Prolonged sedation of critically ill patients with midazolam or propofol: impact on weaning and costs


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
Midazolam, infused at 0.1-0.5 mg/kg/hr, for the sedation of critically ill patients undergoing mechanical ventilation.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
All ICU patients (medical, surgical and trauma), aged 14 and over and who required mechanical ventilation for more than 24 hours were included in the study.

Setting
The practice setting was a community hospital. The economic analysis was carried out in Toledo, Spain.

Dates to which data relate
The dates to which data relate were not given.

Source of effectiveness data
Evidence for final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
121 ICU patients requiring mechanical ventilation, who were eligible and for whom consent was obtained, were assigned to one of four diagnostic groups. Patients within each group were sequentially allocated to treatment with midazolam or propofol. Power calculations were used to determine the sample size needed to detect a statistically significant difference in weaning times.

Study design
The randomised controlled trial was carried out at a single centre. Blinding was not undertaken. Of the patients originally included in the trial, 13 (10.7%) were lost to follow up: 7 (11.5%) in the propofol group and 6 (10.0%) in the
midazolam group. Reasons for withdrawal included the use of muscle relaxants, breaches in protocol adhesion and intolerance of the T-bridge trial. Patients were followed up for 14 days from admission.

**Analysis of effectiveness**
The analysis was based on treatment completers only, but including those with an outcome of death or therapeutic failure. Primary health outcomes were deaths, therapeutic failures, and extubations. At analysis, groups were shown to be comparable in demographic characteristics.

**Effectiveness results**
In the midazolam group 15 (27.8%) died and 11 (20.4%) had therapeutic failure. Of the remaining 28, one died during weaning. The remaining 27 (50.0%) patients were extubated. In the propofol group 11 patients died (20.4%) and 18 (33.4%) had therapeutic failure (including 7 due to inadequate sedation, and 11 due to hypertriglyceridemia). The remaining 25 (46.3%) patients were extubated. No statistically significant difference was found between the primary outcomes of the two groups.

**Clinical conclusions**
Propofol and midazolam are equally effective as sedative agents for the treatment of critically ill patients on mechanical ventilation.

**Measure of benefits used in the economic analysis**
Since the effectiveness analysis showed no differences in clinical benefit between the two strategies, the economic analysis was based only on the differences in cost.

**Direct costs**
Quantities and costs were reported separately. The estimate of resources used included sedative use, length of ICU stay during sedation and length of ICU stay during weaning. Drug prices/mg were reported, but the source of this information was not stated. The average hourly stay cost for an ICU patient on mechanical ventilation was taken from a previous study. The cost boundary adopted was that of the hospital. Costs were not discounted and dates were not given.

**Statistical analysis of costs**
Cost categories in the two groups were compared using the 2-tailed student's t-test. Both the mean and standard deviation of the results were reported.

**Indirect Costs**
These were not included in the analysis.

**Currency**
US dollars ($) converted from pesetas (ptas) at a rate of ptas130 = $1.

**Sensitivity analysis**
The authors produced a model to estimate the cost-effectiveness of the intervention and comparator drugs in other settings. The model included ICU 'stay' costs, drug costs, mortality rate and duration of sedation. Three simple one-way sensitivity analyses were reported.

**Estimated benefits used in the economic analysis**
Cost results
The cost per patient in the midazolam group was $10,828 (+/- 5,734). The cost per patient in the propofol group was $9,466 (+/- 5,820). The propofol strategy cost $1,362 per patient less than the midazolam strategy. The statistical significance of this difference was not stated and confidence intervals were not given. Costs were not reported in the original currency. The results of a simple one-way sensitivity analysis on three variables were reported. An increase in the hourly stay cost in the ICU increased the cost-effectiveness ratio of propofol, relative to midazolam. An increase in the duration of sedation or in the mortality rate decreased the ratio. The magnitudes of these effects were not explicitly stated, but were shown diagrammatically.

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
Midazolam and propofol are equally effective as sedative agents for critically ill patients on mechanical ventilation. Although propofol has a higher per patient cost, it is associated with a shorter weaning time in intensive care. Propofol is therefore more cost-effective than midazolam.

CRD COMMENTARY - Selection of comparators
The authors' justification for the choice of comparator was that it was a frequently used sedative for critically ill patients on mechanical ventilation. You, as a user of this database, should judge if this is a widely used sedative in your own setting.

Validity of estimate of measure of benefit
The effectiveness of the two interventions was found to be equivalent. A statistically significant difference between the weaning times for the two interventions was found, but associated health benefits were not considered in the economic analysis.

Validity of estimate of costs
Although a difference in the relative costs of the two interventions was found, the statistical significance of this result was not reported. In addition, it is unclear which costs were included in estimating the hourly ICU stay cost. The validity of the estimate of costs is therefore unknown.

Other issues
Given the uncertain validity of the cost estimates and the inadequate detail reported in the results from the sensitivity analyses, the authors' conclusions are not justified. However, the authors' presentation of a sensitivity analysis model enables the cost-effectiveness of midazolam, relative to propofol, to be investigated in other settings.

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Bibliographic details
Other publications of related interest

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