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Comparison between Effects of Propofol and Dexmedetomidine as Sedative in Elective Caesarean Section under Subarachnoid Anaesthesia

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Abstract

Background: The use of spinal (subarachnoid) anaesthesia is often limited by the unwillingness of patients to remain awake during surgery. **Objective:** This study was undertaken to compare propofol and dexmedetomidine in terms of onset and recovery of sedation, haemodynamic effects, respiratory effects and adverse effects of both the drugs during elective Caesarian section under spinal anaesthesia. **Methodology:** This randomized clinical trial included 60 ASA (American Society of Anaesthesiologists) grade I patients undergoing elective Caesarean sections under Subarachnoid anaesthesia during the period January 2022 to June 2022. Patients were randomly allocated to one of two groups designated as Propofol group (Group A, n=30), who received Propofol in a single dose of 0.5mg/kg and Dexmedetomidine group (Group B, n=30), who received Dexmedetomidine in a single dose of 2mcg/kg. The onset of sedation i.e. time from iv (intravenous) injection of propofol or dexmedetomidine to closure of eye lids (OAA/S score of 3) and the arousal time from sedation i.e. time from closing of the eye lids to OAA/S score of 5 (patient is awake clinically) were noted. Any complication during operation was documented. **Results:** There was no significant difference of mean blood pressure and mean heart rate between the two groups in different time intervals (P>0.05). Time of onset of sedation was significantly delayed in Dexmedetomidine group (P<0.05). The arousal time i.e. duration of sedation was significantly longer with Dexmedetomidine than Propofol (P<0.05). Propofol was associated with significantly higher incidence of some adverse effects like pain in arm during drug administration than Dexmedetomidine (46.66% vs 10.0%, P<0.05). Significant percentage of patients was satisfied with dexmedetomidine than propofol (86.66% vs 13.33%, P<0.001). **Conclusion:** Duration of sedation is significantly longer with dexmedetomidine than propofol which is beneficial for the patient in single dose technique for sedation. *[Journal of National Institute of Neurosciences Bangladesh, January 2023;9(1):65-70]*

Keywords: Propofol; dexmedetomidine; 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].

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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].

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[7]. Dexmedetomidine is a highly selective α2 agonist that has sedative, analgesic, anxiolytic and amnesic effects without a significant respiratory depression. It displays a dose dependent blood pressure response. It has a sympatholytic effect through decreasing the concentration of norepinephrine which in turn decreases the heart rate and blood pressure[8].

There are a good number of studies regarding the use of sedative agents during regional anaesthesia but it is scarce in case of Caesarian section where a pregnant woman has anatomical and physiological changes from a non-pregnant woman. The aim of this study was to compare the time of onset and recovery from sedation with Propofol and Dexmedetomidine, to evaluate and compare the properties of both drugs in terms of haemodynamic effects, respiratory effects and adverse effects, as adjuncts to spinal anaesthesia.

Methodology

Study Settings and Population: This randomized clinical trial included 60 ASA (American Society of Anesthesiologists) grade I patients between age 20 to 40 years undergoing elective Caesarean sections under Subarachnoid anaesthesia during the period January 2022 to June 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.

Randomization and Allocation: Patients were randomly allocated to one of two groups: Propofol group (Group P, n=30), who received Propofol in a single dose of 0.5mg/kg and Dexmedetomidine group (Group D, n=30), who received Dexmedetomidine in a single dose of 2mcg/kg (over 10min). 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 300ml Ringer lactate within 5 t o10 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 to 4 level. After spinal block, patients were placed on the operating table in horizontal position. Sedation with Propofol and Dexmedetomidine was administered after extraction of the fetus. O2 inhalation by ventimask was given when SpO2 (saturation percentage of arterial oxygen) came down below 90% and vasopressor was given if MAP (mean arterial pressure) decreased beyond 20% of baseline.

Follow Up and Outcomes Measure: MAP was measured continually at 5 min interval and heart rate (HR), SpO2 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 Propofol or Dexmedetomidine to closure of eye lids (OAA/S score of 3) and the arousal time from sedation i.e. time from closing of the eye lids to OAA/S (Observer's Assessment of Alertness/ Sedation)5 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'5 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.

Statistical Analysis: Statistical analysis was performed by Windows based software named as Statistical Package for Social Science (SPSS), versions 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Continuous data were expressed as mean, standard deviation, minimum and maximum. Categorical data were summarized in terms of frequency counts and percentages. Chi-square test was used for comparison of categorical variables and Student t test was applied for continuous variables. Every effort was made to obtain missing data. A two-sided P value of less than 0.05 was considered to indicate statistical significance. Differences between two groups were tested. Independent 't' test was used for age, weight, duration of surgery, time for recovery, heart rate, mean arterial pressure and SpO2 at various time intervals. Chi square test was applied for adverse effects. Paired 't' test was applied for intra-group variation in heart rate and mean arterial pressure.

Ethical Clearance: Written informed consent were taken from all participants. Ethical approval was obtained from proper authority. All the procedures of the present study were carried out in accordance with the International Conference on Harmonization Good Clinical Practice guidelines and the principles for human investigations (i.e., Helsinki Declaration) and also with the ethical guidelines of the Institutional research ethics. Before starting the study, the study protocol, patient information sheet, and informed consent form were approved by the independent ethics committees of the study place and the competent regulatory authorities in accordance with local legal requirements in participating centre. Formal ethics approval was granted by the local IRB. Participants in the study were informed about the procedure and purpose of the study and confidentiality of information provided. All participants consented willingly to be a part of the study during the data collection periods. All data were collected anonymously and analyzed using the coding system.

Results

A total number of 60 respondents (30 in each group) were included in this randomized clinical trial. the group A (propofol group) and group B (dexmedetomidine group) were found to be comparable in respect of age, weight, duration of surgery (time from surgical incision to surgical closure) (Table 1).

Table 1: Demographic data of the Patients Under Study (n=60)

Variable	Group A (n=30)	Group B (n=30)	P value
Age (years)	30.53±5.4	29.10±4.6	0.731
Weight (kg)	66.33±10.8	67.53±8.7	0.756
Duration of surgery (min)	49.61±5.3	50.65±3.4	0.779

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, before sedative drug administration and after drug administration (Table 2).

There was no significant difference in Mean heart rate between the two groups before Spinal anaesthesia (baseline), after spinal block, before sedative drug administration and after drug administration (Table 3)

Table 2: Comparison of MAP (mmHg) in study groups at various time intervals (n=60)

Time Interval	Group A (n=30)	Group B (n=30)	P value
Before Anaesthesia (baseline)	83.1±8.54	80.2±6.88	0.749
After Spinal block	75.5±6.47	75.7±5.43	0.754
Before drug administration	74.4±6.41	74.1±6.42	0.744
After drug administration	71.1±7.28	71.7±8.39	0.739

Values are expressed in mean±SD; SD- Standard deviation

Mean values of SpO2 remained stable throughout the surgical procedure in both the groups, with no statistically significant aberrations (P>0.5).

Table 3: Comparison of mean heart rate (bpm) in Study Groups at Various Time Intervals (n=60)

Time Interval	Group A (n=30)	Group B (n=30)	P value
Before Anaesthesia (baseline)	78.3±12.69	78.4±10.39	0.713
After Spinal block	84.9±11.97	88.1±10.51	0.578
Before drug administration	78.7±12.39	78.6±9.84	0.656
After drug administration	83.5±10.08	81.5±11.18	0.483

Values are expressed in mean±SD; SD- Standard deviation

Time of onset of sedation was significantly delayed in Dexmedetomidine group (P<0.05). Duration of sedation i.e. time for arousal from sedation was significantly longer in Dexmedetomidine group (P<0.05). Significant percentage of patient was satisfied with Dexmedetomidine than Propofol (86.66% vs 13.33%, P<0.001) (Table 4).

Table 4: Comparison of Sedation characteristics in study groups (n=60)

Variable	Group A (n=30)	Group B (n=30)	P value
Time required for onset of sedation (eye closure) (min)	1.49±0.51	6.54±2.51	<0.05
Arousal time from sedation in min (OAA/S score of 5)	10.3±2.37	26.2±5.38	<0.05
Satisfaction with sedation (good)	4(13.33%)	26(86.66%)	<0.001

Values are expressed in mean±SD; SD- Standard deviation

Incidence of pain in arm during drug administration was significantly more in Propofol group (P <0.05). Other complications were comparable between the two groups (Table 5).

Table 5: Incidence of Complications in Study Groups (n=60)

Variable	Group A (n=30)	Group B (n=30)	P value
Nausea and Vomiting	8 (26.7%)	4 (13.3%)	0.231
Chills	4 (13.3%)	2 (6.7%)	0.226
Restlessness	7 (23.3%)	4 (13.3%)	0.388
Pain in arm	14(46.7%)	3 (10.0%)	<0.05

Discussion

Pregnant women undergoing elective Caesarean sections under Subarachnoid anaesthesia are often anxious about the unpleasant experience associated with awareness during surgery. After being informed about the possible use of sedative after baby extraction, the patients usually more eagerly accept this suggested method of anaesthesia[2].

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 equipments e.g. syringe pump, BIS monitor which is expensive and not available everywhere. Moreover, it needs more expertise like interpretation of EEG[10].

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].

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]. Dexmedetomidine, a potent and highly selective α2-adrenoceptor agonist, has been safely used to sedate patients under regional anaesthesia. It induces potent sedation through its action on the locus coeruleus, the predominant brainstem nucleus involved in sleep regulation and respiratory control. Compared to traditional sedatives patients treated with dexmedetomidine have better arousability and cooperation, minimal respiratory depression, and better postoperative cognitive function. Dexmedetomidine is usually given initially as a bolus, followed by continuous infusion. Single-dose dexmedetomidine can also provide adequate sedation during short procedures under spinal anaesthesia[14].

Danielak-Nowak et al[2] conducted a prospective randomized study on 56 pregnant women who were sedated with propofol or midazolam via intravenous infusion after extraction of the foetus. A desired level of sedation was easier to obtain in the propofol group (77.7% vs 55.1%), whereas excessive sedation was noted more frequently in the midazolam group (34.5% vs 11.5%). The mean heart rate and arterial pressure were lower in propofol group. No ECG alteration was observed in any patient. SpO2 was comparable in both the groups. The incidence of nausea and vomiting were higher in the midazolam group. Satisfaction with sedation was comparable in both the groups. They concluded that propofol appears to be more useful for Caesarean section sedation when compared with midazolam because of its shorter action, antiemetic effect and better maternal recall of foetal delivery[2]. In our study, we compared the sedative effects between

Propofol and Dexmedetomidine in single dose technique where duration of sedation with Propofol was inadequate. Haemodynamic profile was not changed significantly with Propofol. Satisfaction with sedation was significantly less with Propofol.

Rasooli et al[15] conducted a randomized, double-blind, placebo controlled clinical trial on 90 parturients, ASA I &II, aged 20-30 years, who undergone 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[15]. In this study, incidence of nausea and vomiting was comparable between Propofol and Dexmedetomidine. Control group was not included in this study.

Jo et al[16] conducted a randomized trial on 116 adult patients, who were assigned to receive either midazolam (n=58) or dexmedetomidine (n=58) during spinal anaesthesia. Systolic, diastolic, and mean arterial pressure; heart rate, peripheral oxygen saturation, and bispectral index scores were recorded during surgery, and Ramsay sedation scores and postanaesthesia care unit (PACU) stay were monitored. Hypotension occurred more frequently in the midazolam group ($P<0.001$) and bradycardia occurred more frequently in the dexmedetomidine group ($P<0.001$). Mean Ramsay sedation score was significantly lower in the dexmedetomidine group after arrival in the PACU ($P=0.025$) and PACU stay was significantly longer in the dexmedetomidine group ($P=0.003$). They concluded that BIS guided dexmedetomidine sedation can attenuate intraoperative hypotension, but induces more bradycardia, prolongs PACU stay, and delays recovery from sedation in patients during and after spinal anaesthesia as compared with midazolam sedation[16]. In this study, haemodynamic effects of Propofol and Dexmedetomidine were comparable. There was no incidence of bradycardia with dexmedetomidine. Recovery from sedation was significantly longer with Dexmedetomidine. Duration of PACU stay was not included in this study.

Hasan[8] conducted a randomized clinical trial to compare two techniques of moderate sedation for patients undergoing ERCP, using either dexmedetomidine or ketofol as regards haemodynamic, sedation, pain, respiratory effect, recovery time, patients' and endocopists' satisfaction, and complications during and after the procedure. Fifty patients were randomly allocated in one of two groups; dexmedetomidine group D (n=25) received 1mcg/kg i.v. bolus over 10 min followed by 0.5mcg/kg/h or ketamine-propofol (ketofol) group KP (n=25) received 1mg/kg i.v. bolus followed by 50mcg/kg/min. After loading dose, HR and MAP were significantly lower in group D as compared with group KP ($P<0.05$). HR was significantly lower in group D during the recovery ($P<0.05$). No significant difference between both groups as regards time to achieve RSS, MAS, FPS and total dose of rescue sedation. Personnel restraint was significantly lower in group KP (8% versus 20%) than in group D. Endoscopists' satisfaction was significantly higher in group KP than D group (92% and 80%) respectively. He concluded that ketofol (1:1) provided better haemodynamic stability than dexmedetomidine and standard alternative to it in moderate sedation during ERCP[8]. In this study, we compared the effects between Propofol and Dexmedetomidine. Dexmedetomidine showed stable haemodynamic effects. Patients' satisfaction was significantly more with Dexmedetomidine. Surgeons' satisfaction was not included in our study.

There are some limitations of this study. The intervention was not placebo controlled and blinded to neither clinicians nor patients. Additionally, group sizes were small and it was a single centre study. Consequently, the clinical relevance remains undetermined and further studies are necessary to confirm potential benefits between the two drugs.

Conclusion

In conclusion the arousal time i.e. duration of sedation is significantly longer with Dexmedetomidine which is beneficial for the patient in single dose technique for sedation. Propofol is associated with high incidence of some adverse effects like pain in arm during drug administration. Thus it is recommended that Dexmedetomidine is a better choice than Propofol for sedation in single dose technique during subarachnoid block for Caesarean section.

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Conflict of interest: There is no conflict of interest relevant to this paper to disclose.

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Contribution to authors: Md Enayet Karim was involved in protocol preparation, data collection, literature search and manuscript writing. RAM Mustafijur Rashid and Mohammad Saleh Akram were involved in data collection and testing. Reza Ershad was involved in review of the article. All the authors have read and approved the final version of the manuscript.

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate
Ethical approval for the study was obtained from the Institutional Review Board. As this was a prospective study the written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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