Efficacy of oral rofecoxib versus intravenous ketoprofen as an adjuvant to PCA morphine after urologic surgery


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of oral rofecoxib (a cyclooxygenase-2 inhibitor) and intravenous ketoprofen (a standard nonselective non-steroidal anti-inflammatory drug) as adjuvants to patient-controlled anaesthesia (PCA) with morphine during urologic surgery. Rofecoxib (50 mg orally) was administered 1 hour before surgery, while ketoprofen (100 mg intravenously every 8 hours) was administered for 24 hours after surgery.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised male patients undergoing transurethral resection of the prostate gland under spinal anaesthesia. Patients with known allergies to non-steroidal anti-inflammatory drugs and opioid analgesics were excluded. Also excluded were patients with a history of gastrointestinal bleeding or renal insufficiency.

Setting
The setting was a hospital. The economic study was carried out in Chile.

Dates to which data relate
The dates during which the effectiveness and resource use data were collected were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out on the same sample of patients as that used in the effectiveness analysis.

Study sample
Power calculations were performed in the preliminary phase of the study. These suggested that, assuming a variability of +/- 3 mg in PCA morphine usage in the first 24 hours and a power of 80%, groups of 30 patients should be adequate to detect a 25% difference in the need for rescue analgesic medication. Seventy patients were enrolled in the study, but four were excluded due to a protocol violation. The final study sample comprised 32 patients (mean age: 65 +/- 10
years) in the ketoprofen group and 34 patients (mean age: 69 +/- 10 years) in the rofecoxib group. It was not stated whether some patients refused to participate.

**Study design**
This was a prospective, randomised, controlled, double-blinded, double-dummy clinical trial that was carried out at the Air Force Hospital of Santiago de Chile in Chile. The patients were randomised using a table of computer-generated random numbers. The outcomes were assessed at 1, 2, 6, 12 and 24-hour intervals, and patients were contacted 14 days after surgery for the final assessment. No patient was lost to follow-up. Both the patients and investigators were blinded to the treatment allocation.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on the basis of treatment completers only since patients who violated the study protocol were excluded from the final analysis. The outcome measures used were:

- pain scores, measured using an 11-point verbal rating scale (VRS) that ranged from 0 (no pain) to 10 (worst pain imaginable);
- the incidence of moderate-to-severe pain (pain VRS score =/> 4); and
- PCA morphine usage during the first 24 hours after surgery (the patients were transferred to the post-anaesthesia care unit where they were connected to a PCA device containing morphine).

Surgery and anaesthesia times were also reported. The study groups were comparable at baseline in terms of the demographic and clinical characteristics.

**Effectiveness results**
During the 24-hour assessment period, the median pain VRS scores were 0.8 (interquartile range, IQR: 0.3 - 2.2) in the ketoprofen group and 0.7 (IQR: 0.2 - 2.1) in the rofecoxib group. The difference was not statistically significant.

The mean pain VRS scores assessed at different time intervals were also comparable.

The incidence of moderate-to-severe pain was:

- 0 in both groups after 1 hour,
- 6% in the ketoprofen group versus 0% in the rofecoxib group after 2 hours,
- 16% in the ketoprofen group versus 6% in the rofecoxib group after 6 hours,
- 16% in the ketoprofen group versus 9% in the rofecoxib group after 12 hours, and
- 9% in both groups after 24 hours.

The overall incidence of moderate-to-severe pain was 22% in the ketoprofen group versus 12% in the rofecoxib group, (p<0.05).

The use of morphine during the first 24 hours was non significantly higher in the ketoprofen group than in the rofecoxib group (37 +/- 4 mg versus 28 +/- 2 mg; p>0.05).

Surgery and anaesthesia times were comparable.

**Clinical conclusions**
The effectiveness analysis showed that rofecoxib and ketoprofen resulted in comparable pain score and usage of rescue morphine. However, significantly more ketoprofen patients experienced moderate-to-severe pain scores in comparison with rofecoxib patients.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis. In effect, a cost-consequences analysis was performed.

**Direct costs**
Discounting was not relevant since the costs were incurred during a short timeframe. The unit costs were not presented separately from the quantities of resources used. The economic analysis considered only the daily costs of rofecoxib and ketoprofen. The cost/resource boundary of the study appears to have been that of the hospital. The costs were derived from the hospital pharmacy. Resource use was based on patient-level data that were derived from the sample of patients included in the clinical trial. The price year was not reported.

**Statistical analysis of costs**
Statistical tests were carried out to test the statistical significance of differences in the estimated costs.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not performed.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The estimated cost of the study drug for a 24-hour period was $3.06 with ketoprofen and $1.14 with rofecoxib, (p<0.05).

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was, in effect, performed.

**Authors' conclusions**
Oral rofecoxib was as least as effective as intravenous ketoprofen as an adjuvant to patient-controlled anaesthesia (PCA) with morphine in patients who underwent urologic surgery. Rofecoxib patients experienced less severe postoperative pain. The costs of rofecoxib were also lower than those for ketoprofen over the 24-hour postoperative period.

**CRD COMMENTARY - Selection of comparators**
The authors did not provide a specific justification for their choice of the comparators. However, they stated that no study had compared a standard non-selective non-steroidal anti-inflammatory drug with a cyclooxygenase-2 inhibitor. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence came from a clinical trial, which was appropriate for the study question. The study was based on a robust design. The analysis had several strengths, not only randomisation and double-blinding, which reduce the potential impact of confounding and bias, but also an appropriate length of follow-up, baseline comparability of the study groups, and power calculations. These issues enhance the internal validity of the study. However, the basis of the analysis was treatment completers only and it was not stated whether some patients refused to participate. The patients were identified at a single centre and it was unclear whether the study sample was representative of the patient population.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the analysis because, in effect, a cost-consequences analysis was conducted.

**Validity of estimate of costs**
The perspective adopted in the study was not explicitly stated and only the drug costs were considered in the analysis. The source of the data was given. The price year was not reported and the unit costs were not presented separately from the quantities of resources used. This limits the possibility of performing reflation exercises and replicating the study in other settings. Statistical analyses were performed in the cost comparison. However, the cost estimates were specific to the study setting and no sensitivity analyses were carried out.

**Other issues**
The authors reported the results of some studies that assessed the efficacy of the two interventions under evaluation. However, the economic results were not compared with those from other studies. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed. This reduces the external validity of the analysis. The authors noted that the relative effect of the two analgesics on blood loss was not addressed in the analysis. The study referred to patients undergoing minor urologic surgery and this was reflected in the authors' conclusions.

**Implications of the study**
The study results supported the use of rofecoxib as an adjuvant to PCA morphine after minor urologic surgical procedures, owing to its similar efficacy to ketoprofen and the lower cost.

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None stated.

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