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ORIGINAL ARTICLE

Efficacy of dexmedetomidine in suppressing cardiovascular and hormonal responses to general anaesthesia for caesarean delivery: a dose–response study

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ABSTRACT

Background: Preoperative dexmedetomidine administration blunts haemodynamic and hormonal responses to tracheal intubation and reduces anaesthetic requirements. We hypothesized that dexmedetomidine would reduce the maternal haemodynamic and hormonal responses to elective caesarean delivery without harmful neonatal effects.

Methods: After ethical approval, 68 parturients scheduled for elective caesarean delivery under general anaesthesia were randomly allocated to receive either placebo, or 0.2, 0.4 or 0.6 μg/kg/h intravenous dexmedetomidine ($n = 17$ per group) 20 min before induction. Anaesthesia was induced using a rapid-sequence technique with propofol and suxamethonium, and was maintained with 0.5–0.75 minimum alveolar concentration sevoflurane. Changes in maternal heart rate, mean blood pressure, minimum alveolar concentration sevoflurane, uterine tone, serum cortisol level, and Apgar scores, Neurologic Adaptive Capacity Scores and acid–base status were recorded.

Results: After induction, patients receiving dexmedetomidine had smaller increases in heart rate ($P < 0.001$) than those in the placebo group. Patients who received 0.4 and 0.6 μg/kg/h infusions of dexmedetomidine showed slower heart rates (−21.5% and −36%, respectively; $P < 0.001$), lower mean blood pressures (−17% and −25%, respectively; $P < 0.001$), sevoflurane minimum alveolar concentrations (−40% and −44.5%, respectively; $P < 0.001$) and serum cortisol levels (−27% and −34.6%, respectively; $P < 0.001$) and higher sedation scores for the first 15 min after extubation and greater uterine tone ($P < 0.002$). Apgar scores, NACS and acid–base status were similar in the four groups.

Conclusion: Preoperative administration of dexmedetomidine 0.4 and 0.6 μg/kg/h is effective in attenuating the maternal haemodynamic and hormonal responses to caesarean delivery under sevoflurane anaesthesia without adverse neonatal effects.

Keywords: Caesarean section; General anaesthesia; Dexmedetomidine; Cardiovascular response; Hormonal response

Introduction

Central neuraxial blockade has become the standard choice for caesarean delivery but general anaesthesia (GA) is commonly used at the authors' hospital due to patient refusal of neuraxial anaesthesia or extreme urgency. Cardiovascular and hormonal responses to tracheal intubation and surgical stimulation during caesarean delivery may be modulated by a variety of agents including opioids, tenoxicam, ketorolac, lidocaine and paracetamol.[1–4] Maternal opioid administration before delivery may, however, induce neonatal respiratory depression.[1]

Preoperative administration of high doses of dexmedetomidine, a specific alpha 2-adrenoceptor agonist, either as a single dose (0.5–1 μg/kg)[5–7] or continuous infusion (0.6 μg/kg/h),[8] blunts haemodynamic and hormonal responses to tracheal intubation,[9,10] reduces opioid and anaesthetic requirements,[7,10,11] and improves the quality of postoperative analgesia.[12] The use of lower doses (0.3 μg/kg) is associated with insignificant haemodynamic changes.[7] Continuous infusion of dexmedetomidine may be safer than single doses (1–2 μg/kg) by reducing the incidence of bradycardia and hypotension.[5,7,13]

While dexmedetomidine may improve the quality of GA in women undergoing caesarean delivery, there is concern about its effect on neonatal outcome. Dexmetetomidine has been used during caesarean delivery in

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women with myasthenia gravis, spinal muscular atrophy, tethered spinal cord syndrome and primary pulmonary hypertension without adverse neonatal outcome.[14–17] It disappears rapidly from the maternal circulation,[18] and acute exposure at the anticipated delivery time has been shown to have no adverse effects on fetal development and postnatal behaviour in the offspring of pregnant rats.[19]

We hypothesized that preoperative intravenous dexmedetomidine infusion would reduce maternal haemodynamic and hormonal responses to tracheal intubation, surgical stimulation and extubation after uncomplicated caesarean delivery under GA, without adverse neonatal effects. This study aimed to test the effects of preoperative intravenous infusion of dexmedetomidine (0.2, 0.4 or 0.6 μg/kg/h) on perioperative maternal haemodynamics, minimum alveolar concentration of sevoflurane (MAC-Sevo), uterine tone, need for oxytocin, quality of extubation, serum cortisol levels and neonatal outcome at elective caesarean delivery under sevoflurane anaesthesia.

Methods

Approval for this prospective, randomized, double-blinded placebo–controlled study was given by the local ethics committee. The protocol was registered with www.clinicaltrials.gov [NCT01005433]. Written informed consent was obtained from all participants who refused neuraxial block and requested GA for caesarean delivery due to breech presentation, cephalopelvic disproportion or previous caesarean delivery. Sixty-eight American Society of Anesthesiologists class I and II parturients aged 18–35 years, with uncomplicated, singleton pregnancies of at least 36 weeks of gestation scheduled for elective caesarean delivery via a Pfannenstiel incision under GA were recruited. Operations were performed by the same surgeons.

Women with a history of allergy to dexmedetomidine, cardiac, pulmonary, hepatic, renal, neurological or neuromuscular diseases, morbid obesity, diabetes mellitus, anaemia, bleeding disorders, those receiving cardiovascular, antipsychotic or hypnotic medications, alcohol or drug abuse, those with pregnancy-induced hypertension, evidence of intrauterine growth restriction or fetal compromise were excluded from the study.

Anaesthetic management was standardized. Oral ranitidine 150 mg was given the night before and on the morning of surgery, with 0.3 mol/L sodium citrate 30 mL given 15 min before induction. Patients were allocated randomly into four groups by drawing sequentially-numbered sealed opaque envelopes containing a software-generated randomization code (Random Allocation Software, version 1.0.0, Isfahan University of Medical Sciences, Isfahan, Iran). The placebo group ($n = 17$) received an intravenous infusion of 0.9% saline 0.1 mL/kg/h, starting 20 min before induction of anaesthesia. The dexmedetomidine groups ($n = 17$ for each) received an intravenous infusion of 0.1 mL/kg/h of solution containing either 2, 4, and 6 μg/mL of dexmedetomidine (DEX 0.2, DEX 0.4 and DEX 0.6, respectively, supplied by Precedex, Hospira, Inc. Lake Forest, IL, USA), starting 20 min before induction of anesthesia. The placebo and dexmedetomidine solutions looked identical.

After peritoneal closure, infusion rates were reduced by two-thirds to 0.03 mL/kg/h and continued until skin closure. One anaesthesiologist not otherwise involved in the study prepared the study solutions. An anaesthesiologist who was blinded to treatment regimen provided perioperative care. A third anaesthesiologist collected perioperative data. All staff in the operating room were unaware of patient allocation.

Maternal monitoring included electrocardiography, non-invasive blood pressure, pulse oximetry, end-tidal carbon dioxide ($ETCO_2$) and sevoflurane concentrations, response entropy (RE) and state entropy (SE) (Datex-Ohmeda Division, Instrumentarium Corporation, Helsinki, Finland). Left uterine displacement was maintained. After preoxygenation for 5 min, a rapid-sequence induction was performed with propofol 1.5–2.5 mg/kg (to achieve an SE <50 and a difference <10 between RE and SE; RE–SE), and suxamethonium 1 mg/kg. Cricoid pressure was applied, laryngoscopy was performed after the 1-min blood pressure recording, and tracheal intubation was completed before the 2-min reading. Anaesthesia was maintained with a 0.5–0.75 MAC-Sevo with nitrous oxide 50% in oxygen to maintain SE <50 and RE-SE <10. Rocuronium 0.6 mg/kg was given to maintain suppression of the second twitch using a train-of-four stimulation. The patients' lungs were ventilated to maintain an $ETCO_2$ of 30–35 mmHg. Induction-to-delivery time was recorded using a stopwatch. After the umbilical cord was clamped, a 10-IU infusion of oxytocin lactated Ringer's solution 500 mL was started, end-tidal nitrous oxide concentration was increased to 70% and fentanyl 2 μg/kg was administered.

The obstetrician assessed uterine tone by palpation every 3 min after placental delivery and rated the degree of uterine contraction on a 10-cm visual analog scale (VAS) (0=well contracted; 10=completely relaxed). If uterine tone remained unsatisfactory after 3 min, an additional 5 IU bolus of oxytocin was administered.

A paediatrician blinded to study group allocation recorded Apgar scores at 1 and 5 min, umbilical cord blood gas analysis and Neurologic Adaptive Capacity Score (NACS) at 15 min, 2 h and 24 h after delivery. NACS gives a maximum of 40 with a score >35 denoting vigor.[20] The percentage of infants scoring <35 was