A randomized, prospective, double-blind comparison of midazolam (Versed) and emulsified diazepam (Dizac) for opioid-based, conscious sedation in endoscopic procedures

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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
Using emulsified diazepam (e-diazepam) for conscious sedation in upper and lower endoscopic procedures.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients aged over 18 years requiring esophagogastroduodenal endoscopy or colonoscopy (or both).

Setting
Hospital. The economic study was carried out in Michigan, USA.

Dates to which data relate
No dates were reported.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing (for the drug doses used only) was prospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were used to determine the sample size: at least 100 patients in each study group were required to identify a 10% variation in the main health outcome with alpha less than 0.05 and power of 0.8. The study sample consisted of 211 patients randomly assigned to either the e-diazepam group (n=111) or the midazolam group (n=100). The mean (standard deviation) age in the midazolam group was 54.8 (13.3) years versus 55.7 (16.4) in the e-diazepam group. The participation rate was 75%. A total of 4% of patients were excluded from the study.

Study design
The study was a randomised, controlled, double-blinded trial, carried out in a single centre. The duration of follow-up
was until discharge for most patients and until 2 weeks after study completion for those with phlebitis. The loss to follow-up was 3 patients in the e-diazepam group and 1 patient in the midazolam group. A "double-dummy" technique was used to blind investigators: the midazolam group were given placebo emulsion (Intralipid) and active midazolam (2 mg/ml), while the e-diazepam group were prescribed diazepam (5 mg/ml) and placebo normal saline.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness was treatment completers only. The primary health outcome measure was the physician's subjective assessment of the quality of sedation (adequate, somewhat adequate, somewhat inadequate, and inadequate). Nurse's and patient's assessment of the quality of sedation, time to adequate sedation, and the rate of phlebitis were among the secondary measures employed in the study. The study groups were comparable in terms of all characteristics.

**Effectiveness results**
In terms of the physician's subjective assessment of the quality of sedation, the percentage of cases identified as adequate, somewhat adequate, somewhat inadequate, and inadequate were 79%, 15%, 5%, and 1%, respectively, for the e-diazepam group. The corresponding figures for the control group were 85%, 11%, 4%, and 0%. The nurse's assessment of the quality of sedation was very similar to the physician's, and in any case, there were no significant differences between the groups, (p>0.05). Time to adequate sedation was 5.7 minutes for e-diazepam versus 5.4 minutes for midazolam, (p>0.05). In terms of patient's assessment, the only significant difference between the groups was in better amnestic response evaluated in the midazolam group, which was evaluated by the authors as not being clinically significant. The e-diazepam group had a 6% rate of phlebitis versus 2% for the midazolam group, (p>0.05).

**Clinical conclusions**
The study results show that physicians could not detect a difference in the quality of sedation between groups.

**Measure of benefits used in the economic analysis**
The physician's subjective assessment of the quality of sedation (adequate, somewhat adequate, somewhat inadequate, and inadequate) was regarded as the primary benefit measure.

**Direct costs**
Discounting of costs was not required due to the short time frame of the study. Quantities (except for the drug doses used) were not reported separately from the costs. The cost analysis covered the costs of the drug doses used. The perspective adopted in the cost analysis was not explicitly specified. Actual cost data were used in the cost analysis. The date of the price data was not stated.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was performed.

**Estimated benefits used in the economic analysis**
In terms of the physician's subjective assessment of the quality of sedation, the percentage of cases identified as
adequate, somewhat adequate, somewhat inadequate, and inadequate were 79%, 15%, 5%, and 1%, respectively, for the e-diazepam group. The corresponding figures for the control group were 85%, 11%, 4%, and 0%. (p>0.05).

Cost results
The total cost for the e-diazepam group was $281 versus $720 for the midazolam group.

Synthesis of costs and benefits
A synthesis of costs and benefits was not carried out since the use of e-diazepam was the weakly dominant strategy (with equivalent efficacy and less cost) in the context in question.

Authors' conclusions
The authors concluded "that both drugs were equally effective for sedation for both upper and lower endoscopic procedures". Based on the results of this trial, the authors suggested that increased use of emulsified diazepam would "markedly reduce the cost without altering the quality of sedation".

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator. It was stated that the comparator (midazolam) "in conjunction with a narcotic is the most frequently employed combination" in the US. You, as a database user, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of benefit
The estimates of the main measure of benefit are likely to be internally valid due to the use of a randomised design and the use of power calculations in determining sample size.

Validity of estimate of costs
Quantities (apart from the drug doses used) were not reported separately from the costs, but adequate details of methods of cost estimation were given. As only drug costs were considered it is impossible to assess whether any important cost items were omitted from the study.

Other issues
The issue of generalisability to other settings or countries was not addressed.

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