Intravenous dexmedetomidine as an adjunct for labor analgesia and cesarean delivery anesthesia in a parturient with a tethered spinal cord


Abstract

For parturients desiring labor analgesia who have contraindications to neuraxial techniques, intravenous opioid-based patient-controlled analgesia (IVPCA) offers a reasonable alternative, although incomplete analgesia and maternal and neonatal respiratory depression can occur. Dexmedetomidine, a highly selective α2 agonist with negligible placental transfer, may be a valuable adjunct to IVPCA by providing additional analgesia without the respiratory depression associated with increasing opioid usage. The successful use of a dexmedetomidine infusion as an adjunct to unsatisfactory fentanyl IVPCA is reported in a 31-year-old parturient with spina bifida occulta and a tethered spinal cord reaching L5-S1. Dexmedetomidine significantly improved the analgesic quality; increased sedation was observed, but the patient was easily rousable to verbal stimuli. No episodes of maternal hypotension or bradycardia, or fetal heart rate irregularities occurred. Cesarean delivery was required for prolonged first stage of labor and presumed chorioamnionitis; it was conducted under general anesthesia during which the dexmedetomidine infusion was continued. A healthy baby boy was delivered with normal Apgar scores and no discernible neurobehavioral or other deficits.

Introduction

Intravenous patient-controlled analgesia (IVPCA) with opioid remains an acceptable option for establishing labor analgesia, especially when neuraxial techniques are contraindicated. Although relatively safe, opioid-based IVPCA is not uncommonly associated with incomplete analgesia and respiratory depression in the mother and neonate. The α2 agonist clonidine is used occasionally for neuraxial labor analgesia, but rarely by the intravenous route in the obstetric setting due to detrimental effects on uterine tone and fetal heart rate with high plasma concentrations. Dexmedetomidine, an agent with greater α2 selectivity and significantly less placental transfer, may serve as a valuable alternative, particularly when responding to inadequate labor analgesia with systemic opioids. In this report, the successful use of dexmedetomidine as an adjunct to a fentanyl-based IVPCA and general anesthesia in a parturient with spina bifida occulta and a tethered spinal cord is described.

Case report

A 31-year-old G2P0 parturient, measuring 155 cm and 104 kg (BMI 43 kg/m²), presented for elective induction of labor at 40 weeks of gestation. Her past medical history was significant for morbid obesity, medically managed gastroesophageal reflux disease, a significant smoking history and clinically asymptomatic spina bifida occulta with a tethered spinal cord at L5-S1, which was diagnosed incidentally in adult life by magnetic resonance imaging to evaluate a complaint of neck pain. Her medications included sporadic use of omeprazole for acid reflux and a nicotine patch to complement her smoking cessation efforts. She had a modified Mallamp-
of dexmedetomidine were reported by the patient to be requested before vaginal examinations. The bolus doses for the analgesia and the occurrence of complications. A 0.5-g/kg loading dose of dexmedetomidine administered over 10 min resulted in an immediate reduction of NRS scores from 10/10 to 5/10. The maternal blood pressure did not change from baseline, and the fetal heart rate remained between 150 and 160 beats/min with moderate variability. Subsequently, a continuous dexmedetomidine infusion was initiated at 0.2 μg·kg\(^{-1}\)·h\(^{-1}\) and the patient’s NRS score remained <2/10 for 2 h. The dexmedetomidine infusion rate was titrated to maintain a NRS target score <4/10 and ultimately, a maximal infusion rate of 0.6 μg·kg\(^{-1}\)·h\(^{-1}\) was provided. The infusion rate alterations often mirrored the changes in oxytocin infusion used for labor augmentation. Moreover, bolus doses of dexmedetomidine (0.25 μg/kg) were requested before vaginal examinations. The bolus doses of dexmedetomidine were reported by the patient to be significantly more effective than the IVPCA fentanyl boluses that the patient was able to control. Throughout her labor course, the patient maintained an oxygen saturation above 95% and consequently, no supplemental oxygen was given.

Sixteen hours after the initiation of the dexmedetomidine, the patient underwent a cesarean delivery for prolonged first stage of labor and a presumed diagnosis of chorioamnionitis. She received general anesthesia with a rapid sequence induction and subsequent maintenance with an O\(_2\)/N\(_2\)O/sevoflurane mixture. The dexmedetomidine infusion was continued during general anesthesia to maintain cardiovascular stability. The patient remained hemodynamically stable, with no episodes of hypertension or hypotension beyond 20% from baseline, although a total ephedrine dose of 40 mg (given in 10 mg doses) was given to maintain the blood pressure within this range. A healthy baby boy was delivered with Apgar scores of 7 and 8; the baby was taken to the neonatal intensive care unit (NICU) for observation. Maternal and umbilical cord blood samples were collected for planned drug assays. The infusion was gradually discontinued, the patient was extubated, and recovery proceeded uneventfully; intravenous morphine was titrated for postoperative analgesia.

At the postoperative visit on the following day, the patient reported that her labor analgesia significantly improved with the addition of the dexmedetomidine infusion, and that she had a full memory of events, including vaginal examinations. The patient denied, however, any awareness of the cesarean delivery. She expressed genuine satisfaction with her analgesic and anesthetic experience and indicated a desire to receive the same analgesic regimen for future pregnancies; she also gave consent to the written and verbal presentation of her case. No aberrations were noted in the neonate during the 24 h of NICU observation or at any time up to routine discharge to home three days later. Attempts to find a laboratory willing to measure serum concentrations of dexmedetomidine were unsuccessful.

**Discussion**

Among spinal dysraphisms, a tethered spinal cord is of particular anesthetic concern due to the low conus medullaris with limited mobility;\(^4\) this anatomic variation can increase the potential for direct needle trauma to the spinal cord and nerve roots. Neuraxial techniques are consequently avoided and other analgesic and anesthetic alternatives should be discussed. Opioid-based IVPCA is a popular option for labor analgesia in these patients, but unsatisfactory analgesia and maternal and neonatal respiratory depression may result.\(^5\)

Animal studies have confirmed the additive or synergistic effects of \(\alpha_2\) agonists when co-administered with...
Dexmedetomidine, an α2 agonist, has been extensively investigated as an adjunct to spinal and epidural opioids and has an acceptable safety profile. However, to our knowledge, there are no reports detailing the successful use of intravenous clonidine for labor analgesia, possibly due to concerns of maternal sedation and enhanced placental transfer associated with high serum levels.3

Dexmedetomidine, an agonist with greater α2 selectivity, has been shown to have significant analgesic and sympatholytic properties.6 The sedative properties of the drug are produced by stimulation of presynaptic α2 receptors, which results in a presynaptic decrease in norepinephrine release and an inhibition of postsynaptic activation; overall this serves to attenuate central nervous system excitation.7 Because the effects of dexmedetomidine are not mediated by the γ-aminobutyric acid(GABA)-mimetic system, it provides sedation, analgesia and anti-shivering properties without respiratory depression.8 More specifically, dexmedetomidine has been noted to achieve ‘cooperative sedation’ by which procedures can be performed (e.g. awake fiberoptic intubation) with the patient interacting with healthcare providers.9

Although not approved for use during pregnancy, dexmedetomidine has been reported to decrease the total dose of opioids, promote hemodynamic stability and maintain maternal homeostasis and uteroplacental blood flow in pregnant patients undergoing non-obstetric surgery.10 Moreover, in vitro perfusion studies of isolated human placentas have demonstrated lower maternal-to-fetal transfer with dexmedetomidine than clonidine,11 presumably due to the greater lipophilicity enhancing placental retention.12,13 As such, dexmedetomidine, by virtue of its increased α2 selectivity, limited effects on uteroplacental blood flow, and minimal placental transfer, may be a preferred adjunct to opioid-based IVPCA versus clonidine or alterations in the dose or type of opioid. Dexmedetomidine may have other benefits specific to providing labor analgesia: a reduction in maternal shivering with its possible favorable influences on intrapartum fever,14,15 less impairment of recall than benzodiazepines16 (although this is in need of further investigation), which may be valuable for the memory of the birthing experience, and a mild sedative effect that resembles natural drowsiness and sleep.17 Of interest, laboratory studies have indicated that dexmedetomidine can also augment spontaneous contractions in the isolated human myometrium,18 which could possibly have beneficial effects on the progression of labor.

Our case demonstrates the benefits of dexmedetomidine in augmenting the analgesic quality of an opioid IVPCA for labor without any apparent deleterious maternal or fetal effects. No episodes of maternal hypotension or bradycardia, or changes in the fetal heart rate occurred during the 16 h of dexmedetomidine infusion for labor or during the subsequent cesarean delivery. During labor, the patient successfully tolerated oxytocin augmentation after the dexmedetomidine was added, and remained sedated, but able to respond to verbal stimuli in an alert and oriented manner. No discernible neonatal neurobehavioral impairment was present in the postoperative period during a 24-h NICU stay or at any time before routine discharge three days later.

The dosing regimen for dexmedetomidine was selected according to standard dosing regimens for sedation in critically ill patients; while these suggest that a 1 μg/kg loading infusion be administered over 10 min followed by a continuous infusion of 0.2 to 0.7 μg·kg⁻¹·h⁻¹,8 we decided to halve the suggested loading dose and use the lowest known continuous infusion. This dosing regimen was selected because the resulting effects were unknown and a baseline degree of sedation had already been established with opioids; moreover, intravenous bolus administration of dexmedetomidine (1–2 μg/kg in 2 min) has been observed to be associated with hypertension, hypotension, and irregular ventilatory patterns with short episodes of apnea.19,20 By contrast, significant stable–plasma concentrations of dexmedetomidine have been associated with either absent or mildly affected ventilatory alterations.21 Further work will be necessary to evaluate these effects during pregnancy and labor, particularly when dexmedetomidine is combined with opioids or other analgesics. Like any sedative or analgesic, the drug will require titration parameters based on efficacy and safety. Moreover, the opioid-sparing or analgesic contribution of systemic, versus neuraxial, administration of dexmedetomidine will need to be assessed; human experimental pain studies have demonstrated an analgesic effect with neuraxial administration, but are less clear with systemic administration.22 Finally, the abrupt discontinuation of dexmedetomidine may be accompanied by a 7–10% rise in mean systolic pressure, but unlike reports with clonidine, more severe hypertension or tachycardia has not been observed.8

Maternal and umbilical cord blood samples were collected in order to assay dexmedetomidine concentration, but all commercial and research laboratories approached, including the manufacturer of dexmedetomidine, were either unwilling or unable to perform the assays at a reasonable cost. Further acceptance of dexmedetomidine during pregnancy will depend on a robust assessment of maternal and fetal drug concentrations and effects. In addition, dexmedetomidine dosing regimens with or without opioids and guidelines for the provision of obstetric labor analgesia will need to be developed, because of the risk of respiratory depression. Particularly when dexmedetomidine is combined with an opioid, continuous pulse oximetry should be employed.
Few alternatives for labor analgesia exist when neur-axial administration is contraindicated and a particular i.v. or intramuscular opioid has proven inadequate. A different opioid may be used with IVPCA, and a continu-ous infusion may be added. Remifentanil and alfenta-nil have been used successfully for IVPCA labor analgesia. In our experience, however, as well as that of others, analgesia may be inadequate partly because the parturient is unable to synchronize the timing of the dose with uterine contractions and because the duration of action is too brief to provide relief for the next contraction. The addition of a continuous infusion frequently results in excessive sedation or respiratory depression.

In conclusion, i.v. dexmedetomidine was used success-fully as an adjunct to opioid-based IVPCA and general anesthesia for the respective provision of labor analgesia and cesarean delivery anesthesia in a partur-i ent with a tethered cord. Further evaluation of dex-medetomidine as an adjunct or sole agent for labor analgesia in the obstetric patient, with complete analysis of serum drug levels and maternal, fetal, and neonatal outcomes, is warranted.

References

22. Angst M S, Ramaswamy B, Davies M F, Maze M. Comparative analgesic and mental effects of increasing plasma concentrations of dexmedetomidine and alfentanil in humans.