SHORT COMMUNICATION

PROSPECTIVE, CONTROLLED, DOUBLE-BLIND STUDY OF I.V. TENOXICAM FOR ANALGESIA AFTER THORACOTOMY†

A. F. MERRY, G. J. WARDALL, R. J. CAMERON, M. J. PESKETT AND C. J. WILD

SUMMARY

We have shown that a single i.v. dose of tenoxicam 20 mg, after thoracotomy, when compared with placebo in 20 patients (with one exclusion), was associated with a reduction in consumption of papaveretum, assessed by patient-controlled analgesia, of 2.2 mg h⁻¹ (22%) to 4 h and 1.4 mg h⁻¹ (23%) to 12 h after operation (repeated measures analysis of variance: P < 0.01). There was no reduction from 12 to 24 h. There was no significant difference between groups in pain scores or in side effects.

KEY WORDS


Tenoxicam is a relatively new thienothiazine derivative of the oxicam class of non-steroidal anti-inflammatory drugs (NSAID). Its analgesic and anti-inflammatory efficacy and frequency of side effects compare favourably with those of other NSAID when used orally for long term treatment of rheumatological conditions [2]. NSAID are used widely for postoperative analgesia [3]; for this application, tenoxicam has the advantages of i.v. formulation and a long half-life of plasma concentration (60-75 h) [2].

We have used patient-controlled analgesia (PCA) [4], in a prospective, placebo-controlled, double-blind study, to assess the analgesic efficacy of tenoxicam used as a single i.v. dose after operation.

METHODS AND RESULTS

We decided that an analgesic advantage sufficient to manifest at the 5% significance level with a sample size of 10 would be relevant to our clinical practice. Thus if we nominated a reduction in papaveretum consumption of 1.5 mg h⁻¹ or more as indicative of clinically useful analgesic efficacy for tenoxicam, the power of a one-tailed t test to distinguish this would be greater than 80% (given P < 0.05: estimating placebo group mean = 5 mg h⁻¹ and sample sd = 25% of the mean).

After Ethics Committee approval, informed consent was obtained from 20 patients, older than 18 yr, undergoing lateral thoracotomy. One (who received placebo) was subsequently unable to manage the PCA device and was withdrawn. Exclusion criteria were: hypersensitivity to NSAID; history of peptic ulceration, gastrointestinal bleeding or any bleeding disorder; presence of severe renal (creatinine > 0.2 mg ml⁻¹), hepatic, cardiac or haemopoietic disease; any possibility of pregnancy; and use of NSAID, opioids, diuretics or angiotensin converting enzyme inhibitors in the 24 h preceding surgery.

All patients were premedicated with diazepam and famotidine. Anaesthesia was induced with thiopentone and maintained with fentanyl (1 µg kg⁻¹ initially, and then up to 0.5 µg kg⁻¹ half-hourly), nitrous oxide and isoflurane or halothane in oxygen. No regional anaesthetic techniques, nerve blocks, other NSAID or other analgesics were used. Either tenoxicam 20 mg or placebo was administered i.v. at the beginning of chest closure from unidentifiable, sequentially numbered ampoules, randomized in blocks of 10. In the recovery room, analgesia was commenced with a Bard PCA pump programmed (in accordance with our then normal clinical practice) to deliver papaveretum with a loading dose of 0.075 mg kg⁻¹ (maximum 6 mg), a background infusion of 0.025 mg kg⁻¹ h⁻¹ (maximum 2 mg h⁻¹), boluses of 0.025 mg kg⁻¹ (maximum 2 mg), a “lockout” interval between boluses of 5 min and an hourly limit of 0.15 mg kg⁻¹ (maximum 12 mg). Papaveretum consumption was measured hourly; all other assessments were made at 1, 2, 4, 8, 12 and 24 h.

Operations undertaken in the tenoxicam group included removal of a recurrent liposarcoma; removal of a metastatic mediastinal teratoma; repair of a hiatus hernia; five lobectomies; two pneumonectomies. In the placebo group there were seven lobectomies and two pneumonectomies.

Mean age (62.5 yr, range 48-74 yr) and weight (69.0 (sd 15.3) kg) of patients receiving tenoxicam did not differ significantly from the mean age (65 yr (range 43-76 yr) and weight (79 (17.3) kg) of those receiving placebo (two-tailed t test: P > 0.18). However, only one of the placebo group was female, in contrast to five of the tenoxicam group.

The pain scores (on unmarked 100-mm visual analogue scales) reported by the two groups were: hypersensitivity to NSAID; history of peptic ulceration, gastrointestinal bleeding or any bleeding disorder; presence of severe renal (creatinine > 0.2 mg ml⁻¹), hepatic, cardiac or haemopoietic disease; any possibility of pregnancy; and use of NSAID, opioids, diuretics or angiotensin converting enzyme inhibitors in the 24 h preceding surgery.

All patients were premedicated with diazepam and famotidine. Anaesthesia was induced with thiopentone and maintained with fentanyl (1 µg kg⁻¹ initially, and then up to 0.5 µg kg⁻¹ half-hourly), nitrous oxide and isoflurane or halothane in oxygen. No regional anaesthetic techniques, nerve blocks, other NSAID or other analgesics were used. Either tenoxicam 20 mg or placebo was administered i.v. at the beginning of chest closure from unidentifiable, sequentially numbered ampoules, randomized in blocks of 10. In the recovery room, analgesia was commenced with a Bard PCA pump programmed (in accordance with our then normal clinical practice) to deliver papaveretum with a loading dose of 0.075 mg kg⁻¹ (maximum 6 mg), a background infusion of 0.025 mg kg⁻¹ h⁻¹ (maximum 2 mg h⁻¹), boluses of 0.025 mg kg⁻¹ (maximum 2 mg), a “lockout” interval between boluses of 5 min and an hourly limit of 0.15 mg kg⁻¹ (maximum 12 mg). Papaveretum consumption was measured hourly; all other assessments were made at 1, 2, 4, 8, 12 and 24 h.

Operations undertaken in the tenoxicam group included removal of a recurrent liposarcoma; removal of a metastatic mediastinal teratoma; repair of a hiatus hernia; five lobectomies; two pneumonectomies. In the placebo group there were seven lobectomies and two pneumonectomies.

Mean age (62.5 yr, range 48-74 yr) and weight (69.0 (sd 15.3) kg) of patients receiving tenoxicam did not differ significantly from the mean age (65 yr (range 43-76 yr) and weight (79 (17.3) kg) of those receiving placebo (two-tailed t test: P > 0.18). However, only one of the placebo group was female, in contrast to five of the tenoxicam group.

The pain scores (on unmarked 100-mm visual analogue scales) reported by the two groups were: hypersensitivity to NSAID; history of peptic ulceration, gastrointestinal bleeding or any bleeding disorder; presence of severe renal (creatinine > 0.2 mg ml⁻¹), hepatic, cardiac or haemopoietic disease; any possibility of pregnancy; and use of NSAID, opioids, diuretics or angiotensin converting enzyme inhibitors in the 24 h preceding surgery.

All patients were premedicated with diazepam and famotidine. Anaesthesia was induced with thiopentone and maintained with fentanyl (1 µg kg⁻¹ initially, and then up to 0.5 µg kg⁻¹ half-hourly), nitrous oxide and isoflurane or halothane in oxygen. No regional anaesthetic techniques, nerve blocks, other NSAID or other analgesics were used. Either tenoxicam 20 mg or placebo was administered i.v. at the beginning of chest closure from unidentifiable, sequentially numbered ampoules, randomized in blocks of 10. In the recovery room, analgesia was commenced with a Bard PCA pump programmed (in accordance with our then normal clinical practice) to deliver papaveretum with a loading dose of 0.075 mg kg⁻¹ (maximum 6 mg), a background infusion of 0.025 mg kg⁻¹ h⁻¹ (maximum 2 mg h⁻¹), boluses of 0.025 mg kg⁻¹ (maximum 2 mg), a “lockout” interval between boluses of 5 min and an hourly limit of 0.15 mg kg⁻¹ (maximum 12 mg). Papaveretum consumption was measured hourly; all other assessments were made at 1, 2, 4, 8, 12 and 24 h.

Operations undertaken in the tenoxicam group included removal of a recurrent liposarcoma; removal of a metastatic mediastinal teratoma; repair of a hiatus hernia; five lobectomies; two pneumonectomies. In the placebo group there were seven lobectomies and two pneumonectomies.

Mean age (62.5 yr, range 48-74 yr) and weight (69.0 (sd 15.3) kg) of patients receiving tenoxicam did not differ significantly from the mean age (65 yr (range 43-76 yr) and weight (79 (17.3) kg) of those receiving placebo (two-tailed t test: P > 0.18). However, only one of the placebo group was female, in contrast to five of the tenoxicam group.

The pain scores (on unmarked 100-mm visual analogue scales) reported by the two groups were: hypersensitivity to NSAID; history of peptic ulceration, gastrointestinal bleeding or any bleeding disorder; presence of severe renal (creatinine > 0.2 mg ml⁻¹), hepatic, cardiac or haemopoietic disease; any possibility of pregnancy; and use of NSAID, opioids, diuretics or angiotensin converting enzyme inhibitors in the 24 h preceding surgery.
The preoperative values of haemoglobin and creatinine were compared with the worst value in the 5 days after surgery. Mean decrease in haemoglobin concentration was 14.0 (9.1) g litre⁻¹ in the tenoxicam group and 14.5 (7.0) g litre⁻¹ in the placebo group (one-tailed paired t tests: \( P < 0.01 \) in each case): there was no significant difference between groups. Mean decrease in creatinine clearance (estimated from creatinine by the Cockcroft Gault correction for age, weight and sex) after operation was smaller in the tenoxicam group (0.03 (0.23) ml s⁻¹) (ns). There were no other adverse reactions to NSAID.

**COMMENT**

Consumption of opioid with postoperative PCA may be influenced by many factors [4]; in this study, because the placebo group had more males and a greater mean weight, the average background infusion and bolus size were larger than in the tenoxicam group and this may have contributed to the result. However, neither the weight difference between groups nor the difference in opioid consumption between males and females overall was significant, and (by contrast) the difference between subjects and controls remained significant even after subtraction of the background infusion from the total papaveretum consumed. Furthermore, the reduced opioid consumption in the tenoxicam group occurred early (0-12 h) and then disappeared (fig. 1), so that from 12 to 24 h the tenoxicam patients actually used slightly more papaveretum than the controls. This fits well with a drug effect, which might have worn off with time, but cannot be attributed to the other factors, which were constant.

When using a drug with a long half-life, it is usual to administer a loading dose. We based our dose of tenoxicam on the only recommendation available, namely that for long term use in rheumatic conditions. However, a single dose of 20 mg i.v. produces blood concentrations of only 3 μg ml⁻¹ compared with more than 10 μg ml⁻¹ at steady state with 20 mg daily by mouth [6]. This may explain the unexpectedly short duration of effect. For single or initial administration, a larger dose would probably be more appropriate.

One important aim of this study was to provide equally effective analgesia to subjects and controls; success in this virtually precludes the demonstration of any clinical advantage, other than opioid sparing, for the drug.

The side effects of NSAID are well known and of concern, particularly in high risk patients, but they must be weighed against the continuing widespread failure to provide adequate analgesia following surgery [7]. We have shown encouraging analgesia after thoracotomy from a single i.v. dose of tenoxicam 20 mg, with no obvious increase in side effects; further studies are now warranted to identify more fully the optimal dose of tenoxicam and its role in the provision of postoperative analgesia.

**REFERENCES**


