https://doi.org/10.31925/farmacia.2025.2.3 **REVIEW**

EFFECTS OF ROPIVACAINE ADMINISTRATION UNDER DIFFERENT OXYGEN CONCENTRATIONS ON PATIENTS UNDERGOING CESAREAN SECTION: A META-ANALYSIS

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Abstract

This meta-analysis evaluated the effects of ropivacaine under varying oxygen concentrations during caesarean section surgeries. A systematic review identified 12 relevant studies, categorizing participants into low-dose (LD) and high-dose (HD) ropivacaine groups. Data were analysed using RevMan 5.3 with fixed- or random-effects models. No significant differences were observed between HD and LD groups regarding surgical duration or anaesthesia duration. However, HD ropivacaine was associated with significantly higher neonatal Apgar scores. A high degree of heterogeneity was observed for sensory block duration, with the LD group showing notably shorter block duration. The findings indicate that oxygen concentration markedly affects ropivacaine's clinical performance in caesarean sections. HD ropivacaine provides enhanced anaesthesia, longer sensory block, better postoperative analgesia, and superior neonatal outcomes, supporting its preferential use in such surgical contexts.

Rezumat

Această meta-analiză a evaluat efectele ropivacainei administrate în timpul operațiilor de cezariană, în funcție de concentrația de oxigen din mediul operator. Au fost incluse 12 studii relevante, iar participantele au fost împărțite în două grupuri, în funcție de doza de ropivacaină administrată: doză mică (LD) și doză mare (HD). Analiza datelor a fost realizată cu ajutorul programului RevMan 5.3. Rezultatele au arătat că nu există diferențe semnificative între cele două grupuri în ceea ce privește durata intervenției chirurgicale sau durata anesteziei. A fost observată o variabilitate ridicată între studii în ceea ce privește durata blocului senzorial, însă aceasta a fost semnificativ mai scurtă în grupul cu doză mică. În concluzie, concentrația de oxigen din mediul operator influențează semnificativ eficiența ropivacainei în timpul operațiilor de cezariană. Administrarea unei doze mari de ropivacaină se asociază cu beneficii superioare: anestezie mai eficientă, durată mai lungă a efectului, control mai bun al durerii postoperatorii și scoruri neonatale îmbunătățite.

Keywords: oxygen concentration, analgesic effect, ropivacaine, caesarean section surgery, anaesthesia

Introduction

Caesarean section is a common procedure in modern obstetrics where anaesthesia management is critical to ensure maternal and foetal safety and surgical success. Ropivacaine, a long-acting amide local anaesthetic, is widely used for anaesthesia in caesarean section due to its superior anaesthetic efficacy and relatively low cardiac toxicity [1]. However, clinical observations suggest that environmental factors, particularly oxygen concentration, may influence the anaesthetic effects of ropivacaine [2].

Ropivacaine is a long-acting amide local anaesthetic known for its dual anaesthetic and analgesic effects. Due to its relatively low cardiac and neurotoxicity, ropivacaine is widely used clinically for local anaesthesia and pain relief in various surgical procedures [3]. Ropivacaine works primarily by blocking sodium channels in nerve fibres, thereby interrupting pain transmission and producing anaesthesia. Compared to other local anaesthetics such as bupivacaine, ropivacaine has less cardiac toxicity, making it safer for prolonged and high-dose (HD) use [4]. In caesarean section, the safety and efficacy of anaesthesia are critical to maternal and foetal well-being. Ropivacaine, with its excellent anaesthetic efficacy and relatively low side effects, has become an ideal choice for caesarean section anaesthesia. Studies have shown that ropivacaine provides effective intraoperative analgesia and prolonged anaesthesia duration, effectively meeting the requirements of caesarean section surgery. In addition to intraoperative anaesthesia, ropivacaine is widely used for postoperative pain management [5, 6]. Postoperative pain management after caesarean section is a critical aspect of maternal recovery. The sustained analgesic effect of ropivacaine helps to reduce postoperative pain, thereby improving maternal comfort and speeding recovery [7]. Typically, administration of ropivacaine by epidural or spinal injection provides long-lasting postoperative analgesia, reducing reliance on opioid analgesics and minimising their side effects. Despite its high safety profile, clinicians should remain vigilant for potential side effects and complications associated with ropivacaine in clinical

use [8]. Common side effects include hypotension, nausea and headache, while serious complications such as cardiac and neurotoxicity are rare when administered in appropriate doses and managed correctly [9]. Therefore, during caesarean section, health care providers must closely monitor maternal vital signs to detect and manage potential complications. In recent years, research has begun to focus on environmental factors that may affect the anaesthetic efficacy of ropivacaine, particularly variations in oxygen concentration. Oxygen concentration not only affects tissue oxygenation but may also influence the distribution and metabolism of local anaesthetics through various mechanisms [10]. Therefore, investigating the anaesthetic effects of ropivacaine under different oxygen concentration environments is of great importance for optimising anaesthetic management and improving the safety and efficacy of caesarean section surgery.

The regulation of oxygen levels in the surgical environment not only involves gas management within the operating room but is also closely related to the physiological status of the patient [11]. Existing research suggests that high oxygen environments may enhance the efficacy of local anaesthetics, improve tissue oxygenation, and consequently improve anaesthetic efficacy and postoperative recovery [12, 13]. However, there is a lack of systematic, comprehensive evaluation of the efficacy of ropivacaine use under different oxygen concentration environments in caesarean section surgery [14].

Therefore, the aim of this study was to systematically evaluate the interventional effects of ropivacaine under different oxygen concentration environments in caesarean sections using meta-analysis (MA) methods. The aim was to provide a more scientific basis for clinical anaesthetic management. This research aimed to add empirical evidence to anaesthesia management in caesarean section surgery and provide guidance for the rational use of ropivacaine in clinical practice.

Materials and Methods

Data inclusion

This study conducted a systematic search of several online databases, including China National Knowledge Infrastructure, Wanfang, PubMed, Nature, Web of Science, Springer and ScienceDirect, to identify relevant literature on the administration of ropivacaine in caesarean section patients under different oxygen concentration environments. The research focused on dividing caesarean section patients into experimental and control groups with respect to different doses of ropivacaine, and then analysing the effects of ropivacaine administration on these patients. The analysis included variables such as the first author's name, year of publication, group allocations, intervention protocols between groups, and the effects of ropivacaine doses on intraoperative parameters relevant to caesarean section procedures.

Criteria

Inclusion criteria: (1) Randomised controlled trials (RCTs) and quasi-experimental studies to ensure the reliability and scientific validity of the data; (2) The participants were pregnant women undergoing caesarean section, regardless of age, race, body mass index and other basic characteristics; (3) The studies must clearly specify the use of ropivacaine for anaesthesia and compare intervention effects under different oxygen concentration environments; (4) The study types were not restricted; (5) Preference for studies published in peer-reviewed journals, written in English or Chinese, within the last 20 years; (6) Detailed and complete documentation of grouping conditions.

Exclusion criteria: (1) Reviews, case reports, conference abstracts and opinion articles were not included in the analysis; (2) Observational studies without control groups and case studies were excluded; (3) Studies lacking original data despite multiple attempts to obtain them; (4) Duplicate publications in different journals; (5) Studies that did not clearly describe the methods of ropivacaine use and oxygen concentration environments; (6) Studies with incomplete data reporting, lack of key outcome measures, or inability to extract valid data; (7) Exclusion of pregnant women with certain health conditions or serious diseases (such as severe heart disease and renal insufficiency) and patients undergoing emergency caesarean section.

Search strategy

A systematic search of online databases was conducted from January 2000 to May 2022 to evaluate the use of ropivacaine in patients undergoing caesarean section. Chinese search terms included “ropivacaine”, “caesarean section”, “analgesic effect” and “ropivacaine anaesthesia”. English search terms included “ropivacaine”, “caesarean section”, “ropivacaine anaesthesia”, “analgesic effect”, “anaesthetic surgery” and “different oxygen concentrations”. The Boolean operators “or” and “and” were used to combine these keywords in different ways to find relevant literature. The search was language-independent.

Literature screening and quality evaluation

Data extraction and quality assessment of the articles were carried out independently by 2 reviewers using the assessment criteria outlined in the Cochrane Reviewer's Handbook 5.1.0. Articles were first screened for titles and abstracts, and then closely read to exclude studies that did not meet the criteria or were of poor quality. In cases of disagreement between the 2 reviewers, a third reviewer made the final decision. The Cochrane Reviewer's Handbook 5.1.0 criteria are as follows: clarity of the description of the study methods, whether the control and experimental groups were randomised, clarity of the description of the study outcome measures and the corresponding numerical values, completeness of the description of the study

results, and whether the intervention, data handling and assessment of the study results were blinded. Each aspect was scored according to the inclusion criteria of our study, with a total score of seven points. Studies scoring ≥ 4 points were high-quality research.

Extraction of literatures

Two reviewers independently extracted data from the included studies. The extracted information mainly included: (1) basic information about the included studies, such as article title, first author, and year of publication; (2) study outcomes: total sample size of included studies, grouping details, number of cases *per* group, patient age, and intervention methods in each group; (3) extracted indicators of patient efficacy and assessment of joint function, including duration of surgery, Apgar scores, adverse effects, duration of analgesia, maximum duration of sensory block, visual analogue scale (VAS) scores, duration of anaesthesia and umbilical artery pH. This systematic extraction process ensured a comprehensive collection of relevant data from the studies that met the inclusion criteria.

Statistical methods

Experimental data from the included literature were extracted individually and compiled for statistical analysis using Excel. Quantitative metrics were expressed as mean ± standard deviation. The data were then subjected to MA using RevMan5.3. This systematic approach ensured a rigorous statistical evaluation and synthesis of the results of the included studies, following standardised methods for MA in scientific research.

For heterogeneity analysis, an initial assessment was performed using a chi-squared test to assess the heterogeneity of the literature, with a significance level of $\alpha = 0.05$ ($p < 0.05$). A quantitative assessment of heterogeneity was then performed using the I2 statistic in RevMan5.3. When I2 was less than 50%, a fixed-effects model (FEM) was used for MA; when I2 was greater than 50%, a random-effects model (REM) was used. Funnel plots were generated in RevMan5.3 to analyse potential publication bias. Forest plots were also generated to visually present the results, with z-values and p-values extracted for the assessment of MA. All effect sizes were reported with 95% confidence intervals (CIs). A p-value of less than 0.05 indicated statistical significance for differences between groups.

Results and Discussion

Search process

One hundred forty-three articles were retrieved. An initial screening based on article titles, following keyword searches, excluded 78 studies unrelated to therapeutic efficacy and assessment of joint function. Further refinement included abstract review, which led to the exclusion of 17 studies that lacked controls or analysis of confounders. Full-text reading and adherence to inclusion criteria resulted in the exclusion of a further 30 articles. After a detailed review, six studies that could not provide original data were excluded. Twelve articles were finally included in the analysis. The literature search and screening process for this study is shown in Figure 1.

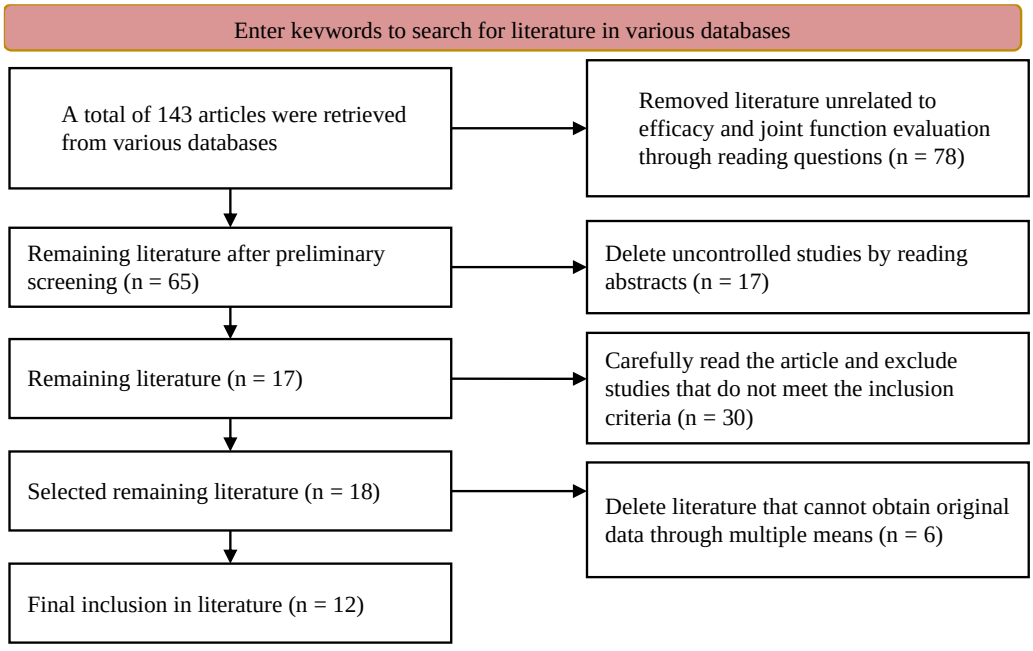

Figure 1.
Basic process of search

Basic literature information

After careful review, 12 articles [15-26] were included in the review. First author, year of publication, number of studies included and demographic details such as age, height and weight of patients in both HD and low-dose (LD) groups were systematically analysed. Detailed statistical results are presented in Table I. A number of 1322 caesarean section patients were included in this study, including 667 patients in the HD group and 655 patients in the LD group. Slight differences in age, height and weight were observed between the two groups.

Table I

Basic literature information

First author	Year	HD group (ex)	LD group (ex)	Age	Height (cm)	Weight (kg)	Outcome indicators
Quan Z [15]	2015	67	67	High: 27 (21 - 40)	163 (152 - 173)	73 (52 - 91)	(2)(3)(5)(8)
				Low: 28 (20 - 43)	162 (154 - 175)	75 (58 - 88)	
Lada Kalagac [16]	2013	20	20	High: 50.35	—	—	(3)(4)(5)(6)(7)
				Low: 53.5	—	—	
Quan ZF [17]	2014	67	67	High: 28 (18 - 41)	162 (152 - 172)	73 (52 - 93)	(2)(3)(4)(5) (7)
				Low: 27 (18 - 37)	160 (146 - 171)	74 (58 - 88)	
Zhang [18]	2017	30	30	High: 27.4 ± 4.1	164.4 ± 4.3	75.2 ± 6.3	(1)(2)(3)(5) (7)
				Low: 26.6 ± 3.2	162.5 ± 2.4	73.1 ± 7.2	
Ashok Jadon [19]	2018	67	67	High: 28.2 ± 4.7	150.5 ± 4	64.5 ± 8.1	(1)(7)(3)
				Low: 28.4 ± 4.5	150.6 ± 4.2	63 ± 6.8	
Pathi S.P [20]	2022	40	40	High: 25.1 ± 2.71	159.7 ± 2.78	71.35 ± 9.58	(2)(3)(4) (5)(7)
				Low: 24.82 ± 2.72	159.7 ± 2.78	71.35 ± 9.58	
Chen [21]	2021	56	56	High: 29.32 ± 6.17	—	68.10 ± 4.08	(3)(4)(5)(8)
				Low: 29.57 ± 7.35	—	68.32 ± 4.12	
Mieszkowski MM [22]	2018	30	28	High: 29.29 ± 4.55	167.80 ± 5.64	82.57 ± 14.26	(1)(2)(3)(4) (5)
				28.74 ± 3.25	166.71 ± 4.93	79.96 ± 9.79	
Yan [23]	2019	39	38	High: 30.8 ± 3.4	—	—	(3)(4)(6)
				Low: 30.3 ± 2.6	—	—	
Wang [24]	2018	135	135	High: 30	161	61	(1)(3)
				Low: 31	161	70	
Yu [25]	2021	79	74	High: 32.4 ± 3.5	159.5 ± 4.8	66.4 ± 6.9	(1)(3)(4)(5)
				Low: 32.5 ± 4.0	160.2 ± 5.0	67.0 ± 7.1	
Nunes [26]	2016	37	33	High: 29.2 ± 6.1	161.8 ± 4.9	76.6 ± 11.8	(2)(3)(4)(5)
				Low: 29.4 ± 6.3	161.7 ± 6.4	79.9 ± 15.1	

(1) = Surgical duration; (2) = Apgar scores; (3) = Adverse reactions; (4) = Duration of analgesia; (5) = Maximum sensory block duration; (6) = VAS scores; (7) = Duration of anaesthesia; (8) = Umbilical artery pH

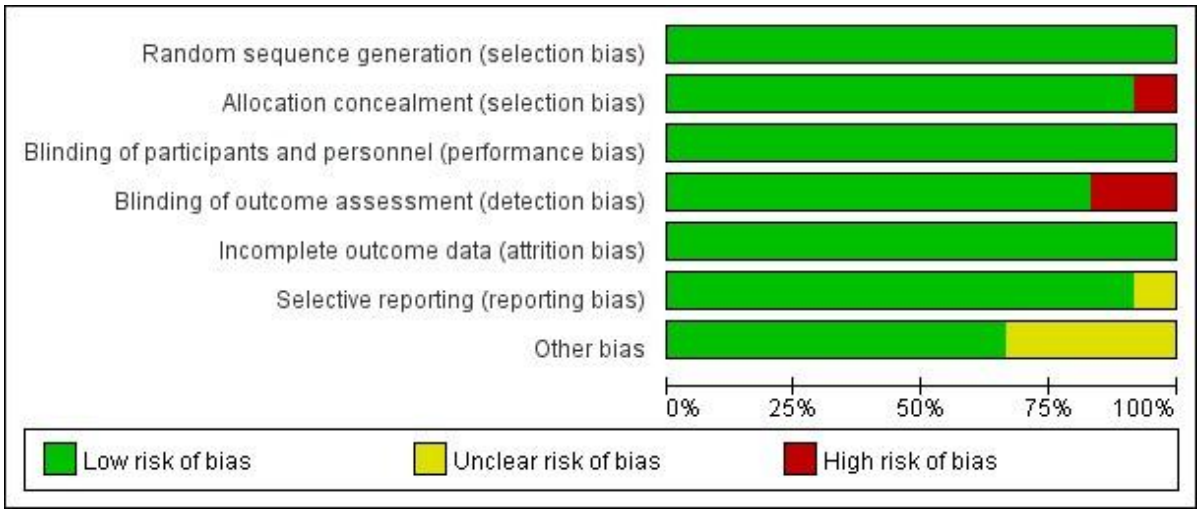

Figure 2.

Bar chart of literature bias risk assessment

Quality evaluation

Figure 2 and Figure 3 show that incomplete outcome data (attribution bias) and selective reporting (reporting bias) were assessed as "low risk" in the 12 included studies. One study was assessed as "high risk" for allocation concealment (selection bias), two studies

were assessed as "high risk" for blinding of outcome assessment (detection bias), and one study was assessed as "unclear" for selective reporting (reporting bias). Other biases were judged to be "unclear" in four studies.

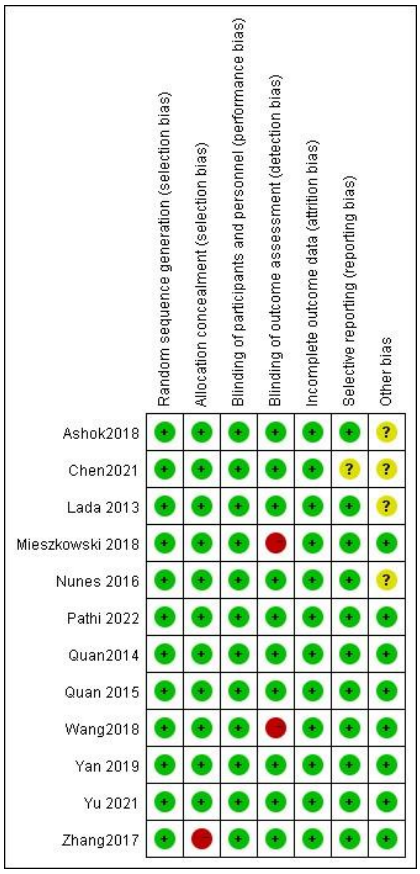

Figure 3.
Summary of literature bias risk assessment

Surgical duration

In the included literature, four studies reported the duration of surgery for patients in different groups. The heterogeneity of operative time among caesarean section patients in these studies was further analysed using MA methods (Figure 4). Negligible heterogeneity was found between the two groups (I2 = 0%, p = 0.84), so a FEM was used for the MA. It was found that there was a negligible difference in operative time between the HD group and the LD group (MD = -1.66, 95% CI: -3.46 ~ 0.14; Z = 1.81, p = 0.07).

Anaesthesia duration

In the included literature, 5 studies reported anaesthesia duration for patients in different groups. MA methods were used to further analyse the heterogeneity of anaesthesia duration among caesarean section patients in these studies (Figure 5). Negligible heterogeneity was found between the LD and HD groups (I2 = 0%, p = 0.75), so a FEM was used for the MA. It was found that there was a negligible difference in the duration of anaesthesia between the 2 groups (MD = -1.65, 95% CI: -4.23 ~ -0.94; Z = 1.25, p = 0.21).

Apgar scores

In the included literature, six studies reported Apgar scores for neonates of caesarean section patients in different groups. MA methods were used to further analyse the heterogeneity of Apgar scores among caesarean section patients in these studies (Figure 6). Significant heterogeneity was found between the LD and HD groups (I2 = 1%, p = 0.41), so a FEM was used for the MA. It was found that neonates of patients in the HD group had significantly higher Apgar scores than those in the LD group (MD = -0.12, 95% CI: -0.22 ~ -0.01; Z = 2.19, p = 0.03).

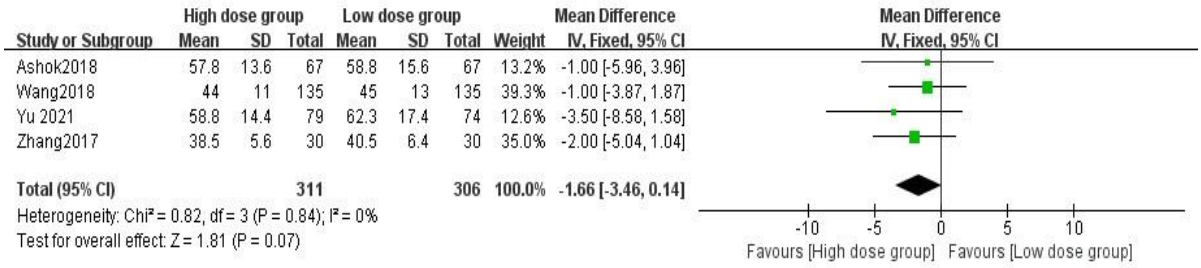

Figure 4.
Forest plot comparing the duration of surgery between two groups of caesarean section patients

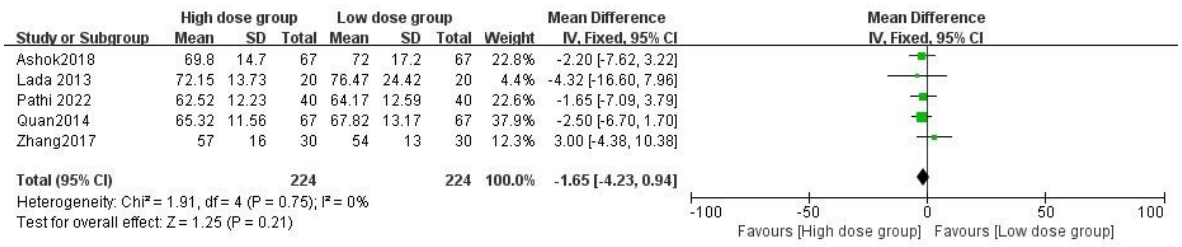

Figure 5.

Forest plot comparing anaesthesia duration between two groups of patients

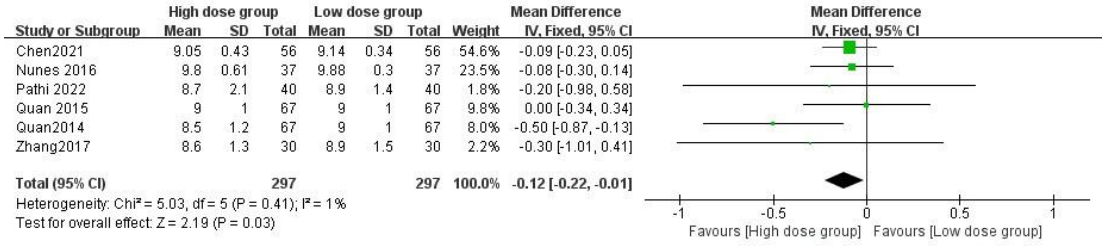

Figure 6.

Forest plot comparing Apgar scores of two groups of patients

Perceived block time

In the included literature, six studies compared the duration of sensory block between different groups of caesarean section patients. MA methods were used to further analyse the heterogeneity of sensory block duration in caesarean section patients across these studies (Figure 7). Notable heterogeneity was observed between the LD and HD groups (I2 = 100%, p < 0.00001), so a REM was applied to the MA. The results showed that patients in the LD group experienced a drastically shorter duration of sensory block than those in the HD group (MD = 6.76, 95% CI: 2.44 ~ 11.08; Z = 3.06, p = 0.002).

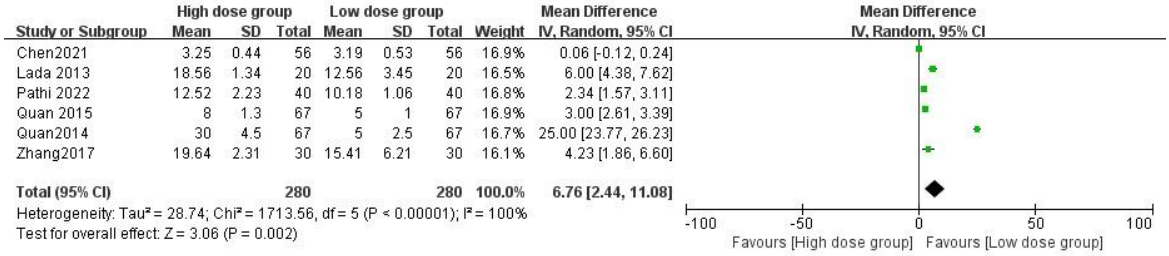

Figure 7.

Comparison of perceived blockade time between LD and HD groups of patients

Analysis of publication bias

In this study, publication bias was analysed by the constructing funnel plots for the included studies. The results showed that the funnel plots for each outcome measure included in this study were generally symmetrical. Most of the included studies fell completely within the boundaries of the funnel plot and were closely clustered around the axis, suggesting low publication bias in the included literature, which all met the required criteria.

This study conducted an MA to compare the interventional effects of ropivacaine administered during caesarean section under different oxygen concentrations. Twelve relevant articles were included through systematic searching and screening, and comprehensive analyses were performed on operative time, anaesthesia time, neonatal Apgar scores, and sensory blockade time. The results showed drastic differences in the effects of different doses of ropivacaine during surgery, particularly in anaesthesia duration and neonatal Apgar scores, where HD ropivacaine showed notable advantages. However, there were negligible differences between HD and LD ropivacaine in terms of operative time and anaesthesia duration, consistent with previous findings showing minimal effects of ropivacaine dose on operative times [27]. Nevertheless, compared to previous studies, this research further emphasises the anaesthetic effects of ropivacaine under varying oxygen concentrations, providing a novel perspective for clinical practice.

Different concentrations of ropivacaine have different effects on anaesthesia, and selection of an appropriate concentration is crucial to achieve optimal anaesthetic outcomes. The MA performed in this study showed that neonatal Apgar scores were significantly higher in the HD group compared to the LD group. This finding is consistent with several studies suggesting that HD ropivacaine not only improves intraoperative analgesia but also has a positive effect on neonatal outcomes. This effect may be due to the efficacy of HD ropivacaine in maintaining maternal stability and reducing pain stress responses, thereby indirectly improving neonatal health. Ropivacaine has a low placental transfer rate, minimising its impact on the foetus and ensuring neonatal safety during caesarean section anaesthesia. Furthermore, the significant improvement in neonatal Apgar scores with HD ropivacaine highlights its unique advantage in ensuring maternal and neonatal safety. Fan *et al*. reported a negligible difference in neonatal Apgar scores with ropivacaine (60 ± 13 mg *vs*. 76 ± 17 mg) [28]. *Białowolska et al*. reported no differences in hypotension,

bradycardia and nausea in parturient receiving different doses of anaesthetics during caesarean section [29]. The high selectivity and low toxicity of ropivacaine contribute to its lower incidence of adverse effects in clinical use. Sun *et al*. demonstrated that ropivacaine concentrations of 0.375% and 0.5% reduced pain scores at 2 hours postoperatively and decreased the incidence of nausea and vomiting [30]. Barney *et al*. highlighted that postoperative pain impairs recovery in several surgical procedures [31]. Local administration of ropivacaine has become an effective strategy for postoperative pain management. Some researchers suggest that wound infiltration with ropivacaine may be a safe and effective rapid route for patients undergoing thoracotomy [32]. The prolonged duration of action of ropivacaine provides a sustained anaesthetic and analgesic effect. In caesarean section, long-acting anaesthesia reduces the need for the intraoperative anaesthetic boluses, simplifying anaesthetic management and providing prolonged postoperative analgesia. Research has shown that ropivacaine provides immediate pain relief after 3rd molar extraction [33] and relatively prolonged pain relief during perineal repair after childbirth [34]. Continuous subcutaneous infusion of ropivacaine at the surgical wound site reduces morphine consumption after caesarean section. Rosetti *et al*. reported negligible differences in the incidence of postoperative nausea/vomiting, pruritus and time to first ambulation between the placebo and ropivacaine groups [35]. Another study suggested that ropivacaine has a weaker inhibitory effect on the cardiac conduction system and myocardium at commonly used doses, resulting in a lower incidence of cardiac toxicity events [21]. Therefore, the use of ropivacaine in caesarean section may better ensure maternal cardiac safety. This study found that the duration of sensory blockade in the LD group was drastically shorter than in the HD group and showed remarkable heterogeneity. This finding is consistent with previous research on the ability of HD local anaesthetics to prolong sensory blockade. However, it is important to note that the presence of heterogeneity may be influenced by study methodology, participant characteristics and other factors that require further investigation.

The results showed major advantages of HD ropivacaine in prolonging the duration of anaesthesia, improving neonatal Apgar scores and prolonging the duration of sensory blockade. The pharmacological theory of anaesthesia suggests a positive correlation between the efficacy of local anaesthetics and their dosage. HDs of ropivacaine increase the depth and duration of local anaesthesia, which is consistent with the results of this study indicating a significantly longer duration of anaesthesia with HD ropivacaine. As an amide-type local anaesthetic, ropivacaine blocks sodium ion channels on neuronal cell membranes, thereby inhibiting the propagation of nerve impulses to induce anaesthesia. HDs of ropivacaine comprehensively block sodium ion channels, providing a deeper and longer lasting anaesthetic effect. This is consistent with the study's observation that the duration of sensory blockade was significantly longer in the HD group than in the LD group. The pharmacokinetics of anaesthetic drugs are influenced by the oxygen concentration environment. High oxygen levels increase tissue oxygenation, which facilitates the distribution and action of anaesthetic drugs and enhances their effects. This study used ropivacaine in a high oxygen environment and found superior anaesthetic effects in the HD group compared to the LD group, supporting this theoretical framework. Oxygen plays a critical role in tissue repair and neonatal health. In high oxygen environments, both maternal and foetal tissue oxygen levels are increased, which contributes to wound healing and healthy neonatal development. This study found that neonatal Apgar scores were significantly higher in the HD ropivacaine group compared to the LD group, indicating a beneficial effect of combining high oxygen environments with HD ropivacaine on neonatal health. Apgar scores are critical indicators for assessing the immediate health status of newborns. The depth and efficacy of anaesthesia have a direct impact on maternal physiological status, and therefore on foetal oxygenation and health. HD ropivacaine provides a prolonged anaesthetic effect, reducing maternal stress responses, maintaining stable haemodynamic and helping to improve neonatal Apgar scores. Effective anaesthesia can reduce maternal pain and stress responses, minimising negative physiological responses to pain during labour and maintaining a stable foetal environment. The efficacy of HD ropivacaine in improving neonatal Apgar scores observed in this study supports this theory. Ropivacaine has a slow metabolism and a longer half-life in the body, allowing it to provide prolonged anaesthesia and analgesia in HDs. This study found that the duration of anaesthesia was significantly longer in the HD ropivacaine group than in the LD group, consistent with its pharmacokinetic properties. The steep concentration gradient of HD ropivacaine in tissues allows it to maintain effective anaesthetic levels for a longer period, thereby prolonging both the duration of anaesthesia and sensory blockade time. This finding is consistent with the theory of local anaesthetic concentration gradients. The results of this study are closely related to relevant theories and validate the relationship between local anaesthetic dose and anaesthetic efficacy. It elucidates the effect of oxygen concentration on the action of anaesthetics, further supporting the importance of depth and efficacy of anaesthesia for neonatal health. These findings not only enrich existing anaesthetic theories, but also provide an important theoretical basis and guidance for optimising the use of the ropivacaine in clinical practice.

Conclusions

This study conducted a systematic search and meta-analysis to compare the interventional effects of ropivacaine at different oxygen concentrations during caesarean section. The results show significant benefits of using high oxygen environments and HD ropivacaine, including improved intraoperative analgesia, longer duration of anaesthesia, improved postoperative pain management and significantly higher neonatal Apgar scores. Clinically, tailoring oxygen concentration and ropivacaine dose to surgical needs and patient-specific conditions can optimise surgical and anaesthetic outcomes and ensure maternal and neonatal safety. This research provides valuable insights into anaesthetic management during caesarean section and promises important clinical applications in this area.

Conflict of interest

The authors declare no conflict of interest.

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