Research Article

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Study of the Effect of Dexmedetomidine in Reducing Hemodynamic Responses to General Anesthesia for Elective Cesarean Section in Patients with Preeclampsia

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Abstract

Background: Depending on the effect of dexmedetomidine in haemodynamic stability, it was started to be used as a sedative prior to and/or during surgical and other procedures in non-intubated adult and pediatric patients. In 2009, dexmedetomidine has been successfully used in laboring parturients. It provides maternal hemodynamic stability, anxiolysis, and stimulation of uterine contractions. Literature describes that dexmedetomidine has a high placental retention and does not cross the placenta, with less incidence of fetal bradycardia. We hypothesized that dexmamedetomidine would be effective in reducing the maternal hemodynamic responses to elective cesarean section in preeclmaptic patients without adverse neonatal effects.

Methods: The series of the present study included forty parturients with preeclampsia who were planned for elective caesarean delivery for different indications under general anesthesia. The patients were divided in 2 groups and they were selected randomly to receive either fentanyl (control group), or 0.4 µg/kg/h intravenous dexmedetomidine 10 min before induction (n=20 per group). Changes in maternal heart rate, mean blood pressure, time from induction to delivery, the full anesthesia time, uterine contraction after placental delivery, umbilical blood gas parameters and Sedation scores were recorded.

Results: The heart rate in the dexmedetomidine group was lower than that in fentanyl group, patients in dexamedetomidine group had statistically significant lower change in mean arterial blood pressure, while patients taken fentanyl showed much higher mean arterial blood pressure from the induction till 5 minutes after extubation, Also the dexamedetomidine group showed greater uterine contraction, while there was no difference between both groups in Apgar score at 1 and 5 minute, NACS<35 and the umbilical blood gas analysis.

Conclusion: It could be concluded that, this study suggests the effective use of dexmedetomidine in preeclamptic patients undergoing elective cesarean as it stabilizes the maternal hemodynamic parameters with negligible effect on the fetus.

Introduction

The approval of Dexmedetomidine (DEX) to be used in humans by United States Food and Drug Administration (US FDA) dated on 1999. It was approved to be used as a sedative and analgesia for a short duration in Intensive Care Unit (ICU) patients and for less than 24 hours.

Dexmedetomidine acts as highly selective α-2 adrenergic receptor agonist, so that it has many actions like: sedation, analgesia decreasing intraoperative anesthetic requirements. Also it preserves the respiratory function with smooth recovery when used as an adjunct to general anesthesia [1,2].

Depending on the effect of Dexmedetomidine in hemodynamic stability it was started to be used as a sedative prior to and/or during surgical and other procedures in non-intubated adult and pediatric patients in 2008 [3].

Since then DEX has been growing in popularity and expanding its role in anesthesia. But with reluctance to be used in parturients; because of the possibility of uteroplacental transfer and untoward effects on the baby [4].

In 2009 Dexmedetomidine has been successfully used in laboring parturients, as an adjunct to labor epidural if pain relief was not satisfactory. Continuous intravenous DEX infusion has been successfully used as an adjuvant to systemic opioids in laboring parturients who could not benefit from epidural analgesia [5,6]. It provides maternal hemodynamic stability, anxiolysis, and stimulation of uterine contractions. Literature describes that dexmedetomidine has a high placental retention and does not cross the placenta, with less incidence of fetal bradycardia [5,7].

The choice of anesthetic technique in severely preeclamptic women requiring caesarean section has been controversial for a number of years, with a relative safety to epidural anesthesia [8]. There is a high risk in doing caesarean section under general anesthesia in preeclampsia because of the increased risk of difficult airway and intubation and marked pressor response at laryngoscopy, intubation

and extubation resulting in dangerous surges in blood pressure. There is a significant risk of intracranial hemorrhage secondary to uncontrolled severe hypertension at induction of general anesthesia [9].

Successful use of dexmedetomidine in laboring parturients who could not benefit from epidural analgesia besides its effect in maternal hemodynamic stability encourage us to use it in preeclampsia patients doing caesarian section under general anesthesia

Methods

After approval by local research ethics committee, informed consent was obtained from all patients participating in the study. The series of the present study included forty full term parturients aged 20-35 years with preeclampsia who were planned for elective caesarean delivery for different indications under general anesthesia. The sample size was calculated according to sample size calculated by the High institute of Public Health, Biostatistics Department, Alexandria University. The patients were divided in 2 groups and they were selected randomly to receive either 1 µg/kg fentanyl (control group) at the induction of anesthesia, or 0.4 µg/kg/h intravenous dexmedetomidine starting at 10 min before induction and stopped after peritoneal closure (n=20 per group). For randomization, patients drew a sealed opaque envelope from a shuffled deck containing a card representing one of the treatment groups. Patients were not informed of their treatment group.

Demographic data of the patients were recorded including: the maternal age, parity, body weight, gestational age and birth weight. The exclusion criteria were parturients with any medical illness rather than the pregnancy induced hypertension (sever renal, hepatic and cardiac illness, neurological or muscular disease, anemia), allergy to dexamedetomidine or with evidence of any fetal compromise.

For prophylaxis against aspiration, all patients were received 30 ml sodium citrate 30 minutes prior to induction. Monitoring of the patients was done using ECG, non-invasive blood pressure and pulse oximetry. Left uterine displacement was established, denitrogenation was accomplished with 100% oxygen for 3 min. A rapid sequence induction was performed using propofol 2 mg/kg and suxamethonium 1 mg/kg, anesthesia was maintained with 0.5-0.75 MAC isoflurane, and cisatracurium 0.1 mg/kg. After the neonate and placenta were delivered an infusion of 10 IU oxytocin in 500 ml Ringer lactate solution was given. Changes in maternal heart rate, mean blood pressure, were recorded preoperatively, 1 min, 3 min, 5 min, 10 min, 20 min, and 30 min after the induction. Then after extubation by 1 min, 3 min and 5 min. Time from induction to delivery and the full anesthesia time were also recorded. The uterine contraction after placental delivery was assessed by the obstetrician and scored from 0 to 10 according to the linear analogue scale (LAS) [10] as 0 means the compete uterine relaxation and 10 refers to the best contraction. The maternal sedation in the first postoperative hour was reported every 15 min. Apgar score of the neonates and neurologic Adaptive Capacity Scores were assessed by the pediatrician, also all neonates observed for respiratory depression and bradycardia during the first hour after delivery. Umbilical blood sample was taken for blood gas analysis.

Sedation scores were recorded using five-point scale (1=completely awake, 2=awake but drowsy, 3=asleep but responsive to verbal commands, 4=asleep but responsive to tactile stimulus, 5=asleep and not responsive to any stimulus) [11], every 15 min during the first hour after the surgery.

Statistical analysis was undertaken using the statistical program for social sciences (SPSS) version 20.0 (IBM, Armonk, New York). Paired t tests and comparing means were used to analyze the relations between the obtained results in both groups. Statistical significance was set at P=0.05.

Results

The demographic data (age, weight, gestational age) and induction to delivery time were similar in both groups (Table1).

Variable	Mean (range)	
	DEX group	**Fentanyl group**
Age (years)	28.15	29.65
Patient body Weight (kg)	82.95 ± 5.49	80.63 ± 5.27
Gestational age (weeks)	34.05 ± 1.2	36.25 ± 1.3
Birth weight (kg)	2.385 ± 0.41	2.680 ± 0.52
Time from induction to delivery (min)	8.6 (7-10)	8.86 (7- 10)
Anesthesia time (min)	29.41 (25-34)	31.68 (27- 35)

Table 1: Demographic data of the studied groups.

On comparing the means of the two groups the preoperative heart rate (HR) and mean arterial blood pressure (MAP) were the same in both groups. The heart rate in the DEX group was lower than that in fentanyl group and the difference was proved to be statistically highly significant (p=0.001) (Figure 1).
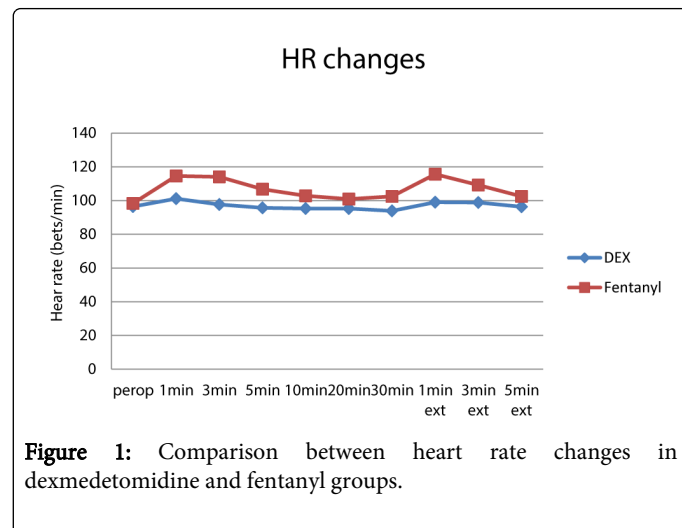

Figure 1: Comparison between heart rate changes in dexmedetomidine and fentanyl groups.

Patients in DEX group had statistically significant lower change in mean arterial blood pressure, while patients taken fentanyl showed much higher mean arterial blood pressure from the induction till 5 minutes after extubation. This relation was proved to be highly significant, (p=0.001) (Figure 2). Also the dexamedetomidine group showed greater uterine tone and less postoperative nausea and vomiting than the fentanyl group.
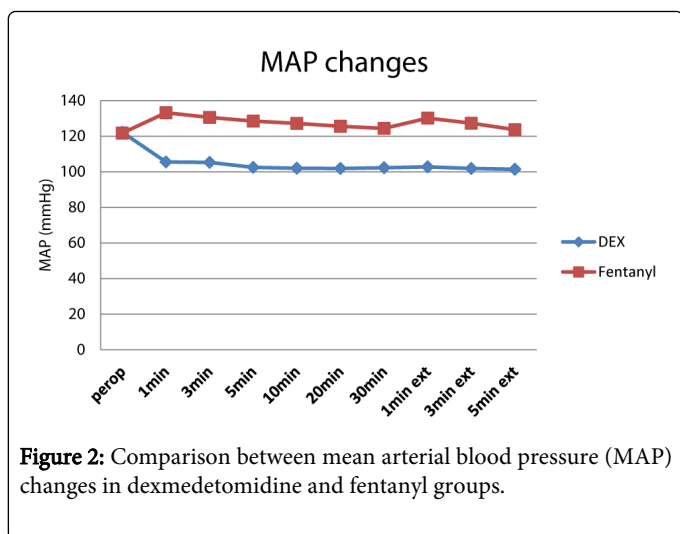
Figure 2: Comparison between mean arterial blood pressure (MAP) changes in dexmedetomidine and fentanyl groups.

As regards the neonatal parameters, there was no difference between both groups in Apgar score at 1 and 5 minute, NACS<35 and the umbilical blood gas analysis, (Table 2). On the other hand the Dexa group showed a statistically significant higher sedation score than the fentanyl group (Figure 3).

	Dexa	Fentanyl
Uterine contraction	8 (8-9)	6 (6-8)
Sedation score		
5 min	2(1-3)	1.3 (1-2)
15 min	1.9 (1-3)	1 (1-1)
30 min	1	1
60 min	1	1
Postoperative nausea and vomiting	0%	3 (15%)
Apgar score		
I min	8 (7-9)	8 (7-9)
5 min	9.3 (8-10)	9.5 (8-10)
NACS<35		
15 min	4	5
2 hr	2	3
24 hr	1	1
Umbilical blood gases		
PH	7.282 ± 0.88	7.274 ± 1.20
PO_2	26.80 ± 0.75	27.92 ± 0.86
PCO_2	47.35 ± 0.02	48.54 ± 0.04

Table 2: Maternal and neonatal assessment.

Discussion

Since the FDA approval of dexmedetomidine for use in humans for short term sedation and analgesia in 1999, it has been studied in several other perioperative settings. There are many series reported in the literature about the efficacy of dexmedetomidine in

haemodynamical stability of the patients on general anesthesia. Talkeel et al. [12] performed a placebo controlled study in vascular surgery and reported that dexmedetomidine-treated patients showed less increase in heart rates and noradrenaline levels when administered via intravenous infusion at a dose of 0.8 μg /kg.
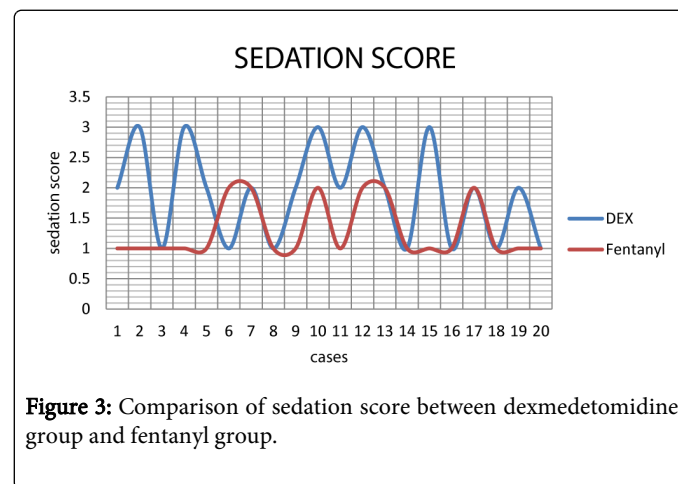

Figure 3: Comparison of sedation score between dexmedetomidine group and fentanyl group.

Hall et al. [13] used dexmedetomidine in a dose of 0.2 and 0.6 μg/kg via intravenous infusion and reported on a reduction in heart rate without any change in mean arterial pressure.

The same were reported by Yildiz et al. [14] and Ozkose et al. [15] who demonstrated a decrease in mean arterial pressures and heart rates after a single dose of 1 μg/kg dexmedetomidine.

Gogus et al. [16], compared between the effects of use of fentanyl, dexmedetomidine and esmolol on prevention of hemodynamic response to intubation in 90 patients undergoing elective surgery and who were in ASA I or II and between 21- 65 years, and they concluded that esmolol was more effective than dexmedetomidine and fentanyl in prevention of the increases in systolic, diastolic and mean arterial pressures following endotracheal intubation. On the other hand, dexmedetomidine was more effective than esmolol and fentanyl in preventing the increase in heart rate.

Our understanding of the existing literature is that there was a reluctance of the use of dexmedetomidine in pregnant women because of the fear of passing the uteroplacenta barrier and causing neonatal respiratory depression.

There were many case reports of use of dexmedetomidine in parturients after the proof of its retention in the placenta with negligible effect on the fetus [17,18].

It was recorded in the entire previous studies that dexamedetomidine can be used in parturients safely without affecting the delivered babies who were delivered with normal Apgar score [19-21].

El Tahan et al. [22] reported on the comparison of the use of different concentration of dexmedetomidine and placebo in caesarian section and they proved its effect in lowering the heart rate and lowering the mean arterial blood pressure and they concluded that pre-operative administration of dexmedetomidine in a dose of 0.4 and 0.6 μg /kg attenuates maternal hemodynamic and hormonal responses to caesarean section. But they did not used dexmedetomedine in preeclampsia and they excluded preeclamptic patients from their study.

In this study we tried to get benefit from cardiovascular stabilizing effect of dexmedetomidine to use it in preeclamptic patients and we randomly take forty patients with preeclampsia undergoing elective CS, twenty were given dexmedetomidine preoperatively and the other twenty were given fentanyl as a premedication. Comparing our results with the control group result (fentanyl group), the preoperative infusion of dexmedetomidine in a rate 0.4 µg/kg/h showed a significant slowing in heart rate and lowering of the mean arterial blood pressure during CS in preeclamptic patients, also it was noticed that babies were delivered with normal Apgar score and normal gas parameters.

Our results were, in fact, comparable to a previous study carried out by Abu-Halaweh et al. [5] who reported on the successful use of intravenous dexmedetomidine infusion in pregnant women with diabetes mellitus and pregnancy-induced hypertension under general anesthesia without any untoward maternal and child adverse events.

The limitation of this study is that we studied the effect of dexamedetomidine in only a single dose and we did not study the effect of increasing the dose on the hemodynamic parameters as it is known that the effect of dexmedetomidine on blood pressure and heart rate is dose dependent [23,24]. The other limitation is that although the cases were randomly allocated into 2 groups, it was not a blinded study to the demonstrators.

Conclusion

It could be concluded that this study supported the previous series in the literature which proved the success of preoperative administration of dexmedetomidine in attenuating the hemodynamic responses to caesarean section, beside that this study also proved the effective use of dexmedetomidine in preeclamptic patients undergoing elective cesarean as it stabilizes the maternal hemodynamic parameters with negligible effect on the fetus.

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