Costs and effectiveness of rofecoxib, celecoxib, and acetaminophen for preventing pain after ambulatory otolaryngologic surgery

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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
Three oral analgesic regimens for preventing pain after ambulatory surgery were examined. The regimens were acetaminophen (2 g), celecoxib (200 mg) and rofecoxib (50 mg). The drugs were administered 15 to 45 minutes before entering the operating room.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised healthy patients (ASA physical status I-II) aged 18 to 75 years who were undergoing outpatient ENT procedures. Patients who had received analgesic medication within 12 hours before surgery were excluded, as were those with a history of drug abuse and those with clinically significant cardiovascular, renal, hepatic, or gastrointestinal disease. Women who were pregnant or breast-feeding were also excluded.

Setting
The setting was an outpatient department. The economic study was carried out in the USA.

Dates to which data relate
The dates during which the effectiveness and resource use data were gathered were not reported. The price year was 2001.

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

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

Study sample
A priori power calculations were performed on the basis of the results of published studies. These calculations showed that at least 55 individuals were required in each group to have 90% power (5% level of significance) of detecting a relative reduction of 33% in the peak verbal pain score rating (i.e. from 6 in the placebo group to 4 in the treatment group) after log transformation. Also, to have 80% power (1% level of significance) to detect a change in the
proportion of patients requiring rescue analgesia in the post-anaesthesia care unit (PACU), from 82% in the placebo group to 40% in the treatment group. Details of the method used to select the sample were not reported. Sixty patients were enrolled in each group. The mean age was 43 (+/- 11) years in the placebo group, 44 (+/- 14) years in the acetaminophen group, 40 (+/- 12) years in the celecoxib group, and 47 (+/- 12) years in the rofecoxib group. The numbers of male participants were 32 (placebo group), 34 (acetaminophen group), 28 (celecoxib group) and 20 (rofecoxib group), respectively.

Study design
This was a prospective, randomised, double-blind, placebo-controlled trial that appears to have been carried out in a single centre, the University of Texas Southwestern Medical Center. Randomisation was based on a computer-generated random number schedule. The length of follow-up was 48 hours after surgery. No patients appear to have been lost to the follow-up assessment. Patients, observers, and all individuals directly involved in direct patient care were blinded to the patients’ allocation to the study groups.

Analysis of effectiveness
The analysis of the clinical study appears to have been conducted on an intention to treat basis, as no patient was lost to the follow-up assessment. The primary outcome measure was the dose of fentanyl used for rescue analgesia in the PACU. The secondary outcome measures were:

- the maximum (peak) pain score at any time during the study (in the PACU and at home);
- the proportion of patients requiring pre-discharge analgesic rescue medication;
- the peak nausea score;
- the rate of patients vomiting;
- the proportion of patients receiving antiemetics in the PACU;
- the use of oral analgesic medication after discharge;
- the maximum verbal nausea score post-discharge;
- the rate of patients completely satisfied with pain management;
- patient satisfaction scores with anaesthetic management and postoperative pain control; and
- the quality of recovery score.

The number-needed-to-treat (NNT) for complete satisfaction was also calculated as the reciprocal of the absolute difference in the incidence of complete satisfaction between the two groups. Pain was assessed using a verbal rating scale, which ranged from 0 (no pain) to 10 (worst possible pain or nausea). Scores of 6 or higher were considered severe pain, while patients with a score higher than 3 were considered as having moderate-to-severe pain. Analgesic treatment was provided according to the pain score. Patient satisfaction was estimated using a verbal analogue scale at 24 hours after surgery, which ranged from 0 (poor) to 100 (excellent). The authors stated that the study groups were comparable at baseline in terms of demographics, clinical characteristics and operating room characteristics, such as anaesthesia time, use of anaesthetics, and recovery (although patients who received rofecoxib had shorter stay in the PACU in comparison with acetaminophen).

Effectiveness results
The dose of fentanyl rescue was 112 (+/- 64) microg in the placebo group, 114 (+/- 90) microg in the acetaminophen group, 78 (+/- 80) microg in the celecoxib group, (p<0.05 versus placebo and acetaminophen), and 45 (+/- 60) microg in the rofecoxib group, (p<0.05 versus all the other drugs).
The median peak pain score during PACU stay was 5 (interquartile range, IQR: 0 - 9.5) in the placebo group, 5 (IQR: 1 - 9) in the acetaminophen group, 4 (IQR: 1 - 7) in the celecoxib group, (p<0.05 versus placebo), and 2.5 (IQR: 0 - 6) in the rofecoxib group, (p<0.05 versus all other groups).

The median peak pain score at home was 5 (IQR: 1 - 9) in the placebo group, 2 (IQR: 0 - 7) in the acetaminophen group, (p<0.05 versus placebo), 0 (IQR: 0 - 4) in the celecoxib group, (p<0.05 versus placebo), and 0 (IQR: 0 - 2) in the rofecoxib group, (p<0.05 versus placebo and acetaminophen).

The proportion of patients requiring pre-discharge analgesic rescue medication was 88% in the placebo group, 85% in the acetaminophen group, 70% in the celecoxib group, (p<0.05 versus placebo), and 47% in the rofecoxib group, (p<0.05 versus all other groups).

The peak nausea score, rate of patients vomiting, and proportion of patients receiving antiemetics in the PACU were not significantly different across the groups.

The maximum verbal pain score after discharge was 5 (IQR: 1 - 9) in the placebo group, 2 (IQR: 0 - 7) in the acetaminophen group, (p<0.05 versus placebo), 0 (IQR: 0 - 4) in the celecoxib group, (p<0.05 versus placebo and acetaminophen), and 0 (IQR: 0 - 2) in the rofecoxib group, (p<0.05 versus placebo and acetaminophen).

The number of doses of oral analgesic medication after discharge was 3 (+/- 2) in the placebo group, 3 (+/- 2) in the acetaminophen group, 2 (+/- 2) in the celecoxib group, (p<0.05 versus placebo and acetaminophen), and 1 (+/- 1) in the rofecoxib group, (p<0.05 versus all other groups).

The maximum verbal nausea score post-discharge was 1.5 (+/- 2.1) in the placebo group, 1.2 (+/- 2.4) in the acetaminophen group, 0.7 (+/- 2) in the celecoxib group, and 0.1 (+/- 0.6) in the rofecoxib group, (p<0.05 versus placebo and acetaminophen).

The rate of patients completely satisfied with pain management was 15% in the placebo group, 34% in the acetaminophen group, (p<0.05 versus placebo), 48% in the celecoxib group, (p<0.05 versus placebo and acetaminophen), and 70% in the rofecoxib group, (p<0.05 versus all other groups).

The patient satisfaction scores with anaesthetic management were 95 (+/- 9) in the placebo group, 98 (+/- 5) in the acetaminophen group, (p<0.05 versus placebo), 96 (+/- 7) in the celecoxib group, and 99 (+/- 3) in the rofecoxib group, (p<0.05 versus placebo and celecoxib).

The patient satisfaction scores with postoperative pain control were 83 (+/- 15) in the placebo group, 88 (+/- 15) in the acetaminophen group, (p<0.05 versus placebo), 93 (+/- 10) in the celecoxib group, (p<0.05 versus placebo and acetaminophen), and 97 (+/- 5) in the rofecoxib group, (p<0.05 versus all other groups).

The quality of recovery score was 84 (+/- 15) in the placebo group, 86 (+/- 16) in the acetaminophen group, 89 (+/- 14) in the celecoxib group, 95 (+/- 7) in the rofecoxib group (p<0.05 versus all other groups).

The NNT for complete patient satisfaction with pain control compared with placebo was 5.5 (95% confidence interval, CI: 3.1 - 73.8) with acetaminophen, 3.2 (95% CI: 2.2 - 7.3) with celecoxib, and 1.9 (95% CI: 1.5 - 3.0) with rofecoxib.

The NNT for complete patient satisfaction with pain control compared with acetaminophen was 7.5 (95% CI: 3.2 - 17.8) with celecoxib and 3.0 (95% CI: 2.0 - 7.2) with rofecoxib.

The NNT for complete patient satisfaction with pain control with rofecoxib compared with celecoxib was 5.0 (95% CI: 2.6 - 166).

**Clinical conclusions**

The effectiveness study showed that, in general, patients treated with rofecoxib and celecoxib experienced less pain than patients receiving placebo or acetaminophen. However, patients treated with rofecoxib were more satisfied with pain management than all other patients. Acetaminophen had limited efficacy in the early recovery phase.
Measure of benefits used in the economic analysis
The summary benefit measure used was the rate of patients completely satisfied with pain management. This was obtained directly from the effectiveness study.

Direct costs
Discounting was not relevant since the costs were incurred during a short timeframe. The unit costs were presented, but information on resource use was less clear. The health services included in the economic evaluation were all drugs involved in patient management. A breakdown of the drugs was reported. The costs common to the four treatment groups were not included. Similarly, the costs of drug preparation and administration and nursing services were not considered because these were assumed to be comparable across groups. The cost/resource boundary of the outpatient surgical centre was used. Resource use was estimated using patient-level data, which were obtained from the sample of patients included in the effectiveness study. The costs came from the authors' institution. The price year was 2001.

Statistical analysis of costs
The costs were presented as mean values plus or minus the standard deviation. Statistical tests were carried out to test the statistical significance of differences in the estimated costs.

Indirect Costs
The indirect costs were not included in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
The authors reported some discursive results of the sensitivity analyses, although no details of the methods used were provided.

Estimated benefits used in the economic analysis
The rate of patients completely satisfied with pain management was 15% with placebo, 34% with acetaminophen, (p<0.05 versus placebo), 48% with celecoxib, (p<0.05 versus placebo and acetaminophen), and 70% with rofecoxib, (p<0.05 versus all other groups).

Cost results
The mean total perioperative drug costs were $62.09 (+/- 24.17) in the placebo group, $71.08 (+/- 21.87) in the acetaminophen group, $78.63 (+/- 16.78) in the celecoxib group, (p<0.05 versus placebo), and $63.81 (+/- 20.70) in the rofecoxib group, (p<0.05 versus celecoxib).

Synthesis of costs and benefits
The average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative strategies.

The average cost per completely satisfied patient was $414 (95% CI: 298 - 730) in the placebo group, $209 (95% CI: 83 - 335) in the acetaminophen group, $164 (95% CI: 95 - 232) in the celecoxib group, (p<0.05 versus placebo), and $92 (95% CI: 33 - 149) in the rofecoxib group, (p<0.05 versus placebo).

The incremental cost per additional completely satisfied patient over acetaminophen would be $45.68 (95% CI: 0 - 306)
with celecoxib and $23.75 (95% CI: 0 - 75.70) with rofecoxib.

The incremental cost per additional completely satisfied patient with rofecoxib over celecoxib would be $6.70 (95% CI: 7 - 20.68).

The authors stated that the results were sensitive to the costs and efficacy of oral pre-medications, the duration of action of the drug used for rescue analgesia, the incidence of postoperative nausea and vomiting (PONV), and the costs and efficacy of drugs used to treat PONV before hospital discharge.

**Authors' conclusions**
Rofecoxib led to superior outcomes, both in terms of clinical end point and patient satisfaction, in comparison with the other analgesic regimens. The drug costs associated with rofecoxib were lower than those associated with celecoxib. Overall, rofecoxib offered a more convenient cost-effectiveness ratio.

**CRD COMMENTARY - Selection of comparators**
The authors discussed the choice of the analgesic regimens under evaluation and it would appear that the selection was appropriate. The option of no therapy (i.e. placebo) was also considered. The authors noted that traditional nonsteroidal anti-inflammatory drugs (NSAIDs) were not selected as comparators because most experts agreed that nonselective NSAIDs were relatively contraindicated in ENT patients. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The internal validity of the analysis was ensured by its robust design, which was based on a clinical trial. The methods of randomisation and outcome assessment were reported in detail. The study groups were comparable at baseline and the sample size was based on power calculations. The length of follow-up appears to have been appropriate. No patients were lost to follow-up. The outcomes were assessed in a blinded manner. Statistical analyses were carried out to test the statistical significance of differences in the outcome measures. However, it was unclear whether the study sample was representative of the patient population. In addition, the sample selection process was not described and the patients appear to have been recruited from a single centre.

**Validity of estimate of measure of benefit**
The summary benefit measure was specific to the interventions considered in the study. Hence, it would be difficult to compare with the benefits of other health care interventions. The measure was derived directly from the effectiveness study.

**Validity of estimate of costs**
The authors stated explicitly which perspective was adopted in the study. However, only the drug costs were considered in the analysis. The authors justified their exclusion of other categories of costs. The unit costs were presented, but there was limited information on resource usage. This limits the possibility of replicating the study. The source of the data was reported. Statistical analyses were carried out to assess the significance of differences in costs between the groups. The price year was reported, which makes reflation exercises in other settings easy.

**Other issues**
The authors compared some of their findings with those from other studies. In general, the superiority of rofecoxib was confirmed. However, the issue of the generalisability of the study results to other settings was not addressed, which reduces the external validity of the analysis. The study results referred to patients undergoing ENT surgery and this was reflected in the authors' conclusions. The authors acknowledged and discussed some potential limitations of their analysis.
Implications of the study
The study results suggested that rofecoxib represents the most cost-effective strategy for treating the pain experienced by patients undergoing ENT surgery. The authors stated that acetaminophen could be useful in the post-discharge period as part of a multimodal analgesic regimen.

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Other publications of related interest


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