Cost-consequence analysis of remifentanil-based analgo-sedation vs conventional analgesia and sedation for patients on mechanical ventilation in the Netherlands

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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.

CRD summary
The aim was to assess the cost consequences of sedation using remifentanil, compared with the usual sedation, for patients in the intensive care unit (ICU) who required mechanical ventilation. The authors concluded that remifentanil reduced the average length of stay in the ICU and the overall costs. There were a few limitations to the methods, but they and the results were well reported. The authors' conclusions appear to be appropriate and to reflect the evidence available.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to assess the cost consequences of sedation using remifentanil, compared with conventional sedation, for patients in the intensive care unit (ICU) who required mechanical ventilation.

Interventions
Remifentanil was given with propofol, if required, and this was compared with the usual care, which consisted of morphine or fentanyl, with propofol or lorazepam, according to Dutch guidelines.

Location/setting
Netherlands/secondary care.

Methods
Analytical approach:
This study used a micro-simulation state-transition Markov model, with one-hour cycles, to estimate the cost of remifentanil, compared with usual care, using data from published trials. The time horizon was 28 days and the authors stated that the perspective was that of the hospital.

Effectiveness data:
The clinical effectiveness estimates were from a clinical, open-label, randomised crossover trial (Rozendaal, et al. 2009, see 'Other Publications of Related Interest' below for bibliographic details). This trial was conducted in 2004 to 2005 at 15 Dutch universities or other centres. Patients were randomised to either remifentanil (n=96) or usual care (n=109); if a patient randomised to remifentanil was not extubated after 10 days, they were switched to usual care. The follow-up was a maximum of 28 days. The key clinical parameters were the time to extubation and the time until discharge from the ICU.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The primary clinical outcomes were the length of stay on mechanical ventilation and the length of stay in the ICU.

Cost data:
The two key cost components were the sedation drugs and the stay in the ICU, which included diagnostic tests,
consumables, accommodation, and staff. The costs of sedation were from the open-label trial (Rozendaal, et al. 2009) and the ICU costs were from a micro-costing study (Tan, et al. 2008, see 'Other Publications of Related Interest' below for bibliographic details). The price year was 2006 and all costs were reported in Euros (EUR).

Analysis of uncertainty:
A probabilistic sensitivity analysis was performed, varying all the input parameters. The model was re-run 1,500 times to determine confidence intervals for the outcomes. The results of the sensitivity analysis were presented as the probability of costs being saved by one intervention compared with the other. A subgroup of patients who started the removal of mechanical ventilation within 72 hours was analysed.

Results
On average, patients on remifentanil spent 7.6 days in the ICU, compared with 8.5 days for patients on usual care. This was a reduction of 0.9 days (95% CI -0.7 to 2.6) with remifentanil.

The average 28-day total costs were EUR 15,626 with remifentanil, compared with EUR 17,100 with usual care. This was a reduction in costs (cost saving) of EUR 1,474 (95% CI -2,163 to 5,110) with remifentanil.

The likelihood of cost savings using remifentanil, compared with usual care, was 79% and the likelihood of ICU stay and costs being reduced, with remifentanil, was 89%. The results were consistent in the subgroup analyses.

Authors’ conclusions
The authors concluded that, compared with usual care, remifentanil reduced the average length of stay in the ICU and the overall costs.

CRD commentary
Interventions:
The reporting was good; both the intervention and the comparator were described. The new intervention, remifentanil, was compared with the usual clinical practice in the study setting.

Effectiveness/benefits:
The clinical evidence came from one study, with a high-quality design, and the authors described this source in full. It was not clear whether other relevant studies were available, as no systematic review to identify the clinical sources was reported and other high-quality evidence might have been missed.

Costs:
The inclusion of the direct costs to the hospital was consistent with the perspective stated. All the relevant costs appear to have been included. The source for these cost data was relevant to the study setting and was well reported. The costs in one table (Table 2) did not match those in the text and abstract. It was appropriate not to discount costs given the short time horizon, but it was not clear if this 28-day horizon was sufficient to capture all the differences in costs between the methods of sedation. The price year was given, which will aid future reflation exercises.

Analysis and results:
The model was described and a diagram was provided. The incremental analysis was appropriate for determining the relative costs and effectiveness of the sedation strategies; these were not combined as a cost-consequences analysis was conducted. The uncertainty was appropriately addressed in probabilistic sensitivity analyses and subgroup analyses. The results were adequately reported, which enhances the generalisability of the findings to other settings. The authors highlighted some limitations of their study including the fact that the trial that supplied the clinical data was not blinded, which might have introduced bias, and that adverse events, such as ventilator-associated pneumonia, were not considered. These were justified due to a lack of available data.

Concluding remarks:
There were a few limitations to the methods, but they and the results were generally well reported. The authors’ conclusions appear to be appropriate and to reflect the evidence available.
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