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Letter to Editor

# The Impact of Intrathecal Dexmedetomidine Administration on Fetuses During Cesarean Sections Performed Using Spinal Anesthesia

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Questions and doubts surround the use of intrathecal dexmedetomidine for spinal anesthesia in cesarean sections. Some evidence suggests that adding dexmedetomidine to local anesthetics may enhance the quality and prolong the analgesia of spinal anesthesia, but its safety and effects on the fetus remain inconclusive [1-2].

Cesarean section is a safe method to prevent high-risk births and obstetric complications while spinal anesthesia (SA) is the preferred anesthetic method during cesarean delivery as it avoids the risks of general anesthesia and offers pain relief post-surgery [3].

Anesthetic drugs may harm the fetus if they cross the placenta. General anesthesia negatively impacted the Apgar score of newborns in the past but advancements in anesthetic techniques and drug development have since reduced its effects on umbilical cord blood gas parameters and Apgar scores. Spinal anesthesia offers a significant advantage over general anesthesia by minimizing the systemic effects of anesthetic agents, particularly opioids on fetus and mother. Spinal anesthesia reduces the risk of substance transfer, thereby offering better protection from medication exposure during anesthesia. Spinal anesthesia can offer longer-lasting pain relief, which early mobilization is crucial as it prevent complications related to immobility, such as deep vein thrombosis and respiratory issues [1,4].

In clinical practice, small doses of local anesthetics in spinal anesthesia often inadequately manage visceral pain, leading to maternal discomfort and short postoperative analgesia. Conversely, high doses can lead to adverse effects such as maternal hypotension, central nervous system toxicity, cardiac toxicity and neonatal acidosis. To address these challenges, anesthesiologists are focusing on enhancing spinal anesthesia through the combination of local anesthetics with adjuvants. Adjuvants are not essential in spinal anesthesia and can lead to adverse reactions, including itching from opioids and bradycardia from Dexmedetomidine [2,5].

Studies show that Dexmedetomidine is a superior adjunct to local anesthetics for intrathecal use compared to fentanyl, morphine, and clonidine, as it enhances spinal anesthesia quality, prolongs pain relief, and has minimal side effects. However, during cesarean sections, concerns arise about its potential effects on the fetus, including neonatal respiratory depression, lower Apgar scores, and acidosis [1-2,5].

Dexmedetomidine offers sedative, analgesic, and anti-sympathetic properties while having minimal respiratory effects. It was initially approved as an ICU sedative thus,

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it's crucial to evaluate the effects of intrathecal Dexmedetomidine on the fetus during cesarean sections. Research indicates that it can enhance intrathecal anesthesia by improving local anesthesia efficacy, reducing side effects, and lowering anesthetic dosages. However, concerns about potential adverse effects on the fetus remain. There is a lack of high-quality studies on the impact of intrathecal Dexmedetomidine during cesarean sections. Although, its use in cesarean section anesthesia is being increasingly recognized and previous reports indicating that its fat-soluble properties limit its transfer across the placenta [1-2,5-6]. We studied intrathecal Dexmedetomidine for cesarean delivery as part of a residency thesis and compared our findings on short-term neonatal outcomes like Apgar scores and umbilical cord blood gas analysis parameters with similar research. We received approval from the university ethics committee (IR.GOUMS.REC.1397.181) and registered our clinical trial (IRCT20181107041590N1).

This study was a double-blind, randomized clinical trial involving 82 patients aged 18 to 40 years. Participants received one of two drug combinations: either 2.5 ml of 5% Bupivacaine (12.5 mg hyperbaric solution) mixed with 0.5 ml normal saline, or 2.5 ml of 0.5% Bupivacaine (12.5 mg hyperbaric solution) combined with 5 μg diluted Dexmedetomidine, both totaling 3 ml.

Based on our findings, Dexmedetomidine as an adjunct to intrathecal bupivacaine accelerated the onset of motor and sensory block. It increased the duration of sensory and motor blockade, reduced postoperative shivering, and increased comfort, facilitating a smoother recovery for mothers. The analgesic properties of Dexmedetomidine may help reduce postoperative pain and the reliance on systemic opioids, which are associated with adverse side effects. The investigator proposed that intrathecal dexmedetomidine enhances analgesia and improves pain relief after cesarean delivery by inhibiting C-fiber transmitters, reducing substance P release, hyperpolarizing post-synaptic neurons via α2 receptor activation, and upregulating adrenergic receptors in the dorsal root ganglia [1-2,7].

We observed reduced postoperative shivering in pregnant mothers who received intrathecal dexmedetomidine. We considered intrathecal dexmedetomidine could potentially reduce postoperative shivering by inhibiting central thermoregulation and minimizing stress responses during the perioperative period, without increasing the risk of adverse effects like maternal bradycardia and hypotension. Intrathecal Dexmedetomidine did not increase maternal hypotension or bradycardia compared to placebo, nor did it raise the incidence of other spinal anesthesia-related complications like itching, nausea, and vomiting. These findings suggest that intrathecal dexmedetomidine may improve intraoperative and post-cesarean care, though further research is required on long-term effects and optimal dosing.

Our analysis revealed no significant differences in neonatal outcomes between the two groups across key parameters. Apgar scores at 1 and 5 minutes, as well as cord blood gas measures—including umbilical artery oxygen partial pressure, carbon dioxide pressure, and pH—were comparable to the placebo group. Furthermore, umbilical glucose and lactate levels were similar in both groups. These findings suggest that intrathecal dexmedetomidine administration with local anesthesia during cesarean sections did not increase adverse reactions in neonates, indicating similar neonatal well-being between the groups.

A major concern with intrathecal dexmedetomidine is its potential neurotoxicity. While animal studies suggest that side effects and demyelination occur only at high doses, there are no clinical reports of neurotoxicity [1-2]. However, the long-term risks need further investigation. Our findings are based on low-dose dexmedetomidine (5 mcg), leaving uncertainty about whether higher doses could pose risks to maternal or fetal health. The effects of increased dosages remain unexplored, creating a gap in our understanding of potential outcomes. Moreover, the absence of empirical data on higher doses raises serious concerns for both maternal and fetal well-being. Maternal physiological changes during pregnancy can affect drug metabolism and clearance, potentially increasing fetal drug exposure. Therefore, a thorough investigation is needed to understand these dynamics and evaluate the safety and efficacy of higher dexmedetomidine doses. Without comprehensive studies on the pharmacokinetics and pharmacodynamics of elevated dexmedetomidine doses, we cannot rule out possible teratogenic effects or long-term neurodevelopmental implications.

We concentrated on the short-term effects, so the long-term impact of intrathecal dexmedetomidine on the fetus remains unclear. One should strive to avoid using dexmedetomidine in cases of brady arrhythmias, severe left ventricular or biventricular dysfunction, and hypovolemic states. Additionally, dose adjustments are necessary in the presence of hepatic and renal dysfunction, as recommended. Future research should include a wider range of pregnancy stages and diverse patient populations to enhance the generalizability of findings across clinical scenarios. Addressing this knowledge gap is crucial for guiding clinical decision-making and optimizing therapeutic strategies while minimizing risks to both the mother and the developing fetus.

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