An economic evaluation of bupivacaine plus fentanyl versus ropivacaine alone for patient-controlled epidural analgesia after total-knee replacement procedure: a double-blinded randomized study

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
Two strategies of patient-controlled epidural analgesia (PCEA) after total-knee replacement (TKR) surgery were examined. One strategy was 0.0625% bupivacaine plus fentanyl (BF) 3 microg/mL, the other was 0.15% ropivacaine alone (RA).

Type of intervention
Palliative care (analgesia).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients diagnosed with degenerative osteoarthritis of the knee and who underwent elective unilateral TKR surgery. The exclusion criteria were ASA physical status greater than III, re-operation of TKR, study drugs allergy, narcotic dependence, contraindication for epidural block, and inability to use the PCEA device.

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

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

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 analysis of effectiveness.

Study sample
Power calculations were based on a pilot study. These suggested a sample of 32 patients per group for an equivalence study in which a pre-specified difference of the mean visual analogue scale (VAS) pain score on movement equalled 10 mm (one-sided type I error = 0.05; type II error = 0.2). A sample of 70 patients (35 in each group) was enrolled. Details of sample selection (i.e. patients who refused to participate or who were excluded from the study sample) were not
reported. The mean age of the patients was 65.86 (+/- 6.43) years in the BF group and 67.61 (+/- 6.25) years in the RA group. There were 32 women in the BF group and 31 in the RA group.

**Study design**
This was a prospective, randomised, double-blind clinical trial that was carried out at a single institution. On the day before surgery, patients were informed of how to use the PCEA device and assess an unmarked 100-mm line VAS. After surgery, PCEA was started and continued for 48 hours postoperatively to deliver a 5 mL/hour basal rate, 3-mL bolus dose, with a lock-out duration of 10 minutes without a 4-hour limit. No patient was lost to the follow-up assessment. A blinded evaluator assessed the data after surgery.

**Analysis of effectiveness**
The analysis of effectiveness was conducted on an intention to treat basis since all patients were considered. The primary outcome measure was the mean VAS pain score upon movement over the first 48-hour postoperative period. Other clinical end points were:

- cardiovascular and respiratory complications;
- other side effects (e.g. nausea, vomiting and pruritus);
- the number of patients requiring a rescue analgesic drug;
- evaluation of motor block, according to a 4-point modified Bromage scale; and satisfaction with pain treatment (assessed on a 4-point scale).

Pain upon movement was defined as pain evoked by movement that was similar to what patients did to move around in their beds by themselves or with assistance. The patients were asked to score postoperative nausea and vomiting (PONV) and pruritus during the first 20 and 48 postoperative hours. Side effects such as bradycardia, hypotension and respiratory depression were abstracted from nursing and medical records. The two study groups were comparable at baseline in terms of their clinical and demographic aspects.

**Effectiveness results**
No statistically significant difference in pain relief at rest and upon movement over the 48 hours for postoperative TKR was observed between the groups. Thus, the main clinical outcome was considered equivalent.

Patients in the BF group experienced significantly more pruritus and had more vomiting episodes than those in the RA group. No differences in the other side effects were observed. Significantly more patients in the RA group required a rescue analgesic drug (21 versus 11 in the BF group; p=0.016).

Other end points were comparable between the groups.

Patient satisfaction with pain management was higher in the BF group than in the RA group. Thirty-five patients (94%) in the BF group and 25 (71%) in the RA group rated satisfaction with their pain treatment as excellent or good. None of the patients in either group rated satisfaction with their pain relief as poor.

**Clinical conclusions**
The effectiveness analysis showed that pain relief and several clinical end points were comparable between the groups. However, patient satisfaction was higher in the BF group despite a higher frequency of side effects.

**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 carried out.

**Direct costs**
The analysis of the costs was carried out from the perspective of the health care provider. It included the costs of all drugs involved in the care of the patients, materials and labour. The unit costs were not presented separately from the quantities of resources used. Resource use was derived from the sample of patients included in the clinical trial. The costs were estimated from the hospital pharmacy and administrative departments. Drug costs took into account the amount wasted. Material costs included the unit cost of the PCEA device per day and the costs of disposable syringes, the infusion set and needles. Labour costs included fixed salaries and fringe benefits calculated for the period of vomiting management. Since postoperative care in both groups was similar, labour costs were only considered for managing emesis. Discounting was not relevant since the costs were incurred during a short timeframe. The price year was not stated.

**Statistical analysis of costs**
Statistical analyses of the costs were carried out to test for cost-differences.

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

**Currency**
Thailand baht (THB). The exchange rate at the time of the study was approximately THB 40 to 1 US dollar.

**Sensitivity analysis**
A univariate sensitivity analysis was carried out by varying the cost of emesis care and substituting the cost of ondansetron with that of another drug. The authors presumably set the alternative values.

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

**Cost results**
The mean total costs (35 patients in each group) were THB 2,185 (+/- 246.87) in the BF group and THB 2,674.49 (+/- 222.07) in the RA group.

The cost-difference was THB 489 (95% confidence interval: 376.98 to 601.02; p<0.001). The sensitivity analysis corroborated the results of the base-case analysis.

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was carried out.

**Authors' conclusions**
Patient-controlled epidural analgesia (PCEA) with 0.0625% bupivacaine plus fentanyl 3 microg/mL (BF) after total knee replacement (TKR) surgery was as effective as ropivacaine alone (RA), but provided more patient satisfaction and was significantly cheaper. However, the use of epidural ropivacaine led to fewer opioid-related side effects, particularly pruritus and vomiting.
CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators, which were appropriate given the objective of the study. The dosages and modalities of administration were clearly described. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis was based on a clinical trial, which was appropriate for the study question. Further, the use of a randomised design should have reduced the impact of selection bias. The methods of randomisation and sample selection were not described. In effect, it was not stated whether some patients refused to participate, or were excluded for any reasons from the initial study sample. The study groups were well balanced at baseline and no patient was lost to follow-up assessment, as patients were followed during their hospital stay. The use of blinding limits the impact of assessment bias. Further strengths of the analysis were the use of intention to treat and the appropriateness of the study sample, which was justified on the basis of statistical analyses. The patients were presumably enrolled at a single institution, which might reduce how representative they were of the patient population.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The cost analysis reflected the perspective of the health care provider, as the authors stated, and the cost categories included were appropriate. The authors justified the exclusion of some labour costs. The unit costs and quantities of resources used were not given, which limits the possibility of replicating the analysis in other settings. The source of the data was reported for all items. Statistical analyses of the costs were carried out, and the impact of changing some key cost items was investigated in a sensitivity analysis. The price year was not given, thus limiting the possibility of reflating the costs in different time periods.

Other issues
The authors reported some results from other studies and stated that their findings were quite comparable to those obtained in other economic evaluations. The issue of the generalisability of the study results to other settings was not explicitly addressed, and few cost estimates were varied in the sensitivity analysis. The external validity of the analysis is therefore low and caution is required when extrapolating the results of the analysis to other countries. The study referred to patients requiring sedation after TKR surgery and this was reflected in the authors' conclusions.

Implications of the study
The study results would appear to support the use of PCEA with BF after TKR surgery in comparison with RA.

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