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Ketorolac as a component of balanced analgesia after thoracotomy

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SUMMARY

Ketorolac 10 mg or 30 mg i.m., 6 hourly or placebo was given to 75 patients who had undergone thoracotomy, in a randomized double-blind study. All subjects were given intercostal nerve blocks with bupivacaine and had access to i.v. patient-controlled morphine. I.m. ketorolac improved the success rate of the analgesic regimen, with fewer patients withdrawing from the study because of inadequate pain relief. (Br. J. Anaesth. 1994; **72**: 224–226)

KEY WORDS

Analgesia Pharmacology: ketorolac.

It is our practice to use intercostal nerve block with morphine via patient-controlled analgesia (PCA) for analgesia after thoracotomy. Unfortunately, many patients find this inadequate and repeat intercostal nerve block has to be performed, probably because the intercostal nerve block regresses within 12–24 h [1]. In this study, we investigated whether the addition of regular i.m. ketorolac trometamol (Toradol, Syntex Pharmaceuticals Ltd) to our basic regimen improved patient comfort. This was performed in a double-blind, placebo-controlled, randomized study after thoracotomy.

METHODS AND RESULTS

Seventy-five patients (18–75 yr) participated in the study, which was approved by the regional Ethics Committee. Exclusion criteria were peptic ulcer disease, asthma, bleeding diathesis and renal or hepatic impairment. The nature of the study and the use of PCA were explained and written consent obtained. The groups did not differ significantly in age, height, weight or sex (table I). Surgery was elective pneumonectomy or lobectomy for carcinoma, but in 10 patients segmental resection was performed (placebo group, three; ketorolac 10 mg, two; ketorolac 30 mg, five). In eight patients removal of the lesion was not possible and only thoracotomy was carried out (placebo, one; ketorolac 10 mg, four; ketorolac 30 mg, three).

After premedication with i.m. papaveretum and atropine, anaesthesia was induced with thiopentone and maintained with nitrous oxide and enflurane in oxygen. Suxamethonium and alcuronium were used for neuromuscular block. Intercostal nerve block was performed after induction of anaesthesia, using 0.5% bupivacaine with 1/200000 adrenaline 30 ml. All patients had an intercostal incision for thoracotomy. At the end of surgery, neuromuscular block was antagonized, the tracheal tube removed and the patient transferred to the high dependency unit.

The study began at the end of surgery and lasted for 2 days, with one nurse-observer organizing all the assessments. Subjects had access to i.v. PCA morphine (Abbott Lifecare PCA plus); bolus 2 mg and lock out time 15 min.

Patients were given i.m. ketorolac 30 mg, ketorolac 10 mg or placebo 6 hourly in a double-blind fashion by allocation of a study number (1–75) corresponding to a box of medication containing nine unlabelled ampoules of ketorolac 30 mg or 10 mg, or placebo. The first dose of study drug was given at the end of surgery, before anaesthesia was discontinued and the others were given 6 hourly. The study ended 2 h after the last dose, 50 h after the end of surgery. Patients were withdrawn if they were not given nine doses of study medication, and the reason noted. Patients were withdrawn also (and intercostal block repeated) if they had more than mild pain at rest which did not respond to PCA morphine in 1 h.

PCA morphine consumption was recorded hourly, and visual analogue pain scores (VAS) at rest and after taking a deep breath were performed by the patient 2 h after the first, fifth and ninth i.m. injections (days 1, 2 and 3).

The variable used to determine the size of this study was the use of PCA morphine by the subjects. We predicted that morphine consumption in the first 24 h would be 60 mg with an SD of 20 mg. A 33% difference in morphine usage between groups would be clinically significant and had been found in similar studies using ketorolac after abdominal surgery [2] and with indomethacin after thoracotomy [3]. Such a difference could be detected with a statistical power of 75%, at the 5% significance

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TABLE I. *Patient details (mean (range or SD)); study completion rates, reasons for withdrawal and the number who withdrew because of inadequate analgesia (No.); PCA morphine consumption in the subjects remaining in the three study groups at 24 and 48 h, and VAS pain assessments made by the patients on the three study days; morphine and VAS (mean (SE)).* * *Significantly different (P < 0.05) from the two other groups*

	Placebo	Ketorolac 10 mg	Ketorolac 30 mg
Sex (M/F)	19/6	20/5	23/2
Age (yr)	60 (39–73)	59.2 (30–74)	56.5 (32–75)
Height (cm)	172 (12)	170 (8)	170 (9)
Weight (kg)	69.4 (13.1)	68.5 (13)	70 (14.7)
Completed study	12	17	22
Withdrawals			
Day 1	4	1	2
Day 2	6	5	0
Day 3	3	2	1
Reasons for withdrawal			
Inadequate analgesia	12	4	2
Bleeding	1	—	1
Myocardial infarction	—	1	—
Dyspepsia	—	1	—
Required bronchoscopy	—	1	—
Violation of procedure	—	1	—
Withdrew because of inadequate analgesia?			
Yes	12*	4	2
No	13	21	23
PCA morphine (mg)			
24 h	61 (4)	52 (6)	55 (7)
48 h	97 (7)	82 (10)	82 (10)
Pain at rest (mm)			
Day 1	26 (5)	20 (5)	27 (5)
Day 2	23 (6)	29 (5)	19 (5)
Day 3	19 (5)	20 (5)	11 (3)
Pain on deep breathing (mm)			
Day 1	31 (5)	26 (5)	36 (6)
Day 2	37 (7)	39 (5)	32 (5)
Day 3	26 (6)	28 (6)	18 (4)

level, with 25 patients in the three treatment groups [4].

The chi-square test was used to analyse rates of withdrawal as a result of inadequate analgesia in the three study groups. One-way analysis of variance was used to analyse morphine consumption and VAS results for the patients remaining in the study.

More patients were withdrawn from the placebo group because of inadequate analgesia than from either the ketorolac 10 mg ($P < 0.05$, chi-square) or the ketorolac 30 mg group ($P < 0.01$). There was no difference between the ketorolac groups. The success rate of the balanced analgesic regimens which included ketorolac was therefore significantly greater.

There was no statistically significant difference between the ketorolac groups in morphine consumption at any time. At 48 h, the placebo group had used an average of 15 mg more morphine than the ketorolac 10 mg group (95% CI −14 to 43 mg, $P = 0.18$) and the ketorolac 30 mg group (95% CI −12 to 42 mg, $P = 0.32$). VAS pain scores in the three groups were not significantly different.

One patient in the placebo group required ligation of a bleeding bronchial artery. In the ketorolac 10 mg group, one patient had postoperative myocardial infarction, one mild dyspepsia and one required suction bronchoscopy to remove retained secretions. One patient in the ketorolac 30 mg group had a postoperative bleed after a difficult operation with many adhesions; coagulation studies and the skin bleeding time were normal and no treatment other than transfusion of 2 u. blood was required.

COMMENT

In this study, the addition of ketorolac improved analgesia after thoracotomy significantly as intercostal local anaesthesia and PCA morphine were less acceptable to patients than when the i.m. non-steroidal anti-inflammatory drug (NSAID) was added. This may be further evidence in support of the use of balanced analgesia, using combinations of opioids, local anaesthetics and NSAID [5]. As the design of this study required that patients were withdrawn if they had more than mild pain at rest, it was difficult to show any differences in PCA morphine use or pain scores, because so many withdrew from the control group.

There was little evidence that ketorolac 30 mg was better than 10 mg and this may indicate that ketorolac had a ceiling analgesic effect in this clinical situation. The dose recommendations for ketorolac have been reduced recently, and this study would support the use of the smaller dose of 10 mg when used as a component of balanced analgesia. There were no serious adverse effects and, despite the known effects of NSAID on the kidneys [6], no acute renal problems were encountered. We conclude that addition of ketorolac improved the success rate of analgesia after thoracotomy when intercostal nerve blocks and PCA morphine were used.

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REFERENCES

1. Swann DG, Armstrong PT, Douglas E, Brockway M, Bowler GMR. The alkalinisation of bupivacaine for intercostal nerve blockade. *Anaesthesia* 1991; **46**: 174–176.
2. Gillies GWA, Kenny GNC, Bullingham RES, McArdle CS. The morphine sparing effect of ketorolac tromethamine. *Anaesthesia* 1987; **42**: 727–731.
3. Pavy T, Medley C, Murphy DF. Effect of indomethacin on pain relief after thoracotomy. *British Journal of Anaesthesia* 1990; **65**: 624–627.
4. Gore SM, Altman DG. *Statistics in Practice*. London: British Medical Association, 1982: 6–8.
5. Dahl JB, Rosenberg J, Dirkes WE, Mogensen T, Kehlet H. Prevention of postoperative pain by balanced analgesia. *British Journal of Anaesthesia* 1990; **64**: 518–520.
6. Power I, Cumming AD, Pugh GC. Effect of diclofenac on renal function and prostacyclin generation after surgery. *British Journal of Anaesthesia* 1992; **69**: 451–456.