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Is pain prophylaxis in minor gynaecological surgery of clinical value? a double-blind placebo controlled study of paracetamol 1 g versus lornoxicam 8 mg given orally

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Abstract

Methods: In a prospective randomised placebo controlled double-blind study 210 ASA I–II women scheduled for elective termination of pregnancy received 1 g paracetamol, 8 mg lornoxicam or placebo orally 60 min before anaesthesia which was standardised with propofol, fentanyl and oxygen in nitrous oxide 1:2. Postoperative pain was assessed by VAS-score at 30 and 60 min after end of surgery and at discharge as primary endpoints. Need for rescue medication and time to discharge were secondary endpoints. *Results:* All patients had an uncomplicated course. Overall pain intensity was low, however, the patients pretreated with lornoxicam had significantly less pain after surgery, no difference could however, be seen in need for rescue medication or time to discharge between the three groups. *Conclusion:* General pain prophylaxis may be argued in minor gynaecological surgical procedures where postoperative pain is of low intensity. If general prophylaxis is to be given in minor gynaecological surgery, a non steroidal anti-inflammatory (NSAID) such as lornoxicam, seems more efficacious as compared to a standard dose of 1 g paracetamol.

Keywords: Analgesics; Paracetamol; Lornoxicam; Ambulatory surgery; Postoperative pain

1. Introduction

Postoperative pain is one of major complaints after ambulatory surgery [1]. Paracetamol is widely used for prophylactic postoperative pain relief because it is well tolerated and not expensive. In previous studies we found prophylactic paracetamol 1 g given rectally at the end of minor gynaecological surgery not efficacious in reducing postoperative pain, however, prophylactic non steroidal anti-inflammatory therapy (NSAID) with ketoralac or diclofenac given parenteral just before surgery decreased pain and the need for postoperative analgesics [2,3]. In the present study we wanted to evaluate the effects of prophylactic paracetamol 1 g or lornoxicam 8 mg given orally 1 h prior to anaesthesia on postoperative pain. Lornoxicam is a new non steroidal anti-inflammatory drug, non selective with a tolerability profile similar to diclofenac but superior to indometacin [4,5].

2. Methods

The Ethics Committee of the Karolinska Institute approved the study and the patients were included after informed consent. Two hundred and ten ASA I–II women scheduled for elective termination of pregnancy under general anaesthesia were randomly assigned to one of three groups: paracetamol 1 g, lornoxicam 8 mg or placebo given orally 60 min before anaesthesia in a prospective, double-blind randomised fashion. Randomisation was done by an envelope technique by a nurse not otherwise involved in the study while another nurse, also not otherwise involved in the study, gave the pretreatment. No other premedication was given.

Anaesthesia was induced with 0.1 mg fentanyl and 2–2.5 mg/kg propofol and maintained with oxygen in

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nitrous oxide 1:2 and additional small doses (20–30 mg) of propofol when needed. The patients breathed spontaneously and ventilation was assisted only when necessary.

Patients received uterine cervical pretreatment with laminaria tab, at the discretion of the gynaecologist. Cervical dilatation and vacuum aspiration was done in accordance with routines at the gynaecological department All patients were given 5 U oxytocin i.v. at the end of the surgery. After surgery all patients were transferred to the recovery unit and observed by the nurses on duty who as well as the patients were blinded to the randomisation.

The patients were asked to quantify their postoperative pain on a 100 mm baseline visual analogue scale (VAS) where 0 = no pain and 100 = unbearable pain. This was done 30 and 60 min after surgery and at discharge. Patients with a VAS pain score of >45 or who requested an analgesic were given paracetamol 1 g rectally. If this was insufficient to alleviate pain, morphine 2–3 mg at the time was administered intravenously. Persistent nausea or vomiting was treated with 10 mg metoclopramide intravenously. Patients were defined as street fit when awake, oriented and able to drink and eat and to void and walk unassisted without pain or nausea. For statistical evaluation pain less than or equal to 30 was transformed to no pain, pain >30 at any time during the observation period was transformed to pain.

3. Statistics

All values are given as mean and standard deviation (SD) unless stated otherwise. The groups were compared with analysis of variance (ANOVA) for continuous data, to identify differences between the three groups Scheffe F-test was used. The χ^2-test was used for the analysis of class data. A P value of less than 0.05 was considered statistically significant. A sample size of 70 for each group was determined adequate by power analysis prior to the study to create a power of 80% at an α of 0.05. The power analysis assumed that: (a) the incidence of patients needing postoperative analgesics in the control group would be 25–30%; (b) a reduction of approximately 50% in the incidence of patients needing analgesics would be considered a clinically valuable treatment.

4. Results

Demographic data and preoperative observations are presented in Table 1. The groups were comparable in terms of age and weight. There were more first pregnancies and number of females without previous childbirth in the group receiving lornoxicam and therefore as well more patients given cervical pretreatment in that group. All procedures were uneventful and no complications were noted.

Overall pain intensity was low and pain decreased over time in all three groups, VAS-evaluation of pain is shown in Fig. 1. There were significantly fewer patients that experienced pain in the lornoxicam group $P<0.016$. No differences in need for rescue analgesics or time to discharge were noticed (Table 2). The uneven distribution of females with no prior childbirth did not influence the frequency of patients experience postoperative pain.

5. Discussion

There are three major findings in the present study. First; overall quite low postoperative pain intensity. Second; paracetamol 1 given orally was not more effective than placebo in this patient population. Third; lornoxicam 8 mg orally did have a significant pain reducing effect. Taking the overall low pain intensity into perspective one may argue, however, about the clinical value of this effect and to question whether pain prophylaxis have a place in such procedures.

Table 1
Patients characteristics and preoperative observations

	Paracetamol ($n=70$)	Lornoxicam ($n=70$)	Placebo ($n=70$)
Age (mean ± SD)	29 ± 6	29 ± 6	29 ± 6
Weight (kg) (mean ± SD)	62.8 ± 9.3	63.2 ± 8.4	62.0 ± 7.8
No prior childbirth (no. of patients)	33	42[a]	32
Gestational week (mean ± SD)	8.9 ± 1.6	8.6 ± 1.2	9.0 ± 1.4
Laminaria pretreatment (no. of patients)	32	43	35
Oral pretreatement (min) (mean ± SD)	65.7 ± 31.5	61.3 ± 32.3	63.7 ± 30.2
Propofol (mg/kg) (mean ± SD)	3.5 ± 0.8	3.5 ± 0.7	3.5 ± 0.7
Hegar 9/11 (no. of patients)	56/14	60/10	52/18
Spiral (no. of patients)	19	13	19

[a] $P<0.05$ χ^2-test lornoxicam versus placebo or paracetamol.

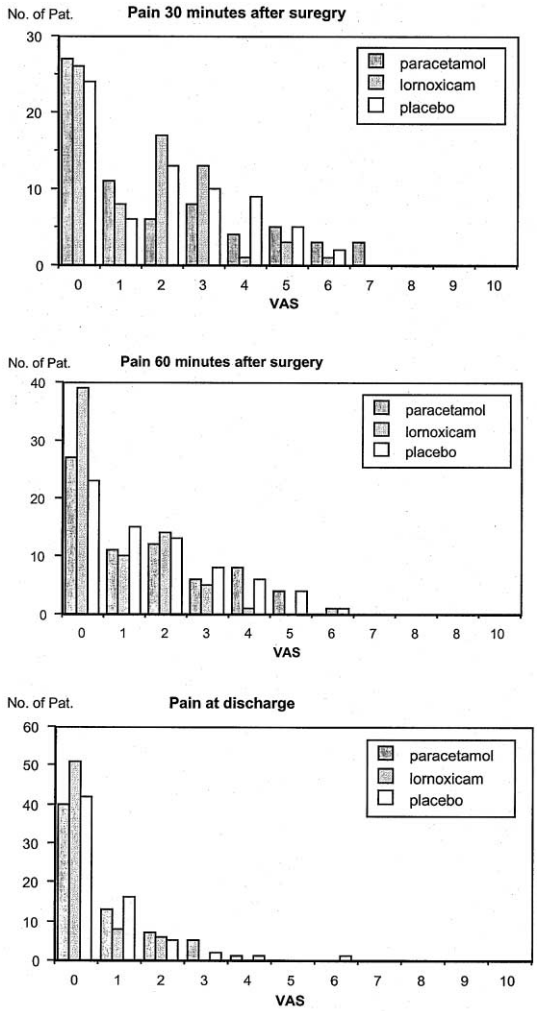

Fig. 1. Pain after surgery: (a) 30 min; (b) 60 min; (c) at discharge.

Pain and emesis are the most common complaints after minor out patient surgery and is also known to be one of most important factors for delayed discharge and to increase unanticipated hospital admission [1,6]. Minimising postoperative pain is an important part of optimising recovery process, however, it is also of great interest to evaluate treatments, to show that they are efficacious and cost effective. The knowledge about pain mechanisms and of the pharmacology for pain treatment has grown tremendously during recent years [7]. Meta-analytic comparisons of oral pain therapy have shown NSAIDs as well as paracetamol to be most effective in reducing acute pain [8]. In a previous study we were unable to show any beneficial effects from 1 g paracetamol given rectally at the end of surgery [2]. Oral administration is easier and paracetamol is also better absorbed when administered orally as compared to rectally [9]. In the present study we could however not see any major impact of pretreatment with paracetamol 1 g given orally approximately 1 h before surgery. This is a finding in agreement with Cade and Ashley also studying patients scheduled for termination of pregnancy [10]. Bjune et al. studying postcaesarean pain, which most certainly has a more complex pathophysiology than pain after termination of pregnancy, found paracetamol effective only in severe pain but not in moderate pain [11].

The bioavailability of paracetamol, given orally, has been shown to be higher and more stable than with rectal administration [12,13]. Our patients, in the paracetamol group, received an average of 16 mg/kg. This is a dose that has been shown ineffective in some studies where doses of more than 20 mg/kg have been shown effective [14,15]. Maybe the frequently used dose of 1 g orally, is insufficient to change the postoperative course, especially in mild to moderate baseline pain.

The surgical procedure may have an impact. In a study by Beaver and McMillan on postpartum pain paracetamol seemed less effective in uterine cramp pain than in pain associated with episiotomy [16]. Pain induced by termination of pregnancy is probably related to prostaglandin release, producing painful contractions of myosalpinx and the myometrium. In pain associated with contractions of the uterus NSAID's has been shown to be more effective than paracetamol [17].

We have, in a previous study, shown a positive effect from pretreatment with intramuscular diclofenac and ketorolac [3]. In a recent meta-analytic comparison Tramer et al. have shown that, concerning NSAID's, the oral route is comparable to intravenous injections and as well preferable in pain conditions other than renal [18]. Pretreatment with oral lornoxicam reduced postoperative pain, however, the clinical relevance of this may be argued in a patient population with low pain ratings. Furthermore, we could find no difference

Table 2
Postoperative observations

	Paracetamol ($n = 70$)	Lornoxicam ($n = 70$)	Placebo ($n = 70$)
No pain (no. of patients)	47	60[a]	47
Pain (no. of patients)	23	10	23
Analgesics postoperative (no. of patients)	19	12	18
Antiemetics (no. of patients)	7	2	4
Time to discharge (min) (mean $\pm$ SD)	99 ± 30	91 ± 20	93 ± 27

[a] $P < 0.016$ χ^2-test lornoxicam versus placebo.

in need for rescue analgesia or time to discharge. The overall low pain intensity may be explained by the use of fentanyl as preoperative opioid. We have in previous studies looked at the effects of the anaesthetic technique on postoperative pain after termination of pregnancy [19,20]. A combination of propofol with an opioid did decrease postoperative pain [19].

Our results should be put into the perspective of the over all low pain intensity during the postoperative period. That makes the assessment of the analgesic drugs more difficult because it is harder to point out differences between groups with low pain intensity [11]. Still, the present study clearly shows that pain intensity after minor gynaecological surgery is overall low, thus general use of analgesics given prophylactically should be weighed against the potential risks and costs. If a prophylaxis is to be given the routine use of preoperative paracetamol 1 g given orally is not effective while preoperative administration of an NSAID orally seems to have a significant impact on pain perception.

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