Original Article

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Comparison between Effects of Diazepam and Propofol as Sedative in Elective Caesarean Section Under Subarachnoid Anaesthesia

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ABSTRACT

Background: Regional anaesthesia has become an important anaesthetic technique now a days. The use of spinal (Subarachnoid) anaesthesia is often limited by the unwillingness of patients to remain awake during surgery. Pharmacologically induced tranquility improves acceptance of regional technique. This study compares diazepam and propofol in terms of onset and recovery of sedation, haemodynamic effects and adverse effects of both the drugs during elective caesarian section under spinal anaesthesia.

Materials and methods: This randomized clinical trial included 60 ASA (American Society of Anaesthesiologists) grade I patients between age 20-40 years underwent elective Caesarean sections under Subarachnoid anaesthesia during the period January 2022 to April 2022. Patients were randomly allocated to one of two groups: Diazepam group (Group D, n=30), who received diazepam in a single dose of 0.15mg/kg and Propofol group (Group p, n=30), who received propofol in a single dose of 0.5mg/kg.

Results: There was no significant difference of mean blood pressure and mean heart rate between the two groups ($p>0.05$). Time of onset of sedation was comparable between the two groups (p value 0.682). Arousal time from sedation was significantly less with propofol ($p<0.001$). Significant percentageof patients was satisfied with diazepam than propofol (83.33% vs 13.33%, $p<0.001$). Incidence of adverse effects were comparable between the two groups ($p>0.05$).

Conclusion: The study showed that duration of sedation was significantly less with propofol than diazepam in single dose technique for sedation in caesarean section which is not beneficial for the patient.

KEY WORDS

Diazepam; Propofol; Sedation; Subarachnoid anaesthesia.

INTRODUCTION

Spinal anaesthesia is the method of choice for elective caesarean section. It allows mother to be involved in the child's delivery but also exposes them to awareness related stress during the procedure. The stress intensity is higher in women undergoing a Caesarean section compared with women delivering spontaneously.[1] The use of pharmacological sedation after extraction of the foetus by caesarean section under subarachnoid anaesthesia is useful in some patients e.g those presenting with high stress. Enhanced stress can result from poor foetal health after delivery, discomfort associated with immobilization on the operating table, chills that accompany anatethesia, nausea, vomiting and environment of operating room.[2]

Sedation is a valuable tool to provide general comfort for the patient. Oversedation may jeopardize the safety of the patient. While levels of sedation progress in a dose response continuum, it is not always possible to predict precisely how an individual patient will respond to a particular dose.[3] Oversedation may be associated with untoward effect of respiratory and cardiovascular depression resulting in higher chances of 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.[4,5] Thus judicious use of sedation can make surgeries under spinal anaesthesia more comfortable for the patient, the surgeon and the anaesthesiologist. As a result, it can increase the patient's acceptance of regional anaesthetic technique.[6]

Diazepam is a long acting benzodiazepine, insoluble in water, so diluted in propylene glycol solution. It has onset of action up to 30 min. and elimination half life of

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20-100 hours as a result of its biphasic elimination. It can be administered Intravenously (IV) Intramuscularly (IM) and orally. It is one of the cheapest benzodiazepines available in market. It has sedative, amnesic and anticonvulsant properties.[7] Propofol, a non-benzodiazepine anaesthetic agent, 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 it has the propensity of greater cardiovascular and respiratory depression when used in higher doses.[8]

The aim of this study was to find out the time of onset and recovery from sedation with diazepam and propofol, to evaluate and compare the properties of both drugs in terms of haemodynamic effects, respiratory effects and adverse effects, as adjuncts to spinal anaesthesia.

METHODS AND MATERIALS

This randomized clinical trial included 60 ASA (American Society of Anesthesiologists) grade I patients between age 20-40 years undergoing elective caesarean sections under Subarachnoid anaesthesia during the period January 2022 to April 2022. The exclusion criteria were positive history of drug allergies, patients suffering from heart disease, hypertension, diabetes, spinal deformity, neurological disorder, any bleeding disorder and unwilling to accept sedation during spinal anaesthesia. Patients were randomly allocated to one of two groups: Diazepam group (Group D, n=30), who received diazepam in a single dose of 0.15mg/kg and propofol group (Group P, n=30), who received propofol in a single dose of 0.5mg/kg. A written informed consent was taken from all patients. Ethical approval was obtained from proper authority. They were fasted for a minimum of 6 hours before surgery. No preoperative opioid or prophylactic antiemetic were given. No other preoperative medication was allowed. All patients were monitored with electrocardiograph, non-invasive blood pressure and pulse oximeter monitor. Baseline vital parameters were recorded. Preloading was done with 300 ml Ringer lactate within 5-10 minutes prior to block. Spinal anaesthesia was conducted by injecting a hyperbaric solution of 0.5% bupivacaine 3ml through a 25G spinal needle at L3-4 level. After spinal block, patients were placed on the operating table in horizontal position. Sedation with diazepam and propofol was administered after extraction of the foetus. O_2 inhalation by ventimask was given when SpO_2 (Saturation Percentage of Arterial Oxygen) came down below 90% and vasopressor was given if MAP (Mean Arterial Pressure) decreased beyond 20% of baseline. MAP was measured continually at 5 min interval and Heart Rate (HR), SpO_2 were monitored throughout the surgery. All parameters were documented at 5 min intervals until arousal of the patient. The onset of sedation i.e. time from iv injection of diazepam or propofol to closure of eye lids and the arousal time from sedation i.e. time from closing of the eye lids to OAA/S (Observer's Assessment of Alertness/ Sedation) score of 5 (Patient is awake clinically) were noted. Any complication during operation was documented. The patient's satisfaction with the sedation was assessed by the 5 point 'Likert verbal rating scale' with some questions like 'where will you put your experience with this sedation on the scale?' in a language which the patient understands, at a point of time when the patient had a mental state suitable for communication.

Observer's Assessment of Alertness/ Sedation (OAA/S) Scale

Category	Observation	Score Level
Responsoveness	Responds readily to name spoken in normal tone	5
	Lethargic response to name spoken in normal tone	4
	Responds only after name is called loudly and/or repeatedly	3
	Responds only after mild prodding or shaking	2
	Does not respond to mild prodding or shaking	1
Speech	Normal	5
	Mild slowing or thickening	4
	Slurring or prominent slowing	3
	Few recognizable words	2
Facial expression	Normal	5
	Mild relaxation	4
	Marked relaxation (Slack jaw)	3
Eyes	Clear, no ptosis	5
	Glazed, or mild ptosis (Less than half the eye)	4
	Glazed and marked ptosis (half of the eye or more)	3

Figure 1 Likert Scale for satisfaction

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Data were analysed using Statistical Package for the Social Science (SPSS) for Windows (Version 12.0, SPSS Inc,. Chicago, IL, USA). Independent 't' test was used for age, weight, duration of surgery, time for recovery, heart rate, mean arterial pressure and SpO_2 at various time intervals. Chi square test was applied for adverse effects and oxygen supplementation. Paired 't' test was applied for intra-group variation in heart rate and mean arterial pressure. Data were expressed in mean, SD and percentage. $p<0.05$ was taken to be of statistically significant.

RESULTS

In this randomized clinical trial, 60 patients (30 in each group) were taken. The Group D (Diazepam group) and Group P (Propofol group) were found to be comparable in respect of age, weight, duration of surgery (time from surgical incision to surgical closure) (Table I).

Table I Demographic data of the patients under study (n=60)

Variable	Group D(n=30)	Group P(n=30)	p value
Age (Years)	29.49±5.4	30.53±5.4	0.753
Weight (Kg)	67.39±10.8	66.33±9.8	0.831
Duration of surgery (min)	49.66±5.6	49.61±5.3	0.865

Values are expressed in mean±SD
SD- Standard Deviation.

There was no significant difference in Mean arterial pressure between the two groups before spinal anaesthesia (Baseline) after spinal block and before sedative drug administration. Fall in mean arterial pressure was observed in both groups immediately after drug administration but that was not statistically significant (Table II).

Table II Comparison of MAP (mmHg) in study groups at various time intervals (n=60)

Time Interval	Group D (n=30)	Group P (n=30)	p value
Before Anaesthesia (Baseline)	83.3±7.54	83.1±8.54	0.768
After Spinal block	77.7±5.47	75.5±6.47	0.656
Before drug administration	74.4±7.39	74.4±6.41	0.781
After drug administration	72.7±6.43	71.1±7.28	0.661

Values are expressed in mean±SD
SD- Standard Deviation.

There was no significant difference in mean heart rate between the two groups before spinal anaesthesia (baseline) after spinal block and before sedative drug administration. Rise in mean heart rate was observed inboth groups immediately after drug administration but that was not statistically significant (Table III). Mean values of SpO_2 remained stable throughout the surgical procedure in both the groups, with no statistically significant aberrations ($p>0.5$).

Table III Comparison of mean heart rate (bpm) in study groups at various time intervals (n=60)

Time Interval	Group D (n=30)	Group P (n=30)	p value
Before Anaesthesia (Baseline)	77.9±11.89	78.3±12.69	0.852
After Spinal block	85.3±11.93	84.9±11.97	0.771
Before drug administration	77.6±11.86	78.7±12.39	0.763
After drug administration	83.4±9.87	90.5±2.08	0.085

Values are expressed in mean±SD
SD- Standard Deviation.

Time of onset of sedation was comparable between the two groups (p value 0.682) but arousal time from sedation was significantly less with propofol ($p<0.001$). Significant percentage of patient was satisfied with diazepam than propofol ($p<0.001$) (Table IV).

Table IV Comparison of Sedation characteristics in study groups (n=60)

Variable	Group D (n=30)	Group P (n=30)	p value
Time required for onset of sedation (Eye closure) (min)	1.39±0.41	1.49±0.51	0.682
Arousal time from sedation in min (OAA/S score of 5)	45.3±5.32	10.3±2.37	<0.001
Satisfaction with sedation (Good)	25 (83.33%)	4 (13.33%)	<0.001

Values are expressed in mean±SD
SD- Standard Deviation.

Although incidence of pain in arm was more with diazepam than propofol, it was not statistically significant (p value 0.241) (Table V).

Table V Incidence of complications in study groups (n=60)

Variable	Group D (n=30)	Group P (n=30)	p value
Nausea and Vomiting	5 (16.7%)	4 (13.33%)	0.862
Chills	3 (10%)	3 (10%)	0.946
Restlessness	4 (13.33%)	6 (20%)	0.673
Pain in arm	30 (100%)	24 (80%)	0.241

DISCUSSION

The most widely used technique for administering sedation in regional anaesthesia is the intermittent bolus dose technique. This technique has been shown to be associated with peaks and troughs in plasma concentration producing significant side effects and delayed recovery.[9] Continuous infusions have been proved to produce, lesser side effects, faster recovery, easy controllability over the desired depth of sedation but requires some especial equipment e.g. syringe pump, BIS monitor etc, which is expensive and not available everywhere. Moreover, it needs more expertise like interpretation of EEG.[10]

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When using sedative medication during regional anaesthesia technique, the anaesthesiologist attempts to titrate the drug to optimize patient comfort while maintaining cardiorespiratory stability and intact protective reflexes. The assessment of depth of sedation has been traditionally performed by observing clinical parameters such as appearance, response to voice, and pain on surgical stimulation. These parameters are qualitative and assessment of response to voice requires patient stimulation, which may itself alter depth of sedation.[11]

We chose the OAA/S scale for assessment of sedation over other scales as it was easier to use, comprehensive and inclusive of parameters such as facial expression and eyelid ptosis in addition to speech and responsiveness, which are not there in other sedation scales.[12] Similarly the OAA/S scale has been shown to have an inter-rater agreement that varies between 85% and 96% depending on the level of sedation, which is higher than most of the other scales used for the same purpose, making it the most suitable choice if precise assessment of sedation is required.[10]

Benzodiazepines via GABAergic receptors produce anxiolysis as well as sedation and anterograde amnesia. Diazepam is a long acting benzodiazepine, which is insoluble in water and has an onset of action upto 30 min. It has long half life of 20-80 hrs as a result of its biphasic elimination. It can also be administered intramuscularly or intravenously. Benzodiazepines at higher doses leas to cardiorespiratory depression, so require monitoring.[7] Propofol via Gamma Amino Butyric Acid (GABA) receptors produce sedation, anxiolysis and amnesia in subhypnotic doses. It is associated with faster onset in achieving the desired sedation score and faster offset of sedation leads to less post-operative impairment of recall with clear headed rapid recovery and higher patient satisfaction. Propofol at higher doses leads to hypotension, bradycardia and respiratory depression. In addition, propofol has antiemetic effect which leads to decreased incidence of nausea and vomiting especially during eye surgeries.[13]

In midazolam group, blood pressure, heart rate and SpO_2 were lower. Postoperative recovery was similar in the two groups. After midazolam, patients experienced greater amnesia for local anaesthesia and drowsiness. Satisfaction was high with both treatments.The recovery and satisfaction were comparable in the two groups.[14] In our study, we did not quantify the level of sedation, because we thought that it would cause interruption of sedation. There was no significant difference of blood pressure changes, heart rate and saturation between diazepam and propofolgroups. Patient's satisfaction was significantly more in diazepam group. Recovery characteristics were not included in our study.

Agbakwuru et al carried out a prospective observational study on 50 adult patients who underwent hydrocelectomy using intramuscular diazepam sedation and spermatic cord block with 0.5% plane xylocaine. 4% of the patients were converted to general anaesthesia. All patients except one preferred to have future surgery under such local anaesthesia and sedation.[15] In our study, we compared the sedative characteristics between diazepam and propofol during spinal anaesthesia which showed better outcome with Diazepam.

The physicians were more comfortable in performing endoscopic procedure in sedated patients, however, the difference between patients in diazepam group and midazolam group was not statistically significant (p= 0.0461). They concluded that both diazepam and midazolam fared equally well in increasing physician's comfort (p=0.617) and there was no difference in the patient's discomfort with regard to the sedative used (Midazolam or diazepam).[16] In our study, we did not include placebo and patient's satisfaction was measured by 'Likert like Scale'. Surgeon's satisfaction was not included in our study. Patients satisfaction was significantly more with diazepam than propofol in our study.

Rasooli et al conducted a randomized, double-blind, placebo controlled clinical trial on 90 parturients, ASA I & II, aged 20-30 years, who underwent spinal anaesthesia for caesarean section, randomly allocated to one of three groups receiving midazolam or propofol infusion immediately after umbilical cord clamping and compared to placebo. Bupivacaine hydrochloride (10 mg) was used for spinal anaesthesia. The incidence of nausea, retching and vomiting was significantly higher in the control group compared to propofol and midazolam groups. Overall IONV (Intra Operative Nausea and Vomiting) and PONV (Post-operative Nausea and Vomiting) in midazolam group was as low as propofol group without any significant haemodynamic changes as seen in placebo group or even with propofol group.[17] In our study, incidence of intra-operative nausea and vomiting was comparable between diazepam and propofol group. There was no significant haemodynamic changes (Mean arterial pressure and mean heart rate) between diazepam and propofol.

LIMITATION

The intervention was not placebo controlled and blinded to neither clinicians nor patients. Additionally, group sizes were small. Consequently the clinical relevance remains undetermined and further studies are necessary to confirm potential benefits between the two commonly used sedatives.

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CONCLUSION

The study showed that duration of sedation was significantly less with propofol than diazepamin single dose technique for sedation in caesarean section which is not beneficial for the patient.

RECOMMENDATION

The study shows that, patients satisfaction was significantly more with diazepam. Thus it is recommended that diazepam is a better choice that propofol for sedation in single dose technique during subarachnoid block for c/s.

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DISCLOSURE

All the authors declared no competing interest.

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