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J. of Ambulatory Surgery 12 (2006) 139–142

Ambulatory Surgery

www.elsevier.com/locate/ambsur

Oral or rectal diclofenac for laparoscopic sterilization☆

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Received 4 March 2005; accepted 21 October 2005
Available online 5 December 2005

Abstract

In the UK, perioperative non-steroidal anti-inflammatory drugs are commonly administered via the rectal route even though suppositories are unpopular with patients. This prospective, randomised, double-blind study compares the analgesic effectiveness of diclofenac 100 mg given either orally or rectally to 42 ASA grades 1 and 2 patients scheduled to undergo day-case laparoscopic sterilization by the application of Filshie clips. General anaesthesia was induced with fentanyl 2 μg kg^{-1} and propofol and maintained with isoflurane and nitrous oxide in oxygen. No difference was observed between the two groups in postoperative pain scores, morphine requirement, nausea and vomiting rates and time to achievement of street fitness. One patient in the rectal group and none in the oral group required in-patient admission. We conclude that oral and rectal diclofenac are of equal effectiveness in this approach to day-case laparoscopic sterilization.

Keywords: Postoperative analgesia; Analgesics; Diclofenac; Surgery; Gynaecological laparoscopy

1. Introduction

In the UK, laparoscopic sterilization is commonly performed as an outpatient procedure. Postoperative pain may be severe and difficult to manage [1]. The efficacy of analgesic methods such as applying local anaesthetic gel to the Filshie clips [2], intravenous glycopyrrolate [3] and rectal diclofenac [4] has been demonstrated.

In other published studies investigating its efficacy, diclofenac has been administered intramuscularly [1] and intravenously [5] following the induction of anaesthesia. Neither has been shown to be superior to placebo. Suppositories are unpopular with patients [6], and their use without consent has been the subject of a serious professional misconduct ruling by the General Medical Council (GMC) [7]. The oral route avoids this problem but there has been no previous examination of its effectiveness in the perioperative setting. This study was designed to compare the analgesic and morphine-sparing properties of oral diclofenac premedication with the administration of suppositories after induction of general anaesthesia—the current practice in our day case unit.

2. Method

After approval by the local ethics committee, written informed consent was obtained from 42 female outpatients (ASA I or II) aged 25–45 years scheduled for laparoscopic sterilization. Exclusion criteria included allergy to non-steroidal anti-inflammatory drugs (NSAIDs), asthma, renal impairment, history of peptic ulceration, bleeding disorder, and prior regular analgesia. Patients were allocated to either group O (oral dosing) or group R (rectal dosing) by computer generated random number tables. All patients and the investigators were blind to the treatment allocations. Group O patients received oral diclofenac 100 mg modified release (Diclovol® Retard, Arun Pharmaceuticals Ltd, UK) 75 min preoperatively and a placebo suppository immediately after

☆ Presented as a oral presentation at the Group of Anaesthetists in Training Annual Scientific Meeting, Bristol, 2003 and as a poster at the WCA 2004 Meeting, Paris.

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doi:10.1016/j.ambsur.2005.10.002

induction of anaesthesia. Group R patients received an oral placebo preoperatively and diclofenac 100 mg (Voltarol®, Novartis Pharmaceuticals, UK) rectally immediately after induction of anaesthesia. Placebos were manufactured by the St Thomas' Hospital Pharmacy and supplied with the corresponding active preparation in numbered sealed packs.

All patients received a standardised anaesthetic. No other premedication was given. Anaesthesia was induced with fentanyl 2 μg kg^{-1} and propofol 2–4 mg kg^{-1} followed by cyclizine 50 mg. A laryngeal mask airway was inserted and the lungs were ventilated via a circle system. Anaesthesia was maintained with nitrous oxide 70% and isoflurane 1–2% in oxygen. When required, neuromuscular blockade was facilitated with mivacurium 5–10 mg. Atropine, glycopyrrolate and neostigmine were avoided in all cases.

Surgery was carried out via a 5 mm laparoscope using Filshie clips. To standardise the procedure as much as possible, 38 operations were performed by the same Consultant Gynaecologist, 4 by Specialist Registrars under his direct supervision. No definable anaesthetic or surgical complications occurred. No additional surgical procedures were required by any patient. Incision sites were infiltrated with 10 ml of bupivacaine 0.5%.

Postoperatively, patients were prescribed morphine intravenously in 2 mg aliquots for severe pain, dihydrocodeine 60 mg for moderate pain, and paracetamol 1000 mg for mild pain, to be given as and when the nursing staff considered it necessary. Ondansetron 4 mg was used for rescue antiemesis.

Patients were asked to score their pain on a 100 mm visual analogue scale (VAS, 0: no pain; 100: worst pain imaginable) on waking, 1 h postoperatively, 2 h postoperatively and on discharge. A further VAS at 24 h was returned via a questionnaire.

A power calculation, based on the standard deviation from a previous study [2], suggested that 20 patients per group would be required to detect a 20 mm difference in pain scores ($\alpha = 0.05$, $\beta = 0.8$). Data were analysed using Student's *t*-test for the patient's age and weight, the χ^2-test for categorical data and the Mann–Whitney *U* test for ordinal data. Statistical tests were performed using Microsoft™ Excel and Microsoft™ SPSS.

Table 1
Demographic data values are median (range), mean (S.D.) or number where appropriate

	Group O ($n = 21$)	Group R ($n = 21$)
Age (year)	36 (3.4)	34 (5.5)
Weight (kg)	66 (10.3)	65 (13.8)
ASA grade		
1 (*n*)	20	21
2 (*n*)	1	0
Duration of surgery (min)	15 (6–33)	11 (6–20)

3. Results

All 42 of the patients in this study gave informed consent, 21 in each group. Both groups were of similar age, weight, ASA score and duration of surgery (Table 1). One patient required subsequent in-patient admission as a result of inadequate pain management. Twenty-eight patients (66%) returned their 24 h questionnaire (Tables 2 and 3).

There were no statistically significant differences in postoperative pain scores, morphine dose, nausea and vomiting, time to discharge, and in-patient admission rates (Tables 2 and 3).

4. Discussion

In this study we were unable to demonstrate any difference in analgesic effects between patients premedicated with oral

Table 2
Pain scores are median (range)

Time	Group O ($n = 21$)	Group R ($n = 21$)	*p*	95% confidence interval
Waking	25 (1–97)	37 (0–100)	0.92	−17 to +19
1 h postoperatively	28 (3–74)	26 (0–100)	0.64	−16 to +16
2 h postoperatively	10 (0–73)	11 (0–68)	0.94	−10 to +6
Discharge	4 (0–31)	5 (0–56)	0.61	−5 to +3
Time	**Group O ($n = 16$)**	**Group R ($n = 12$)**	***p***	**95% confidence interval**
24 h postoperatively	4 (0–42)	5 (0–24)	0.76	−4 to +6

Table 3
Postoperative outcome values are median (range) or number (proportion) where appropriate

	Group O ($n = 21$)	Group R ($n = 21$)	*p*	95% confidence interval
Morphine dose (mg)	4 (0–15)	0 (0–26)	0.09	0–4
Time to discharge after surgery (min)	161 (120–232)	142 (120–219)	0.06	0–34
Nausea	9 (43%)	7 (33%)	0.53	
Vomiting	2 (10%)	1 (5%)	0.55	
In-patient admission	0	1 (5%)	0.31	

diclofenac and those given rectal diclofenac after induction of anaesthesia. The in-patient admission rate was acceptable. Pain scores were similar and low for both groups at all stages. The power calculation was based on the standard deviation of the control group pain scores from Ezeh's study [2]. There are few standard deviations reported in the literature. The anaesthetic technique was similar to that used in our study, although the dose of fentanyl was lower at $1\,\mu g\,kg^{-1}$. This accounts for the lower pain scores reported by our patients, making it less likely that a statistically significant difference would occur. Notwithstanding, 20% of our patients reported pain scores greater than 50 mm and 65% required rescue opioid analgesia.

The 66% response rate for the 24 h pain score was disappointing. This may be due to the high level of domestic commitments of the study group. In retrospect, telephoning the patients may have produced a greater response. However, this problem arose after a substantial proportion of the patients had been recruited, and to rectify it would have required a change of study design.

The relative efficacy of drugs given via different routes can be evaluated only after considering the dose, the timing of administration, the duration of anaesthesia and any other analgesic use. At equal doses, a higher peak plasma diclofenac concentration is achieved by the oral, compared to the rectal, route [8,9]. The same dose was given to both groups because both tablets and suppositories are readily available as 100 mg preparations. No data was available to guide an alteration of the oral dose to produce an identical peak plasma concentration in the two groups. It has been demonstrated that after oral and rectal administration of the drug, peak plasma diclofenac concentrations are attained at 2 and 1 h, respectively, in healthy volunteers. The drug regimen used in this study, based on known pharmacokinetic data, was designed to achieve peak plasma levels of diclofenac during the first postoperative hour. Given the short duration of surgery, neither group would have achieved peak plasma levels on waking. It is likely that the residual effect of fentanyl, given at induction, would have accounted for most of the analgesic effect at this time. After 1 h, pain scores were similar. Many patients had, by then, received rescue analgesia. Morphine was used for rescue analgesia because our recovery staff were already trained in its' use. The onset of peak analgesic effect is slower than with fentanyl, but the duration of action allows for prolonged pain relief. It is not possible to quantify the contribution of the NSAID to the overall analgesic effect. However, given the low pain scores and admission rate, the doses of opioid given were not excessive.

Previous studies investigating the analgesic efficacy and effectiveness of NSAIDs after laparoscopic sterilization have given conflicting results. Rectal diclofenac [4] and oral naproxen [10,11] have shown greater efficacy than placebo. Regimens of unproven efficacy include rectal indomethacin [12], intramuscular ketorolac [13], intramuscular [1] and intravenous diclofenac [5]. The reason for this discrepancy is not certain. Residual effects of anaesthetic and other analgesic drugs may mask differences in analgesic effect. The onset of action may occur late in the postoperative period, by which time many of the patients will have required rescue opioid analgesia. However, the use of this class of drugs is widespread, often administered by the rectal route [14–18].

In the UK, suppositories are not popular. A recent survey indicated that 54% of patients found the idea of drugs administered by the rectal route unacceptable, all preferring the alternative oral route [6]. It is the practice of the Day Surgical Unit at our hospital to gain informed consent prior to the rectal administration of diclofenac to help patients manage their postoperative pain, in line with the guidelines published by the Association of Anaesthetists of Great Britain and Ireland [19]. The use of oral tablets avoids this need. This study has shown that after laparoscopic sterilization, when combined with early rescue analgesia, oral diclofenac provides an effective alternative to rectal suppositories. It is now our practice to avoid this route of administration where possible.

Acknowledgement

The pharmacy costs of this study were covered by a grant from the St Thomas' Hospital Anaesthetic Research Fund.

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