Original Article

Comparison of Three Doses of Dexmedetomidine on Cardiovascular, Maternal and Neonatal Outcome in Patients undergoing Elective Caesarean Delivery

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ABSTRACT

Background: Many institutions frequently use general anaesthesia (GA) when a patient refuses neuraxial anaesthesia or when there is an urgent need for a caesarean delivery, even though central neuraxial blocking is now the preferred method. There is need to find effective drug and best dose to attenuate endocrine and haemodynamic respone of caesarean section under GA.

Objective: To compare the impact of pre-operative IV administration of dexmedetomidine (0.2, 0.4, and 0.6 µg/kg/h) on perioperative maternal hemodynamic, maternal and neonatal outcome.

Methods: Twenty minutes before to inducing anaesthesia, the three groups (n = 30 each) were given an IV infusion of 0.1 mL/kg/h of a solution comprising 2, 4, as well as 6 µg/mL of "dexmedetomidine (DEX 0.2, DEX 0.4, and DEX 0.6, respectively)". Two-thirds of the infusion rates were cut to 0.03 mL/kg/h following peritoneal closing, and this reduction was maintained until skin closure. Maternal outcome, haemodynamic parameters and neonatal outcomes were recorded.

Results: There was significantly greater uterine relaxation with more need of oxytocin in lower doses of dexmedetomidine (p <0.001 and p = 0.0002 respectively). Time to extubation was significantly lower in lower doses of dexmedetomidine (p=0.0147) with better quality of intubation (p= 0.0003). MAC-sevo was significantly less in higher doses of dexmedetomidine with greater degree of sedation (p<0.0001). There was one case of PONV in DEX (0.2) group as compared to no cases in DEX (0.4) or DEX (0.6) group.

Conclusion: Pre-operative administration of dexmedetomidine at dosage of 0.4 or 0.6 mcg/kg/hour is more effective with more effective uterine contraction and greater sedation level. Haemodynamic as well as endocrine reactions of caesarean section under GA was also better attenuated at these doses.

Keywords: Caeserian Section, Dexmedetomidine, Dose, General Anaesthesia, Haemodynamic.

INTRODUCTION

Many institutions frequently use general anaesthesia (GA) when a patient refuses neuraxial anaesthesia or when there is an urgent need for a caesarean delivery, even though central neuraxial blocking is now the preferred method. Many drugs, such as opioids, tenoxicam, ketorolac, lidocaine, or paracetamol, can alter the hormonal and cardiovascular reactions to intubation of the trachea or surgical stimulation during caesarean delivery.[1-4]

However, newborn respiratory problems may be brought on by the mother's prenatal opiate medication. High levels of dexmedetomidine, a particular alpha 2-adrenoceptor agonist, given prior to surgery, either as a constant infusion (0.6 µg/kg/h) or via one dose (0.5–1 µg/kg),[5-7] blunts the body's hormonal and hemodynamic reactions to tracheal intubation, reduces the need for opioids and anesthetics,[7,10,11] and enhances the effectiveness of postoperative pain relief.[12] Use of lesser dosages (0.3 µg/kg) is linked to negligible alterations in hemodynamic.

A constant infusion of dexmedetomidine has the potential to be less dangerous compared to a single injection of 1-2 µg/kg since it lowers the risk of hypotension as well as bradycardia.[5, 7, 13] Although dexmedetomidine may enhance the standard of GA in women having caesarean sections, its impact on the result of the newborn is a matter of concern.

Women having myasthenia gravis, progressive spinal muscle atrophy, tethered spinal cord injury syndrome, as well as primary pulmonary hypertension have had caesarean deliveries using dexmedetomidine without experiencing a negative outcome for the newborn.[14–17] Acute exposure at the expected time of delivery has been demonstrated to have no adverse impacts on foetal development or postnatal behaviour in children of pregnant rats, and it swiftly leaves the mother's circulation.[18, 19]

Our hypothesis was that, in the event of a straightforward caesarean birth under GA, pre-operative IV dexmedetomidine administration would lessen the mother's hormonal and hemodynamic reactions to intubation of the trachea, operative stimulation, as well as extubation, all without having a negative impact on the newborn.

During a planned caesarean delivery under sevoflurane anaesthesia, this study was done to compare the impact of

pre-operative IV administration of dexmedetomidine (0.2, 0.4, and 0.6 µg/kg/h) on perioperative maternal hemodynamic, "minimum alveolar concentration of sevoflurane", "uterine tone", requirement for oxytocin, ease of extubation, and neonatal outcome.

MATERIALS AND METHODS

This was a randomised controlled open label study with parallel 1:1:1 allocation conducted in Department of Anaesthesiology of NMCH, Patna from January 2024 to June 2024. Informed consent was taken from patients undergoing caesarean section under General Anaesthesia before enrolment under the guidelines of ICH-GCP and Declaration of Helsinki.

Sample Size: With approximate mean arterial pressure of 105 mmHg in DEX (0.2), 90 mmHg in DEX (0.4) and 85 mmHg ± 20 in DEX (0.6) at 60 minutes after extubation from study of El-Tahan MR (2012), the effect size was calculated to be 0.43.[20] At this effect size minimum sample size required at 95% power with 0.05 alpha value was found to be 87 as per A-priori analysis of one-way ANOVA using G*Power. So, 30 patients were enrolled in each group.

Inclusion Criteria:

- Patients of either gender of age 18-65 years planned for caesarean under GA
- Patients of ASA class I or II

Exclusion Criteria:

- History of hypersensitivity to dexmedetomidine
- Patients diagnosed with cardiovascular, renal, hepatic or neurological disease
- Patients receiving any drug acting on cardiovascular system

Methodology:

The administration of anaesthesia was codified. On the night before as well as morning of the procedure, 150 mg of ranitidine was taken orally, and 15 minutes prior to induction, 30 milliliters of 0.3 mol per litre sodium citrate was administered. By selecting sequentially numbered closed opaque packets with a randomly created randomization code produced by software, patients were divided into three groups at random. Twenty minutes before to inducing anaesthesia, the three groups (n = 30 each) were given an IV infusion of 0.1 mL/kg/h of a solution comprising 2, 4, as well as 6 µg/mL of "dexmedetomidine (DEX 0.2, DEX 0.4, and DEX 0.6, respectively)". Two-thirds of the infusion rates were cut to 0.03 mL/kg/h following peritoneal closing, and this reduction was maintained until skin closure.

Following a 5-minute preoxygenation period, a rapid sequence induction was carried out using 1 mg of suxamethonium and 1.5–2.5 mg of propofol (to attain a SE less than 50 along with a difference less than 10 across RE and SE; RE–SE). Cricoid pressure was used, tracheal intubation was finished prior to the 2-minute measurement, and laryngoscopy was conducted following the 1-minute blood pressure recording. In order to keep SE <50 and RE-SE <10, anaesthesia was maintained using a 0.5 to 0.75 sevoflurane along with fifty percent oxygen plus nitrous oxide. Using a train-of-four stimulus, rocuronium 0.6 mg/kg was administered to sustain inhibition of the subsequent twitch.

Every three minutes following placental delivery, the obstetrician palpated the uterus to determine the level of contraction and recorded the result on a 10-scale "visual analog scale (VAS)" (0 being fully contracted, and 10 being entirely relaxed).

Prior to (baseline), 10 minutes into the infusion, carefully for the first 10 minutes following induction, 15 and 30 minutes after birth, skin closure, along with 0, 1, 5, 15, 30, as well as 60 minutes following extubation, the heart rate & MAP were recorded. A 5-point grading system was used to assess the standard of the tracheal extubation:

- 1: no coughing or straining
- 2: very smooth, minimum coughing
- 3: for moderate coughing
- 4: significant coughing or straining
- 5: poor extubation, very uncomfortable.21

Throughout the first hour following surgery, the existence and level of peri-operative sedation (4-point verbal rating scores):

- 1: awake
- 2: drowsy
- 3: rousable
- 4: deep sleep

45 minutes after the extubation, the blood glucose level was tested.

Statistical Analysis:

Data from patients undergoing elective caesarean under general anaesthesia were presented in tabular form using Microsoft Excel 365 and transferred to SPSS version 24 for further statistical analysis. Continuous data such as age, weight, height, induction to delivery time, duration of anaesthesia, DBP, MAP, and heart rate were expressed as mean ± SD (standard deviation). Statistical significance of difference in continuous data between groups was evaluated by one way ANOVA. Categorical data, including gender, and complications were reported as percentages and frequencies and then compared by chi-square. A p-value of less than 0.05 was taken as cut-off for statistical significance.

RESULTS

Most of the patients belonged to 26-32 years of age group, and 36-38 weeks of gestation in DEX (0.2), DEX (0.4) as well as DEX (0.6) groups. Induction to delivery time was slightly lower in DEX (0.2) group and duration of anaesthesia was slightly higher in DEX (0.2) group, but the differences were not statistically significant (p>0.05). Birth weight of most of the study participants ranged from 2.5 to 3.5 kg [Table 1].

There was significantly greater uterine relaxation with more need of oxytocin in lower doses of dexmedetomidine (p <0.001 and p = 0.0002 respectively). Time to extubation was significantly lower in lower doses of dexmedetomidine (p=0.0147) with better quality of intubation (p= 0.0003). MAC-sevo was significantly less in higher doses of dexmedetomidine with greater degree of sedation (p<0.0001). There was one case of PONV in DEX (0.2) group as compared to no cases in DEX (0.4) or DEX (0.6) group. [Table 2]

There was no significant association of APGAR score of neonate with dexmedetomidine dose (p>0.05). Oxygen saturation was significantly greater in lower dose of dexmedetomidine (p<0.0001). [Table 3]

Table 1: Comparison of Baseline Demographic and Clinical Characteristics between DEX (0.2), DEX (0.4) and DEX (0.6) Groups

Parameters	Value in Mean ± SD			P-Value (One Way ANOVA)
	DEX (0.2) (n =30)	DEX (0.4) (n =30)	DEX (0.6) (n =30)	
Age in years	27.86 ± 3.29	28.09 ± 3.94	28.23 ± 4.02	0.9288
BMI in kg/m^2	23.79 ± 1.67	23.95 ± 1.86	24.08 ± 1.93	0.8270
Gestational age in weeks	37.14 ± 1.03	37.09 ± 1.15	37.26 ± 0.97	0.8137
Induction to delivery time	9.62 ± 1.96	9.97 ± 2.1	10.05 ± 2.06	0.6872
Duration of anaesthesia in minutes	66.94 ± 14.56	57.54 ± 15.25	63.07 ± 16.65	0.0674
Birth weight of new-born in kg	2.94 ± 0.43	2.89 ± 0.36	2.92 ± 0.29	0.8670

Table 2: Comparison of Maternal Outcomes between DEX (0.2), DEX (0.4) and DEX (0.6) Groups

Parameters	Value in Mean ± SD			P-Value (One Way ANOVA)
	DEX (0.2) (n =30)	DEX (0.4) (n =30)	DEX (0.6) (n =30)	
VAS (Uterine Relaxation)	3.05 ± 0.46	2.32 ± 0.37	1.68 ± 0.25	**<0.0001***
Supplementary Oxytocin in IU	12.34 ± 2.67	12.75 ± 2.88	10.13 ± 1.94	**0.0002***
Time to spontaneous ventilation in min	5.15 ± 1.17	4.96 ± 1.98	5.61 ± 2.16	0.3685
Time to extubation in min	7.37 ± 1.45	7.26 ± 2.29	8.74 ± 2.54	**0.0147***
Quality of Tracheal Intubation	2.16 ± 0.36	1.95 ± 0.29	1.83 ± 0.26	**0.0003***
MAC-Sevoflurane				
After Intubation	0.62 ± 0.14	0.39 ± 0.15	0.36 ± 0.15	**<0.0001***
15 min after delivery	0.55 ± 0.12	0.36 ± 0.09	0.34 ± 0.07	**<0.0001***
30 min after delivery	0.55 ± 0.11	0.34 ± 0.08	0.33 ± 0.1	**<0.0001***
Sedation Score				
5 min	1.56 ± 0.23	1.93 ± 0.28	2.15 ± 0.37	**<0.0001***
15 min	1.27 ± 0.19	1.09 ± 0.11	1.84 ± 0.21	**<0.0001***
30 min	1.05 ± 0.06	1.05 ± 0.09	1.06 ± 0.1	0.8711
60 min	1.01 ± 0.02	1.02 ± 0.05	1.03 ± 0.06	0.2559

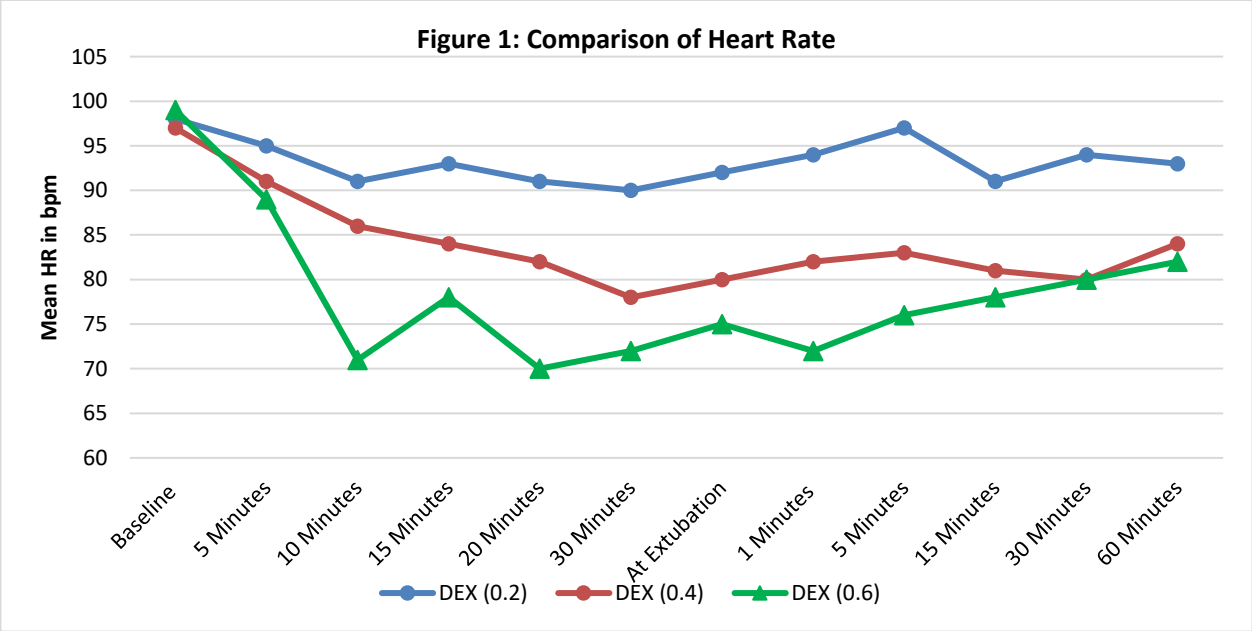
*Significant

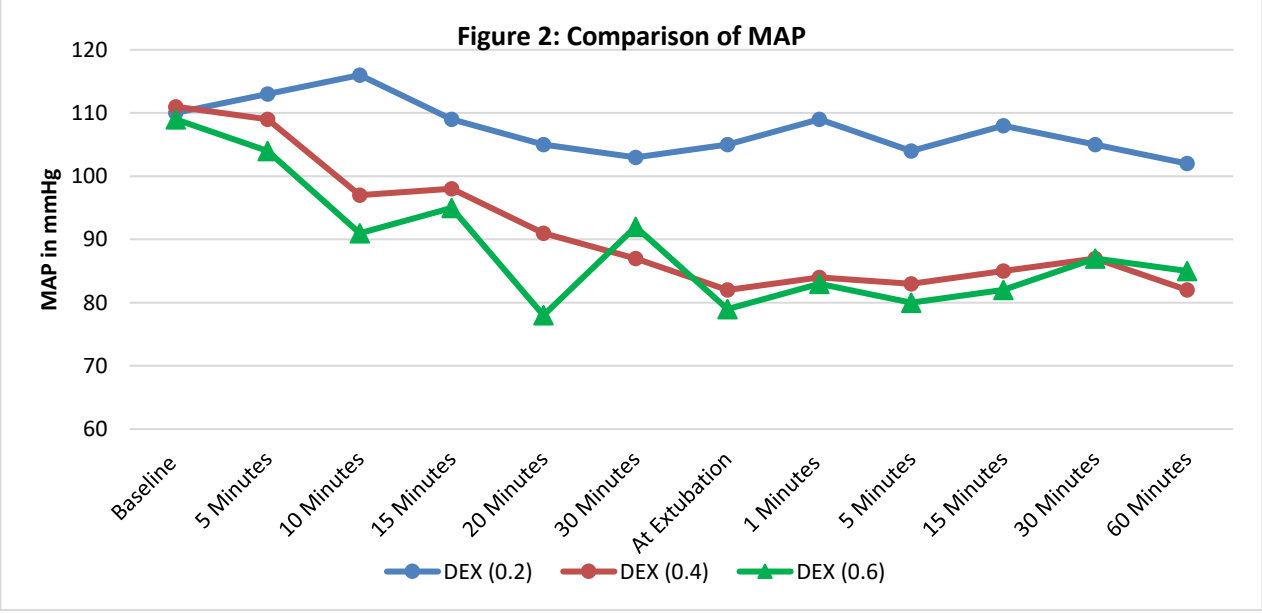
Table 3: Comparison of Neonatal Outcome between DEX (0.2), DEX (0.4) and DEX (0.6) Groups

Parameters	Value in Mean ± SD			P-Value (One Way ANOVA)
	DEX (0.2) (n =30)	DEX (0.4) (n =30)	DEX (0.6) (n =30)	
APGAR Score				
1 Min	8.06 ± 1.09	8.13 ± 1.08	7.98 ± 0.96	0.8569
5 Min	9.73 ± 1.22	9.82 ± 1.18	9.61 ± 1.25	0.7991
Umbilical Blood Gases				
pH	7.22 ± 0.06	7.24 ± 0.02	7.23 ± 0.04	0.2064
$PaCO_2$ (mmHg)	46.64 ± 1.5	45.28 ± 2.68	48.83 ± 2.96	**<0.0001***
PaO_2 (mmHg)	29.24 ± 1.15	26.93 ± 2.51	27.68 ± 2.51	0.0003*
SaO_2 (%)	61.03 ± 2.07	57.49 ± 3.1	58.77 ± 2.52	**<0.0001***
Base Excess (mEq/L)	-4.87 ± 0.59	-4.68 ± 0.4	-4.13 ± 0.42	**<0.0001***

*Significant

There was significantly greater fall in heart rate and MAP in higher dose of dexmedetomidine with stable haemodynamic in DEX (0.2) group. [Figure 1 & 2]





DISCUSSION

The primary conclusion of this study was that administering dexmedetomidine at dosages of 0.4–0.6 mcg/kg/h correlated with reduced HR, MAP, MAC-Sevo, a greater contraction of uterus, and elevated sedation scores post-delivery, without any detrimental effects on neonates. Dexmedetomidine infusions commenced 20 minutes prior to to anaesthesia induction to attain levels in the blood sufficient to mitigate the neuroendocrine reactions to anaesthesia and operation. The infusion rates employed (0.2–0.6 mcg/kg/h) were comparable to those utilized in earlier trials.[21, 22]

Our study shown that the preoperative administration of dexmedetomidine at doses of 0.4–0.6 mcg/kg/h led to significant reductions in HR (21.5% & 36%, respectively) and MAP (17% & 25%, respectively) during caesarean birth. Numerous investigations have demonstrated comparable attenuation of cardiovascular reactions to intubation, surgical stimulation, as well as extubation when employing dexmedetomidine during abdominal hysterectomy, minor orthopaedic and general surgeries, and intracranial procedures. [23-26]

A prior study demonstrated that 0.5–0.75 MAC-Sevo in NO diminishes the entropy responses to painful stimuli.[27] The preoperative dosing of dexmedetomidine has demonstrated a 44.5 percent drop in sevoflurane demands, as indicated by entropy factors.[28] The effects of dexmedetomidine on cardiovascular as well as endocrine reactions following tracheal intubation along with MAC-Sevo are predictable.[29, 30]

Alpha 2-adrenergic agonists exert a direct influence on the human myometrium. At approximated clinical levels in the blood, dexmedetomidine enhances the amplitude while frequency of uterine contractions in a dose-responsive manner. [31, 32] Clonidine exhibits same effects, albeit at elevated tissue amounts. [32] The current study found that administering 0.4–0.6 mcg/kg/h of dexmedetomidine throughout caesarean birth resulted in enhanced uterine tone and a reduced requirement for supplemental oxytocin. This was linked to a simultaneous decrease in MAC-Sevo as well as a reduction in instances of sickness and vomit.[33] No mother experienced intraoperative consciousness or associated adverse reactions of dexmedetomidine, including bradyarrhythmia, low blood pressure, or hyperglycemia. The administration of 0.6 mcg/kg/h dexmedetomidine correlated with elevated sedation scores for 15 minutes post-extubation.

To mitigate the possibility of low blood pressure and bradycardia, all dexmedetomidine administrations omitted a loading dosage, and the infusion commenced 20 minutes before induction to attain a specified effective concentration.[24] The premature termination of the dexmedetomidine its administration, 30 minutes prior to the conclusion of surgery, correlates with enhanced clinical recovery. The administration pace of dexmedetomidine was decreased by two-thirds following peritoneal closure to enhance recovery and expedite extubation. Enhanced efficiency in tracheal extubation without extending the duration of extubation was seen following dexmedetomidine infusion. This contrasts with other reported research and may come from a decreased infusion rate.[26]

The current study has few limitations administration on the level of postoperative analgesia following caesarean birth. We intend to examine this in subsequent research. The researchers did not employ a specific plasma level of dexmedetomidine, but rather chose a dosage range frequently utilized in other trials. The results should exclusively pertain to parturients receiving elective caesarean delivery following an otherwise uncomplicated pregnancy.

CONCLUSION

Pre-operative administration of dexmedetomidine at dosage of 0.4 or 0.6 mcg/kg/hour is more effective with more effective uterine contraction and greater sedation level. Haemodynamic as well as endocrine reactions of caesarean section under GA was also better attenuated at these doses. However, quality of extubation and oxygen saturation was more effective with 0.2 mcg/kg/hour dose of dexmedetomidine. There is need of some research to correlate plasma concentration of these drugs to these responses.

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