Sedation with Midazolam or Propofol for Diagnostic Upper Gastrointestinal Endoscopy: A Prospective Randomized Study


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ABSTRACT

Background and objectives: Adequate patient sedation is necessary for diagnostic and therapeutic upper gastrointestinal endoscopic procedures. Propofol is being increasingly used due to its potential advantages of rapid action and clear headed recovery. The aim of this prospective, randomized study was to compare propofol and midazolam for conscious sedation during upper gastrointestinal tract endoscopy with respect to quality of sedation, safety and recovery profile along with the satisfaction of endoscopist in carrying out the procedure on an outpatient setting.

Methods: Eighty-one consecutive patients of (ASA) status I-III undergoing upper GI endoscopy were randomly assigned to receive sedation with midazolam (n = 42) or propofol (n = 39). The doses of drugs were titrated according to patient’s requirement. The level of sedation during the procedure was assessed on a 5-point scale. Safety profile was assessed by monitoring heart rate, electrocardiography, blood pressure and oxygen saturation. Endoscopist rated their satisfaction on a 10-point scale.

Results: Change in heart rate, BP, SPO₂ and procedural discomfort was comparable in both the groups. Thirty-nine patients (93%) in propofol group had a sedation score of 3-4 as compared to 31 of the 42 patients (74%) in the midazolam group (p<0.03). Mean recovery score was higher at 5 min in propofol group than midazolam group. The endoscopist satisfaction score regarding ease of carrying out the procedure was significantly higher in propofol group compared to the midazolam group, [8.62 ± 0.91 vs 7.0± 1.07; (p<0.01). The median time to discharge from the endoscopic unit was shorter in propofol group than in the midazolam group (20 vs 40 min; p = 0.03).

Conclusion: We concluded that propofol is a suitable and safe alternative to midazolam, as its duration of action corresponds well to that of the procedure. Moreover it had a rapid onset, quick and clear headed recovery as well as higher endoscopist satisfaction. (J Dig Endos 2010;1(4):176-79)

Key words: Propofol - Midazolam - Upper GI Endoscopy - Sedation

Introduction

Although many endoscopists perform upper GI endoscopic procedures under topical anaesthesia, sedation is often required not only for patients’ comfort but also to improve the quality of endoscopy. Sedation during endoscopy requires high degree of patient satisfaction, quality of care and safety as well as increased efficiency of endoscopic suite. The use of intravenous benzodiazepines with or without opioids has been the standard practice for undertaking endoscopic procedures for many years, but sedation achieve may not provide adequate patient comfort. Recently, propofol is fast becoming an attractive choice for conscious sedation during endoscopy due to its ideal pharmacokinetic profile for conscious sedation. It is a potent hypnotic drug with a short duration of

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action (1/2 distribution 2–4 min) and quick recovery time for the patient (10–20 min) compared with benzodiazepines and/or opioids.

The aim of this prospective randomized controlled study was to compare midazolam and propofol as sedative agents with particular reference to quality of sedation, safety, recovery profile and satisfaction of endoscopist in carrying out diagnostic upper GI endoscopy.

Methods

Patient population

The present study included 81 adult patients of both sexes of ASA (American Society of Anesthesiologist) status I–III requiring diagnostic upper gastrointestinal endoscopy under sedation. Exclusion criteria were pregnant females, morbidly obese patients, patients who had history of lipid allergy and those not accompanied by a responsible adult person. No patient had received any sedative or analgesic drug 24 hours prior to procedure.

Place of study

The patients as well as endoscopist were unaware of the drug used for sedation. The study was done in the endoscopy unit of Post Graduate department of Medicine. Written informed consent was obtained from all patients and study was approved by institutional ethics committee.

Drug protocol

The anesthesiologists administered drugs in all patients and a single experienced endoscopist did all the endoscopies. Each patient received 4% lignocaine spray about 5 minutes before the procedure. The patients were randomly allocated using a random number table to receive midazolam or propofol. Patients in the propofol group received propofol mixed with 0.02 mg/kg of lignocaine at a rate of 10 mg every 10 seconds while in midazolam group patients received midazolam at a rate 0.5 mg every 15 seconds. The end point of injection in both groups was dysarthria or ptosis. Further increments of propofol (10mg) or midazolam (0.5 mg) were titrated according to patient’s need to ensure adequate sedation (drowsy but able to swallow on command). The patients breathed room air but oxygen with nasal cannula was available if SpO2 decreased below 90% and remained at this or lower level for 30 sec.

Data recording

The maximum level of sedation during the procedure was assessed on a 5-point score ranging from 1, awake; 2, drowsy; 3, arousable on command; 4, arousable to stimulus; and 5, not arousable). Our aim was to keep the patients at the score of 3 or 4. Heart rate and arterial saturation (SpO2) were monitored continuously and blood pressure was monitored non-invasively every minute using a multipara monitor.

The endoscopist satisfaction regarding ease of carrying out the procedure was rated on a 10 point verbal rating score where 0, not satisfied and 10, most satisfied. After the procedure the patients were transferred to recovery room. Adverse events during endoscopy and in the recovery room were also recorded.

In the recovery room degree and level of residual sedation were assessed every 2 minutes using Steward recovery score (Table 1) till the highest score of 6 was attained. Prior to discharge the patients were asked about any discomfort during the procedure (None / some / excessive). The patients were sent home accompanied by a responsible adult, when fully alert, conversant, vitals stable, SpO2 >95% on air and were able to walk unsupported.

### Table 1: The Steward score (post-anaesthesia recovery score)

<table>
<thead>
<tr>
<th>Consciousness</th>
<th>Airway Function</th>
<th>Motor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awake</td>
<td>2 Points</td>
<td>Coughs on command</td>
</tr>
<tr>
<td>Arousable by stimuli</td>
<td>1 point</td>
<td>Breaths independently</td>
</tr>
<tr>
<td>Not Arousable</td>
<td>0 point</td>
<td>Airway remains open</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control of Extremities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uncontrollable movements</td>
</tr>
</tbody>
</table>

Statistical analysis

The sample size was calculated as minimum of 39 patients per group for the projected difference of 20% between the two groups for type I error of 0.01 & power of 90%. The data are presented as mean±SD, median or number of patients. For statistical comparison paired or unpaired tests were used wherever appropriate and value of <0.05 was regarded as significant. Data analysis was performed by SPSS version 10 statistical software.

Results

The two groups were well matched in demographic characteristics, ASA status and duration of procedure (Table 2).

The median dose of propofol was 60mg (range 40–150mg) and of midazolam was 2.5 mg (range 1-3 mg).

### Table 2: Demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Propofol (n=39)</th>
<th>Midazolam (n=42)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs); Mean</td>
<td>38.6±10.3</td>
<td>39.23±</td>
<td>0.79</td>
</tr>
<tr>
<td>(Range)</td>
<td>(21.59)</td>
<td>(19-65)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg), Mean±SD</td>
<td>64±10</td>
<td>67 ±9</td>
<td>0.77</td>
</tr>
<tr>
<td>Male / Female</td>
<td>28/11</td>
<td>31/11</td>
<td>-</td>
</tr>
<tr>
<td>ASA* Status I/II/III</td>
<td>20/10/9</td>
<td>19/14/9</td>
<td>0.81</td>
</tr>
<tr>
<td>Duration of procedure (min)</td>
<td>5 [3-7]</td>
<td>5 [2-8]</td>
<td>0.65</td>
</tr>
<tr>
<td>Drug dose, Median (Range)</td>
<td>75mg (40-150)</td>
<td>3mg[1-3.5]</td>
<td>-</td>
</tr>
</tbody>
</table>

*American Society of Anaesthesiologist
Hemodynamic parameters

Haemodynamic parameters are depicted in Table 3. The mean increase in heart rate (baseline vs maximum heart rate during endoscopy) was similar in both groups (p > 0.05). A transient fall in heart rate occurred after propofol but was not significant. The systolic and diastolic arterial blood pressure decreased after administration of both propofol and midazolam. Compared with baseline, systolic BP decreased by 19% in propofol group and 14% in midazolam group (p > 0.05) while diastolic BP decreased by 12% and 9% in propofol group and midazolam group respectively (p > 0.05). In both the groups there was some rise in BP during endoscopy (systolic BP 9% vs. 11% and diastolic BP 8% vs. 10% in propofol and midazolam groups respectively). The fall in O₂ saturation was seen more frequently in patients receiving propofol compared to those receiving midazolam, but the difference did not reach statistical significance. SpO₂ below 90% occurred in 3 patients given propofol and in 1 given midazolam but was transient and improved upon itself.

Sedation score, endoscopist satisfaction, patients’ discomfort and post-anaesthesia recovery score

The median time from start of injection until endoscopy could be commenced was almost double (1 min vs 2 min) in midazolam than in propofol group. Significantly more patients in propofol group (93% vs 74) had a desired level of sedation ( arousable on command or light stimulus ) than in midazolam group (p < 0.03). None of the patients in any group had a score of 5 (not arousable) (Table 4). The endoscopist satisfaction score regarding ease of carrying out the procedure was significantly higher in propofol group compared to the midazolam group. [8.62 ± 0.91 vs 7.0 ± 1.07; (p <0.01)] indicating better conditions of endoscopy in propofol group (Table 3). At 2 minutes after the procedure mean Steward Score was higher in the propofol group than in the midazolam group (p <0.032) suggesting faster recovery in propofol group. The highest scores 2 minutes after the procedure were attained significantly more among patients in propofol group compared to midazolam group (87% vs 68%; p < 0.05). Procedural discomfort was either nil or slight in most patients in each group (Table 3). The median time to discharge from the endoscopic unit was shorter in propofol group than in the midazolam group (20 vs 40 min; p = 0.03). No serious adverse event was seen in any patient.

Discussion

Conscious or moderate sedation is a state that allows patients to tolerate unpleasant procedures (diagnostic or therapeutic) with minimal or no discomfort while maintaining ability to respond purposefully to verbal commands or tactile stimulation. Although few authors claim that most endoscopies can be done without any need for sedation, given the choice, most patients would demand sedation. There has been a general consensus that it provides adequate control of anxiety, pain, improves comfort, reduces risk of physical injury and confers sufficient amnesia. Apart from providing comfort to the patients, sedation also facilitates endoscopy especially difficult interventions. Traditionally sedation was provided by benzodiazepines but there is growing evidence in favor of propofol during endoscopy worldwide. Propofol is a pure sedative/anaesthetic that acts on GABA receptors. Its main advantages include rapid onset and offset of sedation, fast recovery and normalization of neuro-psychiatric functions. Rapid onset and recovery is a virtue for busy endoscopy units as
it allows quick discharge and quick return to workplace. The patients aged between 19 and 65 years were taken in this study. In both the groups majority of patients belonged to ASA status I and II.

The chief findings of this study are that propofol is more effective in providing rapid and adequate sedation and better conditions of endoscopy with safety profile similar to that of midazolam. Many studies concur with our findings.\(^5\) The endoscopists also preferred propofol to midazolam due to its faster onset, optimal endoscopy conditions and rapid recovery. Gagging was lesser after propofol probably due to more suppression of pharyngeal reflexes. Moderate sedation is the ideal desired level of sedation for unpleasant procedures (sedation score of 3–4). This was achieved more consistently and frequently in patients given propofol. Many previously reported studies have shown superiority of propofol over midazolam.\(^6,9,10\) No patient complained of pain on propofol injection as reported by some workers.\(^16\) This was probably due to cannulation of larger veins, addition of lignocaine and use of cooled propofol.

The safety profile as suggested by haemodynamic changes and \(O_2\) saturation were more or less similar in both the groups. Transient hypotension has been reported following propofol administration previously\(^2\), similar to that noted in the present study. But as the endoscope was inserted the BP increased to baseline level or slightly above that. In no case rise was more than 20% from baseline value indicating that sedation offered some protection against haemodynamic response to insertion or manipulation of endoscope.\(^8\) Although some decrease in SpO\(_2\) was seen in both the groups, potentially harmful fall below 90% was seen only in three patients in propofol group and one in Midazolam group. The fall was for short duration and improved upon itself without oxygen supplementation, a finding in agreement with previous reports.\(^6\) But in view of decrease in SpO\(_2\), supplementation by nasal catheter is worthwhile\(^2\) in some patients.

The common adverse events related to sedation techniques are airway and ventilatory problems, hypotension and rarely aspiration. We did not encounter any such event in our patients. This could be due to selection of patients with not many co-morbidities, short duration of procedure, lower doses of drugs, and continuous monitoring. The complications are mainly related to sub optimal monitoring, higher doses and lack of adequate trained staff.\(^2,3,17\)

**Conclusions**

In conclusion, our findings indicate that for short duration upper GI endoscopy, propofol is a suitable choice as the duration of action corresponds well to that of procedure. The additional benefits are rapid onset, quick and clear headed recover, less discomfort and higher level of endoscopist satisfaction along with acceptable safety profile. However close monitoring, titration of dosage and availability of \(O_2\) and resuscitation equipment are mandatory. In the settings where non-anesthetists use propofol, the doctors should be well trained in managing complications especially related to airway management. The presence of a trained personnel other than the endoscopist will certainly increase the safety of patients.\(^3,10\)

**References**


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