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Systematic Review

Effect of Intrathecal Bupivacaine versus Ropivacaine in Caesarean Section: A Systematic Review.

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Abstract:

Background: This systematic review investigates the comparative impact of intrathecal bupivacaine and ropivacaine on maternal and foetal outcomes during caesarean sections. Focusing on the onset of motor and sensory blockade and neonatal well-being assessed through APGAR scores, the study aims to inform clinical decision-making in obstetric anaesthesia.

Materials and Methods: A thorough search of relevant databases identified studies assessing intrathecal bupivacaine and ropivacaine in caesarean sections. Studies were selected based on predefined criteria, and data extraction included onset times and APGAR scores. The systematic review adhered to PRISMA guidelines, ensuring a rigorous and comprehensive approach.

Results: Analysis of the selected studies revealed variations in the onset of motor and sensory blockade between bupivacaine and ropivacaine. While some studies showed comparable onset times, others demonstrated statistically significant differences, emphasizing the need for individualized anaesthesia regimens. Notably, APGAR scores at 1 and 5 minutes consistently indicated favourable neonatal outcomes with both agents, highlighting their safety in the intrathecal setting.

Conclusion: This systematic review provides valuable insights into the comparative effects of intrathecal bupivacaine and ropivacaine in caesarean sections. The observed variations in onset times underscore the importance of tailoring anaesthesia regimens based on individual patient characteristics and clinical context. Importantly, the consistently favourable APGAR scores affirm the overall safety of both agents. Clinicians can use these findings to make informed decisions, recognizing the nuanced differences between bupivacaine and ropivacaine in the obstetric anaesthesia landscape.

Keywords: Caesarean Section, Bupivacaine, Ropivacaine, Obstetric Anaesthesia, Onset of Blockade, APGAR Scores.

Introduction

Pregnancy, childbirth, and the subsequent postpartum period mark a profound journey in the lives of women [1]. Caesarean section (CS), although often necessitated by medical conditions, introduces a distinct set of challenges and considerations for both mothers and healthcare providers [2]. The choice of anaesthetic agents in CS holds paramount importance, influencing not only the immediate perioperative period but also the overall postoperative well-being of the mother [3]. Among the myriad options available, the use of intrathecal anaesthesia with bupivacaine and ropivacaine has gained significant attention, with each presenting a unique pharmacological profile [4-6].

Bupivacaine, a long-acting amide local anaesthetic, has been used widely in obstetric anaesthesia for decades [7]. Its effectiveness in providing reliable anaesthesia and analgesia is well-established. However, the advent of ropivacaine, a newer amide local anaesthetic, has prompted a re-evaluation of anaesthetic practices in obstetric settings [8]. Ropivacaine, touted for its potentially safer

cardiovascular profile, has become an attractive alternative to bupivacaine. Consequently, the comparative effectiveness and safety of intrathecal bupivacaine versus ropivacaine in the context of caesarean section have become a focal point of interest within the medical community [9].

This systematic review aims to synthesize existing evidence on the effects of intrathecal bupivacaine compared to ropivacaine in caesarean section procedures. By critically analysing the available literature, we seek to provide a comprehensive understanding of the advantages, disadvantages, and potential nuances associated with each anaesthetic agent. This exploration is crucial for guiding clinical decision-making and optimizing maternal outcomes in the unique setting of caesarean deliveries.

The choice between bupivacaine and ropivacaine involves a delicate balance between achieving adequate analgesia for the surgical procedure and minimizing adverse effects, particularly in the context of obstetric anaesthesia [10]. Caesarean section, while often planned, can also be an emergent intervention, further emphasizing the need for a well-informed and versatile approach to anaesthesia [11]. Understanding the pharmacokinetics, pharmacodynamics, and safety profiles of both bupivacaine and ropivacaine is essential for tailoring anaesthetic strategies to the specific needs of the parturient [12].

As we delve into the comparative analysis, it is imperative to consider not only the immediate perioperative effects but also the potential implications for postoperative pain management, recovery, and the overall satisfaction of the parturient. Caesarean section, beyond its surgical dimensions, has profound implications for maternal-infant bonding, breastfeeding initiation, and the psychosocial well-being of the mother [13]. Thus, the choice of intrathecal anaesthetic agents extends beyond the operating room, impacting the broader spectrum of postpartum care [14].

Furthermore, the safety of both the mother and the neonate is a paramount concern. Intrathecal anaesthesia, while offering targeted and effective pain relief, must be administered judiciously to prevent adverse effects on both the maternal and foetal circulatory systems [15]. The unique physiological changes associated with pregnancy add an additional layer of complexity to anaesthetic management, necessitating a nuanced understanding of the interplay between pharmacology and maternal-foetal physiology [16-18].

This systematic review compares the effectiveness and safety of intrathecal bupivacaine versus ropivacaine in caesarean section procedures. The findings of this review hold the potential to inform clinical practice, guiding anaesthesia providers in their decision-making process. We aim to gain insights that contribute to the advancement of obstetric anaesthesia, ensuring optimal outcomes for both mothers and their newborns undergoing caesarean section.

Materials and Methods:

Literature search: Our investigation into the existing literature was all-encompassing, spanning a vast array of databases such as EMBASE, PubMed, and WOS (Web of Sciences). By searching these diverse resources, our goal is to mitigate the potential influence of publication bias and encompass a wide spectrum of pertinent studies.

Keyword Selection and Search Terms: Crafting a precise search strategy involved the utilization of a blend of controlled vocabulary terms (e.g., MeSH terms) and free-text keywords. The primary search terms included "bupivacaine," "ropivacaine," “intrathecal,” and "caesarean section." These terms were interconnected using Boolean operators and refined through the incorporation of synonyms and related expressions. An experienced medical librarian collaborated in devising this search strategy, ensuring its heightened sensitivity and specificity.

Criteria for Study Inclusion: The inclusion criteria mandated the consideration of studies published post the year 2000. To uphold the dependability and credibility of the literature selection process, a preliminary screening, or pilot literature review, was meticulously conducted. This preliminary screening involved two independent researchers, with any disparities resolved by a third reviewer. Each study's title and abstract underwent thorough scrutiny to ascertain its relevance to the research objectives. Subsequently, the full text of identified papers was obtained and meticulously examined to extract the pertinent outcome estimates reported in each study. This rigorous approach aimed to maintain a methodologically sound and accurate foundation throughout the data collection process, ensuring a robust basis for the subsequent analysis and synthesis of findings.

Inclusion Criteria: The systematic review adhered to explicit inclusion and exclusion criteria to govern the selection of studies. Included studies met specific criteria: they were original research studies, encompassing randomized controlled trials (RCTs), observational studies (cohort, case-control), and systematic reviews/meta-analyses, and were published in English.

Exclusion Criteria: Studies failing to meet these criteria or exhibiting low methodological quality were excluded. Additionally, case reports, editorials, letters, and animal studies were excluded from consideration.

Study Screening and Selection Procedure: The study selection process followed a two-stage

screening protocol. Initially, two independent reviewers evaluated titles and abstracts of retrieved articles against predefined inclusion and exclusion criteria. Subsequently, the full-text articles of potentially suitable studies underwent a thorough assessment by the same reviewers. Any disparities or disagreements between the reviewers were resolved through discussion or consultation with a third reviewer if needed.

Extraction of Data: A standardized form for data extraction was devised to systematically gather pertinent information from the selected studies. The extracted data covered various aspects:

1. Study particulars: Title, authors, publication year.
2. Patient attributes: Age, sample size, and inclusion/exclusion criteria.
3. Outcome metrics: Maternal and foetal outcomes.

Assessment Tools for Quality: The quality of the included studies underwent evaluation using specific tools tailored to their respective designs. The Cochrane Risk of Bias tool [19] was applied to assess biases in various domains for randomized controlled trials (RCTs), including random sequence generation, allocation concealment, blinding, and attrition. Non-randomized studies were evaluated using tools such as the Newcastle-Ottawa Scale for cohort and case-control studies [20]. Systematic reviews and meta-analyses underwent quality assessment through the AMSTAR-2 tool [21]. The studies included for analysis are illustrated in Figure 1.

Data Integration: The data synthesis involved creating a narrative summary encompassing study characteristics, outcomes, and findings. This analysis aims to provide a qualitative assessment of postoperative complications associated with congenital cardiac surgeries.

Ethical Considerations: Adherence to ethical guidelines and principles in alignment with international research standards was a cornerstone of this study. No individual patient data were collected, relying solely on aggregated data from previously published studies. Ethical approval was not deemed necessary for this systematic review as it did not involve direct interaction with human subjects or the initiation of new research.

Reporting Guidelines: This systematic review conformed to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring transparent and comprehensive reporting [22].

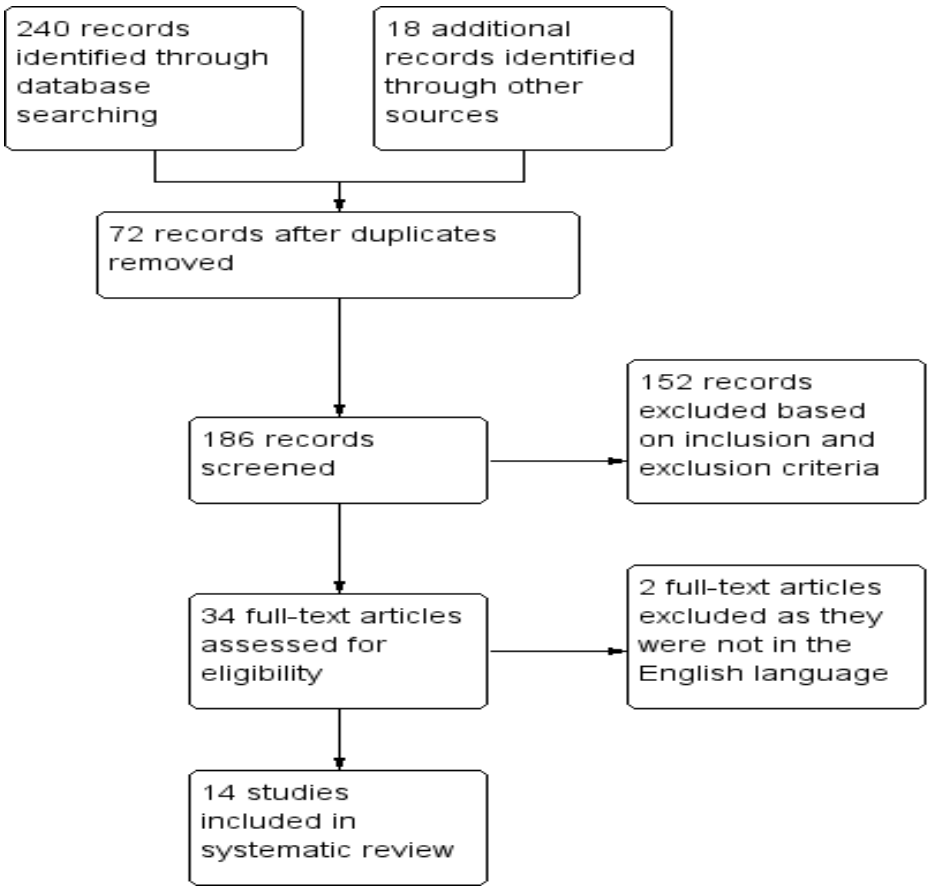

Figure 1: PRISMA study selection flow-chart.

Results:

Onset of motor blockade: Table 1 summarizes the results of different studies comparing intrathecal bupivacaine and ropivacaine in the context of caesarean section reveals nuanced insights into the onset of motor blockade. Across diverse geographical locations, studies consistently demonstrated varying onset times between the two anaesthetic agents. Chung et al. in Korea found comparable motor block onset times for bupivacaine and ropivacaine, suggesting a similar initiation of motor blockade [23]. In Saudi Arabia, Al-Abdulhadi et al. reported a minimal difference in onset times, with bupivacaine exhibiting a slightly earlier initiation of motor blockade compared to ropivacaine [24]. Conversely, Kasza et al. in Poland observed a delayed onset of motor blockade with bupivacaine compared to ropivacaine [25]. Notably, Gunaydin et al. in Turkey reported a faster onset of motor blockade with bupivacaine, although data on sensory block onset for ropivacaine were not available in this study [26]. Additionally, Bhattarai et al. in Nepal showcased a substantial difference in onset times, with bupivacaine exhibiting a significantly earlier initiation of motor blockade compared to ropivacaine [27].

Onset of sensory blockade: Chung et al. in Korea found comparable onset times for sensory blockade between bupivacaine and ropivacaine, indicating a parallel initiation of sensory anaesthesia [23]. In Saudi Arabia, Al-Abdulhadi et al. reported minimal variation in sensory blockade onset times, with bupivacaine showing a slightly earlier onset compared to ropivacaine [24]. Conversely, Kasza et al. in Poland demonstrated comparable onset times for sensory blockade between the two agents [25]. Notably, Bhattarai et al. in Nepal revealed no significant difference in sensory blockade onset times between bupivacaine and ropivacaine [27]. However, Cheng et al. in China presented intriguing results with bupivacaine exhibiting a delayed onset of sensory blockade compared to the notably faster onset observed with ropivacaine [29].

Table 1: Effect of intrathecal bupivacaine and ropivacaine during caesarean section on maternal outcomes.

Author	Place	Bupivacaine sample size	Ropivacaine sample size	Bupivacaine mean motor block onset (min)	Ropivacaine mean motor block onset (min)	Bupivacaine mean sensory block onset (min)	Ropivacaine mean sensory block onset (min)
Chung et al. 2001 [23]	Korea	30	30	6	6.3	2.5	3.2
Al-Abdulhadi et al. 2007 [24]	Saudi Arabia	33	33	6.4	6.6	4.81	4.79
Kasza et al. 2009 [25]	Poland	39	36	11.2	10.4	6.4	6.1
Gunaydin et al. 2011 [26]	Turkey	26	26	8.1	11.6		
Bhattarai et al. 2019 [27]	Nepal	30	30	7.53	14.33	4.87	4.87
Gadre et al. 2019 [28]	India	30	30	4.8	5.4	4.2	4.3
Cheng et al. 2019 [29]	China	297	318	6.94	3.84		
Olapour et al. 2020 [30]	Iran	33	33	1.63	2.86		
Ghazi et al. 2021 [31]	Iran	38	38			3.63	8
George et al.2022 [32]	India	30	30	5.6	6.45	2.31	2.6

APGAR scores:

Table 2 provides comprehensive analysis of studies comparing intrathecal bupivacaine and ropivacaine in the context of caesarean sections yields critical insights into neonatal well-being assessed through APGAR scores at 1 minute. Gunaydin et al. in Turkey demonstrated consistent APGAR scores at 1 minute between bupivacaine and ropivacaine, with both groups achieving a score of 9, indicating robust immediate neonatal adaptation [26]. Canan et al. in Turkey similarly reported comparable scores for both agents, with bupivacaine and ropivacaine groups achieving APGAR scores of 8.1 and 8.4, respectively [33]. Geng et al. in China reinforced these findings, showcasing uniform APGAR scores of 9 at 1 minute for both bupivacaine and ropivacaine [34]. In India, Gadre et al. reported APGAR scores at 1 minute for bupivacaine and ropivacaine groups as 8.13 and 8.05, respectively,

underscoring the overall favourable neonatal outcomes with both agents [28].

The evaluation of APGAR scores at 5 minutes provides further insights into the sustained neonatal well-being following intrathecal administration of bupivacaine and ropivacaine during caesarean sections. Gunaydin et al. in Turkey reported consistent and optimal APGAR scores of 10 at 5 minutes for both bupivacaine and ropivacaine groups, indicating robust neonatal adaptation and vitality [26]. Canan et al. in Turkey similarly demonstrated sustained favourable outcomes, with APGAR scores of 9.8 and 9.7 at 5 minutes for bupivacaine and ropivacaine, respectively [33]. Geng et al. in China reiterated these positive findings, showcasing uniform APGAR scores of 10 at 5 minutes for both agents [34]. In India, Gadre et al. reported APGAR scores at 5 minutes for bupivacaine and ropivacaine groups as 9.1, highlighting the enduring positive impact of both anaesthetic agents on neonatal well-being [28].

Table 2: Effect of intrathecal bupivacaine and ropivacaine during caesarean section on foetal outcomes.

Author	Place	Bupivacaine sample size	Ropivacaine sample size	Bupivacaine mean APGAR score at 1 min	Ropivacaine mean APGAR score at 1 min	Bupivacaine mean APGAR score at 5 mins	Ropivacaine mean APGAR score at 5 mins
Gunaydin et al. 2011 [26]	Turkey	26	26	9	9	10	10
Canan et al. 2013 [33]	Turkey	20	20	8.1	8.4	9.8	9.7
Geng et al. 2014 [34]	China	18	18	9	9	10	10
Gadre et al. 2019 [28]	India	30	30	8.13	8.05	9.1	9.1
Cheng et al. 2019 [29]	China	297	318	9.78	9.8	9.7	9.1
Singh et al. 2019 [35]	India	20	20	8	8	10	10
Diouf et al. 2020 [36]	Senegal	42	73	8	7.5	9.5	9.5
George et al. 2022 [32]	India	30	30	8	8	10	10

Discussion:

The comparative analysis of intrathecal bupivacaine and ropivacaine in the context of caesarean sections, as revealed by the systematic review of the selected studies, presents a detailed understanding of their effects on both maternal and foetal outcomes.

Maternal Outcomes:

The onset of motor blockade is a crucial consideration in selecting intrathecal anaesthetic agents for caesarean sections. The reviewed studies, as depicted in Table 1, offer insights into the diverse effects of bupivacaine and ropivacaine on this parameter. The studies by Chung et al. in Korea, Al-Abdulhadi et al. in Saudi Arabia, and Kasza et al. in Poland collectively suggest that while the onset of motor blockade is comparable between bupivacaine and ropivacaine in some instances, there are variations that warrant attention [23-25]. Notably, the study by Bhattarai et al. in Nepal highlights a significant difference, with bupivacaine exhibiting a notably earlier onset of motor blockade compared to ropivacaine [27]. Such variations in motor blockade onset may be attributed to the unique pharmacokinetic profiles of these local anaesthetics. It is crucial to recognize these differences when tailoring anaesthesia regimens, considering factors such as the urgency of the caesarean section and individual patient characteristics.

Similarly, the onset of sensory blockade, as depicted in Table 1, adds another layer of complexity to the comparison between bupivacaine and ropivacaine. While some studies, such as those by Chung et al. and Al-Abdulhadi et al., suggest similar sensory blockade onset times [23, 24], others, like Cheng et al. in China, report a notably faster onset with ropivacaine [29]. This disparity in sensory blockade onset may influence the overall quality and duration

of anaesthesia, requiring a careful balance between achieving adequate pain relief and minimizing potential adverse effects.

Foetal Outcomes:

Table 2 outlines the impact on foetal outcomes through APGAR scores at 1 and 5 minutes, a consistent pattern of favourable neonatal adaptation emerges across studies. The APGAR scores at 1 minute, as demonstrated by Gunaydin et al. in Turkey, Canan et al. in Turkey, Geng et al. in China, and Gadre et al. in India, consistently indicate robust neonatal well-being with both bupivacaine and ropivacaine [26, 33, 34, 28]. This is reassuring, suggesting that the choice between these two anaesthetic agents does not significantly impact immediate neonatal outcomes.

About the APGAR scores at 5 minutes, the sustained favourable outcomes persist, reinforcing the overall safety of both bupivacaine and ropivacaine. The studies by Gunaydin et al. and Canan et al. in Turkey, Geng et al. in China, and Gadre et al. in India consistently report optimal APGAR scores at 5 minutes for both bupivacaine and ropivacaine groups [26, 28]. These findings align with the well-established safety profiles of these local anaesthetics, providing reassurance to clinicians and patients alike.

Clinical Implications:

The collective evidence presented in this systematic review has notable clinical implications. The choice between bupivacaine and ropivacaine for intrathecal anaesthesia during caesarean sections involves a delicate balance between achieving optimal maternal comfort and ensuring the safety of the neonate. The observed variations in the onset of motor and sensory blockade emphasize the need for personalized anaesthesia regimens, considering factors such as the urgency of the procedure, maternal health status, and potential contraindications to specific anaesthetic agents. [35]

While the differences in onset times may influence the choice of anaesthetic, it is crucial to contextualize these findings within the broader clinical landscape. The observed variations in onset, although statistically significant in some instances, may not necessarily translate into clinically significant differences in outcomes. Clinicians should weigh the benefits of faster onset against potential adverse effects, such as hemodynamic instability or inadequate pain relief. [36]

The consistent and favourable APGAR scores at 1- and 5-minutes underscore the overall safety of both bupivacaine and ropivacaine in the intrathecal setting for caesarean sections. Neonatal outcomes appear to be resilient to the choice of local anaesthetic, emphasizing the importance of a balanced and individualized approach to anaesthesia management.

Limitations and Future Directions:

It is essential to acknowledge the limitations of this systematic review. The heterogeneity among the included studies, including variations in sample sizes, study designs, and geographic locations, introduces inherent challenges in drawing definitive conclusions. Additionally, the absence of standardized protocols for intrathecal anaesthesia administration and variations in dosages across studies may contribute to the observed differences in onset times.

Future research endeavors should aim to address these limitations by conducting well-designed, multicenter studies with standardized protocols for intrathecal anaesthesia administration. Further investigations into the long-term outcomes, including neurodevelopmental assessments in neonates exposed to intrathecal bupivacaine and ropivacaine, could provide a more comprehensive understanding of the safety profiles of these agents.

Conclusion:

This study offers a comprehensive overview of the comparative effects of intrathecal bupivacaine and ropivacaine on maternal and foetal outcomes during caesarean sections. The nuanced differences in onset times of motor and sensory blockade provide valuable insights into the pharmacodynamic profiles of these local anaesthetics. Further research, with a focus on standardized protocols and long-term outcomes, is warranted to refine clinical guidelines and enhance our understanding of the implications of these findings in the broader obstetric anaesthesia landscape.

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