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ABOUT COVER

Peer Reviewer of *World Journal of Clinical Cases*, Dimitra Bacharaki, MD, PhD, Consultant Physician-Scientist, Department of Nephrology, Attikon University Hospital, Chaidari 12462, Greece. bacharaki@gmail.com

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Butorphanol in epidural: Could this be the breakthrough solution for safe and effective labor analgesia that we've been waiting for?

Anju Gupta, Brinda Valecha, Nishkarsh Gupta

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Anju Gupta, Department of Anesthesiology, Pain Medicine and Critical Care, All India Institute of Medical Sciences, New Delhi 110076, Delhi, India

Brinda Valecha, Department of Anaesthesia, All India Institute of Medical Sciences, New Delhi 110029, India

Nishkarsh Gupta, Department of Onco-Anesthesiology and Palliative Medicine, All India Institute of Medical Sciences, New Delhi 110029, India

Corresponding author: Nishkarsh Gupta, MD, Professor, Department of Onco-Anesthesiology and Palliative Medicine, All India Institute of Medical Sciences, Room No 139 FF IRCH AIIMS, New Delhi 110029, India. dmishkarsh@rediffmail.com

Abstract

The authors have conducted a comprehensive investigation into the safety and effectiveness of butorphanol for epidural analgesia during labor. Their critical analysis of the paper and discussion of the technique's advantages and disadvantages provide a thorough understanding of the topic.

Key Words: Metanalysis; Protocol; Labor analgesia; Labor pain

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Core Tip: Labor pain is one of the most agonizing pains a woman experiences, which can affect both the mother and the fetus physiologically. Among the various methods of labor analgesia, pharmacological interventions play a crucial role. Of all these practices, epidural analgesia has been the most effective and thus widely accepted technique. No study has comprehensively examined the effectiveness and safety of using epidural butorphanol as an analgesic during labor. The authors have investigated the safety and effectiveness of butorphanol for epidural analgesia during labor.

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TO THE EDITOR

Labor pain is one of the most agonizing pains a woman experiences, which can affect both the mother and the fetus physiologically[1]. One of the significant physiological changes in maternal physiology due to labor pain is increased minute ventilation, leading to respiratory alkalosis, which causes decreased uterine blood flow, ultimately leading to decreased fetal oxygenation[2]. Pain-induced release of catecholamines and cortisol further leads to vasoconstriction, resulting in decreased uteroplacental blood flow, affecting fetal circulation and oxygenation. Hence, labor pain management is indispensable to modern-day obstetric anesthesia for maternal and fetal well-being. Among the various methods of labor analgesia, pharmacological interventions play a crucial role. Of all these practices, epidural analgesia has been the most effective and thus widely accepted technique.

Along with the local anesthetic agents, epidural opioids have proven to be beneficial in enhancing the analgesic effect in addition to reducing the dose of local anesthetics, thereby decreasing the risk of motor block[3]. However, the concerns regarding the impact of epidural opioids on maternal and fetal cardiorespiratory systems and neonatal Apgar scores remain. Fentanyl is a μ -receptor agonist, which is used commonly but not without concerns long acting μ receptor agonists like Morphine are avoided for the same reason.

PHARMACOKINETICS OF BUTRUM

Butorphanol is a partial agonist at μ -receptors and is an agonist at the κ -receptors[4]. Since the latter is involved in modulation visceral pain, Butorphanol is highly efficacious in combatting labor pain with minimum side effects. While butorphanol exhibits binding to both μ and κ opioid receptors in radioligand binding studies, its predominant behavioral, pharmacological, and therapeutic effects stem from its lower efficacy agonist activity, specifically at μ opioid receptors [5]. Thus, unlike morphine and fentanyl, it doesn't cause μ receptor mediated delayed respiratory depression, pruritis, nausea, and vomiting[6]. Epidural butorphanol, when compared with epidural morphine, provides safer and faster analgesia, but owing to its shorter duration of action, multiple doses are required[7,8]. The potency of Butorphanol is five times that of morphine[9]. Numerous studies have investigated the efficacy of butorphanol in providing pain relief during labor. Its ability to mitigate labor pain while maintaining maternal hemodynamic stability has been well-documented[10,11]. Butorphanol balances adequate analgesia and minimal fetal respiratory depression, making it an attractive choice for obstetric practitioners. Furthermore, its rapid onset of action and moderate duration of effect align well with the dynamic nature of labor, ensuring timely relief without compromising maternal or fetal well-being. Its limited placental transfer and lower fetal exposure further enhance its safety profile, reassuring healthcare providers and expectant mothers.

PRESENT STUDY

We appreciate the author's Tang *et al*[12] for their brilliant efforts to bridge the gap between the knowledge regarding the safety and efficacy of butorphanol in epidural labor analgesia. It has included randomized controlled trials analyzing the use of epidural butorphanol for labor analgesia. By meticulously searching various trusted electronic databases like PubMed, Web of Science, Cochrane Library, China National Knowledge Infrastructure, *etc.*, it offers a sturdy basis for making evidence-driven decisions in a clinical setting. Incorporating randomized controlled trials into the review framework is a significant advantage as it guarantees a stringent methodology, enhancing the conclusions' reliability. This approach lends greater credibility to the evaluation of butorphanol's effectiveness and safety compared to other opioids used along with local anesthetics. Besides the primary outcome of assessing pain during the first stage of labor and Apgar score, it also evaluated first stage of labor duration, side effects, rate of vaginal delivery, and degree of motor block in adult parturients who received epidural analgesia during labor. This gives a holistic overview of the drug used by providing valuable insights into potential impacts on mothers and infants and the course of labor. It explicitly elaborates on the search strategy, making the entire process transparent. They have also included unpublished sources in the meta-analysis, like conference abstracts, non-randomized controlled trials, review articles, case series, and reports. The evaluation of publication bias by the authors further affirms the quality of the study. Cochrane risk of bias methodology is described to assess the bias in all the randomized controlled trials. Results of heterogeneity amongst the studies have also been included in this funnel plot. It is appreciated that they have included research done in all languages for data collection. They have elaborately specified the three author-based data collection and analysis (data collection and analysis were done by two authors, and a third author would solve any resulting discrepancies).

Notwithstanding its strengths, the metanalysis leaves much more to be answered, which would have been pivotal in the clinical applicability of the study results. The study could have further highlighted if any opposing results had been obtained and the unique side effects, if any. A significant limitation of the meta-analysis is that the dose of epidural butorphanol to be studied has not been mentioned. Still, it can significantly influence the meta-analysis results as the effects are dose-dependent. Various doses of epidural butorphanol have been used in literature, varying from 1 mg to 3 mg. Considering the dose of butorphanol given in epidural analgesia, there will be a possibility of subgroup analysis for the same dose range, and the uniformity would yield reliable results; the study will then be able to provide recommendations regarding strategies of dose titration for best safety profile and efficacy of the drug in labor analgesia. They could have also considered including more secondary outcomes like duration of the first stage and second stage of labor, vaginal delivery rate, and degree of motor block. Assessing the requirement of first rescue analgesia would have helped

determine the duration of action. In case of any breakthrough pain, analgesia should have been mentioned too. There should have been more emphasis on side effects, and revealing the most common side effects would have helped weigh the drug's risk-benefit ratio. This would be important for providers in decision-making for the type of opioid to be used in labor analgesia, considering that butorphanol is far from being used as a routine for this purpose. Overall, the study protocol holds promise for a commendable job of throwing light on safe and efficacious labor analgesia, which is a need of the hour.

CONCLUSION

To conclude, Butorphanol represents a valuable addition to the armamentarium of labor analgesia options. Its unique pharmacological properties offer effective pain relief while mitigating the risks associated with traditional opioid analgesics. Despite its promising attributes, challenges persist in the widespread adoption of butorphanol for labor analgesia. The lack of standardized dosing regimens requires further research to optimize its efficacy and safety profile.

We need studies to determine the optimal dose of epidural butorphanol for labour analgesia and evaluate its safety profile across different patient subgroups, such as those with gestational diabetes, placental disorders, or pregnancy-induced hypertension. Additionally, its effects on the duration of the first and second stages of labour need to be investigated.

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Country of origin: India

ORCID number: Nishkarsh Gupta [0000-0002-8444-2564](https://orcid.org/0000-0002-8444-2564).

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