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Evaluation of Cardiovascular, Maternal, and Neonatal Outcomes with Three Different Dexmedetomidine Doses in Elective Caesarean Deliveries

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Abstract: ***Background:*** *Numerous institutions routinely employ general anesthesia (GA) whenever a patient declines neuraxial anesthesia or if there is an urgent requirement for a cesarean delivery, despite central neuraxial blockade being the recommended approach. It is necessary to identify an effective medication and optimal dosage to mitigate the endocrine and hemodynamic responses during cesarean section under general anesthesia.* ***Objective:*** *To compare the effects of pre-operative "intravenous administration of dexmedetomidine (0.2, 0.4, and 0.6 µg/kg/h) " on perioperative maternal hemodynamics and maternal as well as neonatal outcomes.* ***Methods:*** *20 minutes prior to the induction of anesthesia, each of the three groups (n = 50 each) received an intravenous administration of 0.1 mL/kg/h of a solution containing 2, 4, and 6 mcg/mL of "dexmedetomidine (DEX 0.2, DEX 0.4, and DEX 0.6, respectively)". Infusion rates for two-thirds of the subjects were reduced to 0.03 mL/kg/h after peritoneal closure, so this adjustment was sustained until skin closure. Maternal outcomes, hemodynamic parameters, including neonatal outcomes have been recorded.* ***Results:*** *Group C (DEX 0.6) showed the lowest VAS scores for uterine relaxation, indicating better relaxation, and required the least supplementary oxytocin. Additionally, Group C had the highest sedation scores at 5 and 15 minutes, and the longest time to extubation. The quality of tracheal intubation was best in Group C, with the lowest MAC-Sevoflurane values after intubation and at 15 and 30 minutes post-delivery. The comparison of neonatal outcomes showed similar immediate neonatal health across all groups.* ***Conclusion:*** *The pre-operative injection of dexmedetomidine at dosages of 0.4 or 0.6 mcg/kg/hour enhances uterine contractions and increases sedation levels. The hemodynamic and endocrine responses to caesarean section under general anesthesia were more effectively mitigated at these dosages.*

Keywords: Caesarian Section, Dexmedetomidine, Dosage, General Anesthesia, Hemodynamic

1. Introduction

Numerous institutions often employ general anesthesia (GA) whenever a patient declines neuraxial anesthesia especially if there is an urgent requirement for a cesarean delivery, despite central neuraxial blockade being the recommended approach. Numerous pharmaceuticals, including "opioids, tenoxicam, ketorolac, lidocaine, and paracetamol, " can modify the hormonal and circulatory responses to tracheal intubation or surgical stimulation during cesarean delivery.[1-4]

Nonetheless, neonatal respiratory issues may be induced by maternal perinatal opiate therapy. Elevated concentrations of dexmedetomidine, "a specific alpha 2-adrenoceptor agonist, " administered before surgery—either as a continuous infusion (0.6 µg/kg/h) or as a single dose (0.5–1 µg/kg) — attenuate the body's hormonal as well as hemodynamic responses to tracheal intubation, diminish the requirement for opioids and anesthetics, and improve the efficacy of postoperative analgesia.[5-12] The administration of reduced dosage (0.3 µg/kg) is associated with minimal changes in hemodynamics.

A continuous administration of dexmedetomidine may be less hazardous than a solitary injection of 1-2 µg/kg, as it diminishes the likelihood of hypotension and bradycardia.[5, 7, 13] While dexmedetomidine may improve the quality of general anesthesia in women undergoing caesarean sections, its effects on neonatal outcomes raise concerns.

Women with "myasthenia gravis, progressive spinal muscle atrophy, tethered spinal cord injury syndrome, and primary pulmonary hypertension" have undergone cesarean births with dexmedetomidine without adverse effects on the newborn.[14-17] Acute exposure at the anticipated time of birth has been shown to have no detrimental effects on fetal growth or postnatal behavior in offspring of pregnant rodents, and it rapidly dissipates from the circulatory system of the mother.[18, 19]

We hypothesized that, during a straightforward caesarean delivery under general anesthesia, the pre-operative use of intravenous dexmedetomidine would mitigate the maternal endocrine and hemodynamic responses to tracheal intubation, surgical stimulation, and extubation, without adversely affecting the newborn.

This study was conducted during a scheduled caesarean section under sevoflurane anesthesia to compare the effects of pre-operative intramuscular injection of "dexmedetomidine (0.2, 0.4, and 0.6 µg/kg/h) " on maternal hemodynamics, minimum alveolar concentration of sevoflurane, uterine tone, oxytocin requirements, extubation ease, and neonatal outcomes.

2. Materials & Methods

This was a randomized controlled open-label trial with a parallel 1: 1: 1 allocation done in the Department of Anesthesiology at NMCH, Sasaram from December 2023 to March 2024. Informed consent was obtained from participants having caesarean sections during GA before to enrollment, in accordance with ICH-GCP protocols as well as the Declaration of Helsinki.

Sample Size: The mean arterial pressures recorded were around "105 mmHg for DEX (0.2), 90 mmHg for DEX (0.4), and 85 mmHg ± 25 for DEX (0.6) " after 60 minutes post-extubation, as per the study by El-Tahan MR (2012), [20] resulting in an effect size of 0.34. The minimum sample size required for this effect size, at 95% power and a 0.05 alpha level, was determined to be 138 by an "A-priori evaluation of one-way ANOVA using G*Power. " So, 50 Subjects were recruited for each group to adjust for expected attrition of 10%.

Inclusion Criteria: The inclusion criteria for this study encompass patients of both genders, aged between 18 and 65 years, who are scheduled to undergo a caesarean section under general anesthesia. Additionally, eligible participants must be classified as ASA class I or II.

Exclusion Criteria: The exclusion criteria for this study include individuals with a known hypersensitivity to dexmedetomidine. Additionally, patients who have been diagnosed with cardiovascular, renal, hepatic, or neurological diseases are excluded. Furthermore, those who are currently taking any medications that affect the cardiovascular system are also not eligible to participate.

3. Methodology

The administration of anesthesia was standardized. On the evening prior before and on the day of the method, 150 mg of ranitidine was ingested orally, then 15 minutes preceding induction, a thirty-milliliter dose of 0.3 mol/L sodium citrate had been given. Patients were randomly assigned to three groups by picking consecutively numbered sealed opaque packages with a randomly generated code provided by software. Twenty minutes prior to the induction of anaesthesia, each of the three groups (n = 50 each) received an intravenous infusion of 0.1 mL/kg/hour of a solution containing "2, 4, and 6 µg/mL of dexmedetomidine (DEX 0.2, DEX 0.4, and DEX 0.6) in group A, group B and Group C. " Infusion rates were reduced to 0.03 mL/kg/h for two-thirds of the duration following peritoneal closure, and this adjustment was sustained until skin closure.

After a 5-minute preoxygenation interval, a rapid sequence inducement was performed utilizing one milligram of suxamethonium along with 1.5–2.5 mg of propofol to achieve a SE below 50, with a difference of less than 10 between RE and SE (RE–SE). Cricoid pressure was applied, tracheal intubation was completed before the 2-minutely evaluation, and laryngoscopy was performed after the 1-minute arterial blood pressure monitoring. To maintain SE below 50 and RE-SE below 10, anesthesia was administered utilizing 0.5 to 0.75 sevoflurane in conjunction with 50 percent oxygen along with nitrous gas. Employing a train-of-four stimulus, Rocuronium at a dosage of 0.6 milligrams per kg was provided to maintain suppression of the next twitch.

Every three minutes after placenta delivery, the doctor handling the delivery palpated the uterus to assess contraction levels and documented the findings on a 10-point visual analog scale (VAS), with 0 indicating full contraction and 10 signifying complete relaxation.

Heart rate (HR) and mean arterial pressure (MAP) were monitored at baseline, 10 minutes into the infusion, during the first 10 minutes post-induction, as well as "15 and 30 minutes after birth, skin closure, and at 0, 1, 5, 15, 30, and 60 minutes following extubation. "

A 5-point rating system was employed to evaluate the quality of tracheal extubation: [21]

Score	Description
1	No Coughing or Straining
2	Very Smooth, Minimum Coughing
3	Moderate Coughing
4	Significant Coughing or Straining
5	Poor Extubation, Very Uncomfortable

During the initial hour post-surgery, the presence and degree of peri-operative sedation were assessed using 4-point verbal rating scores.

Score	State
1	Awake
2	Drowsy
3	Rousable
4	Deep Sleep

Statistical Analysis:
Data from participants undergoing elective cesarean sections under general anesthesia were organized in tabular format utilizing Microsoft Excel 2010 and subsequently imported into Graph Pad version 8.4.3 for advanced statistical analysis. Continuous variables including "age, weight, height, induction to delivery time, length of anesthesia, diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate" were presented as mean ± standard deviation (SD). The statistical significance of differences in continuous data between three groups was assessed using one-way ANOVA. Categorical data, such as "gender and complications, " were presented as percentages along with frequencies, thereafter analyzed using chi-square tests. A p-value below 0.05 was established as the threshold for statistical significance.

4. Results

Table 1: Comparison of Baseline Demographic and Clinical Characteristics between Group A (DEX 0.2), Group B (DEX 0.4) and Group C (DEX 0.6)

Parameters	Value in Mean ± SD			P-Value (One Way ANOVA)
	Group A (n =50)	Group B (n =50)	Group C (n =50)	
Age in years	26.67 ± 3.18	27.03 ± 3.8	27.13 ± 3.9	0.8021
BMI in kg/m^2	22.69 ± 1.54	22.85 ± 1.77	22.93 ± 1.79	0.7735
Gestational age in weeks	36.04 ± 0.89	36.18 ± 1.02	36.38 ± 0.86	0.1857
Induction to delivery time	9.51 ± 1.87	9.88 ± 1.97	9.96 ± 1.92	0.4597
Duration of anaesthesia in minutes	65.77 ± 14.45	56.86 ± 15.13	62.09 ± 16.57	**0.0165***
Birth weight of new-born in kg	2.83 ± 0.29	2.8 ± 0.25	2.82 ± 0.18	0.8226

*Significant

The baseline demographic and clinical characteristics of the three groups (Group A: DEX 0.2, Group B: DEX 0.4, and Group C: DEX 0.6) were compared using one-way ANOVA. The results showed no significant differences in age, BMI, gestational age, induction to delivery time, and birth weight of the newborns among the groups, as indicated by p-values greater than 0.05. However, there was a significant difference in the duration of anaesthesia, with Group B having a shorter duration compared to Groups A and C (p = 0.0165).

Table 2: Comparison of Maternal Outcomes between Group A (DEX 0.2), Group B (DEX 0.4) and Group C (DEX 0.6)

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)	2.96 ± 0.35	2.23 ± 0.24	1.57 ± 0.11	**<0.0001***
Supplementary Oxytocin in IU	11.54 ± 2.55	11.63 ± 2.77	9.15 ± 1.83	**<0.0001***
Time to spontaneous ventilation in min	5.04 ± 1.09	4.87 ± 1.84	5.51 ± 2.07	0.1592
Time to extubation in min	7.26 ± 1.36	7.16 ± 2.16	8.64 ± 2.43	**0.0004***
Quality of Tracheal Intubation	2.05 ± 0.22	1.86 ± 0.17	1.73 ± 0.18	**<0.0001***
MAC-Sevoflurane				
After Intubation	0.52 ± 0.13	0.31 ± 0.13	0.27 ± 0.1	**<0.0001***
15 min after delivery	0.45 ± 0.1	0.26 ± 0.06	0.23 ± 0.03	**<0.0001***
30 min after delivery	0.45 ± 0.08	0.25 ± 0.07	0.22 ± 0.08	**<0.0001***
Sedation Score				
5 min	1.45 ± 0.15	1.83 ± 0.19	2.05 ± 0.25	**<0.0001***
15 min	1.15 ± 0.18	0.98 ± 0.09	1.74 ± 0.16	**<0.0001***
30 min	0.96 ± 0.04	0.95 ± 0.06	0.97 ± 0.06	0.1854
60 min	0.92 ± -0.01	0.92 ± 0.04	0.94 ± 0.04	0.0030

*Significant

The comparison of maternal outcomes between the three groups (DEX 0.2, DEX 0.4, and DEX 0.6) revealed significant differences in several parameters. Group C (DEX 0.6) showed the lowest VAS scores for uterine relaxation, indicating better relaxation, and required the least supplementary oxytocin. Additionally, Group C had the highest sedation scores at 5 and 15 minutes, and the longest time to extubation. The quality of tracheal intubation was best in Group C, with the lowest MAC-Sevoflurane values after intubation and at 15 and 30 minutes post-delivery.

Table 3: Comparison of Neonatal Outcome between Group A (DEX 0.2), Group B (DEX 0.4) and Group C (DEX 0.6)

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	7.94 ± 0.97	8.02 ± 0.97	7.88 ± 0.82	0.7489
5 Min	9.63 ± 1.09	9.73 ± 1.1	9.5 ± 1.16	0.5880
Umbilical Blood Gases				
pH	7.1 ± 0.05	7.14 ± 0.01	7.12 ± 0.02	**<0.0001***
$PaCO_2$ (mmHg)	45.68 ± 1.37	44.26 ± 2.59	47.73 ± 2.83	**<0.0001***
PaO_2 (mmHg)	28.15 ± 1.06	25.98 ± 2.4	26.66 ± 2.38	**<0.0001***
SaO_2 (%)	60.08 ± 1.96	56.59 ± 3.02	57.77 ± 2.4	**<0.0001***
Base Excess (mEq/L)	-4.97 ± 0.47	-4.79 ± 0.27	-4.23 ± 0.29	**<0.0001***

*Significant

The comparison of neonatal outcomes between the three groups (DEX 0.2, DEX 0.4, and DEX 0.6) showed no significant differences in APGAR scores at 1 and 5 minutes, indicating similar immediate neonatal health across all groups. However, significant differences were observed in umbilical blood gases. Group B (DEX 0.4) had the highest pH and lowest PaCO2 and PaO2 levels, suggesting better acid-base balance and oxygenation. Group C (DEX 0.6) had the highest SaO2 and the least negative base excess, indicating better oxygen saturation and metabolic status.

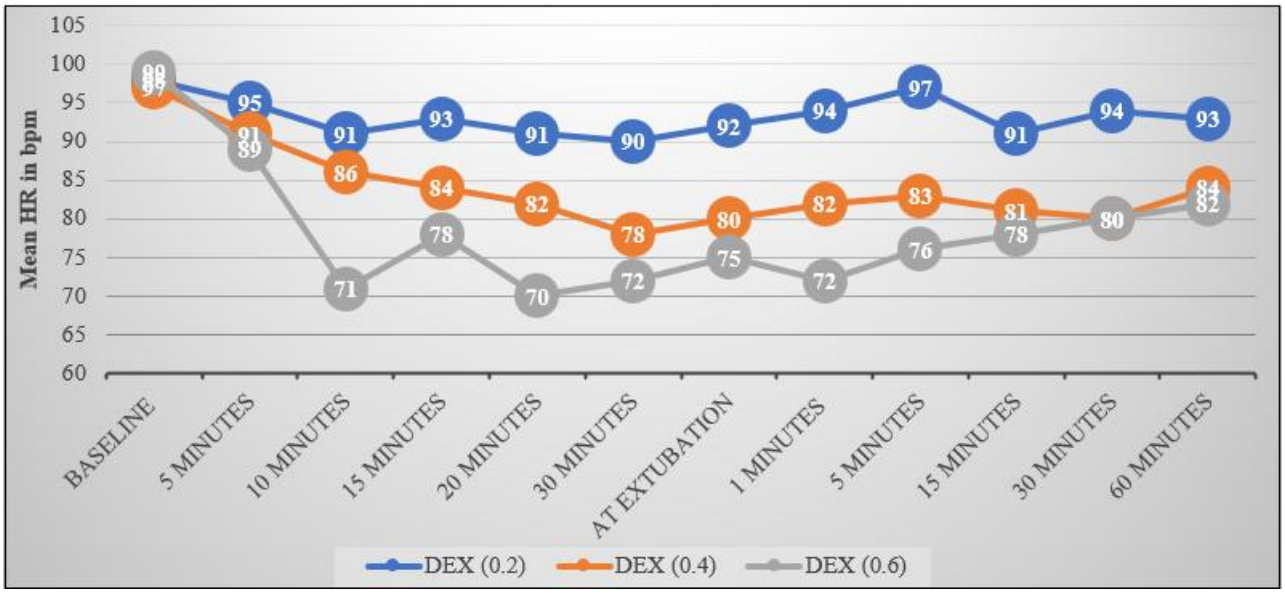

Figure 1: Comparison of Heart Rate

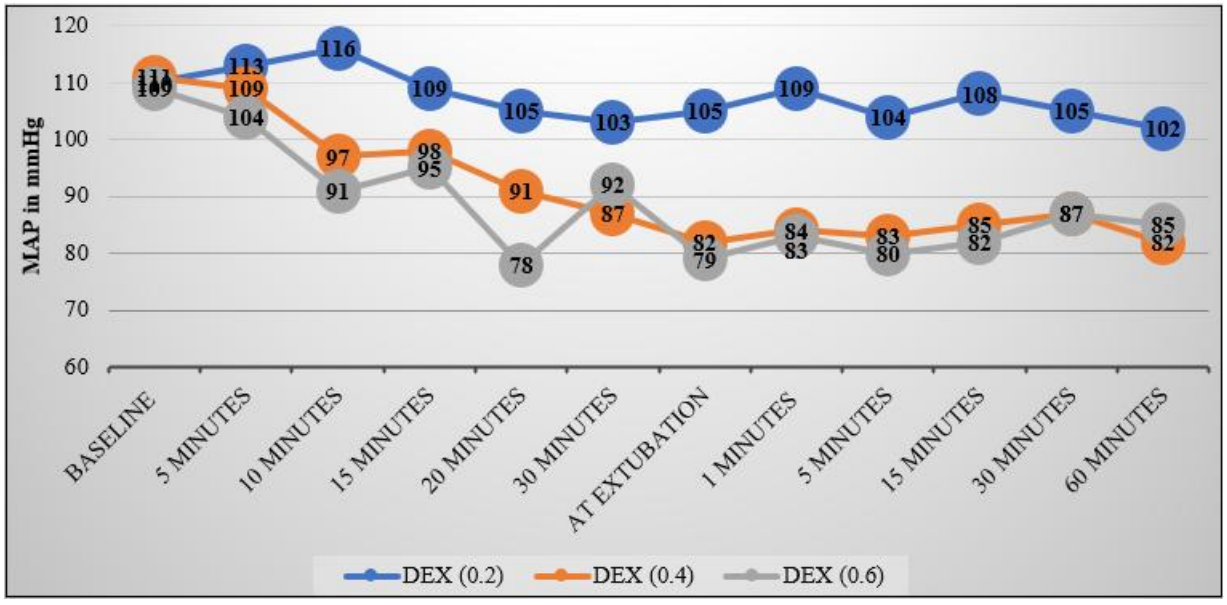

Figure 2: Comparison of MAP

5. Discussion

The principal finding of this study indicated that the administration of Dex at dosage of 0.4–0.6 mcg/kg/h was associated with decreased heart rate, mean arterial pressure, and MAC-Sevo, enhanced uterine contraction, and increased sedation scores following delivery, without adverse effects on newborns. Dex infusions were initiated 20 minutes before anaesthesia induction to achieve blood levels adequate to attenuate the neuroendocrine responses to anaesthesia and surgery. The infusion rates used "0.2–0.6 mcg/kg/h" were analogous to those applied in previous studies.[21, 22]

Our study demonstrated that the preoperative injection of Dex at dosages of 0.4–0.6 mcg/kg/h resulted in substantial drops in heart rate and mean arterial pressure during cesarean delivery. Multiple studies have shown similar reductions in cardiovascular responses to intubation, intraoperative stimulation, along with extubation while utilizing Dex throughout abdominal hysterectomy, minor orthopedic and general operations, or intracranial surgeries.[23-26]

A previous study indicated that "0.5–0.75 MAC-Sevo" in nitrous oxide reduces entropy responses when exposed to painful stimuli.[27] Preoperative administration of Dex has shown a 44.5 percent reduction in sevoflurane requirements, as evidenced by entropy metrics.[28] The impact of Dex on cardiovascular and endocrine responses after tracheal intubation with MAC-Sevo is foreseeable.[29, 30]

Alpha 2-adrenergic agonists directly affect the human myometrium. At estimated clinical concentrations in the bloodstream, dexmedetomidine increases the amplitude and intensity of uterine muscle contractions in a dose-dependent manner.[31, 32] Clonidine demonstrates identical effects, however at increased tissue concentrations.[32] The present investigation demonstrated that the administration of "0.4–0.6 mcg/kg/h of dexmedetomidine" after cesarean delivery improved uterine tone and decreased the need for supplementary oxytocin. This was associated with a

concurrent decline in MAC-Sevo along with a decline in occurrences of nausea and emesis.[33] No mother exhibited intraoperative awareness or any adverse effects from Dex, such as "bradyarrhythmia, hypotension, or hyperglycemia. " The injection of "0.6 mcg/kg/h dexmedetomidine" was associated with increased sedation scores for 15 minutes following extubation.

To reduce the risk of hypotension or bradycardia, all Dex infusions excluded a loading dose, and the infusion began 20 minutes prior to induction to achieve a targeted effective level.[24] The early cessation of Dex therapy, 30 minutes before the completion of surgery, is associated with improved clinical recovery. The administration rate of dexmedetomidine was reduced by two-thirds after peritoneal closure to facilitate recovery and accelerate extubation. Improved effectiveness in tracheal extubation without prolonging the extubation period was observed subsequent to Dex infusion. This differs from other documented studies and may result from a reduced infusion rate.[26]

The present study includes some limitations regarding the provision of analgesia after surgery following cesarean delivery. We plan to investigate this in future studies. The researchers failed to use a precise plasma concentration of dexmedetomidine, but instead selected a dosage range often employed in other studies. The results should solely relate to parturients undergoing elective cesarean birth after an uncomplicated pregnancy.

6. Conclusion

The pre-operative injection of Dex at dosages of "0.4 or 0.6 mcg/kg/hour" enhances uterine contractions and increases sedation levels. The hemodynamic and endocrine responses to cesarean section under general anesthesia were more effectively mitigated at these dosages. The degree of extubation as well as oxygen saturation were more successful at a dosage of 0.2 mcg/kg/hour of dexmedetomidine. Research is necessary to connect the plasma concentrations of these medications with the corresponding responses.

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