A comparison study of dexmedetomidine vs clonidine for sympathoadrenal response, perioperative drug requirements and cost analysis

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.

CRD summary
This study compared the requirements for various drugs and costs of alpha-2 agonists, given before anaesthesia, to maintain anaesthesia in patients undergoing at least three hours of surgery. The authors concluded that dexmedetomidine, before anaesthesia and during surgery, significantly reduced blood pressure and heart rate fluctuation, and reduced opioid and anaesthetic use, compared with clonidine. There were limitations to the study design, which affected its validity and generalisability, and the conclusions should be considered with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study compared the requirements for various drugs and costs of alpha-2 agonists, given before anaesthesia, to maintain anaesthesia, for patients who were undergoing at least a three-hour surgery.

Interventions
Clonidine and dexmedetomidine interventions were compared with a control. Clonidine was defined as standard care. Each drug was given at a dose of one microgram per kg, as a 10-minute infusion, before the induction of anaesthesia.

Location/setting
India/in-patient care.

Methods
Analytical approach:
An economic evaluation was undertaken based on the results of a three-arm randomised trial. The time horizon was 24 hours after surgery. The authors did not state the study perspective.

Effectiveness data:
The effectiveness data were from a prospective, observational, randomised controlled trial, which lasted for six months. There were 60 patients in the trial, with 20 patients in each arm. The main clinical effectiveness estimates were the patients' systolic and diastolic blood pressure, their heart rate, and the drugs' safety and tolerability.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measures of benefit were the reduction in the use of opioids, analgesia and anaesthetics, as well as the patients' systolic and diastolic blood pressure and heart rate, during different phases of surgery. The main drugs of interest that could be reduced were fentanyl, thiopentone, isoflurane and diclofenac.

Cost data:
The cost categories included the drugs. The direct costs were the charges to the patient, by the hospital anaesthetics satellite pharmacy. The resource use estimates were from the trial. All costs were presented in Indian rupees (INR).

Analysis of uncertainty:
There was no formal analysis of uncertainty. The drug requirements and costs were analysed in pairwise comparisons, with probabilities reported.

**Results**

The percentage of patients who required diclofenac was 90 for control, 40 for clonidine, and five for dexmedetomidine. The percentage who required propofol was 50 for control, and 10 for clonidine and dexmedetomidine. Clonidine statistically significantly reduced the use of fentanyl ($p=0.003$) and thiopentone ($p=0.006$) and the costs, compared with control. Dexmedetomidine significantly decreased the use of isoflurane, fentanyl, and thiopentone (all $p<0.01$), compared with control.

No statistically significant differences were found in the drug costs for isoflurane, fentanyl, and thiopentone, between clonidine and dexmedetomidine at a significance threshold of 0.05.

Adding clonidine or dexmedetomidine to the anaesthetic regimen, reduced the fluctuations in blood pressure and heart rate, during intubation, compared with control. Compared with clonidine, dexmedetomidine reduced systolic blood pressure and heart rate fluctuation, during intubation and surgery.

**Authors’ conclusions**

The authors concluded that dexmedetomidine, given before anaesthesia and during surgery, significantly reduced blood pressure and heart rate fluctuation, and reduced opioid and anaesthetic use, compared with clonidine.

**CRD commentary**

**Interventions:**
The interventions were described. It was not clear whether there were other interventions, not used in the trial, that were relevant. Decision-makers should consider whether the drugs used in the analysis are appropriate to their setting.

**Effectiveness/benefits:**
The effectiveness data were appropriately described and reported. The reasons for excluding patients from the study were clearly stated. It appears that the groups were assessed for confounding, as it was stated that there were no statistically significant differences between the three groups, but the factors that were assessed were not described, and so the quality of the assessment is unclear. The three-arm trial was not blinded, which the authors acknowledged could lead to bias in the effectiveness estimates. The benefit measures were useful and clinically important for this study, but not easily generalisable to other study settings and populations.

**Costs:**
The perspective was not stated, but appears to have been that of the hospital. The drug costs were the only category included, which is unlikely to have covered all the costs incurred by the hospital. The authors acknowledged their omission of nurse costs and bed charges. As the drug costs and the resource use estimates were from billing charges to the patient, these may not reflect the actual drug costs, which may reduce the generalisability of the costs to other study settings. Given the short time horizon, the costs were appropriately not discounted. The price year was not stated, so it is unclear if adjustments for inflation were necessary or undertaken.

**Analysis and results:**
No incremental analysis was undertaken, and the study's results were presented in a disaggregated form. These results were adequately reported, but in some instances where differences were found, it was not clear whether they were statistically significant. No analysis of uncertainty was conducted, and so it is unclear if the results were robust; given the very small sample the uncertainty is likely to be substantial. The authors acknowledged that the short time horizon might have excluded potentially important outcomes, as the long-term costs and benefits were not analysed. The lack of blinding within the trial was acknowledged as a study limitation.

**Concluding remarks:**
The methods and results were adequately reported, but there were limitations to the study design, such as a lack of blinding, small sample, and short analysis period, which limit the evaluation of the validity and generalisability of the results. The authors conclusions should be considered with caution.
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