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Review Article

Inadequate neuraxial anaesthesia in patients undergoing elective caesarean section: a systematic review

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Summary

Neuraxial anaesthesia is widely utilised for elective caesarean section, but the prevalence of inadequate intra-operative anaesthesia is unclear. We aimed to determine the prevalence of inadequate neuraxial anaesthesia for elective caesarean section; prevalence of conversion from neuraxial anaesthesia to general anaesthesia following inadequate neuraxial anaesthesia; and the effect of mode of anaesthesia. We searched studies reporting inadequate neuraxial anaesthesia that used ≥ ED95 doses (effective dose in 95% of the population) of neuraxial local anaesthetic agents. Our primary outcome was the prevalence of inadequate neuraxial anaesthesia, defined as the need to convert to general anaesthesia; the need to repeat or abandon a planned primary neuraxial technique following incision; unplanned administration of intra-operative analgesia (excluding sedatives); or unplanned epidural drug supplementation. Fifty-four randomised controlled trials were included (3497 patients). The overall prevalence of requirement for supplemental analgesia or anaesthesia was 14.6% (95%CI 13.3–15.9%); 510 out of 3497 patients. The prevalence of general anaesthesia conversion was 2 out of 3497 patients (0.06% (95%CI 0.0–0.2%)). Spinal/combined spinal–epidural anaesthesia was associated with a lower overall prevalence of inadequate neuraxial anaesthesia than epidural anaesthesia (10.2% (95%CI 9.0–11.4%), 278 out of 2732 patients vs. 30.3% (95%CI 26.5–34.5%), 232 out of 765 patients). Further studies are needed to identify risk factors, optimise detection and management strategies and to determine long-term effects of inadequate neuraxial anaesthesia.

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Introduction

Caesarean section is one of the most commonly performed surgical operations in the world [1]. In the UK alone, 28% of women (annually approximately 178,000) deliver by caesarean section [2] and neuraxial anaesthesia remains the gold standard mode of anaesthesia [3]. It is regarded as superior to general anaesthesia because its use is associated with better patient satisfaction and reduction in serious adverse clinical outcomes including maternal mortality [4, 5].

Neuraxial anaesthesia is not always successful – the reported prevalence of inadequate or failed neuraxial anaesthesia varies widely, ranging from 0.8% to 12% [6–8].

However, the true prevalence of severe breakthrough pain during caesarean section remains unknown. The definition of inadequacy varies. Peri-operative factors such as urgency of surgery, type of neuraxial anaesthesia performed (spinal, epidural or combined spinal–epidural (CSE)), surgical approach and utilisation of epidural top-up as the primary mode of anaesthesia can all impact the success of neuraxial anaesthesia. A small number of single-centre studies [7, 8] reporting failure rates of neuraxial anaesthesia for caesarean section used different definitions for what constitutes neuraxial anaesthesia inadequacy. Definitions include pain during surgery; requirement for additional intra-operative analgesia; the inability to achieve a desired sensory level of anaesthesia; poor maternal satisfaction; and requirement for conversion to an alternative anaesthetic technique (including conversion to general anaesthesia). The percentage of neuraxial anaesthesia cases for caesarean section in which conversion to general anaesthesia is specifically required for neuraxial anaesthesia inadequacy remains unclear [9, 10].

Subspecialty organisations have thus far provided little guidance surrounding optimal management of pain during caesarean section. The French Practice Bulletin is one of the few professional societies that have raised awareness regarding this issue by providing best-practice guidance for the prevention, recognition, treatment and follow-up of insufficient or failed anaesthesia to all stakeholders involved in the care of women undergoing caesarean section under neuraxial anaesthesia [6, 11]. Accurate prevalence data for inadequate neuraxial anaesthesia would be invaluable to help clinicians counsel and consent patients regarding the potential risks associated with caesarean section under neuraxial anaesthesia, to facilitate development of optimal management strategies for this complication and to help direct future research efforts in this area.

To our knowledge, no study has systematically reviewed the prevalence of inadequate neuraxial anaesthesia in women undergoing elective caesarean section. Thus, the primary aim of this systematic review was to estimate the prevalence of inadequate neuraxial anaesthesia in women undergoing elective caesarean section under neuraxial anaesthesia in randomised controlled trials utilising ≥ ED95 (effective dose in 95% of the population) of anaesthesia. Secondary aims were to estimate the prevalence of conversion of neuraxial to general anaesthesia and to compare the prevalence of inadequacy between different modes of anaesthesia.

Methods

A search of the literature was performed with no restrictions on 21 August 2019 and repeated on 27 September 2021 (search strategy provided in online Supporting Information Appendix S1) by a medical librarian (LB). Databases searched included MEDLINE via PubMed, EMBASE, Web of Science, CINAHL and the Cochrane Database of Systematic Reviews. In addition, a 'grey literature' search was conducted looking for English language research on OAIster and OpenGrey. Studies describing the use of neuraxial anaesthesia (epidural, spinal, epidural top-up or CSE) for scheduled caesarean section were sought and reports on intra-operative pain, inadequate neuraxial anaesthesia (as defined by individual study authors), conversion to general anaesthesia or the need for unplanned intra-operative supplementation of analgesia were identified. If a study specifically reported no intra-operative pain or inadequate neuraxial anaesthesia as pre-defined in the study methodology, a 0% prevalence of neuraxial anaesthesia inadequacy was assumed. Opioids, inhalational agents such as sevoflurane or nitrous oxide and ketamine were considered intra-operative analgesic supplementation. The use of benzodiazepines was excluded from this study as these are typically used to treat anxiety, not pain.

Studies evaluating women aged ≥ 18 y, at gestational age ≥ 24 weeks and undergoing elective caesarean section were eligible for inclusion. Any randomised controlled trial that evaluated the effectiveness of intra-operative neuraxial anaesthesia in parturients undergoing caesarean section was eligible for inclusion. If a study included both elective and non-elective caesarean section data, it was included providing the elective data could be extracted. We excluded dose-finding studies, news articles, commentaries, surveys, letters and conference abstracts. There were no restrictions based on the type of neuraxial anaesthesia used. In addition, studies were excluded that utilised unclear methodology; administered neuraxial anaesthesia doses < ED95, as reported by Ginosar et al. and Xu et al. (ED95 doses reported as ≥ 11.2 mg intrathecal bupivacaine [12] or ≥ 15.2 mg ropivacaine [13]); or where a block height less than a T6 level was achieved when epidural anaesthesia was used [14]. If block height was not reported in a study using epidural anaesthesia, the study was excluded. Studies that reported inconclusive data or lacked data regarding intra-operative pain, used non-standardised drugs (local anaesthetics other than bupivacaine, ropivacaine or lidocaine) or used any non-opioid neuraxial adjunct (except adrenaline or sodium bicarbonate) were also excluded.

Titles and abstracts from the search were entered into Rayyan (Rayyan Systems Inc., Cambridge, MA, USA), a web application for performing systemic reviews [15]. Titles and

abstracts were screened by three authors (RP, JK and NS) who determined whether the citation would undergo full-text review. Full-text reviews were performed by two reviewers (RP and JK) based on eligibility criteria. If the two reviewers disagreed, the final decision went to a third reviewer (PS) and the article was discussed until consensus was obtained. A further manual search of citations and reference lists of included manuscripts was also undertaken by two reviewers (RP and JK) in order to ensure completeness; a third reviewer (PS) settled any disagreements for inclusion or exclusion.

A standardised data collection tool using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) was used to extract the following data from included articles: publication characteristics (title, authors, study year, study country); study details (primary and secondary outcomes, study design, single- or multicentre, numbers of participants, groups for comparison studies, urgency of surgery); intervention details (mode of neuraxial anaesthesia, drugs, doses administered); neuraxial anaesthesia procedural details (needle type, injection time, positioning of patient for anaesthesia, lumbar level of procedure); outcome data (method of block assessment, modality of block assessment, documented block height, definition of neuraxial anaesthesia inadequacy); strategies used to treat inadequacy; the most likely reason for inadequacy; and inadequacy data if given (prevalence of neuraxial anaesthesia inadequacy, supplemental analgesia administration, conversion to general anaesthesia). Data extraction was performed by two authors (RP and JK), with a third (PS) resolving any discrepancies.

For the purposes of this study, we defined inadequate neuraxial anaesthesia as: the need to convert to general anaesthesia; the need to repeat or abandon a planned primary neuraxial anaesthesia technique following skin incision; the unplanned administration of intra-operative analgesia (excluding benzodiazepines); or epidural drug supplementation where an epidural catheter was in-situ. The exact definition of inadequate neuraxial anaesthesia varies between individual practitioners and institutions; however, this definition was chosen as it is an extractable, measurable endpoint while also being a broadly comprehensive and applicable definition to clinical practice. The primary outcome was the prevalence of inadequate neuraxial anaesthesia in parturients undergoing elective caesarean section under neuraxial anaesthesia from all randomised controlled trials using ≥ ED95 doses, with the total number of study patients as the denominator. Secondary outcomes included: the prevalence of conversion from neuraxial to general anaesthesia from all randomised controlled trials using ≥ ED95 doses; and the prevalence of inadequate neuraxial anaesthesia (overall prevalence and prevalence of intravenous opioid, epidural top-up or general anaesthesia requirement) when comparing spinal/CSE vs. epidural techniques.

We amended our protocol from the proposal registered with PROSPERO to only include randomised controlled trials in order to reduce the amount of studies to a manageable number, reduce the risk of bias and optimise the levels of evidence among included studies.

Two reviewers (RP and JK) independently assessed each randomised controlled trial that met the ≥ ED95 dose criteria using the Cochrane risk of bias tool for randomised controlled trials [16]. Each study was compared for consistency, with disagreements resolved by discussion between the two reviewers with involvement of a third reviewer (PS) if required. Only the studies that were judged to be at a low risk of bias remained eligible for analysis.

Prevalence was calculated by dividing the numerators for each sub-group by the denominator and converted to a percentage with 95%CIs, assuming a Poisson distribution. A p value < 0.05 was considered statistically significant. All statistical analyses were conducted in R Version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The literature search yielded 2163 articles. Full texts were obtained and read for 363 articles, of which 73 randomised controlled trials (published between 1984 and 2021) met the inclusion criteria.

Cochrane risk of bias assessment was performed for the 73 included randomised controlled trials that reported prevalence data for studies using ≥ ED95 dosing strategies. Overall, 54 randomised controlled trials demonstrated a low risk of bias. A full reference list for these 54 studies is provided in online Supporting Information Appendix S2 and a summary of the study methodology and relevant findings is provided in online Supporting Information Table S1. Eighteen studies had serious limitations and one had very serious limitations relating to their primary outcome (online Supporting Information Table S2). These studies were excluded from further analyses. The number of records identified, included and excluded, along with the reasons for exclusion are provided in Fig. 1. The 54 studies yielded 3497 patients who received neuraxial anaesthesia for caesarean section.

Included articles consisted of predominately single-centre studies from 18 countries. Of the 54 included randomised controlled trials, the UK contributed the majority (18 studies; 33.3%), followed by the USA (seven

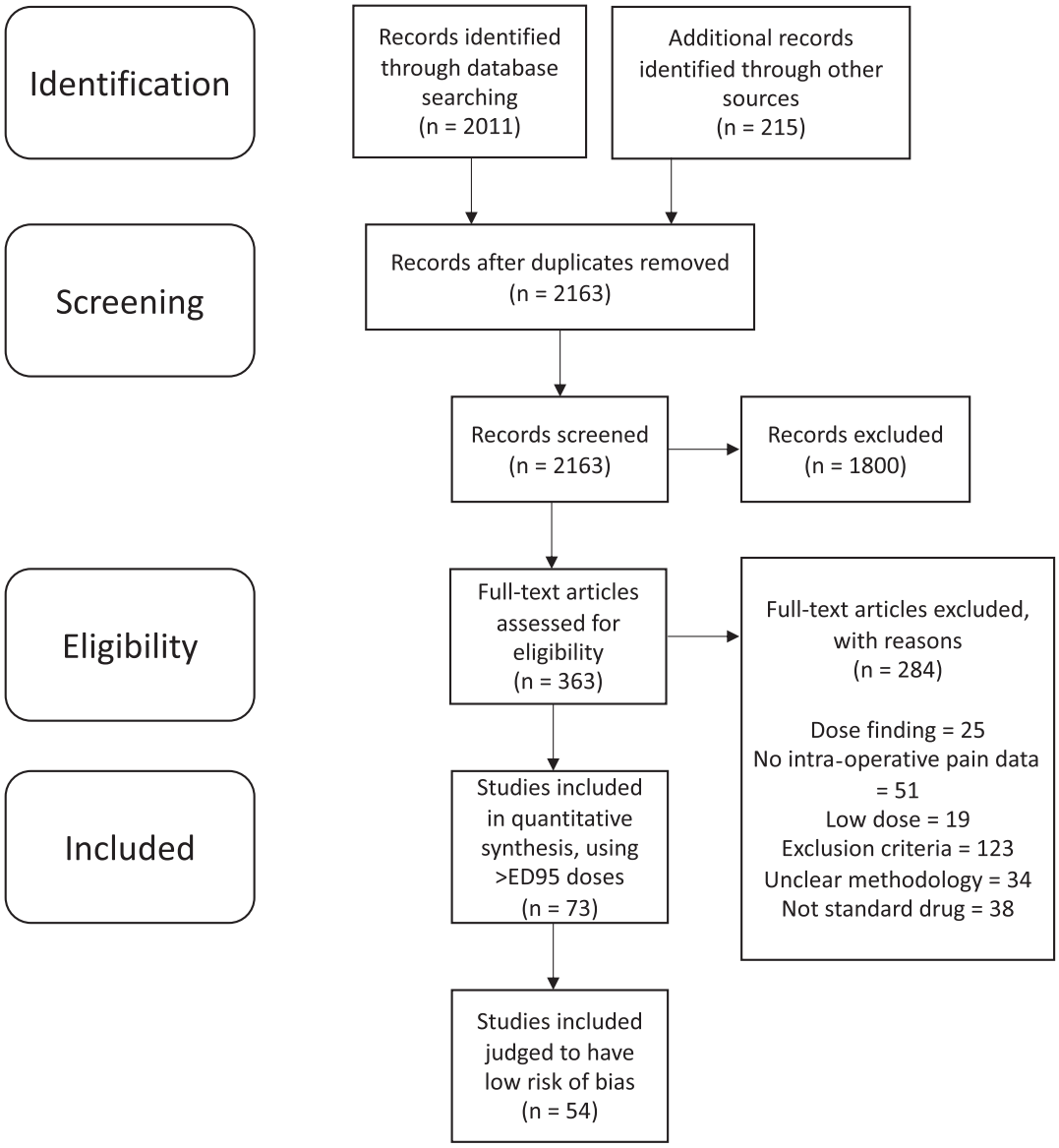

Figure 1 Flow diagram summarising the literature search. A total of 2163 studies were identified. After abstract screening, the full text of 363 studies was assessed for eligibility and 54 were included that used ≥ ED95 dosing as described.

studies; 12.9%). Neuraxial anaesthesia inadequacy, as defined by individual studies (including synonyms such as 'quality of block', 'analgesic efficacy', 'quality of anaesthesia' and/or 'clinical efficacy of anaesthesia'), was the primary outcome measure in 22 of the included studies. Thirty-three studies stated when intra-operative supplementation should be given or provided thresholds for when the neuraxial block should be considered as failed or inadequate within their study protocols.

The most commonly used definition for inadequate anaesthesia was based on 'the use of supplementary intra-operative analgesia' (17 studies). A comprehensive list of definitions of inadequate neuraxial anaesthesia used among the included studies is provided in online Supporting Information Table S3.

Of the 3497 women underwent elective caesarean, 2732 (78.1%) women underwent elective spinal or CSE and 765 (21.9%) underwent epidural anaesthesia.

The prevalence of inadequate neuraxial anaesthesia (ranging from nitrous oxide inhalation to conversion to general anaesthesia) determined from the 54 randomised controlled trials that administered ≥ ED95 doses for women undergoing elective caesarean section was 14.6% (95%CI 13.3–15.9%); 510 out of 3497 patients.

The prevalence of general anaesthesia conversion was 0.1% (95%CI 0.0–0.2); 2 out of 3497 patients.

Spinal/CSE anaesthesia was associated with a lower overall prevalence of inadequate neuraxial anaesthesia than epidural anaesthesia (10.2% (95%CI 9.0–11.4%), 278 out of 2732 vs. 30.3% (95%CI 26.5–34.5%), 232 out of 765 patients). Prevalence data for sub-group comparisons (requirement for intravenous opioid, epidural top-up or general anaesthesia) are provided in Table 1.

Discussion

The main finding from this systematic review is that approximately 15% of women received supplemental analgesia or anaesthesia during elective caesarean section, ranging from the brief use of nitrous oxide to requirement for conversion to general anaesthesia. Within this group are women who experienced 'pulling' or 'tugging' during surgery, anxiety and unexpectedly prolonged surgery where additional epidural anaesthesia was administered pre-emptively. The rate of conversion to general anaesthesia was 1 in 1749, suggesting that significant failure of the neuraxial technique is rare during elective surgery. Spinal and CSE techniques were associated with significantly lower prevalence of inadequate anaesthesia when compared with epidural techniques (10.2% vs. 30.3%).

Our review is the largest systematic review investigating both prevalence and risk factors for neuraxial anaesthesia inadequacy. A small number of single-centre retrospective studies have previously reported failure rates of neuraxial anaesthesia for caesarean section ranging from 1.7% [17] to 19.7% [8, 7, 18]. Kinsella et al. conducted a large audit comprising 5080 cases in a single UK institution over a 5-year period between 1999 and 2004 [7]. The rate of conversion of neuraxial anaesthesia to general anaesthesia during emergency caesarean section in this population was 5%, with a four times greater conversion rate reported for category-1 caesarean section. In our review, the 14.6% prevalence was derived using data from over 3497 women involved in 54 robust randomised controlled trials who underwent elective surgery, which is usually associated with optimum levels of staffing and expertise. The lower conversion rate to general anaesthesia compared with previous reports may be due to our inclusion of only elective cases. It should also be noted that the finding of 14.6% prevalence for inadequate anaesthesia covers a spectrum of interventions ranging from the use of nitrous oxide to general anaesthesia conversion due to incomplete block, which are not comparable clinical interventions. The rate of failure when using epidural anaesthesia (4.3%) has previously been shown to be higher than with spinal (2.1%) or CSE (1.7%) techniques [19]).

Caesarean section is the most commonly performed inpatient surgical operation worldwide. Published guidelines from the UK and USA surrounding management of pain during caesarean section are currently lacking [11]. The French Club Anesthésie Réanimation en Obstérique recently convened to provide a clinical framework and practice bulletin to prevent, recognise and treat acute pain during caesarean section [6]. Prevalence figures reported in this review can be used as a framework to inform patients, guide clinicians and develop national guidelines for optimal management of this complication. Published reports of medicolegal claims made over 21 years related to caesarean section concluded that assessing the level of neuraxial block and management of intra-operative pain are key themes related to litigation [20]. While the conversion

Table 1 Prevalence of different types of inadequate neuraxial anaesthesia in elective section settings. Values are presented as percentage of patients (95%CI) and number of patients.

	Spinal	Epidural de-novo	Combined spinal–epidural
Studies	32	17	9
Patients	1842	765	890
Supplement type (95%CI); n			
Intravenous opioids	6.6 (5.5–7.8%) (121 patients)	6.4 (4.7–8.5%) (49 patients)	1.9 (1.1–3.1%) (17 patients)
Epidural top-up	-	7.2 (5.4–9.4%) (55 patients)	2.9 (1.9–4.3%)* (26 patients)
General anaesthesia	0 (0.0–0.2%) (0 patients)	0.3 (0.0–0.9%) (2 patients)	0 (0.0–0.4%) (0 patients)
Other	4.3 (3.4–5.4%) (80 patients)	16.5 (13.7–19.6%) (126 patients)	3.8 (2.6–5.3%) (34 patients)

*Patients who underwent non-elective caesarean section via epidural top-up, who then had further epidural top-up as a supplement due to neuraxial inadequacy.

rate from neuraxial anaesthesia to general anaesthesia was low (approximately 0.1%), the short- and long-term effects associated with requirement for treatment of intra-operative breakthrough pain remain underexplored. Consenting patients regarding intra-operative pain is a significant issue that requires the most contemporary, up-to-date and accurate information in order to responsibly inform women about these risks.

Further work is urgently needed to determine the proportion of women experiencing clinically significant or severe intra-operative breakthrough pain, rather than sensations such as 'pressure' or 'tugging', which patients are counselled to expect during caesarean section under neuraxial anaesthesia. The impact of severe intra-operative breakthrough pain and its effects on inpatient quality of recovery and medium to longer term outcomes following hospital discharge using validated measures of post-partum recovery, also requires further prospective evaluation [21–25]. Previous studies have described an association between obstetric labour pain and development of symptoms of post-partum depression up to 6 weeks post-partum [26, 27]. Future studies should aim to develop risk stratification tools to predict neuraxial anaesthesia inadequacy and to determine the best management strategies for treating significant intra-operative breakthrough pain.

While this study is the largest of its kind investigating neuraxial anaesthesia inadequacy, there remains no consensus regarding the definition for inadequate neuraxial anaesthesia during caesarean section. Inconsistent definitions across trials investigating similar clinical problems limit their value, as any pooled analyses are difficult and hard to replicate for further research. Clear definitions are required to support research and quality improvement, and obstetric anaesthesia would benefit from the same approach as taken in general peri-operative care to both define core outcomes and standardise key endpoints [28, 29]. Supplemental analgesia included a wide range of clinical interventions. The definition of inadequate anaesthesia is broad and, therefore, open to misinterpretation. Furthermore, studies did not report peri-operative maternal or fetal outcomes for patients experiencing inadequate neuraxial anaesthesia, and infrequently reported how much supplementation was given, at what operative time-points or how effective the supplementation was. Thus, it must be considered that this study's definition of inadequate neuraxial anaesthesia likely overestimates the problem of severe pain due to genuine failure of neuraxial anaesthesia, and the definitive low conversion rate to general anaesthesia demonstrated in this study would support this.

In summary, this review provides the most comprehensive analysis of neuraxial anaesthesia inadequacy to date and encompasses a variety of neuraxial techniques and patient groups. It is likely that approximately 1 in 1750 women require conversion to general anaesthesia due to inadequate neuraxial anaesthesia, and 14.6% of women require supplemental analgesia or anaesthesia, ranging from nitrous oxide administration to requirement for general anaesthesia. These data are derived from the highest quality studies in terms of design, adequacy of dosing and during the optimal working conditions offered by elective work. These figures should be considered by clinicians when counselling and consenting women regarding the potential risks associated with caesarean section under neuraxial anaesthesia. Future studies are needed to determine the prevalence of severe intra-operative breakthrough pain, in addition to risk factor, management strategies and long-term effects of inadequate neuraxial anaesthesia during obstetric surgery.

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Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1. Literature search strategy.

Appendix S2. The 54 included studies used for the primary outcome.

Table S1. Summary table of all 54 studies.

Table S2. Cochrane risk of bias judgements for studies that meet ED95 dose criteria.

Table S3. Frequently utilised definitions for neuraxial anaesthesia inadequacy.