Comparative Evaluation of Propofol and Midazolam as Conscious Sedatives in Minor Oral Surgery

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Abstract

Objective The objective of the study was to assess the efficacy of propofol and midazolam as an intravenous sedative agent in minor oral surgical procedures in terms of: (a) the onset of action, (b) heart rate, (c) oxygen saturation, (d) systolic and diastolic blood pressure, (e) respiratory rate, (f) pain during the injection of sedative agent, (g) recovery period, (h) side effects, (i) patient's cooperation during the surgery.

Methodology This was a double blind randomized study in which one group of 20 patients received propofol with the induction dose of 0.5 mg/kg and 50 µg/kg/min which was administered by syringe infusion pump as a maintenance dose and the other group received midazolam in a single dose of 75 µg/kg and no maintenance dose was given, instead 5 % dextrose was administered by syringe infusion pump at the rate of 50 µg/kg/min. Since propofol was milky white in colour, a green cloth was covered over the infusion pump in all cases. The surgeon, assistants and observers were blind about the medications which would

be given to the patient for sedation. After the administration of the sedative, local anesthesia was achieved with 2 % lignocaine hydrochloride.

Results The onset of action in propofol group was significant as onset of action was faster. The maximum increase in heart rate in propofol group was at 10 min intraoperatively (Mean $\pm$ 80.40 $\pm$ 12.73) and that in midazolam group was at 15 min intraoperatively (Mean 79.25 $\pm$ 13.44). Post operatively the heart rate decreased near to the baseline value in both the groups. The average oxygen saturation before induction in propofol group was 99.7 $\pm$ 0.73 % and that of midazolam group was 99.15 $\pm$ 0.31 $P = 0.314$. None of the patients in this study developed apnea. The systolic blood pressure (Mean $\pm$ SD) before induction in both the groups decreased from the baseline value after the administration of sedatives. The diastolic blood pressure (Mean $\pm$ SD) before induction in both the groups decreased from the baseline value after the administration of sedatives and the decreased diastolic blood pressure was maintained

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throughout the procedure. The respiratory rate (Mean $\pm$ SD) before induction in both the groups decreased from the baseline value after the administration of sedatives. The decreased respiratory rate remained throughout the surgical procedure. Pain during the injection of the sedatives was reported by nine patients (45 %) in the propofol group whereas none of the patients in midazolam group complained of pain during the injection. This is statistically significant ($P = 0.001$). The recovery time (Mean $\pm$ SD) in propofol group was 22.50 ± 3.04 (range 15–25 min) and that in midazolam group was 33.75 ± 3.93 (range 30–40 min), which was statistically significant ($P < 0.001$). Patients in the propofol group were significantly less co-operative than midazolam group at both 10 and 25 min intra operatively.

Conclusion The design of the present study permitted qualitative assessment of propofol and midazolam as sedative agents in minor oral surgical procedures. The ideal anesthetic agent should provide rapid onset of action, profound intra operative amnesia while ensuring rapid recovery without much complications. There were no significant differences in either patient demographics or surgical characteristics between the two groups. The propofol group was less co-operative than midazolam group. Pain during the injection of sedative was a significant adverse effect in the propofol group. Cardiovascular parameters remained stable throughout the procedure in both study groups and no intervention was required. However recovery and onset of action was faster in the propofol group as compared with the midazolam group.

Keywords Propofol · Midazolam · Minor oral surgery · Day care surgery

Introduction

Fear and subsequent avoidance of dental procedures are known to be the major deterrents to oral health. Recognition of this as a serious problem has led to the use of pharmacologic and behavioral therapies to control both the evasiveness of the procedure and patient anxiety. The intravenous administration of variety of anesthetic agents to conscious patients has been prompted as providing optimal control of anxiety with minimal risk [1].

Conscious sedation is a method of depression of the central nervous system that allows the operator to perform a surgical procedure during which the patient retains protective reflexes.

In combination with local anesthesia, it is a safe alternative to general anesthesia for the control of perioperative pain and anxiety in outpatient surgery [2].

Although there are a number of methods to effect conscious sedation, most surgeons rely on the intravenous route to produce rapid and titrable results. Other methods include inhalation sedation with nitrous oxide and oxygen and the less controllable forms of oral and intramuscular premedication. In addition to the variability of individual's response to orally administered sedatives, the time required for onset of effect is more and duration of action often extends well beyond the surgical appointment. Although preoperative intramuscular medication is routinely given in the hospital before a general anesthetic, the situation in the office, which involves an ambulatory patient, is obviously different and requires different criteria and approaches.

Amnesia, analgesia, suppression of stress response, hemodynamic stability, immobilization, sedation and hypnosis are among the effects sought with the administration of anesthetic agents.

Intravenous anesthesia is the principal anesthetic technique used within oral and maxillofacial surgery for office ambulatory surgery to achieve these conditions. An advantage of the intravenous technique is the ability to select specific agents that provide the particular effects just mentioned. The efficacy of intravenous anesthetic agents can be enhanced by using anesthetic agents with rapid onset, short duration of clinical effect, high clearance rate, minimal tendency for drug accumulation and no active metabolites [3].

Benzodiazepines are the most widely used IV anesthetic agents because they have a wide therapeutic margin of safety and provide reliable effects, producing sedation, anxiolysis, anterograde amnesia, anti hallucinatory effects and are devoid of emetic action. Parenteral benzodiazepines that are commonly used in oral and maxillofacial surgery are midazolam and diazepam.

This study was conducted to compare the efficacy of propofol and midazolam as conscious sedatives during minor oral surgical procedures.

Aims and Objectives

The objective of the study was to assess the efficacy of propofol and midazolam as an intravenous sedative agent in minor oral surgical procedures in terms of:

- The onset of action
- Heart rate
- Oxygen saturation
- Systolic and diastolic blood pressure
- Respiratory rate
- Pain during the injection of sedative agent
- Recovery period
- Side effects
- Patient's cooperation during the surgery

Pharmacology

Propofol

Propofol is an alkylphenol and is available as intra lipid [3]. It is chemically unrelated to any other anaesthetic or sedative agent. It is an intravenous general anesthetic agent that in lower doses can be used to induce either conscious or deep sedation. It is formulated as 1 % (10 mg/ml) emulsion that contains soyabean oil, glycerol, and egg lecithin. Disodium edetate can be added to propofol as an anti bacterial agent. Propofol has a dose dependant depression of CNS that gives rise to an anesthetic effect that ranges from sedation to hypnosis [3].

The formulation contains no antimicrobial preservatives, and this vehicle can support growth of micro organisms. Therefore, it should be drawn into sterile syringes or connected to a volumetric infusion device immediately after opening the container and administered promptly. Unused portions of the injection should be discarded at the end of the case, or no later than 6 h after opening the ampule [3].

Propofol possess many of the properties of an ideal anesthetic drug such as rapid onset of action, short duration of action, high clearance rate, minimal tendency for drug accumulation and no active metabolites. It has got antiemetic [6] and antipruritic properties but no analgesic effect.

The characteristics of propofol make it ideal for continuous infusion. It provides sedation, rapidly and predictably alters anesthetic depth and ensures rapid recovery with minimal side effects. Dose and rate dependent ventilatory depression is also associated with propofol. However neither hypotension nor apnea requiring intervention generally occurs with doses normally used in ambulatory office anesthesia for oral and maxillofacial surgical procedures [7, 8].

Pharmacokinetics

Propofol is characterized by a rapid onset of action and short duration of action, compared with other IV anesthetic agents. Its initial distribution half life is short, in the range of 2–8 min. If used alone, the expected duration of action is 5 min. This very short distribution half-life also implies that although it can be administered by intermittent boluses, it is ideally given as infusion. It is highly protein bound, in the range of 97–99 %. Furthermore, propofol has an extremely high clearance rate, which also contributes to its characteristic of rapid recovery.

Dosage

Intravenous conscious sedation can be induced with a dose of 0.5 mg/kg titrated over a period of 3–5 min if used alone

in an ASA I or II patient. A dose of 25–75 µg/kg/min, ideally administered by the infusion, maintains conscious sedation in healthy adults. This dose should be reduced if it is used in addition to other agents such as midazolam and fentanyl, ASA III and IV patients or in elderly. The dose for induction of general anesthesia is 2–2.5 mg/kg.

Cardio Respiratory Activity

The mechanism of action of propofol is believed to involve modulating the binding site of GABA on its receptor, which results in an inhibition of synaptic transmission. In the cardiovascular system propofol can depress mean arterial blood pressure significantly with no effect on heart rate. These hypotensive effects are dose and rate dependant, transient, and rarely require pharmacologic correction. Although well tolerated in healthy patients, significant hypotension may occur in elderly or hypovolemic patients or persons with limited cardiac reserve.

Propofol can cause dose and rate dependant respiratory depression. Apnea is the most significant respiratory effect when propofol is used to induce general anesthesia. In doses used for sedation, ventilatory drive and the normal response to hypercarbia are inhibited. This reaction implies that supplemental oxygen is a valuable adjunct. However, neither hypotension nor apnea requiring intervention generally occurs with doses normally used in ambulatory office anesthesia for oral and maxillofacial surgery. It does not release histamine and therefore should be safe for use in asthmatics.

Adverse Reactions

The most common adverse reaction is the pain from injection, which is noted more frequently when administered in the small caliber veins in the dorsum of the hand, compared with the antecubital fossa. Cooling, diluting, or mixing with lidocaine may produce the incidence of pain. Propofol has no analgesic effect.

Advantages

Propofol's major advantage is its rapid recovery, with more clear headedness noted compared with other agents. This makes it advantageous for parenteral sedation in the outpatient setting. Propofol has antiemetic and antipruritic properties in doses as low as 10–20 mg.

Although it may be intended to induce conscious sedation, propofol easily may induce deep sedation or general anesthesia. Ideally any patient who receives propofol should be monitored to the same minimum level as that for a person under deep sedation.

Midazolam

Midazolam is a 1, 4-benzodiazepine compound that is similar in most of its pharmacological aspects to diazepam. Midazolam was synthesized in 1975 by Walser and Fryer. The chemical formula is 8-chloro-5-(2'-fluorophenyl)-1-methyl-4H-imidazo(1, 5-a)(1-4)benzodiazepine maleate.

It has powerful anxiolytic, amnesic, hypnotic, anticonvulsant, skeletal muscle relaxant and sedative properties. It is considered a fast-acting benzodiazepine, with a short elimination half-life. This drug is considered quite addictive, as should be expected given its potent anxiolytic properties and rapid onset of action.

Midazolam is a colorless crystal in an aqueous solution. Each milliliter contains either 1.0 or 5.0 mg midazolam maleate buffered to a pH of 3.3. The acidic pH maintains the benzodiazepines ring in the open configuration, which is required for its water solubility. This water solubility eliminates the requirement for potentially irritating solvents such as propylene glycol and responsible for the positive finding of lack of burning sensation and the absence of phlebotic sequelae at the injection site.

However, when it is injected, the physiologic pH (7.4) acts to close the ring, providing the chemical structure of the drug that is required for its clinical efficiency. Now it becomes much more lipid soluble, facilitating its rapid uptake into nerve tissue. This partly accounts for its rapid onset of action and its high protein binding in the blood (up to 97 %). The water solubility of midazolam is produced by the substitution of imidazole at the 1, 2 position of the 1, 4 benzodiazepine ring structure and is aided because midazolam is the salt of an acid.

Pharmacokinetics and Biotransformation

Midazolam undergoes metabolism in the liver by hydroxylation into three major metabolites. When compared to diazepam the major metabolites of midazolam have no pharmacological activity. It is rapidly metabolized to 1-hydroxy methyl midazolam and 4-hydroxymidazolam. Midazolam is mainly excreted through the renal route as glucuronide conjugates. Less than 0.03 % of an IV dose is excreted unchanged. In addition because of lack of active metabolites and its shorter plasma half-life rebound effect is not evidenced by midazolam.

Mechanism of Action

The half-life produced by the distribution and redistribution of midazolam has been recorded as 4–18 min and the half-life of metabolism and excretion is 1.7–2.4 h. The shorter half life of midazolam appears to make the drug more ideally suited to ambulatory sedation procedures.

All benzodiazepines including midazolam act by stimulating the benzodiazepine receptors, which are a part of the gamma amino butyric acid (GABA) receptor complex. Stimulation of the benzodiazepine receptor affects the GABA-A receptor specifically, which in turn increases chloride ion conductance and results in neuronal inhibition.

Dosage Conscious sedation is achieved with doses approximating 0.07 mg/kg (i.e. 5 mg in a typical adult), titrated slowly in 1-mg increments. If using the 5-mg/ml formulations for IV administration, it is strongly recommended to dilute this to a 1-mg/ml concentration to facilitate slow titration.

Amnesia Midazolam is superior to other benzodiazepines in providing anterograde amnesia. Retrograde amnesia is not produced by midazolam.

Cardio Respiratory Activity Midazolam has minimal effect on the cardiovascular and respiratory dynamics of ASA I or II patients in the usual doses. Studies show that IV doses of 0.15 mg/kg of midazolam in healthy persons have produced statistically significant, but clinically insignificant decrease in arterial blood pressure and increase in heart rate.

Intravenous administration of midazolam produces significant respiratory depression; this is due to the result of direct depression of the central respiratory drive rather than being caused by a simultaneous depression of the muscles of respiration, although this cannot be excluded. No cardiac dysrhythmias were provoked by midazolam administration.

Adverse Reaction The most frequently voiced complaint after administration of midazolam is dizziness. Others are cough, over sedation, pain at the site of injection, nausea, vomiting, headache, hypotension, respiratory arrest/depression (especially when given rapidly).

Materials and Methodology

The study was conducted in the department of Oral and Maxillofacial Surgery of the Oxford Dental College, Hospital and Research Centre, Bangalore. The study included 40 adult patients of American Society of Anesthesiologist (ASA) Class I and Class II between the age group of 20–40 years, both male and female requiring minor oral surgical procedures (removal of impacted mandibular 3rd molar). All patients were subjected to a thorough pre-anesthetic evaluation and routine hematological investigations.

Inclusion Criteria

- American Society of Anesthesiologist(ASA) Class I and Class II
- Patients within the age group of 20–40 years, both males and females.

Exclusion Criteria

- Patients with history of psychiatric illness.
- Chronic use of CNS depressants/antidepressants.
- Alcohol abusers.
- Morbidly obese patients.
- Patients suffering from systemic complications/symptoms.
- Pregnant or with history of anesthetic related complications.
- Surgical procedures which took more than 30 min.

The study was approved by the ethics committee of our institution. All the patients were advised for a minimum of 6 h of NPO (nil per oral). The surgical procedures including the administration of intravenous sedatives were explained to the patient and an informed consent was taken.

In the operating room the patient was connected to a pulse oximeter, ECG monitor and non-invasive blood pressure cuff (NIBP) for continuous monitoring of heart rate, oxygen saturation, blood pressure and respiratory rate. The patient was allowed to relax in the operation theatre for 10 min with constant reassurance following which the baseline parameters were noted and recorded.

A 20 gauge IV canula was placed on the largest available vein on the hand. Oxygen was administered at the rate of 4 l/min via nasal canula.

This was a double blind randomized study in which one group of 20 patients received propofol with the induction dose of 0.5 mg/kg and 50 µg/kg/min which was administered by syringe infusion pump as a maintenance dose and the other group received midazolam in a single dose of 75 µg/kg and no maintenance dose was given, instead 5 % dextrose was administered by syringe infusion pump at the rate of 50 µg/kg/min.

Since propofol was milky white in colour, a green cloth was covered over the infusion pump in all cases.

The surgeon, assistants and observers were blind about the medications which were be given to the patient for sedation. After the administration of the sedative, local anesthesia was achieved with 2 % lignocaine hydrochloride.

All patients who were subjected to minor oral surgical procedure ex: removal of impacted mandibular 3rd molar were performed by the same surgeon

Onset of Action

This was calculated from the time of induction of anesthetic agent to the loss of eye lash reflex.

Duration of Surgery

This was calculated from the time of first incision to the last suture placement, or till the end of surgical procedure.

Co-operation Score

1. Did the patient's movements during the injection of local anesthesia or during the surgery interfere or delay the treatment?	
At 5 min	No interfering movements [0] Minor movements, positioning remained appropriate [1]
At 15 min	Minor movements, patient had to be repositioned [2]
At 25 min	Movements grossly interfered with the procedure [3]
2. To what extent did the patient verbalize discomfort during procedure?	
At 5 min	No verbalization [0] Some verbalization, but did not indicate pain or discomfort [1]
At 15 min	Some verbalization indicating pain or discomfort [2]
At 25 min	Complained frequently during the procedure [3]
3. Did the patient show nonverbal signs of discomfort?	
At 5 min	Not at all [0] Slight discomfort, occasional grimaces [1]
At 15 min	Moderate discomfort, feet/hands tensed, tears in eyes [2]
At 25 min	Marked discomfort apparent during procedure [3]
Sum the numbers next to each response and record as the score of 0 to 9.	
Co operation score:	
At 5 min	
At 15 min	
At 25 min	

Side Effects

- Head ache
- Drowsiness
- Cough/hiccough
- Nausea/vomiting
- Restlessness

Recovery

It was calculated from the end of surgery to when the patient could walk in a straight line without support.

Preoperative, intra-operative and postoperative monitoring of the oxygen saturation, heart rate, systolic, diastolic, mean arterial blood pressure and respiratory rate were continuously monitored and recorded.

These parameters were recorded before induction, after induction, every 5 min intra operatively and every 10 min

post operatively for the first 40 min. Pain during the injection of sedatives, the onset of action, recovery period, and side effects were also noted and recorded by the blind observer.

Patient co-operation during the surgery was evaluated using the co-operation score at 5, 15, and 25 min intra operatively. After completion of the surgery the administration of the drug through infusion pump was stopped and patient was immediately transferred to recovery room with the same monitor where postoperative data were obtained by the observer.

Discharge

Criteria set for safe discharge:

- Orientation to place, person and time
- Stable vital signs for at least 1 h
- Ability to ambulate unassisted
- Ability to tolerate oral liquid
- Absence of significant pain and bleeding at the surgical site.

The patient was discharged with patient's adult attender.

Results

The study was conducted on 40 patients who reported to the Dept of Oral and Maxillofacial Surgery of The Oxford Dental College Hospital and Research Center, Bangalore for minor oral surgical procedures (removal of impacted mandibular 3rd molar). The patients were in the age group of 20–40 years, ASA I and II physical status, both males and females.

The mean age of the patients in Group A (propofol group) was 26.15 ± 4.45 years, 14 male and 6 female patients with a mean weight of 57 ± 7.08 kg. In Group B (midazolam group) the mean age of the patients was 26.70 ± 6.74 years, 12 male and 8 female patients with a mean weight of 58.05 ± 12.94 kg. There were no statistically significant differences between the two groups in terms of basic characteristics.

Pain during the injection of the sedatives was reported by nine patients (45 %) in the propofol group whereas none of the patients in midazolam group complained of pain during the injection. This is statistically significant. ($P = 0.001$) (Table 1).

The onset of action in propofol group was 60.25 ± 8.66 s (range 50–80 s) and that in Midazolam group was 83.75 ± 11.11 s (range 65–100 s). ($P \leq 0.001$) (Fig. 6).

The average oxygen saturation before induction in propofol group was 99.7 ± 0.73 % and that of midazolam group was 99.15 ± 0.31 % $P = 0.314$. None of the patients in this study developed apnea (Fig. 1).

Table 1 Comparison of incidence of pain

Pain	Group A		Group B	
	No	%	No	%
Absent	11	55.0	20	100.0
Present	9	45.0	0	0
Total	20	100.0	20	100.0

Inference incidence of pain is significantly more in Group A compared to Group B with $P = 0.001^{**}$ (** = Statistical significance)

The heart rate (Mean $\pm$ SD) before induction in propofol group was 81.30 ± 13.25 beats/min and that of midazolam group was 78.80 ± 14.16 beats/min ($P = 0.568$) (Fig. 2). Following administration of sedative and local anesthesia the heart rate increased from the base line value in both the groups and this increased heart rate remained throughout the procedure. The maximum increase in heart rate in propofol group was at 10 min intraoperatively (Mean $\pm$ 80.40 ± 12.73) and that of midazolam group was at 15 min intraoperatively (Mean 79.25 ± 13.44). Post operatively the heart rate decreased near to the baseline value in both the groups. None of the patients developed cardiac arrhythmias.

The systolic blood pressure (Mean $\pm$ SD) before induction in propofol group was 127.20 ± 11.54 mmHg and that of midazolam group was 128.00 ± 13.54 mmHg ($P = 0.842$) (Fig. 3). In both the groups the systolic blood pressure decreased from the baseline value after the administration of sedatives.

The diastolic blood pressure (Mean $\pm$ SD) before induction in propofol group was 82.50 ± 10.4 mmHg and that of midazolam group was 85.05 ± 8.03 mmHg ($P = 0.391$) (Fig. 4). In both the groups the diastolic blood pressure decreased from the baseline value after the administration of sedatives and the decreased diastolic blood pressure was maintained throughout the procedure.

The respiratory rate (Mean $\pm$ SD) before induction in propofol group was 16.35 ± 0.67 cycles/min and that of midazolam group was 16.65 ± 1.35 cycles/min ($P = 0.379$) (Fig. 5). In both the groups the respiratory rate decreased from the baseline value after the administration of sedatives. The decreased respiratory rate remained throughout the surgical procedure. None of the patients in the study group had respiratory rate of less than 14 cycles/min (Fig. 6).

The Recovery time (Mean $\pm$ SD) in propofol group was 22.50 ± 3.04 (range 15–25 min) and that of midazolam group was 33.75 ± 3.93 (range 30–40 min), which was statistically significant ($P < 0.001$) (Fig. 7).

Patients in the propofol group were significantly less co-operative than midazolam group at both 10 and 25 min intra operatively (Fig. 8).

Fig. 1 Comparison of drugs on oxygen saturation [SpO_2].

Inference The average oxygen saturation before induction in Propofol Group was $99.7 \pm 0.73\%$ and that of Midazolam group was $99.15 \pm 0.31\%$. $P = 0.314$

Fig. 2 Comparison of drugs on heart rate (per min) **Fig. 3** Comparison of SBP (mm Hg) between two groups

Discussion

Conscious sedation is a minimally depressed level of consciousness that retains the patient's ability to maintain an airway independently, continuously and respond

appropriately to physical stimulation and verbal command. It is produced by the pharmacologic and non pharmacologic methods or a combination of it. Sedation allows outpatient surgery for many patients who otherwise need general anesthesia.

Fig. 4 Comparison of DBP (mm Hg) between two groups. *Inference* The maximum increase in heart rate in propofol group was at 10 min intraoperatively (Mean $\pm$ 80.40 $\pm$ 12.73) and that of midazolam group was at 15 min intraoperatively (Mean 79.25 $\pm$ 13.44)

Fig. 5 Comparison of respiratory rate between two groups

Fig. 6 Comparison of onset of action in seconds (after loss of lash reflex). *Inference* Onset of action is significantly early in Group A when compared to Group B (60.25 vs. 83.75 s) with $P < 0.001^{**}$

This study examined four measures of therapeutic efficacy: onset of action, recovery period, pain reaction, and patient's co-operation and three measures of clinical toxicity: cardiovascular impairment, respiratory depression and liability to side effects.

Bennet stated that narcotics decreased the discomfort associated with administration of local anesthesia during oral and maxillofacial surgical procedures [3]. Opioids provide strong profound analgesia and sedation with minimal cardiovascular effects [4]. Although the addition of an opioid will increase the potential for respiratory depression, with additional oxygen supplementation and prudent monitoring, it is not problematic.

Pain during the injection of propofol was a complication found in this study. Nine patients (30 %) in the propofol group complained of pain during the injection where as

Fig. 7 Comparison of Recovery period in minutes. *Inference* Recovery is significantly early in Group A compared to Group B with $P < 0.001^{**}$

Fig. 8 Comparison of Co-operative score. *Inference* Patients in the propofol group were significantly less co-operative than midazolam group at both 10 and 25 min intra operatively

none of the patients in midazolam group complained of it. But, once it was explained to the patient that it was normal to have pain along the vein during administration, they did not complain again.

The most common adverse effect of propofol was the pain caused during injection, where as there was no pain recorded during the administration of midazolam [2].

In the current study the onset of action in propofol group was 60.25 ± 8.66 s (range 50–80 s) and that of midazolam group was 83.75 ± 11.11 s (range 65–100 s). Cook et al. [10] in his study stated that onset of action in propofol group (70.6 ± 22.4 s) was significantly more rapid as compared with the midazolam group (106.3 ± 50.7 s).

The arterial oxygen desaturation has always been a significant cause of concern during minor oral surgical procedures, under local anesthesia alone or in combination with sedatives. In our study the oxygen saturation (Mean $\pm$ SD) before induction in propofol group was 99.7 ± 0.73 and that of midazolam group was 99.15 ± 1.31 , ($P = 0.314$). The average oxygen saturation increased from baseline value in

both the study groups after the administration of sedatives and remained above 98 % throughout the procedure. The drugs used in this study propofol, midazolam are known to cause respiratory depression and oxygen desaturation. Many authors recommended the administration of supplemental oxygen during sedation to prevent oxygen desaturation. [4, 11, 15] The increased oxygen saturation after the administration of the sedatives in this study was due to the addition of supplemental oxygen.

Similar results have been obtained by other researchers [2, 12, 16]. None of the patient in this study developed apnea.

Meyers et al. [15] reported no incidence of apnea with propofol sedation in third molar surgery. Tucker et al. [11] reported no incidence of apnea after midazolam sedation with or without Fentanyl for outpatient oral surgical procedures. In a similar study conducted by Parworth et al. [2] there was 4 % incidence of apnea in propofol group and 6 % in midazolam group. The difference may be due to the use of increased dose in their study. Further clinical studies will be required to differentiate the effect of dosage and rate of infusion on apnea.

In this study the heart rate (Mean $\pm$ SD) before induction in propofol group was 81.30 ± 13.25 beats/min and that of midazolam group was 78.80 ± 14.16 beats/min. In both the groups the heart rate increased from the baseline value after the administration of sedatives and local anesthesia. The maximum increase in heart rate in propofol group was just after induction (Mean $\pm$ SD 85.00 ± 12.17) and that of midazolam (Mean $\pm$ SD $79.85.30 \pm 12.66$) group was 5 min intraoperatively.

Post operatively the heart rate decreased near to the baseline value in both the groups. None of the patients developed cardiac arrhythmias. Bennet [15] stated that when propofol is administered a central sympatholytic effect blunts the barostatic reflex resulting in increased heart rate [3]. Meyers et al. reported 13.9 % increase in heart rate after deep sedation with propofol [15]. In a study conducted by Parworth et al. [2] to compare propofol and midazolam each in combination with fentanyl for third molar surgery, there was significant increase in heart rate at 10 and 15 min intraoperatively in both the groups [2].

Dembo [5] stated that propofol causes central sympatholytic effect that serves to maintain stable heart rate. Rodrigo et al. [12] reported a slight increase in heart rate following injection of local anesthesia during patient controlled sedation with midazolam. Rodrigo et al. [12] reported a slight fall in blood pressure following the onset of action of sedative during patient controlled sedation with midazolam.

In the current study the systolic blood pressure decreased from the baseline value after the administration of sedatives in both the groups. Zacharias et al. in their study on patient controlled sedation using midazolam showed that the systolic

blood pressure and heart rate was not significantly affected by the procedure. The mean values of systolic blood pressure ranged between 118 and 129 mm of Hg for the infusion method and 120 and 128 mm of Hg for the patient controlled method.

In another study conducted by Parworth et al. [2] both the groups exhibited statistically significant decrease in diastolic blood pressure at 5, 15 and 20 min period and significant drop in systolic blood pressure at 5 min period [2].

The mean arterial blood pressure decreased from the baseline value after the administration of the sedative and this decreased value remained throughout the procedure. This was statistically significant but clinically non significant.

Dose and rate dependant ventilatory depression is associated with Propofol. Midazolam causes significant respiratory depression. Opioids depress respiration which seen as a decrease in rate of breathing. This is due to dose- dependent decrease in response to the respiratory center to carbon dioxide [4]. A modified study conducted by Parworth et al. [2] showed that there was no significant respiratory depression or decrease in respiratory rate seen in both the groups [2].

In this study there was no much change in the respiratory rate after administration of sedative in both the groups. The difference was not clinically significant and no intervention was required. This may be due to the administration of supplemental oxygen in all patients before administration of the sedatives. None of the patients in the study group had respiratory rate less than 15 cycles/min.

Patients in the propofol group were significantly less co-operative than midazolam group at both 15 and 25 min intra operatively. In a study conducted by Parworth et al. [2] the mean co-operation score of propofol group was significantly more than midazolam group indicating less patient co-operation in propofol group (more the score, less the patient co-operation). This increased score in propofol group was due to the increased talkativeness of patient [14]. However, difference in the co-operation scores cannot be explained by differences in pharmacokinetics between the two sedative techniques.

Recovery is rapid with propofol sedation [3, 9, 14, 15]. A high clearance rate and minimal tendency for drug accumulation contribute to this rapid recovery. Midazolam compared to propofol is usually associated with a more prolonged recovery cognitive function, which may be compounded by excessive postoperative sedation and amnesia [13]. Propofol's major advantage is its rapid recovery, with more clear headedness compared to other sedative agents [4].

The recovery time (Mean $\pm$ SD) in propofol group was 22.50 ± 3.04 (range 15–25 min) and that of midazolam group was 33.75 ± 3.93 (range 30–90 min), which was statistically significant ($P < 0.001$).

Conclusion

The design of the present study permitted qualitative assessment of propofol and midazolam as sedative agents in minor oral surgical procedures. The ideal anesthetic agent should provide rapid onset of action, profound intra operative amnesia while ensuring rapid recovery without much complications.

There were no significant differences in either patient demographics or surgical characteristics between the two groups. The propofol group was less co-operative than midazolam group. Pain during the injection of sedative was a significant adverse effect in the propofol group. Cardiovascular parameters remained stable throughout the procedure in both study groups and no intervention was required. However recovery and onset of action was faster in the propofol group as compared with the midazolam group.

Based on this study the following conclusions have been made

1. Cardiovascular parameters and respiration were well maintained in both the study groups.
2. No incidence of apnea was noticed in both the study groups.
3. Pain during the injection of propofol was a side effect noticed.
4. Onset of action was faster in the propofol group.
5. Propofol group was less co-operative than midazolam group but this was clinically insignificant.
6. Midazolam group showed slower recovery than propofol group restricting and wasting the productive time of the patient.
7. Qualities such as short plasma half-life period, absence of postoperative nausea and vomiting, make propofol a better choice for sedation.

Thus propofol is a fast acting, safe and easily controllable sedative with rapid recovery. This offered the advantage of early patient discharge and better patient compliance.

Summary

In the present study propofol produced rapid onset of action, reliable sedation, good operating conditions, stable vital signs and rapid recovery with practically nil side effects. Pain during the injection of propofol was a complication found in this study. However, the patients were informed about the same and hence did not complain again during the administration.

On the basis of this study, propofol appears to a safe and efficacious alternative to midazolam to use as an intravenous sedative agent in minor oral surgical procedures.

Since the patients in the present study were selected after a careful inclusion and exclusion criteria, it is suggested that larger randomized study covering even patients in high risk category be carried out to assess the efficacy and safety profile of these sedative agents for minor oral surgical procedures.

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