PROPOFOL SEDATION FOR OUTPATIENT UPPER GASTROINTESTINAL ENDOSCOPY: COMPARISON WITH MIDAZOLAM

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SUMMARY
The objectives of this study were to assess midazolam and propofol as sedative agents for outpatient gastrointestinal endoscopy, with particular reference to recovery profile, amnesic effects, and haemodynamic state and oxygenation during the procedure. Forty consecutive patients were allocated randomly to two groups. Patients in group I (n = 19) received midazolam 81 (SEM 32) μg kg⁻¹; those in group II (n = 21) received propofol 950 (400) μg kg⁻¹. Both agents were administered as single injections to similar end-points of sedation. Psychomotor function was assessed using the digit symbol substitution test (DSST). Amnesia was measured with a visual memory test and subjective questionnaire. Patients in group I had a lower DSST score than those in group II (P < 0.01), indicating a hangover effect from midazolam. Amnesia was similar in the two groups up to the time of removal of the endoscope. More patients in group II remembered removal of the endoscope (P < 0.001). Oxygen desaturation from baseline was similar in both groups (P < 0.01). An increase in heart rate and decrease in mean arterial pressure were noted in both groups. Propofol provided more rapid recovery compared with midazolam, but was associated with pain on injection, a short amnesia span, and reduced patient acceptance.

KEY WORDS

Outpatient endoscopy requires reliable sedation of short duration and devoid of side effects. The i.v. use of benzodiazepines is a popular technique. Midazolam is chosen frequently because of its short elimination half-life, lack of active metabolites and potent amnesic properties [1, 2]. Propofol (2,6-diisopropylphenol), a sterically hindered phenol, has a rapid onset, large volume of distribution, lack of active metabolites and short elimination half-life; these properties suggest that it may be suitable for outpatient gastrointestinal endoscopy.

The objectives of the study were to compare midazolam and propofol as sedative agents for outpatient endoscopy, with particular reference to recovery profile, amnesic effects and cardiorespiratory changes.

METHODS AND RESULTS
Following institutional Ethics Committee approval and informed consent, we studied 40 patients (ASA I—II) undergoing elective outpatient gastrointestinal endoscopy; they were allocated randomly to receive midazolam (group I) or propofol (group II). Patients receiving psychotropic medication or drugs known to interact with benzodiazepines or propofol were excluded. After topical anaesthesia of the oropharynx with 120 mg lignocaine, each agent was administered as a single injection to the same end-points of sedation (dysarthria, nystagmus or ptosis). The same physician, who was not blinded to the agent, administered all drugs. As the onset time for propofol is approximately one arm–brain...
PROPOFOL SEDATION FOR UPPER GASTROINTESTINAL ENDOSCOPY

circulation time, whereas that for midazolam is about 2 min, a separate injection scheme was adopted in each group. Midazolam was diluted to a concentration of 0.5 mg ml\(^{-1}\) and injected at a rate of 1 ml every 15 s until the patient demonstrated signs of sedation; propofol was injected undiluted at a rate of 1 ml every 5 s to the same end-points. In an effort to avoid pain on injection, lignocaine 1 ml was added to the propofol immediately before injection.

All patients breathed room air throughout the procedure. Monitoring included oxygen saturation, automatic arterial pressure and ECG. Cardiorespiratory data were recorded at the following times: baseline, i.v. cannulation, topical anaesthesia of the oropharynx, administration of drug, insertion of mouth gag, insertion of endoscope, biopsy, removal of endoscope and 5 min after endoscopy.

Endoscopies were carried out by the same endoscopist using an Olympus endoscope and blinded to the drug administered. Gastric or oesophageal biopsies were taken from all patients.

The study was blind to the investigator assessing the patients.

Psychomotor function using the digit symbol substitution test (DSST), administered in the standard manner, was assessed before endoscopy and at 30 and 90 min after administration of drug. This test has been found previously to be sensitive to the effects of benzodiazepines and to be appropriate for outpatient use [3].

The degree of amnesia was measured with a visual memory test and a subjective questionnaire [3]. Questions regarding complications and patient satisfaction with the sedation were included also.

Statistical methods included analysis of variance (ANOVA), the Mann–Whitney \(U\) test, Fisher’s Exact Probability test, Wilcoxon Matched Pairs test, and the chi-square test. \(P < 0.05\) was considered significant. Data are expressed as mean (SEM), unless stated otherwise.

The two patient groups were similar with regard to age, weight, sex distribution and duration of procedure; 63% of patients in group I and 52% of patients in group II were having repeat endoscopy. Mean doses of midazolam and propofol to achieve sedation were 81 (32) \(\mu g \text{ kg}^{-1}\) and 950 (400) \(\mu g \text{ kg}^{-1}\) in groups I and II, respectively. All patients remained conscious during endoscopy.

The change in DSST score from before endoscopy to 30 and 90 min after injection is illustrated in figure 1. Deterioration in psychomotor function at 30 min was noted in group I (midazolam) (\(P < 0.01\)). Group II patients (propofol) show no change from baseline. At 90 min, psychomotor function had returned to baseline values in both groups.

Both drugs showed similar amnesic properties up to the time of removal of the endoscope. However, 68% of group I patients were amnesic for this event, compared with 14% of group II patients (\(P < 0.001\)). Early amnesic effects were similar in the two groups; however, 74% of patients in group I were amnesic for the third photograph shown immediately after removal of the endoscope, compared with 38% of patients in group II (\(P < 0.05\)).
The main complication was pain on injection: 29% of patients in group II experienced moderate to severe pain, compared with 5% in group I ($P < 0.05$). Twenty-four percent of patients in group II indicated that they would prefer another method of sedation during future endoscopy, compared with 5% in group I ($P < 0.05$). All the patients who expressed dissatisfaction with the procedure had experienced pain on injection. Other complications were similar in the two groups.

Oxygen saturation decreased in both groups after administration of drug ($P < 0.01$). There was no difference between the groups (fig. 1).

Heart rate increased in both groups during the procedure, but was less in the propofol group at insertion of the mouth gag ($P < 0.05$) and 5 min after endoscopy ($P < 0.05$). Both drugs caused a reduction in mean arterial pressure following administration of drug, but baseline mean arterial pressure was less in group II ($P < 0.05$).

**COMMENT**

Propofol and midazolam produced satisfactory sedation and acceptable amnesia during upper gastrointestinal endoscopy. Both drugs produced similar arterial desaturation. The decrease in saturation as a mean value was not clinically important (from 98% to 94%). However, when one considers that oxygen saturation decreased to 90% or less in 26% of patients in group I and 19% of patients in group II, its clinical importance becomes apparent. In the presence of pre-existing cardiac disease, hypoxaemia of this magnitude could predispose to cardiac arrhythmias.

Propofol-treated patients had a greater DSST score 30 min after endoscopy, indicating more rapid recovery than those in the midazolam group and implying that the use of propofol may allow earlier discharge. However, to demonstrate improved “street fitness” after use of propofol, more elaborate recovery tests would be needed.

More patients in the propofol group indicated that they would prefer an alternative method of sedation if future endoscopy was necessary. This may reflect the fact that 29% of patients in group II experienced moderate to severe pain on injection, compared with 5% in group I. The addition of 1% lignocaine 1 ml to the propofol before administration of drug failed to eliminate pain on injection.

There is a wide dose variation reported in the literature when midazolam is used for sedation (50–110 μg kg$^{-1}$) [1]. The mean dose in our study (81 (32) μg kg$^{-1}$) was comparable to the doses used by other workers. The mean dose of propofol was 950 (400) μg kg$^{-1}$, which is considerably smaller than that reported previously for sedation. Gepts and colleagues used propofol 2 mg kg$^{-1}$ followed by an infusion as a sedative technique for colonoscopy [4] and Dubois and colleagues used 1.76 mg kg$^{-1}$ followed by an infusion for sedation during gastrointestinal endoscopy [5]. These doses are in the range used for induction of anaesthesia. No control groups were included in these studies, presumably because it is difficult to compare fixed doses of agents with differing onset times. We overcame this problem by titrating both drugs to the same clinical endpoints of sedation using an injection technique which allowed for the variation in onset time.

Our study confirms the amnesic effects of both drugs [1, 4]. Amnesia for the total procedure may be important in that it improves patient acceptance of a repeat endoscopy. To increase duration of amnesia in group II it would probably be necessary to give patients an infusion of propofol. It is worth noting that the long duration of amnesia associated with midazolam may delay early discharge from a day-case unit and be hazardous in unsupervised patients.

Patients in the propofol group had a significantly slower heart rate than those in the midazolam group, and this persisted in spite of a decreased mean arterial pressure. This effect of propofol has been demonstrated previously and may be of benefit in patients as it reduces myocardial oxygen demand [6]. However, a reduction in mean arterial pressure and its effect in reducing myocardial blood supply may offset any benefits gained by a reduced heart rate.

In conclusion, both agents are suitable for sedation during gastrointestinal endoscopy. Propofol may offer some advantages in a day-case setting, with its rapid recovery profile and limited amnesic effects. However, its disadvantages include pain on injection, a short amnesia span when administered by single injection and reduced patient acceptance compared with midazolam. We recommend that supplementary oxygen be administered to all patients undergoing endoscopy when either propofol or midazolam is used for sedation. Monitoring should include ECG, arterial pressure and oxygen saturation. It
is the practice in many endoscopy units for the endoscopist to administer the sedative and then carry out the procedure with a nurse assistant. In view of our findings, we strongly recommend that a second doctor, other than the endoscopist, administer the sedation and remain with the patient for the duration of the procedure.

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REFERENCES