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# COMPARISON BETWEEN PROPOFOL AND MIDAZOLAM FOR AROUSAL TIME IN INFRAUMBILICAL SURGERIES REQUIRING SPINAL ANAESTHESIA.

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Conflicts of Interest: Nil

**ABSTRACT:**

***Introduction****: The use of spinal anesthesia is often limited by the unwillingness of patients to remain awake during surgery. Intravenous sedative medications are useful as positioning for surgery can be uncomfortable and spontaneous movements by an inadequately sedated patient can cause interference with the surgical procedure. Over sedation may compromise the safety of the patient. Also it is not always possible to predict precisely how an individual patient will respond to a particular dose. Over sedation may be associated with deleterious effects of respiratory and cardiovascular depression which results in airway instrumentation and hypotension leading to a prolonged stay in the post-anaesthetic care unit. Bispectral index (BIS) monitoring may be helpful when over sedation has to be avoided as clinical scales do not allow a discrimination of deep sedation.*

***Material and Methods****: A total of 100 patients 50 in each groups were randomly selected and were included in the study. Patients posted for elective infraumbilical operations were included. Weight and height of all patients were noted during the pre-anaesthetic check-up also BMI was calculated. They were also given a demonstration about the use of the 7-point Likert-like verbal rating scale to express their satisfaction about the quality of sedation they would receive during the intra-operative period. In operation theatre blood pressure, electrocardiogram, pulse oximeter was attached to the patient and mean arterial pressure [MAP], heart rate [HR] and peripheral arterial oxygen saturation [$SpO_2$]) were recorded. Spinal anaesthesia was given in the left lateral decubitus position. Injection propofol or injection midazolam was injected through infusion pump as per the study group.*

***Results****: A total of 100 patients were included in the study of which 50 were in the propofol group and 50 were in the midazolam group. No significant difference in propofol and midazolam group was observed in respect to age, sex, BMI, height and weight. The intra-operative parameters (MAP and HR) and the peripheral oxygen saturation (SPO2) were compared at various time points. The MAP and the HR were lower in the Group P than in Group M, but the intra-group MAP and HR in both the groups were stable throughout. The MAP and HR in both the group showed no significant differences in both the group. Also in SPO2 no difference was observed. The mean arousal time from sedation with BIS score 90 with injection propofol was 8.23±2.94 min, whereas, with injection midazolam it was 16.22 ±3.17min, p value < 0.0001 the difference was statistically significant. The time taken to reach an OAA score of 5 was 7.54± 1.98 min with propofol versus 14.59± 3.24 min with midazolam.*

***Conclusion****: A shorter arousal time from sedation during spinal anaesthesia can be achieved using propofol compared with midazolam. Midazolam and propofol are effective sedative agents but the time to reach effective sedation was less with propofol than midazolam and time to recovery time from sedation was lesser with propofol.*

***Keywords****: SPO2, MAP, HR, hypnosis stage, areflexiastage and CNS.*

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## Introduction

Supplemental sedation with an intravenous agent is often required to reduce fear and anxiety in patients' subjected to spinal anaesthesia. The use of spinal anaesthesia is often limited by the unwillingness of patients to remain awake during surgery[i]. Intravenous sedative medications are useful as positioning for surgery can be uncomfortable and spontaneous movements by an inadequately sedated patient can cause interference with the surgical procedure. But there are some constraints on the choice of these supplemental medications, though, as long acting amnesia is also undesirable[ii]. Recently regional techniques have taken an upper hand in anaesthesia over general anaesthesia because of its certain, often underestimated advantages such as lesser chances of airway compromise and aspiration, facilitation of postoperative analgesia, inherent benefit in some pre-existing medical conditions and avoidance of operation theatre pollution. The concept of Monitored Anaesthesia Care has becoming more popular because of the fact that a vigil on patient's vitals and monitoring of various aspects of regional anaesthesia are as important as in general anaesthesia[iii]. Bispectral Index monitoring (BIS) is the best suited tool for monitoring equipment available to the modern anaesthetist[iv].

The term general anaesthesia shows a state in which three principal stages are fulfilled: (a) unconsciousness and amnesia (hypnosis stage), (b) complete analgesia (areflexia stage), and (c) immobilization (muscle relaxation stage)[v,vi].Each phase is accomplished by drug actions at distinct locations within the central nervous system (CNS), and only the inhalation anaesthetics are capable of providing all 3 components. The term "general anaesthetic" is used spuriously when describing potent sedative-hypnotics such as propofol and methohexital. Unconsciousness (deep sedation) alone does not define general anaesthesia and unconsciousness or deep sedation does not define general anaesthesia proper. Patients in the ICU which are on mechanical ventilators also require sedation and analgesia in order to tolerate the endotracheal tube, to prevent dysynchrony with the ventilator, to tolerate the procedures and for optimization of oxygenation and for patient safety[vii].

Over sedation may compromise the safety of the patient. Also it is not always possible to predict precisely how an individual patient will respond to a particular dose. Over sedation may be associated with deleterious effects of respiratory and cardiovascular depression which results in airway instrumentation and hypotension leading to a prolonged stay in the post-anaesthetic care unit, entailing increased burden on staff, bed availability and associated costs[viii]. Midazolam which is a short-acting benzodiazepine is frequently used as a sedative during spinal anaesthesia. It has a property of rapid onset and offset of action after intravenous (IV) injection. It has the advantage of producing anxiolysis and amnesia. Propofol gives hypnosis but a surgical stimulus typically evokes autonomic and somatic reflexes that confirm absence of significant analgesia. Propofol is a non-benzodiazepine anaesthetic agent, and is frequently being used as an IV sedative agent during regional anaesthetic procedures, as it has a quick onset and offset of action with easy arousability. Lower doses of propofol as sedative also produces amnesia and anxiolysis, but has the propensity of greater cardiovascular and respiratory depression when used in higher dose[ix]. Bispectral index (BIS) monitoring may be helpful when over sedation has to be avoided as clinical scales do not allow a discrimination of deep sedation[8].

## Material and Methods

The present study was conducted in the department of Anesthesiology at Rama Medical College Hospital and Research centre Hapur; for comparison of the two drugs propofol and midazolam for intra-operative sedation during spinal anaesthesia in respect to 'arousal time from sedation' following stoppage of infusion. The arousal times were assessed by utilising BIS score. Correlation between the arousal times of propofol and midazolam was observed. Intra-operative hemodynamic changes and patients' satisfaction regarding quality of intra-operative sedation by utilizing 7-point Likert-like verbal rating scale. Patients were fasted for a minimum of 6 hours before surgery. No preoperative opioids or prophylactic antiemetic were given.

A total of 100 patients 50 in each groups were randomly selected and were included in the study. Patients posted for elective infraumbilical operations were included. Patients not willing to accept spinal anaesthesia, those not willing to receive sedation during surgery, or having any contraindication to spinal anaesthesia were excluded. Informed consent was taken from all the patients who were included in the study. Weight and height of all patients were noted during the pre-anaesthetic check-up also BMI was calculated. They were also given a demonstration about the use of the 7-point Likert-like verbal rating scale to express their satisfaction about the quality of sedation they would receive during the intra-operative period.

Premedication was given with injection ranitidine 50 mg, injection tramadol 50 mg, injection ondansetron 4 mg and injection. In operation theatre blood pressure, electrocardiogram, pulse oximeter was attached to the patient and mean arterial pressure [MAP], heart rate [HR] and peripheral arterial oxygen saturation [$SpO_2$]) were recorded. Spinal anaesthesia was given in the left lateral decubitus position. Injection propofol or injection midazolam was injected through infusion pump as per the study group.

Patients in propofol group was given a bolus of propofol (1 mg/kg) followed by infusion of propofol (at 3 mg/kg/hour). The Group midazolam received a bolus of midazolam (0.05 mg/kg), followed by infusion of midazolam at 0.06 mg/kg/h. The infusion was continued until a BIS score of 70 was reached. MAP was measured continually at 5 min intervals and

HR, $SpO_2$ were monitored continuously throughout the surgery. All parameters were documented at 10 min intervals until arousal of the patient. Infusion was stopped 5 min before the end of surgery. Te arousal of the patient was defined as achieving a BIS score of 90.

All data was inserted in Excel sheet and analysed using Statistical Package for the Social Sciences (SPSS) for Windows

**Observations and Results**

A total of 100 patients were included in the study of which 50 were in the propofol group and 50 were in the midazolam group.

**Table 1 Demographic variable of the patients in both groups**

| variable | Propofol group (mean ±SD) n=50 | Midazolam group (mean ±SD) n=50 | P value |
|---|---|---|---|
| **Height in cms** | 159± 10.41 | 158±9.42 | 0.6156 |
| **Weight** | 57.2 ± 11.79 | 56.9± 10.22 | 0.8921 |
| **BMI** | 26± 3.11 | 26.2 ±3.43 | 0.7607 |
| **Age** | 38.4±12.44 | 37.7 ± 11.29 | 0.7689 |
| **Males** | 33 (66%) | 30 (60%) | 0.5364 |
| **Females** | 17 (34%) | 20 (40%) | 0.1167 |

No significant difference in propofol and midazolam group was observed in respect to age, sex, BMI, height and weight.

The intra-operative parameters (MAP and HR) and the peripheral oxygen saturation (SPO2) were compared at various time points. The MAP and the HR were lower in the Group P than in Group M, but the intra-group MAP and HR in both the groups were stable throughout. The MAP and HR in both the group showed no significant differences in both the group. Also in SPO2 no difference was observed.

**Table 2 Recovery of the patients**

| Time | Propofol group | midazolam group | P value |
|---|---|---|---|
| **Arousal time from sedation in min** | 8.23±2.94 | 16.22 ±3.17 | < 0.0001 |
| **Time taken to reach an OAA score of 5** | 7.54± 1.98 | 14.59± 3.24 | < 0.0001 |

OAA: Observers assessment of awareness

The mean arousal time from sedation with BIS score 90 with injection propofol was 8.23±2.94 min, whereas, with injection midazolam it was 16.22 ±3.17min, p value < 0.0001 the difference was statistically significant. The time taken to reach an OAA score of 5 was 7.54± 1.98 min with propofol versus 14.59± 3.24 min with midazolam.

In patients satisfaction score no statistically significant difference was observed

**Discussion and Conclusion:**

BIS provides an idea about the hypnotic state of the patient and also enables titration of anaesthetic agents so as to avoid adverse effects as awareness due to inappropriate dosage as well as unwanted effects of over dosage. Propofol and midazolam both are good sedative both intraoperatively and in an ICU[x]. While using sedation during regional anaesthesia, the anaesthesiologist attempts to titrate the drug to optimize patient comfort while maintaining cardio respiratory stability and intact protective reflexes. The assessment of sedation has been performed by observing clinical parameters such as appearance, response to voice, and pain on surgical stimulation. BIS has advantage of not requiring patient stimulation and provide a quantitative measure. During recovery the MAP reached almost baseline in midazolam group.

In propofol group, MAP remained below baseline in our study. Similar results were shown by Hidaka *et al*[5] in a comparison of the effects of propofol and midazolam on the cardiovascular autonomic nervous system in spinal epidural anaesthesia[xi].

In our study BIS score of 90 i.e. arousal time from sedation was lower with injection propofol than midazolam (Propofol group 8.23±2.94 min and midazolam group 16.22 ±3.17) . Also, the patients became clinically awake earlier (time taken to reach an OAA/S score of 5) when sedated with propofol . 6.81 ± 2.54 min with propofol and 14.59± 3.24min with midazolam. Similar results were observed by Yaddanapudi et al[9] and Bagchi D et al.[xii] Khurana *et al*.[xiii] found a recovery at 10.1 min with propofol compared with 18.6 min with midazolam.

Enhances the Higher clearance rate of propofol (around 30 ml/kg/min) with respect to that of midazolam (6-11 ml/kg/min) reversibility of sedation is more rapid with propofol also, the concentration of propofol in the brain falls rapidly owing to its redistribution, leading to quick recovery. Midazolam in the liver produces an active metabolite, 1-hydroxy midazolam, which may be responsible for its delayed offset of action[12]. Clearance of the drug from the body compartments when an infusion is given, is much lower for propofol than for midazolam. This perhaps explains the earlier recovery from sedation with propofol when compared with midazolam.

Bispectral index monitoring for assessing the level of sedation can help in better titration of propofol and thus it reduces dose requirement of propofol and potential economic benefits compared with clinical monitoring of depth of sedation. Verma *et al*.[xiv] in their study showed that BIS monitoring reduced propofol requirement by 47% during combined spinal epidural anaesthesia. Propofol can cause hypotension when given in bolus or infusion as a result of vasodilatation and negative inotropic action on the heart[xv].

The present study showed that midazolam and propofol are effective sedative agents but the time to reach effective sedation was less with propofol than midazolam and time to recovery time from sedation was lesser with propofol. A shorter arousal time from sedation during spinal anaesthesia can be achieved using propofol compared with midazolam.

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