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Research Article

Remifentanil *vs* dexmedetomidine for severely preeclamptic parturients scheduled for cesarean section under general anesthesia: A randomized controlled trial

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KEYWORDS

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Abstract *Objectives:* To compare the effect of remifentanil *vs* dexmedetomidine on hemodynamic response of noxious stimuli and neonatal outcome in preeclamptic parturient underwent C.S. under G.A.

Methods: This blinded, prospective, randomized trial included 50 preeclamptic parturients underwent C.S under G.A., randomized into two equal groups [25 patients each]: group **R** [remifentanil]: received 1 μg/kg loading and 0.05 μg/kg/min infusion doses and group **D** [dexmedetomidine] received 1/kg loading and 0.2 μg/kg/h infusion doses. Maternal MAP and HR were assessed before medication ($\mathbf{T_0}$), just after induction of GA ($\mathbf{T_I}$), just after intubation ($\mathbf{T_T}$), two minutes after intubation ($\mathbf{T_{T2}}$), just after skin incision ($\mathbf{T_S}$), two minutes after skin incision ($\mathbf{T_{S2}}$), just after delivery of the baby ($\mathbf{T_D}$), and at the end of operation ($\mathbf{T_E}$). Time between induction and fetal delivery **(I-D interval)**, time between incision of the uterus and delivery **(U-D interval)**, and time between stop of the infusion of the tested drugs and delivery **(D-D interval)** were recorded. Neonatal **Apgar score** was recorded at 1 and 5 min and the need for resuscitative measures.

Results: Maternal MAP and HR in group R were statistically lower at ($\mathbf{T_I}$), ($\mathbf{T_T}$), ($\mathbf{T_{T2}}$), ($\mathbf{T_S}$) and ($\mathbf{T_{S2}}$). Neonatal Apgar score was statistically lower in group R with higher incidence for tactile stimulation.

Conclusion: Both remifentanil and dexmedetomidine were effective on blunting the pressor response to noxious stimuli in severely preeclamptic parturients. While remifentanil was marginally more effective in suppressing the pressor response, dexmedetomidine was safer for the neonates.

1. Introduction

General anesthesia (GA) is typically used for Cesarean Section (CS) when neuraxial anesthesia is contraindicated: such

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as with coagulation abnormalities, vertebral deformity, local infection, and patient refusal, or for emergency situations. Endotracheal intubation usually increases arterial blood pressure (ABP) and heart rate (HR) [1]. With preeclampsia, this pressor response to intubation is exaggerated [2]. This abrupt increase in ABP can cause cerebral edema, intracranial hemorrhage [3], cardiac failure, and pulmonary edema, with increased rate of morbidity and mortality in both the mother and fetus [4]. In addition, this pressor response raises maternal plasma catecholamine levels, that can induce utero-placental vasoconstriction and placental insufficiency [5,6]. Therefore, close control of pressor responses during intubation and surgical stimulation can protect both the mother and the fetus in preeclamptic parturients. Opioids are commonly used to attenuate this pressor response. However, because of its adverse neonatal effects, opioids are classically avoided at induction of GA for CS.

Remifentanil was a potent opioid with rapid onset (maximum effect at 1–3 min) [7] and ultra-short duration of action, with a consistent half-time of 3–5 min, regardless of the duration of the infusion [8]. It is an attractive option when GA is required for CS. It has been proved to blunt the pressor response to intubation in healthy [9,10] and severely preeclamptic [11,12] parturients, but the concern of neonatal respiratory depression still exists [13]. The success to blunt the pressor response was defined as a systolic blood pressure (SBP) did not exceed 160 mmHg, a critical point for the risk of intracranial hemorrhage to occur in preeclamptic parturients [14].

Dexmedetomidine, a highly selective α-$_2$ adrenergic agonist, can induce sedation, analgesia, and amnesia without respiratory depression [15,16]. Preoperative administration of dexmedetomidine, either as a single dose (0.5–1 μg/kg) [17,18] or as continuous infusion (0.6 μg/kg/h) [19], showed to effectively blunt hemodynamic and hormonal responses to tracheal intubation [20], reduce anesthetic requirements [21], and enhance postoperative analgesia [22]. Several studies successfully used dexmedetomidine for labor analgesia or CS under GA, or to improve the quality of pain relief with opioid-based analgesia [23,24]. Other studies employed dexmedetomidine in the healthy [25] and the preeclamptic [26,27] parturients for control of maternal hemodynamics. Later on, a study carried out on 2015, compared the efficacy of remifentanil on hemodynamics, depth of anesthesia, anesthetic consumption and neonatal outcome with that of dexmedetomidine in non-preeclamptic parturients [28]. However, to our knowledge, no study compared the efficacy of these drugs with severe preeclampsia.

In our study, we aimed to compare the efficacy of remifentanil (1 μg/kg *iv* bolus followed by 0.05 μg/kg/min continuous infusion), with dexmedetomidine (1 μg/kg *iv* bolus followed by 0.2 μg/kg/min continuous infusion), for attenuation of the pressor response to endotracheal intubation and surgical stimulation, in severely preeclamptic parturient candidate for CS under GA, and to evaluate the neonatal outcome in both studied groups.

2. Materials and methods

Following approval of our institutional ethical committee and obtaining written informed consents, 50 parturients scheduled for elective CS under GA, of ASA grade I or II, 20–40 years old, presented with severe preeclampsia [29,30] were recruited in this blinded, prospective, and randomized, trial. This study was blinded to the data-collecting investigator and the studied drugs were prepared and administered by other investigators blind to the data collected.

GA was required when regional anesthesia was contraindicated or failed, or with patient refusal to regional anesthesia. This study was performed in the Kasr Al-Ainy University Hospitals over a period of six months started from March 2015.

Exclusion criteria included emergency cases, evidence of fetal compromise or intrauterine growth retardation, HELLP syndrome (**h**emolysis, **e**levated **l**iver enzymes, and **l**ow **p**latelet levels), morbid obesity, diabetes mellitus, or known allergies to the tested drugs. Parturients with history of cardiac, pulmonary, hepatic, renal or other diseases were also excluded. Preoperative monitoring of fetal heart sounds was applied to exclude fetal distress. Preoperatively, all patients were assessed clinically and investigated for the exclusion criteria. Complete blood count, bleeding profile, liver and kidney function tests were routinely recorded for all patients.

All patients were randomly allocated into two groups, ***Group R*** (remifentanil) and ***Group D*** (dexmedetomidine), using a computer generated randomization list and a sealed envelope technique (n = 25/group). An intravenous line was established and infusion of lactated Ringer's solution was started at a rate of 15 ml/kg/h till delivery. All patients received a loading dose of *iv* magnesium sulfate (4 gm), followed by 1 gm/h *iv* infusion for seizure prophylaxis, and *iv* hydralazine (5 mg) at 20 min intervals when SBP > 160 mmHg or diastolic arterial pressure (DBP) >110 mmHg. All patients were fasted for six hours and pre-medicated with 30 ml of oral sodium citrate and iv ranitidine 150 mg and ondansetron 4 mg. Patients were placed in the supine position with left lateral tilt and preoxygenated with 100% O_2 face mask over three minutes. ECG, pulse oximetry, capnography and train-of-four monitoring were applied. A left radial artery catheter was inserted under local anesthesia for invasive continuous blood pressure measurement.

In group **(R)**, a bolus of intravenous (*iv*) remifentanil (1 μg/kg) was given over 30–60 sec, followed by a continuous infusion of (0.05 μg/kg/min), while in group **(D)**, a bolus of *iv* dexmedetomidine (1 μg/kg) was given over 10 min, followed by a continuous infusion of (0.2 μg/kg/h). In both groups, the infusion was stopped with peritoneal incision.

Anesthesia was then induced in both groups with *iv* bolus of propofol (2 mg/kg) followed by a continuous infusion of 6–10 mg/kg/h, succinylcholine (1.5 mg/kg) was given, cricoid pressure was applied, the trachea was intubated and the patient was ventilated with a mixture of oxygen in air (50%). Atracurium 0.5 mg/kg was given after succinylcholine effect faded. After delivery, fentanyl 3 μg/kg and oxytocin (30 IU) in 500 ml Ringer's solution were given. When skin suturing started, propofol infusion was stopped, atropine 0.02 mg/kg and neostigmine 0.05 mg/kg were used for reversal of neuromuscular block under train-of-four monitoring, and the patient was extubated when she was able to localize. Extubation time (from cessation of propofol infusion to extubation) was recorded.

Mean arterial blood pressure (MAP) and heart rate (HR) were recorded five minutes after radial arterial puncture **(T_0)**, just after induction of GA **(T_I)**, just after intubation **(T_T)**,