Opioid analgesics versus ketorolac in spine and joint procedures: impact on healthcare resources

Gora-Harper M L, Record K E, Darkow T, Tibbs P A

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 ketorolac as analgesia for a minimum of 24 hours after spine and joint surgery was compared with the use of narcotics (morphine or meperidine).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who had undergone spine or joint surgery in the preceding 24 months. Patients were included if they had received at least 3 doses of intramuscular (IM) or intravenous (IV) ketorolac, 3 doses of IV or IM narcotic analgesia, or 1 dose of patient-controlled narcotic analgesia. To enter the analysis, the patients were required not to have undergone a concurrent unrelated procedure, and to have received IV or IM analgesia for at least 24 hours postoperatively. Patients were excluded from the trial if they had a known allergy or hypersensitivity to any analgesic, had a medical history that contraindicated the study analgesics, or had a history of alcohol or drug abuse. Patients were also ineligible to enter the study if they received high doses of ketorolac. High doses were specified as more than 120 mg/24 hours for patients aged 65 years or younger, or 60 mg/24 hours for patients aged over 65 years.

Setting
The setting was tertiary care. The economic study was set in the USA.

Dates to which data relate
The years during which data were collected for the effectiveness analysis, resource use and prices were not reported.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was based on actual resource use in the study. It was taken from medical records at the same time that the effectiveness data were collected.

Study sample
A power calculation established that a sample of 500 patient records was required to identify a difference of one day of hospitalisation using an alpha value of 0.05 and a power of 80%. Investigators compiled a database of cases, which met the study inclusion criteria, from the preceding 24 months. Physician preference dictated which analgesic had been prescribed postoperatively. The patients were matched to try to minimise selection bias. A random selection process was used to select the sample from the matched patient groups to which a second screening process was applied. A total of 559 patients were included in the analysis, of whom 275 had received ketorolac and 284 had received narcotic analgesia.

**Study design**
The study employed a retrospective cohort design. The study was multi-centred, with data being collected from 6 sites. Follow-up continued until discharge from the hospital.

**Analysis of effectiveness**
All the patients observed in the study were accounted for in the analysis. The primary health outcomes reported were the times to reach recovery milestones. The recovery milestones were resumed bowel sounds, first bowel movement, first oral intake and first unassisted walk. Serious adverse events and central nervous system (CNS), gastrointestinal (GI) and genitourinary disruptions were also recorded. At baseline, the ketorolac group contained more males than the narcotic group (59% versus 50%; p>0.05), while the narcotic group contained more patients aged over 60. There was a significant difference in the number of patients in each group receiving hip and knee surgery. More specifically, 7.7% of the ketorolac group versus 22.8% of the narcotic group received hip surgery, (p<0.05), and 25.7% (ketorolac) and 15.7% (narcotic), respectively, received knee surgery, (p<0.05). The ketorolac group also included more obese patients, (p<0.05).

**Effectiveness results**
Several recovery milestones were reached sooner in the ketorolac group. These were times to first bowel movement, first oral intake and first unassisted ambulation. Patients in this group also had a shorter mean length of postoperative stay, (p<0.05), and less time in the recovery room, (p=0.05).

The group who received narcotic analgesia suffered significantly more adverse CNS and GI events (p<0.05), but the rate of serious adverse events was similar between the two groups.

**Clinical conclusions**
Health care resource use was lower for patients in the ketorolac group. However, 95% of the patients receiving ketorolac as their primary analgesic were also given narcotic analgesics for uncontrolled pain. This was not significantly different from those receiving narcotics as their primary analgesic, 94% of which also required supplementary doses of narcotics.

**Measure of benefits used in the economic analysis**
The authors did not derive a summary measure of benefit. In effect, a cost-consequences analysis was performed.

**Direct costs**
In general, the costs and the quantities were not reported separately, although the average number of days the patients received the study medication was stated. Only the direct costs of the hospitals were analysed. The costs included were for hospitalisation, study medication, as-needed procedures, and medications for relief of supplementary pain and GI and CNS disturbances. The overall treatment costs were calculated by multiplying the average resource use by the per-item unit cost. The costs were also obtained from the participating hospitals. However, it was unclear whether the unit cost was an average calculated on the basis of data obtained from each hospital in the study, or it was derived in an alternative manner. The costs were incurred during a 2-year period, hence discounting should have been applied. The average costs were reported. The date of the price data was not stated.
Statistical analysis of costs
The cost data were deterministic. No statistical analysis of the costs was reported.

Indirect Costs
The indirect costs were not reported as the perspective of a hospital was adopted.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was undertaken.

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

Cost results
The total postoperative cost for each patient was $949.73 in the ketorolac group compared with $1,250.63 in the narcotic group.

The cost of adverse effects was captured by including the costs of hospitalisation and of the medications given for relief of breakthrough pain and CNS or GI events.

Synthesis of costs and benefits
Not applicable because, in effect, a cost-consequences analysis was performed.

Authors' conclusions
Although the cost of using ketorolac was greater than using narcotics, ketorolac was associated with lower overall resource use and a lower total per-patient cost among patients undergoing spine and joint procedures. The authors noted that, as most patients in the ketorolac group also received supplementary narcotic analgesia, the beneficial effects might have been due to the combination of medication rather than to ketorolac alone.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. Morphine sulphate and meperidine are commonly administered agents for postoperative pain management after orthopaedic procedures.

Validity of estimate of measure of effectiveness
The basis of the analysis was a retrospective cohort design. The study sample was not representative of the study population to the degree that it was altered by the strict inclusion criteria, such as the absence of co-morbidities. The retrospective nature of the study means that selection bias is an issue, even though the authors tried to minimise this by matching patients as much as possible. However, an (unspecified) element of random selection was employed in choosing the study sample. The patients were shown to be comparable at analysis, although differences in the age, gender and type of procedure undergone were identified. The authors used strict inclusion criteria in an attempt to control for confounding variables. A power calculation was reported and an appropriate sample size was used.
Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was, in effect, a cost-consequences study.

Validity of estimate of costs
All the categories of cost relevant to the hospital perspective adopted were included in the analysis. Some relevant cost items were omitted from the analysis. The additional costs involved in the storage and administration of narcotics as controlled substances were not included. Therefore, the cost of using narcotics might have been underestimated. The costs and the quantities were not reported separately. A statistical analysis of the quantities was limited to a sub analysis by site of orthopaedic procedure, and a regression analysis that explored the factors predicting postoperative length of stay and intensive care unit stay. A statistical analysis of the prices was not performed. The authors noted that giving generic versions, which are now available, rather than the branded product used in this study, could reduce the costs of the ketorolac group. Consequently, exploration of the variation in cost estimates would have been appropriate. The costs were incurred during 2 years but discounting was not undertaken. The date of the prices was not reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability was addressed by comparing the findings with those from studies with patients undergoing other types of surgery. The authors do not appear to have presented their results selectively. The study enrolled patients who had incision and excision of joint structures, or repair and plastic operations on joint structures, and this was reflected in the authors’ conclusions. The authors acknowledged the limitations imposed on the study by using a retrospective design rather than a randomised controlled trial, but maintained that their strict inclusion and exclusion criteria reduced the effect of bias.

Implications of the study
Patients in the study who received ketorolac had lower overall per-patient costs, primarily because of the shorter length of hospital stay, fewer adverse events and a quicker time to reach recovery milestones. Since most patients who were prescribed ketorolac as their primary postoperative analgesic also received narcotic analgesia concurrently, it was unclear whether the observed benefits might be due to the combination of ketorolac with narcotic analgesia.

Source of funding
Funded by a grant from Roche.

Bibliographic details

PubMedID
11724076

Indexing Status
Subject indexing assigned by NLM

MeSH
Analgesics, Opioid /economics /therapeutic use; Anti-Inflammatory Agents, Non-Steroidal /economics /therapeutic use; Hospitalization /economics; Humans; Joints /surgery; Ketalorolac /economics /therapeutic use; Orthopedic Procedures; Pain, Postoperative /drug therapy /economics; Retrospective Studies; Spine /surgery

AccessionNumber
22001002092

Date bibliographic record published
31/12/2004

Date abstract record published
31/12/2004