INTRAVENOUS SEDATION FOR UPPER GASTROINTESTINAL ENDOSCOPY: MIDAZOLAM VERSUS PROPOFOL

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ABSTRACT

Propofol was compared with Midazolam for sedation during upper gastrointestinal endoscopy in a randomised, double blind study. Both drugs were equally acceptable to endoscopists and patients. There was significant oxygen desaturation after sedation and during endoscopy ($p < 10^{-6}$). Significantly more patients in the propofol group could remember the diagnosis which was revealed to them immediately after the gastroscopy ($p<0.001$).

Keywords: Oxygen desaturation, amnesia.

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INTRODUCTION

The increasing popularity of day case surgery has produced a strong demand from both patients and clinicians for sedation techniques with better recovery characteristics and minimal adverse side-effects. In many endoscopy units, Midazolam is the intravenous sedative of choice[1].

Propofol has also been found to be a satisfactory agent[2]. Propofol or 2,6 di-isopropylphenol represents a newer intravenous anaesthetics used for sedation during endoscopy. In low doses, propofol produces sedation and drowsiness and as the dose is increased progressively there is loss of consciousness and anaesthesia.

The aim of this study was to compare midazolam and low dose propofol in terms of effectiveness of sedation, quality of recovery and complications.

MATERIALS AND METHOD

In the present study, 60 patients aged 15 to 75 years, all ASA I and II, undergoing elective upper gastrointestinal endoscopy were allocated randomly to receive either midazolam or propofol.

Patients with clinically significant hepatic, renal or respiratory disease and those who have taken major or minor tranquillisers within 24 hours were excluded from the study. No premedication was given to any patient. The study was blind to the endoscopists and the investigators assessing the patients.

Following an overnight fast, patients were given a 4% lignocaine spray (lignocaine 50 - 100 mg). Five minutes after the application of the spray, the drugs were injected into a vein on the dorsum of the hand or forearm.

Two groups of patients were randomly selected. One group received midazolam, 0.07 mg/kg[3] given over 30 seconds with 1 mg increment at 60 seconds interval, thereafter according to patient's response. The other group received propofol, 1.5 mg/kg over 30 seconds with 10 mg increments at 30 seconds interval, thereafter according to patient's response.

The desired level of sedation was to maintain the patient drowsy, but able to swallow on command. The total dose of drug administered and the duration of the procedure were noted. The gastroscopy was performed with an Olympus GIF PQ 20 gastroscope in all patients.

The patient's ECG and oxygen saturation were monitored continuously. Blood pressure was recorded non-invasively with a Critikon Dinamap 1846 SX. The blood pressure, heart rate and respiratory rate were recorded pre-induction, 2 minutes later and every 3 minutes thereafter.

During recovery, the patients were assessed for orientation in time, place and person. When they were orientated, the results of gastroscopy were revealed to them and they were assessed for ability to recall the diagnosis subsequently during the interview.

Immediately after the procedure, the endoscopist completed a questionnaire on the ease of examination and patient co-operation. Five to six hours after the procedure, the patients were asked to complete a questionnaire concerning adequacy of sedation, amnesia and their willingness to undergo further endoscopy.

STATISTICAL ANALYSIS

The results were analysed using t-tests and one way analysis of variance (ANOVA), chi-square contingency tables or Fisher's exact test to determine the significance of changes from

Table I - Treatment groups characteristics

	Midazolam n = 29	Propofol n = 31
Age (years) mean ± s.d.	47 ± 15	46 ± 18
Weight (kg) mean ± s.d.	57.2 ± 8.9	56.0 ± 9.0
Sex		
male	21	20
female	8	11
ASA classification		
I	17	20
II	12	11
Total dose (mg) mean ± s.d.	5.3 ± 1.3	94 ± 22
Dose (mg/kg) mean ± s.d.	0.09 ± 0.02	1.72 ± 0.35
Duration (min) mean ± s.d.	6 ± 4	6 ± 3

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baseline in each group and differences between groups. A p value <0.05 was taken as significant.

RESULTS

Treatment groups characteristics

The two treatment groups were similar as to patient's age, sex, weight and ASA classification. (Table I).

There was no significant difference in the duration of the procedure in the two treatment groups. A complete examination of the upper gastrointestinal tract, up to the second part of the duodenum was successful in all patients.

Significantly, none of the patients in the midazolam group complained of pain on injection, while 12 in the propofol group did. ($p< 0.01$).

Table II - Cardiorespiratory parameters

	Midazolam n=29		Propofol n=31	
	Baseline measurements	2 min measurements	Baseline measurements	2 min measurements
Arterial pressure (mm Hg)				
Systolic	127	135* (+6.3%)	124	111* (-10.5%)
Diastolic	77	85* (+10.4%)	79	69* (-12.7%)
mean	93	101* (+8.6%)	94	94* (-11.7%)
Heart rate (beats/min)	80	97* (+21.2%)	78	85* (-11.7%)
Respiratory rate (/min)	18	23* (+27.8%)	18	22* (+22.2%)

* Significantly different from measurement before induction ($p< 0.04$)

Cardiorespiratory parameters

There was a significant increase in blood pressure and heart rate after injection of midazolam and during gastroscopy. In the case of propofol, there was a significant decrease in blood pressure and an increase in heart rate (Table II). However, in no patient was there any serious haemodynamic complications such as arrhythmias.

Table III - Oxygen saturation

	Midazolam n=29	Propofol n=31
Baseline saturation (%)		
mean	97	97
s.d.	1	2
range	93 - 99	93 - 100
Lowest saturation (%)		
mean	91	90
s.d.	3	4
range	85 - 96	77 - 95
Breakdown of lowest saturation (% of patients)		
>90	41.4	48.4
90-86	55.2	45.2
≤85	3.4	6.5

In both groups of patients, the respiratory rate increased significantly and in no patient was apnoea of more than 30 seconds observed.

Oxygen saturation

In both groups of patients, there was a significant fall in oxygen saturation ($p<10^{-6}$) between the baseline value and the lowest value recorded after sedation and during endoscopy. However, a comparison of the mean fall in oxygen saturation of the 2 groups, showed no significant diffcrence (Table III).

In 58.6% of patients in the midazolam group and 51.6% in the propofol group, the lowest oxygen saturation was 90% or less.

Endoscopists' Assessment

The endoscopists rated both drugs as being equally satisfactory. Co-operation was assessed to be good in 69% and 77% of patients in the midazolam and propofol groups respectively. In no patient was co-operation described as being poor.

There were no significant differences when patient co-operation, presence of gagging, coughing, vomiting, retching and excessive salivation were compared between the two groups (Table IV).

Table IV - Assessment of patients during endoscopy (No. of patients)

	Co-operation			Gagging		Coughing	
	good	satisfactory	poor	Yes	No	Yes	No
Midazolam	20	9	-	10	19	5	24
Propofol	24	7	-	12	19	4	27
p		n.s.			n.s.		n.s.
	Vomiting			Retching		Excessive salivation	
	Yes		No	Yes	No	Yes	No
Midazolam	1		28	11	18	1	28
Propofol	0		31	5	26	2	29
p		n.s.			n.s.		n.s.

n.s.: differences not statistically significant.

Amnesia

The percentage of patients who remembered the insertion of the gastroscope in the 2 groups were similar, although at the time of removal of gastroscope 72% of patients in the midazolam group had amnesia compared to 55% in the propofol group. However, there was no significant difference in amnesia rates between the 2 groups (Table V).

Table V - Number of patients recalling the injection, passage and removal of gastroscope

	Injection		Gastroscope passed		Gastroscope removed	
	Yes	No	Yes	No	Yes	No
Midazolam	18	11	9	20	8	21
Propofol	17	14	10	21	13	18
p	n.s.		n.s.		n.s.	

n.s.: differences not statistically significant

Patients' Assessment

Both methods of sedation were equally acceptable to the patients. Twenty-seven patients in each group found the procedure not unpleasant and only one patient in the midazolam group and 2 in the propofol group felt that further endoscopy with these methods of sedation were unacceptable.

Significantly 12 patients in the Propofol group could remember the diagnosis in the subsequent interview, while only one patient in the Midazolam group could (Table VI).

DISCUSSION

Successful endoscopy requires patient co-operation. The ideal

Table VI - Patients' Assessment (Number of patients)

	Midazolam n=29	Propofol n=31	P value
Endoscopy			
Not unpleasant	27	27	
Somewhat unpleasant	2	4	n.s.
Very unpleasant	0	0	
Quality of sedation			
Good	25	27	
Satisfactory	3	3	n.s.
Poor	1	1	
Remember the gastroscopy result			
Yes	1	12	
Partially	-	1	p
No	28	18	<0.01
Further endoscopy acceptable			
Yes	28	29	n.s.
No	1	2	

n.s.: differences not statistically significant.

agent for sedation should produce anxiolysis, optimal relaxation and have rapid onset of action. While its action should outlast the operative procedure it should be devoid of unwanted residual effects, as many of these procedures are done on an outpatient basis. It should maintain cardiovascular stability and not depress respiration.

Cardiorespiratory changes during sedation for endoscopy are well known. Haemodynamic changes will depend on the drugs used, the dosages and whether measurements were made at the point when there was stimulation (insertion of gastroscope).

Midazolam has been reported to cause no significant haemodynamic changes even with larger doses[3]. It has also been reported to cause a 5-15 % decrease in arterial blood pressure[4].

It is known that midazolam causes a fall in systemic vascular resistance and a fall in preload. Significant increase in blood pressure in our study can be explained by the fact that the usual peripheral vasodilation and slight drop in cardiac output and peripheral resistance are reversed by surgical stimulation, as our measurements were made at the time of stimulation.

Haemodynamic variations in the propofol group similar to ours have been reported in other studies[5,6].

Incidence of apnoea can be as high as 48% with a mean duration of 51 seconds with the use of propofol for sedation[5]. Apnoea was not seen in this study. This can be explained by the relatively low doses of propofol used (mean dose of 1.72 mg/kg), the drug being given slowly and the gastroscope was introduced as soon as the patients became drowsy.

It is clear from several studies that there is a consistent fall in oxygen saturation during sedation with a benzodiazepine[7-9], which is exacerbated by passage of the gastroscope. This has been postulated to be due to the combination of hypoventilation produced by midazolam, plus the mechanical effect of the instrument partly occluding the patient's upper airway or a reflex stimulated by it.

Our findings confirm the results of others where benzodiazepines have been used either alone or in combination with opioids. We have also shown that a significant fall in oxygen saturation also occurred when propofol was used. Thus all patients should be monitored closely with a pulse oximeter during gastroscopy. This hypoxia can be reversed by providing supplemental oxygen through nasal cannulae at 2 litres/minute[10].

This study showed that both midazolam and propofol are suitable agents for sedation during gastroscopy. They are equally acceptable to both endoscopists and patients. A common side effect was pain on injection in the propofol group, which is a well known side effect and has been reported by other workers[11,12]. There are numerous studies of this problem and its management. In a study assessing eight different methods of administration of propofol, using large veins either in the forearm or antecubital fossa, was the only method that did not cause pain on injection[13]. It has been shown that lignocaine given before or with propofol reduced the frequency of pain. The dose of lignocaine used varied from 0.1 mg/kg[14] to 40 mg given either as pretreatment or mixed with propofol[15].

The amnesia rates for insertion of gastroscope was similar in both groups of patients (68% for midazolam, 69% for propofol). Similar rates for midazolam have been reported[3]. Amnesia for the procedure is important since it helps patients accept repeated endoscopies, which are often necessary in many of our patients. The ability to produce short periods of anterograde amnesia forms part of the efficacy of midazolam as sedative for endoscopy. This property of the benzodiazepines has also been demonstrated in propofol in this study.

The amnesia is mainly anterograde with less retrograde component, since many of the patients could remember the injection. At the time of interview, 5 to 6 hours after the procedure, all the patients could complete the questionnaire.

The major point of difference in the two drugs was that a significant proportion of patients in the propofol group could remember the gastroscopy results that the doctor told them after the procedure, while only one in the midazolam group could. This can be explained by the faster recovery of patients who have received propofol. A number of clinical studies have even shown that when given by intermittent injections for short procedures, recovery from propofol occurs rapidly[16].

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