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A comparison of the effect of intramuscular dicofenac, ketorolac or piroxicam on postoperative pain following laparoscopy

J J O'Hanlon, H Beers, B K D Huss, K R Milligan

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SUMMARY

Sixty patients presenting for in-patient gynaecological laparoscopic surgery were randomly allocated to receive either diclofenac 75mg (n=20), ketorolac 30mg (n=20) or piroxicam 20mg (n=20) as an intra-muscular injection immediately after induction of anaesthesia. Postoperative visual analogue scores over the first 24 hours, using a 10cm scale, ranged from 3.2–0.5 in the diclofenac group, 2.7–0.85 in the ketorolac group and 2.8–0.5 in the piroxicam group. The scores did not differ significantly between the three groups (p>0.05). Mean time (SD) to first analgesia was 27(94) minutes in the piroxicam group, 16 (30) minutes in the diclofenac group and 62 (120) minutes in the piroxicam group. Six out of twenty patients in the diclofenac group required further analgesia compared to nine out of twenty in the other two drug groups. This difference was not significant. There were no reports of increased bleeding, bronchoconstriction, bleeding from the upper gastrointestinal tract, renal impairment or pain from the intra-muscular injection site in any of the groups. The administration of a non-steroidal anti-inflammatory drug to patients presenting for laparoscopic surgery reduces postoperative pain. There were no obvious differences between the agents used.

INTRODUCTION

Non-steroidal anti-inflammatory drugs [NSAIDS] are useful adjuncts to opioids for postoperative analgesia.[1] NSAIDS can provide similar analgesia to the opioids,[2] but avoid the sedation, respiratory depression, nausea and vomiting caused by them. Many workers have shown that both diclofenac and ketorolac can reduce opioid requirements following major gynaecological and upper abdominal surgery.[3,4,5] Diclofenac can provide similar analgesia to fentanyl following knee arthroscopy.[6] Unfortunately intramuscularly administered diclofenac has been associated with muscle damage,[7] and due to increased reporting of severe bleeding and renal impairment, especially in the elderly[8] the recommended dose of ketorolac has been reduced to a maximum daily dosage of 30mg.

We compared the analgesic efficacy and incidence of side-effects of diclofenac, ketorolac and piroxicam, given intramuscularly after induction of anaesthesia, in patients undergoing inpatient gynaecological laparoscopic surgery.

METHODS

The study protocol was approved by the Regional Medical Ethics Committee and written informed consent was obtained from 60 ASA 1-2 (ie patients who are healthy or have a mild systemic illness) female patients scheduled for either in-patient diagnostic laparoscopy or laparoscopic sterilisation. Patients with a history of upper gastrointestinal symptoms, known hypersensitivity to the study

Department of Anaesthesia, Lagan Valley Hospital, Hillsborough Road, Lisburn, BT28 1JP.

J J O'Hanlon, BSc, FFARCSI, Registrar.

H Beers, MD, FFARCSI, Consultant.

B K D Huss, MB, FRCA, Consultant.

Department of Anaesthetics, Belfast City Hospital, Lisburn Road, Belfast BT9.

K R Milligan, MD, FFARCSI, Consultant.

Correspondence to Dr J O'Hanlon, Anaesthetic Senior Registrar, Department of Clinical Anaesthesia, Royal Group of Hospitals, Grosvenor Road, Belfast BT12 6BA.

drugs, impaired renal function, asthma or on medication likely to interfere with the study results were excluded. We explained the use of the visual analogue scale (VAS) 0-10 at the preoperative visit. (The VAS was 10cm in length with 0 at the left end, representing "no pain" and 10 at the right end scoring "the worst pain imaginable").

Patients were premedicated with lorazepam 2mg by mouth 2 hours before surgery. Anaesthesia was induced with propofol 2mg/kg and fentanyl lmcg/kg. Atracurium 0.5mg/kg was given to facilitate tracheal intubation and intraoperative ventilation. Anaesthesia was maintained with 1–1.5% isoflurane in 65% nitrous oxide in oxygen. At the end of the procedure neuromuscular blockade was reversed with neostigmine 2.5mg and glycopyrrolate 0.5mg.

Following induction the patients were randomly allocated to receive a 3ml deep intra-muscular injection in the lateral compartment of the right thigh of either diclofenac 75mg (group D), ketorolac 30mg (group K) or piroxicam 20mg (group P).

The patients' age, height, and weight were recorded, and the interval from the end of surgery until the first request for analgesia was noted. Postoperative analgesia was prescribed in the form of either paracetamol lg or intra-muscular 'Cyclimorph 10' 0.01 ml/kg. This was administered to the patient by the recovery ward nurses who were unaware of the study drug given. Oral analgesia was administered if the patient's pain score was 3 or greater and and cyclimorph was given if the pain score was 5 or greater. The dose and timing of any postoperative analgesia was noted. Patients completed their VAS scores for pain on movement at the following times: on admission to recovery ward, at 1 hour, 2 hours, 4 hours and 24 hours after completion of surgery. They were also asked about the presence of musculoskeletal pain and pain from the NSAID injection site.

For statistical analysis we used an independent samples Student's t-test for continuous variables, the Kruskal-Wallis test for VAS scores and Chi-square for categorical samples. A P value of < 0.05 was considered statistically significant.

RESULTS

Data were obtained from 60 patients and treatment groups were similar in respect of age, height, weight and nature of surgery. There was no difference in the dosages of propofol or fentanyl between the three groups (Table I).

The VAS pain scores (Table II) in the three different groups were not significantly different at any time in the 24 hour postoperative study period. Median (Interquartile range) VAS scores (Table II) in the study groups were diclofenac 2.1(2.6), ketorolac 2.1(2.7) and piroxicam 2.3(2.5). The mean (SD) intervals to first analgesia (Table II) were 27(93.7), 16.3(30.2) and 62(120) minutes in the diclofenac, ketorolac and piroxicam groups respectively ($p>0.05$), although the time to first analgesia seems longer in the piroxicam group the results were skewed by one patient who required cyclimorph 420 minutes after surgery. Six patients in the diclofenac group, nine in the ketorolac group and nine in the piroxicam group required further analgesia in the form of a single opioid intramuscular injection, but this difference was not statistically significant. Of the twenty four patients who received an intra-muscular opioid, six patients received co-codamol initially, but this did not provide sufficient analgesia.

DISCUSSION

The NSAIDS can reduce postoperative pain by central and peripheral cyclooxygenase inhibition.[9] This has led to their use as single analgesics[10] or in combination with opioids. Prostaglandins are present in menstrual fluid, and the NSAIDS can reduce the pain associated with menstruation.[11] Similarly they might be expected to reduce pain after surgical manipulation of the Fallopian tubes.[12]

Piroxicam is an oxicam and not related to acetylsalicylic acid. It has different characteristics from other NSAIDS such as a longer half-life (30 hours).[13] This is due to extensive protein binding allowing a once daily dosage which should provide longer duration analgesia compared to the other NSAIDS.[14] Previous studies have demonstrated that piroxicam, in oral and intramuscular formulations is superior to placebo and other widely used NSAIDS in providing analgesia. In dental patients oral piroxicam 20mg was shown to be superior to 50mg diclofenac, and in a similar group of patients there was no difference between 50 and 100mg of diclofenac.[15] In arthroscopy patients Morrow et al[16] showed 30mg of ketorolac to be clinically superior to 75mg diclofenac. When piroxicam was compared with other commonly used NSAIDS in patients with osteoarthritis it showed good clinical efficacy and as there were fewer reported side-effects it was thought generally more tolerable.[14, 17, 18]

TABLE I

Physical characteristics in the treatment groups shown. Values are mean. Standard deviation shown in brackets.

	Diclofenac (n=20)	*Ketorolac (n=20)*	*Piroxicam (n=20)*
Age: years	34 (7.7)	30 (6.1)	31 (7.88)
Height: cm	156 (7.2)	157 (7.2)	155 (6.8)
Weight: kg	68 (6.7)	62 (8.8)	61 (6.2)
Laparoscopic sterilization:	6	6	6
Diagnostic laparoscopy:	14	14	14
Propofol dose: mg	155 (30)	153 (30)	156 (26)
Fentanyl dose: mcg	74 (14)	70 (15)	74 (16)

TABLE II

Median (interquartile range) VAS scores over the first 24 hours after surgery and mean (SD) time to first analgesia.

	Diclofenac (n=20)	*Ketorolac (n=20)*	*Piroxicam (n=20)*
Median VAS scores	2.1 (2.6)	2.1 (2.7)	2.3 (2.5)
Time to first analgesia (minites)	27 (93.7)	16 (30.1)	62 (120)

However there was no difference in VAS scores between the three study groups postoperatively but there was a difference in the time to first analgesia in the ketorolac group compared to the diclofenac and piroxicam groups. In the latter two groups there were patients requesting analgesia 360–420 minutes after surgery as compared to 130 minutes in the ketorolac group. Although not statistically significant, due to the small number, it would suggest that diclofenac and piroxicam may have a longer effect than ketorolac. By giving the NSAID to gynaecological laparoscopy patients the number of patients requiring postoperative analgesia was reduced, and most patients reported adequate analgesia. Despite the longer half-life of piroxicam, all three drugs produced similar results, suggesting the reduction in postoperative pain occurred in the immediate perioperative period. Preoperative nerve blocks in patients undergoing inguinal hernia repair have been shown to provide better postoperative analgesia than postoperative nerve blockade.[19] The preoperative reduction of the inflammatory response by the NSAIDS provided the patient with good analgesia. However is immediately post induction the most beneficial time of administration of NSAIDS? More work is required to answer this question.

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