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Original Article

Comparison between Effects of Fentanyl and Dexmedetomidine 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 Fentanyl 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.*

Materials and methods: *This randomized clinical trial included 60 ASA (American Society of Anaesthesiologists) grade I patients between age 20-40 years undergoing elective caesarean sections under subarachnoid anaesthesia during the period January 2022 to June 2022.Patients were randomly allocated to one of two groups: Fentanyl group (Group F, n=30), who received Fentanyl in a single dose of 0.5mcg/kg and Dexmedetomidine group (Group D, n=30), who received Dexmedetomidine in a single dose of 2mcg/kg. Spinal anaesthesia was conducted by injecting a hyperbaric solution of 0.5% bupivacaine 3ml through a 25G spinal needle at L3-4 level. All parameters were documented at 5 min intervals until arousal of the patient. The onset of sedation i.e. time from iv (Intravenous) injection of Fentanyl 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. The patient's satisfaction with the sedation was assessed by the 5 point 'Likert verbal rating scale.'*

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 comparable between Fentanyl and Dexmedetomidine (p value 0.210). The arousal time i.e. duration of sedation was significantly longer with Dexmedetomidine than Fentanyl ($p<0.05$). Fentanyl was associated with significantly higher incidence of some adverse effects like nausea, vomiting than Dexmedetomidine (46.66% vs 13.33%, $p<0.05$). Significant percentage of patients was satisfied with Dexmedetomidine than Fentanyl (86.66% vs 20%,$p<0.001$).*

Conclusion: *The study showed that the arousal time i.e. duration of sedation was significantly longer with Dexmedetomidine which is beneficial for the patient in single dose technique for sedation. Moreover, Fentanyl was associated with high incidence of some adverse effects like nausea, vomiting. Thus it is recommended that Dexmedetomidine is a better choice than Fentanyl for sedation in single dose technique during subarachnoid block for caesarean section.*

Key words: Dexmedetomidine; Fentanyl; Sedation; Subarachnoid anaesthesia.

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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]

Fentanyl is a potent narcotic analgesic with rapid onset and short duration of effect following a single intravenous dose. It provides analgesia with sedation but it has the propensity of respiratory depression when used in higher doses.[7] Dexmedetomidine is a highly selective α 2 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]

The aim of this study was to compare the time of onset and recovery from sedation with Fentanyl 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.

MATERIALS AND METHODS

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 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. Patients were randomly allocatedto one of two groups: Fentanyl group (Group F, n=30) who received Fentanyl in a single dose of 0.5mcg/kg and Dexmedetomidine group (Group D, n=30) who received Dexmedetomidine in a single dose of 2mcg/kg. Written informed consent were taken from all participants. 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 300ml Ringer lactate within 5-10 minutes prior to block. Spinal anaesthesiawas 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 Fentanyl and Dexmedetomidine 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 Fentanyl 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) 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
Responsiveness	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

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. 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

60 respondents (30 in each group) were included in this randomized clinical trial. The Group F (Fentanyl group) and Group D (Dexmedetomidine group) were found to be comparable in respect of age, weight, duration of surgery (Time from surgical incision to surgical closure) (Table I).

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 II).

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 III). Mean values of SpO_2 remained stable throughout the surgical procedure in both the groups, with no statistically significantaberrations ($p>0.5$).

Time of onset of sedation was comparable between the two groups (p value 0.210). Duration of sedation i.e time for arousal from sedation was significantly more in Dexmedetomidine group ($p<0.05$). Significant percentage of patient was satisfied with Dexmedetomidine than Fentanyl (86.66% vs 20%, $p<0.001$) (Table IV).

Incidence of nausea and vomiting was significantly more in Fentanyl group ($p <0.05$). Other complications were comparable between the two groups (Table V).

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

Variable	Group F(n=30)	Group D (n=30)	p value
Age (years)	30.46±4.5	29.10±4.6	0.713
Weight (kg)	66.53±9.8	67.53±8.7	0.761
Duration of surgery (min)	48.66±3.6	50.65±3.4	0.679

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

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

Time Interval	Group F (n=30)	Group D (n=30)	p value
Before Anaesthesia (baseline)	83.1±6.53	80.2±6.88	0.651
After Spinal block	77.5±5.69	75.7±5.43	0.643
Before drug administration	73.6±6.57	74.1±6.42	0.734
After drug administration	72.1±7.28	71.7±8.39	0.739

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

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

Time Interval	Group F (n=30)	Group D (n=30)	p value
Before Anaesthesia (Baseline)	79.6±11.69	78.4±10.39	0.737
After Spinal block	86.5±11.97	88.1±10.51	0.688
Before drug administration	82.6±12.31	78.6±9.84	0.551
After drug administration	86.5±2.08	81.5±11.18	0.381

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

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

Variable	Group F (n=30)	Group D (n=30)	p value
Time required for onset of sedation (Eye closure) (min)	4.3±0.25	6.54±2.51	0.210
Arousal time from sedation in min (OAA/S score of 5)	9.3±2.37	26.2±5.38	<0.05
Satisfaction with sedation (Good)	6 (20%)	26 (86.66%)	<0.001

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

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

Variable	Group F (n=30)	Group D (n=30)	p value
Nausea and Vomiting	14 (46.66%)	4 (13.33%)	<0.05
Chills	3 (10%)	2 (6.66%)	0.526
Restlessness	6 (20%)	4 (13.33%)	0.488
Pain in arm	2 (6.66%)	3 (10%)	0.526

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 equipments e.g. syringe pump, BIS monitor etc, 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 maintaning 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]

Opioids bind to specific receptors located throughout the central nervous system and other tissues. Four major types of receptors have been identified. Fentanyl bind mostly to mu (μ) receptor. Opioid receptor activation inhibits the presynaptic release and post synaptic response to excitatory neurotransmitters (e.g. acetylcholine, substance P) from nociceptive neurons. The cellular mechanism for this neuromodulation may involve alteration in potassium and calcium ion conductance.[13]Dexmedetomidine, a potent and highly selective α 2-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]

Minami et al. conducted a prospective clinical trial on safety and discomfort during bronchoscopy performed under sedation with Fentanyl and Midazolam. Fentanyl 20 mcg was administered to the patients just before bronchoscopy, and Fentanyl (10 mcg) and Midazolam (1mg) were added as needed during the procedure. A questionnaire was completed 2 hours after the examination. 70.2% patients agreed to undergo a second bronchoscopic examination and only 37.8% of the patients remembered the bronchoscopic examination. No severe complication was reported.[15] In our study, we compared the sedative effect between Fentanyl and Dexmedetomidine during Caesarean section which showed more favorable sedative effect with Dexmedetomidine. Fentanyl was associated with more adverse effects like nausea and vomiting than Dexmedetomidine.

Frolich et al. conducted a double blinded, randomized, placebo controlled trial, where 60 healthy pregnant women received either a combination of Fentanyl (1mcg/kg) and Midazolam (0.02mg/kg) intravenously or an equal volume of iv saline at the time of their skin preparation for a bupivacaine spinal anaesthetic. Foetal outcome measures included Apgar Score, continuous pulse oximetry, and neurobehavioral Scores. Maternal outcomes included catecholamine levels, recall of anaesthesia and delivery. There were no between-group differences of neonatal outcome variables. Mothers in both groups showed no difference in their ability to recall the birth of the babies. So, they concluded that maternal analgesia and sedation with Fentanyl and Midazolam immediately prior to spinal anaesthesia is not associated with adverse neonatal effects.[16] In our study, we compared the sedative effect between Fentanyl and Dexmedetomidine after delivery of the baby which showed more favorable sedative effect with Dexmedetomidine. Foetal outcome was not included in our study. Maternal satisfaction was significantly more with Dexmedetomidine.

Jo et al. 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 Post Anaesthesia 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.[17] In our study, haemodynamic effects of Fentanyl 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 our study.

In our study, we compared the effects between Fentanyl and Dexmedetomidine. Dexmedetomidine showed stable haemodynamic effects. Patients' satisfaction was significantly more with Dexmedetomidine.

LIMITATIONS

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 drugs.

CONCLUSION

The study showed that the arousal time i.e. duration of sedation was significantly longer with Dexmedetomidine which is beneficial for the patient in single dose technique for sedation. Moreover, Fentanyl was associated with high incidence of some adverse effects like nausea, vomiting.

RECOMMENDATION

It is recommended that Dexmedetomidine is a better choice than Fentanyl for sedation in single dose technique during subarachnoid block for Caesarean section.

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DISCLOSURE

All the authors declared no competing interest.

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