovery period [5]. Likewise, administration of postoperative intravenous paracetamol improves pain control [6]. Nevertheless, we did not find any studies that compared the efficacies of postoperative intravenous lornoxicam vs. paracetamol.

Lornoxicam is a short acting NSAID [7-10]. Drugs of the NSAID family have been widely used in the management of postoperative pain due to their dual analgesic effect. They have impact on the peripheral and central nervous system, and their anti-inflammatory properties are generally well-tolerated [11]. Lornoxicam inhibits the peripheral receptors cyclooxygenase (COX)-I and COX-II and increases levels of prostaglandins, endogenous dynorphins, and beta-endorphins [12]. Lornoxicam has been shown to reduce the use of morphine and tramadol in the treatment of postoperative pain following hysterectomy [13]. Reduced tramadol consumption contributed to decreased side effects as well as shorter hospitalization [7,11,14]. Fewer side effects with better tolerability were reported in patients treated with lornoxicam compared to other analgesics. Lornoxicam was also reported to be the most effective drug of the NSAID family due to its short-acting properties and significant opioid sparing effect, especially for patients undergoing major surgeries [11,15].

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Paracetamol is believed to inhibit the synthesis of prostaglandins in the central nervous system, work peripherally to block pain impulse generation, and produce antipyresis by inhibiting the hypothalamic heat-regulating center. As the most popular over-the-counter analgesic, paracetamol has been widely accepted in lieu of NSAIDs. Due to its lack of antiplatelet activity, paracetamol has fewer severe side effects, such as gastric bleeding or toxicity, which could explain its popularity over NSAIDs. Extensive clinical trials have demonstrated that paracetamol is a safe and effective analgesic for the relief of mild to moderate pain associated with oral surgery, episiotomy, postpartum pain, and many other conditions [16].

We also chose these two drugs because of their short onset of analgesia. For paracetamol, the onset of analgesia is known to start 15 minutes after infusion and reach its peak concentration after 1 hour, with relief duration of approximately 4 to 6 hours. The onset of lornoxicam's analgesic effect is also known to start 15 minutes after infusion, yet its peak is reached after 1 to 2 hours, with a half-life of 3 to 5 hours.

The aim of this study was to compare the efficiency in pain management of two drugs , lornoxicam and paracetamol, given intravenously postoperatively to women undergoing abortion with dilation and curettage.

PATIENTS AND METHODS

This randomized, double-blind controlled trial compared the efficacy of intravenous 1000 mg paracetamol (Perfalgan 10 mg/ml) to 8 mg lornoxicam for pain control in women undergoing dilation and curettage for pregnancy termination. The study was conducted at the Rambam Health Care campus and was approved by the institutional review board and in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. The inclusion criteria was scheduled dilation and curettage for pregnancy termination at 6–12 gestational weeks, which was approved by a special committee nominated by the Israel Ministry of Health. Exclusion criteria included chronic pelvic pain, fibromyalgia, pelvic infection, cervical stenosis, kidney disease, liver disease, peptic ulcers, gastrointestinal bleeding in the past, and sensitivity to one of the investigated drugs.

Demographic and medical data were collected, a physical examination was done, and women were allocated to either the paracetamol or the lornoxicam group by computer-generated simple randomization. The drugs were prepared by a pharmacologist in identical 100 ml vials, without labeling, and were covered by a carton bag to conceal the different appearances: paracetamol is a clear colorless solution and lornoxicam is a yellow colored solution.

The procedure was conducted under general anesthesia. A 20-gauge venous catheter was inserted into a superficial vein for the administration of the medications and for safety purposes. The abortions were performed by vacuum aspiration of the uterine content followed by curettage after prior dilation of the cervix. No local anesthesia was used. During the procedure, patients were monitored by means of electrocardiogram, noninvasive blood pressure measurements, and pulse oximetry.

The anesthesiologist gave the trial medications soon after starting the procedure and according to the randomization table. The medications were administrated in a 15 minute infusion, finished by the end of the procedure. After the completion of the abortion, patients were followed in the postoperative unit for 2 hours. The medical staff caring for the patients in the recovery room, as well as the patients, were blinded to the drug allocation. Time of arrival to the postoperative care unit was defined as time 0. Pain levels were evaluated five times (at 0, 30, 60, 90, and 120 minutes) by a visual analogue scale (VAS). The 10-cm VAS ranges from 0 (no pain) to 10 (the most pain imaginable). For rescue analgesia in the recovery room, oral tramadol (100 mg) was provided on patient request.

Following the procedure and during the recovery period, hemodynamic status was recorded by monitoring oxygen saturation, blood pressure, and heart rate. In addition, vaginal blood loss was assessed by the quantity of blood on the patient's pads as well as by the number of pads required during the follow-up period.

STATISTICAL ANALYSIS

IBM SPSS Statistics version 21 software (IBM Corp, Armonk, New York, USA) was used for data management and statistical analysis. Histograms were used to evaluate data homogeneity. Women's age, parity, and gestational week were compared using analysis of variance (ANOVA). The pain levels in the two groups during the 2 hours of the study period were compared using an independent *t*-test. Chi-square tests were used to compare the prevalence of rescue analgesia among study groups. According to the Cohen power tables, a sample size of 34 patients was needed for each treatment group to detect a difference of 1.5 cm on VAS between the largest and smallest mean, at the 5% significance level, with 80% power. Taking into consideration a dropout rate of 20%, 40 women were required for each group. All tests were considered significant at the 0.05 level. No one-sided tests were conducted.

RESULTS

Eighty women were included in the study. Ten women who were approached refused to participate. Social and medical information according to the postoperative analgesic drug administered are reported in Table 1. There were no statistically significant differences between the women who received paracetamol and lornoxicam with regard to age, parity, gestational week of pregnancy, and number of previous pregnancy terminations.

For both groups, the maximal mean pain levels were at 15 to 30 minutes following the procedure, 2.6 ± 0.448 and 3.6 ± 0.42

Table 1. Socio-medical information according to the postoperative analgesic drug administered

	Lornoxicam (N=40)	Paracetamol (N=40)	*P*
Age (years), mean and SD	29.93 ± 8	30.83 ± 7.34	0.59*
BMI, mean and SD	23.86 ± 4.11	24.48 ± 5	0.55*
Gestational week	7.8 ± 1.9	7.6 ± 1.9	0.64*
Parity, median (range)	0 (0–6)	0 (0–4)	0.41*
Previous TOP, median (range)	0 (0–5)	0 (0–5)	0.24*
Previous C/S, median (range)	0 (0–2)	0 (0–2)	0.65*
Smoking, number (percentage)	34 (14)	22 (53)	0.059∞
Hypertension, number (percentage)	0	1 (2.4)	0.50†

*independent t-test, ∞chi-square test of association, †Fisher's exact test, $P < 0.05$ significant

SD = standard deviation, TOP = termination of pregnancy, C/S = cesarean section

cm on the VAS, for lornoxicam and paracetamol, respectively [Table 2]. Mean levels of pain decreased during the second hour postoperative, reaching minimum levels of 0.8 ± 0.19 and 1.5 ± 0.28, respectively [Table 2]. The mean pain levels were significantly higher ($P < 0.05$) during coughing as well as at rest among women who received paracetamol than among those who received lornoxicam [Table 2].

None of the patients reported having adverse effects following administration of either drug. There was no statistically significant difference in the number of women who requested rescue analgesic medication during their stay in the recovery room, three (7.5%) for lornoxicam, vs. two for paracetamol (5%), $P = 0.39$.

DISCUSSION

In this study, lornoxicam and paracetamol demonstrated similar efficiency in reducing pain up to 30 minutes following termination of pregnancy via dilation and curettage. However, from 60 minutes postoperative until the time of discharge (2 hours after the procedure), lornoxicam showed statistically significant greater reduction in pain level.

The lack of statistically significant difference between the groups in reported pain at 30 minutes can be attributed to the effect of propofol, which was received by all patients during anesthesia. Indeed, propofol is an intravenous anesthetic that is commonly used when rapid sedation and rapid awakening are desirable. Propofol works through the activation of the central gamma-aminobutyric acid receptors along with modulation of hypothalamic sleep pathways [17], by which it influences postoperative pain levels. However, a study conducted by the Department of Anesthesia and Intensive Care Medicine at the University Hospital Basel, Switzerland in 2010 [18] described a biphasic elimination time for propofol, with an initial phase at 40 minutes and a terminal phase 4 to 7 hours later. Due to this

Table 2. Mean pain levels for the treatment groups, as assessed by visual analogue scale

Time from procedure	Lornoxicam (N=40) mean ± SD	Paracetamol (N=40) mean ± SD	*P* < 0.05 significant*
15 minutes rest	2.6 ± 0.448	3.3 ± 0.465	0.54
Cough	2.6 ± 0.455	3.5 ± 0.5	0.24
30 minutes rest	2.4 ± 0.40	3.4 ± 0.43	0.4
Cough	2.5 ± 0.43	3.6 ± 0.42	0.57
60 minutes rest	1.7 ± 0.33	3.0 ± 0.47	0.01
Cough	1.7 ± 0.34	3.1 ± 0.48	0.01
90 minutes rest	1.2 ± 0.29	2.4 ± 0.46	0.001
Cough	1.3 ± 0.29	2.4 ± 0.46	0.002
120 minutes rest	0.8 ± 0.19	1.5 ± 0.28	0.03
Cough	0.9 ± 0.2	1.5 ± 0.27	0.05

Values are measured on a 10-cm visual analogue scale

*independent *t*-test

SD = standard deviation

elimination pattern, propofol's analgesic effect seems to decrease according to its concentration. With their target concentration of 2 µg/m, the analgesic effect decreased, and matched the control level 30 to 40 minutes following the end of the infusion [18]. This pattern is similar to what was observed in the current study.

Although mean differences between the groups in reported pain were statistically significant after 60 minutes, the clinical relevance of these findings is not clear. The VAS, a sensitive method for pain level measurement, has been used for many years with good reliability [19]. The VAS has demonstrated simplicity and adaptability to a wide range of populations. A difference of 1.3 cm on the VAS is considered clinically significant [20]. Accordingly, the only clinically significant difference observed in the current study was between the measures taken at rest and at 90 minutes after the procedure (difference of 1.4). Thus, the statistically significant differences observed at other testing points do not necessarily reflect clinically significant differences.

This work follows a previous study, which evaluated the efficacy of suppository analgesia in post-abortion pain reduction [21]. That study comprised four groups of patients according to the following treatment options: suppository of indomethacin (100 mg), suppository of paracetamol (1000 mg), suppository of tramadol (100 mg), and a control group with no suppository treatment. Those findings showed that the application of analgesia at the end of the abortion procedure significantly reduced pain levels. A single suppository of 100 mg indomethacin was found to be the most potent analgesic agent. Indomethacin is a well-known analgesic drug, which inhibits the synthesis of prostaglandins and belongs to the NSAID family [22]. As such, patients receiving lornoxicam in the current study can be compared with patients receiving indomethacin in the previous

study. Although the modes of administration of the analgesic agents differ between the studies, the results are statistically similar. These results support the notion that the mode of administration of an analgesic, intravenous or by means of a suppository, may not be a major factor in pain reduction. Furthermore, a study published in 2002 [23] reinforces our findings. The qualitative review comparing the effect of paracetamol and NSAIDs in postoperative pain management suggested that their efficacies in pain reduction may depend on the type of surgery. However, the lack of statistically significant differences between the drugs precludes reaching a conclusion regarding the superiority of either drug type. Nonetheless, that study also concluded that paracetamol was a sustainable alternative to NSAID and should be the preferred choice of analgesia in high risk patients.

Moreover, drugs of the NSAID family are known to confer risks of side effects, such as gastrointestinal and hemostatic disturbances. Since paracetamol confers a considerably lower risk of side effects and has a lower cost, at least for the population in Israel, it can be considered a good alternative in postoperative pain management, especially in patients with contraindications for medication from the NSAID family. Considering the current and previous studies [23], we recommend the use of paracetamol intravenously following abortion procedures. Paracetamol neither interferes with platelet activity nor increases bleeding time, both of which are important considerations in gynecological procedures [24], thus, paracetamol is considered safer than NSAIDs for patients with ST-elevation myocardial infarction or when aspirin is contraindicated. Future research is needed to compare the efficacies of paracetamol and lornoxicam in the pain management of women undergoing termination of pregnancy at more advanced gestational weeks, as well as following different procedures.

A possible limitation of the current study is the 80% rate of participation of eligible patients. The main reason for non-participation was the requirement to stay 2 hours following the procedure.

CONCLUSIONS

In conclusion, patients receiving lornoxicam after dilation and curettage for termination of pregnancy reported a slightly greater reduction in pain level 60 minutes after the procedure and until the time of discharge at 120 minutes. However, due to the well-known side effects of NSAID drugs, and the absence of a clear clinical difference between lornoxicam and paracetamol given intravenously, we recommend giving paracetamol intravenously for pain management after dilation and curettage.

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