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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. Dexmedetomidine as an adjunct to spinal anesthesia may enhance its quality and duration, but further research is required to confirm its safety profile, especially regarding fetal effects. [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].

If anesthetic agents are able to cross the placenta, which functions to nourish and protect the fetus, they may exert harmful effects on the unborn child. 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 the 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, for which early mobilization is crucial, as it prevents 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].

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Dexmedetomidine offers sedative, analgesic, and anti-sympathetic properties while having minimal respiratory effects. It was initially approved as an ICU sedative; thus, 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, 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 may reduce postoperative shivering by modulating central thermoregulation and minimizing perioperative stress responses, without increasing maternal bradycardia or hypotension risk. 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, and umbilical artery blood gas values (oxygen partial pressure, carbon dioxide pressure, and pH), were similar 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. inother word, Intrathecal dexmedetomidine with local anesthesia during cesarean sections did not negatively impact neonatal well-being, showing similar outcomes compared to local anesthesia alone.

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. High-dose dexmedetomidine's potential adverse effects and long-term neurodevelopmental risks remain uncertain due to a lack of specific pharmacokinetic and pharmacodynamic studies.

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 bradyarrhythmias, severe left ventricular or biventricular dysfunction, and hypovolemic states. Additionally, dose adjustments are necessary in the presence of hepatic and renal dysfunction, as recommended. To ensure the applicability of research findings to a broader spectrum of real-world clinical practice, future studies should consider expanding the scope of investigation to encompass a greater variety of pregnancy stages. This would allow for a more comprehensive understanding of the phenomena under investigation across the entire gestational period. Furthermore, it is crucial to incorporate more diverse patient populations in subsequent research endeavors. This emphasis on diversity, including variations in ethnicity, coexisting

disease, and pre-existing health conditions, will significantly enhance the generalizability of the results. By studying a wider array of individuals, the findings will be more representative of the broader pregnant population, ultimately increasing their relevance and utility in a multitude of 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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