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OBSTETRICS

Labour analgesia and obstetric outcomes

C. R. Cambic and C. A. Wong*

Department of Anesthesiology, Northwestern University Feinberg School of Medicine, 251 E. Huron, F5-704, Chicago, IL 60611, USA

* Corresponding author. E-mail: c-wong2@northwestern.edu

Key points

- The effects of neuraxial labour analgesia on the progress of labour and labour outcomes have generated considerable controversy.
- The evidence indicates that effective labour analgesia does not increase the rate of Caesarean delivery.
- Effective labour analgesia can prolong the second stage of labour, and might also increase the rate of instrumental vaginal delivery.
- The potential benefits and risks of neuraxial labour analgesia must be tailored to the needs of each parturient.

Summary. Neuraxial analgesic techniques are the gold standards for pain relief during labour and delivery. Despite the increased use and known benefits of neuraxial labour analgesia, there has been significant controversy regarding the impact of neuraxial analgesia on labour outcomes. Review of the evidence suggests that effective neuraxial labour analgesia does not increase the rate of Caesarean delivery, even when administered early in the course of labour; however, its use is associated with a prolonged second stage of labour. Effective second-stage analgesia might also be associated with an increased rate of instrumental vaginal delivery.

Keywords: analgesia, obstetric; analgesic techniques, epidural; analgesic techniques, subarachnoid; obstetric

Neuraxial techniques are the gold standard for intrapartum labour analgesia. Multiple randomized controlled trials comparing epidural analgesia with systemic opioids, nitrous oxide, or both have demonstrated lower maternal pain scores and higher maternal satisfaction with neuraxial analgesia.[1–4] In addition to their analgesic benefits, the physiological benefits of neuraxial analgesia for the mother and fetus are well-documented: neuraxial analgesia has been shown to improve maternal cardiovascular and pulmonary physiology, and the acid–base status of the fetus.[5–8] As a result of the superior analgesia and maternal–fetal benefits afforded by neuraxial techniques, and their improved safety, use of neuraxial labour analgesia has progressively increased over the past three decades. In the USA, the percentage of parturients receiving neuraxial analgesia for labour rose to 77% in 2001 from 21% in 1981; in the UK, a little over 33% of parturients chose neuraxial analgesia for childbirth in 2008–09.[9 10]

In spite of the proposed benefits and increased use of intrapartum neuraxial analgesia, considerable debate has existed in the obstetric and anaesthesiology communities regarding the impact of neuraxial analgesia on the progress of labour and mode of delivery. While observational studies uniformly conclude that parturients who have neuraxial analgesia for labour have higher Caesarean and instrumental vaginal delivery rates and longer durations of labour, the cause–effect relationship of this association, particularly for the duration of labour and incidence of instrumental vaginal delivery, is unclear. The purpose of this article is to review and summarize the available evidence regarding the impact of neuraxial analgesia on labour outcomes and provide clinicians with a clearer understanding of the issues.

The effect of neuraxial analgesia on Caesarean delivery rates

Impact studies

Impact studies are a type of study design used to investigate the effect of a certain treatment modality on patient outcomes. Also known as before–after studies, these studies are designed to assess the incidence of a patient outcome before and after the implementation of a specific treatment. An advantage of this type of study design compared with the gold standard randomized controlled trial is that it eliminates the potential development of a Hawthorne effect. As such, in some circumstances, the external validity of the results from these studies might be more robust, as patients have not chosen to participate in the study, and therefore might present a more realistic representation of the general population. Additionally, this study design eliminates cross-over between treatment groups, as the control group is the time period before the treatment implementation. However, a limitation of this study design is the assumption that there were no other changes in the medical management of patients between the 'before' and 'after' time periods that could influence the outcome of interest.

Yancey and colleagues[11] published the largest impact study investigating the impact of the introduction of neuraxial labour analgesia on Caesarean delivery rates by

examining the incidence of Caesarean delivery at the Tripler United States Army Hospital in Hawaii before and after 1993. Before 1993, the rate of epidural analgesia in this hospital was less than 1%. In 1993, a policy change within the United States Department of Defense mandating on-demand availability of neuraxial labour analgesia in US military hospitals resulted in an increase in the rate of epidural labour analgesia to 80% over a 1-yr time period. Despite this increased use of neuraxial labour analgesia, the Caesarean delivery rate in nulliparous women in spontaneous labour remained unchanged (19.0% *vs* 19.4%).

For years, the low Caesarean delivery rate at the National Maternity Hospital in Dublin, Ireland was partially attributed to the low rates of intrapartum epidural analgesia. However, Impey and colleagues[12] disproved this theory in an impact study comparing obstetric outcomes for the first 1000 nulliparous, term, spontaneously labouring parturients who delivered at the National Maternity Hospital in 1987 with similar groups of women who delivered in 1992 and 1994. The epidural analgesia rate increased during this time period (10% in 1987, 45% in 1992, and 57% in 1994), yet the Caesarean delivery rate remained unchanged (4% in 1987, 5% in 1992, and 4% in 1994; not significant). Based on these findings, the authors concluded that the initial low rates of epidural analgesia could not explain this institution's low rate of Caesarean delivery.

Several other impact studies have shown no association between Caesarean delivery rates and rates of epidural administration.[13–17] These findings were confirmed in a meta-analysis by Segal and colleagues[18] that included nine impact studies involving more than 37 000 parturients. There was no increase in the rate of Caesarean delivery during a period of increased usage of epidural analgesia compared with a historical control period (Fig. 1).

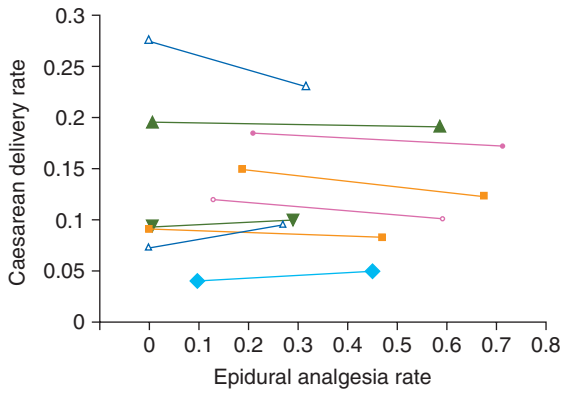

Fig 1 Meta-analyses of impact studies of the influence of neuraxial labour analgesia on the rate of Caesarean delivery. Each pair of symbols shows data from one investigation: the left symbol is the epidural analgesia rate and Caesarean rate during the period of low epidural availability and the right symbol is the epidural analgesia rate and Caesarean delivery rate during the period of high epidural availability. The size of the plot symbol is proportional to the number of patients included in the analysis. Reprinted from Segal *et al.*,[18] © (2000) with permission from Elsevier.

Randomized controlled trials

Randomized controlled trials are the gold standard study design to investigate the impact of medical interventions on clinical outcomes, as they mitigate or eliminate the potential biases seen in other study designs, including impact studies. Unfortunately, randomized controlled trials of the effect of neuraxial labour analgesia on the progress of labour suffer a number of limitations. These trials cannot be placebo controlled, as it would be unethical to randomize women to a no-analgesia group, and presumably, few women would agree to participate in such a study. Another obvious limitation is the lack of blinding owing to the marked difference in the quality of analgesia between neuraxial and other types of analgesia. Additionally, because neuraxial analgesia is significantly superior to other forms of analgesia, many studies suffer from a high group crossover rate. Other limitations include lack of control for other factors known to influence the Caesarean delivery rate, including parity, obstetric provider, labour management, and insurance status, among others.

Given these limitations, multiple randomized controlled trials have investigated the effect of neuraxial analgesia on Caesarean delivery rates compared with systemic opioid analgesia. A 2005 Cochrane review involving 20 studies reported no increase in Caesarean delivery rates between women who received epidural *vs* systemic analgesia for labour (RR 1.07, 95% CI 0.93–1.23).[1] Similarly, a 2005 meta-analysis by Halpern and Leighton[19] of 17 studies involving 6701 women concluded that the risk of Caesarean delivery was no different between women who received systemic opioid *vs* neuraxial analgesia [odds ratio (OR) 1.03; 95% CI 0.86–1.22] (Fig. 2). Although differing in many variables (e.g. parity, type of neuraxial analgesia, cross-over rate, labour management), all of the studies analysed in these meta-analyses, save one, found no difference in Caesarean delivery rates between women who received neuraxial *vs* systemic analgesia.

The single, dissenting study by Thorp and colleagues[20] randomized 93 nulliparous women to receive epidural analgesia or systemic analgesia with meperidine. Twelve (25%) of the women in the epidural group underwent Caesarean delivery compared with one (2%) woman in the meperidine group. However, there were several flaws with this study's methodology and results which were of concern. First, the investigators were ultimately responsible for deciding the method of delivery, potentially leading to significant selection bias. Second, there was no standardization between groups of other factors known to influence labour outcomes, specifically timing and dose of oxytocin and timing of rupture of membranes. Third, there was an anomalous outcome in the Caesarean delivery rate for both groups: the Caesarean delivery rate in the epidural group was significantly higher, and that in the

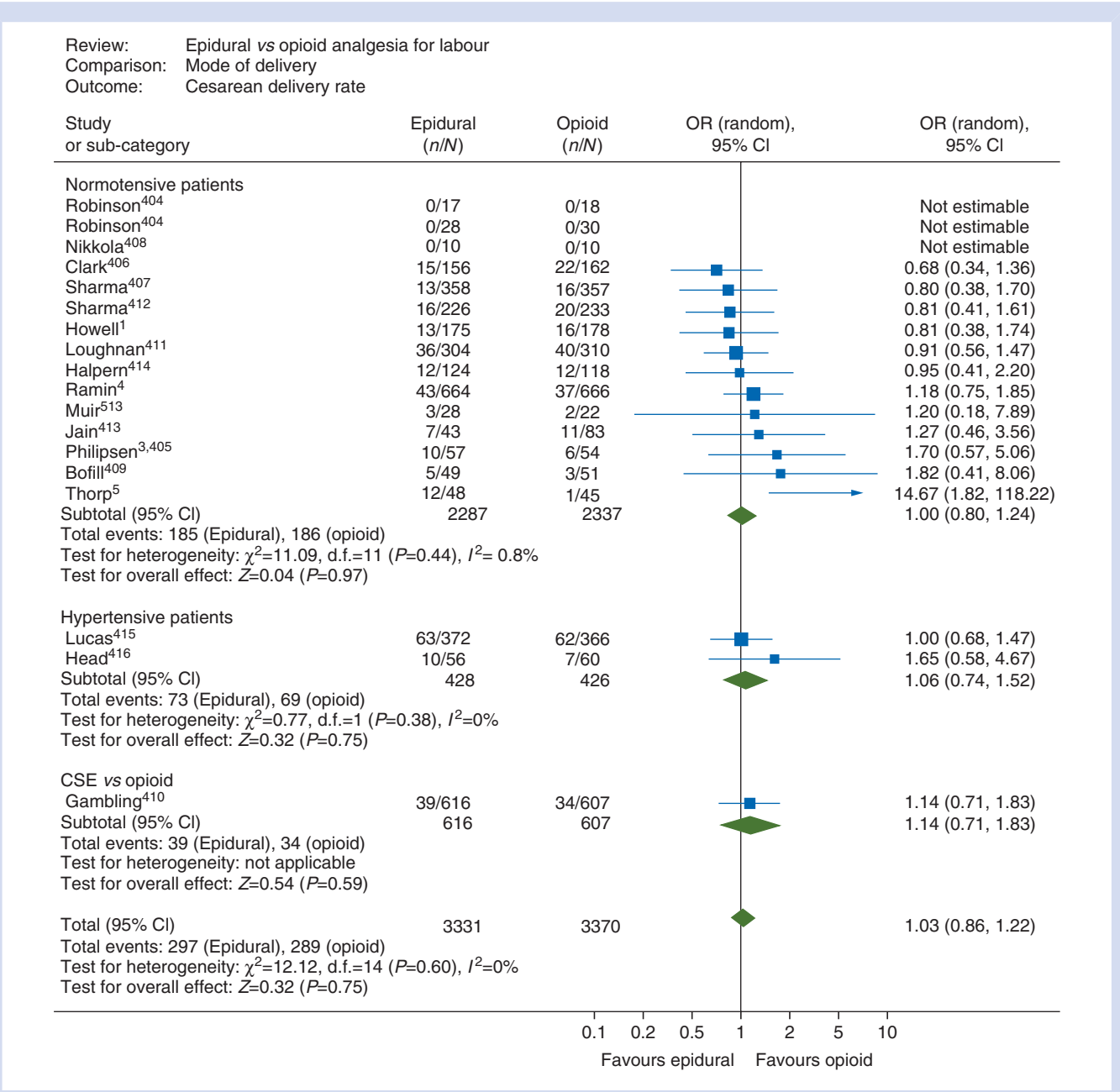

Fig 2 Meta-analysis of Caesarean delivery rate in women randomized to neuraxial *vs* systemic opioid analgesia. The number of women who had Caesarean delivery, the OR, and 95% CI of the OR (random effects model) are shown for each study. The size of the box is proportional to the weight of the study in the meta-analysis. The scale is logarithmic. For studies with no Caesarean deliveries, the OR cannot be calculated. Reprinted from Halpern and Leighton,[19] © (2005) with permission from John Wiley and Sons, Inc.

meperidine group significantly lower, than the historical norm (15%) for the study institution. Taken together, these study design flaws significantly limit the external validity and applicability of the results, and might have contributed to the anomalous results.

Investigators from Parkland Hospital in Dallas, TX, USA also performed several randomized trials investigating this topic.[4 21–23] This institution is unique in that its patient population is composed primarily of indigent Hispanic parturients. Labour was managed by the same group of resident physicians and midwives who were supervised by a core group of attending obstetricians. This distinctive organizational set-up eliminates several factors that are known to confound results of similar studies (i.e. parturient and obstetric provider variability, and labour management).

In their first study, more than 1300 women of mixed parity were randomized to receive epidural bupivacaine-fentanyl or i.v. meperidine for labour analgesia.[4] Although they demonstrated a Caesarean delivery rate of 9.0% in the epidural group *vs* 3.9% in the meperidine group, there was

a lack of an intent-to-treat analysis of the data despite a high cross-over rate. As approximately one-third of the women in each group did not receive the treatment to which they were randomized, it was unclear whether there was actually a higher incidence of Caesarean delivery in the women randomly assigned to receive epidural analgesia. The investigators subsequently performed an intent-to-treat analysis that revealed a Caesarean delivery rate of 6% in both groups.[22] The authors, in hopes of decreasing the cross-over rate of the meperidine group, designed a second study in which meperidine was administered by patient-controlled i.v. analgesia (PCIA).[24] Despite a significant number of women not receiving the treatment to which they were randomized owing to rapid labour, only 5 of 357 parturients in the PCIA group crossed-over to the epidural group. Again, the investigators found no difference in the rate of Caesarean delivery between groups; using an intent-to-treat analysis, the Caesarean delivery rate was 4% in the epidural group *vs* 5% in the PCIA group.

In a third randomized trial, the Parkland investigators randomized women of mixed parity to receive combined spinal–epidural (CSE) analgesia (intrathecal sufentanil 10 μg, followed by epidural bupivacaine with fentanyl at the second request for analgesia) or i.v. meperidine (50 mg h^{-1} on request).[21] Although only 60% of the parturients received the treatment to which they were allocated, an intent-to-treat analysis of the data revealed a Caesarean delivery rate of 6% in the CSE group *vs* 5.5% in the meperidine group. Finally, the Parkland investigators conducted an individual patient meta-analysis of all previous studies (n=4465) comparing Caesarean delivery rates in women randomized to epidural analgesia *vs* systemic opioids; the OR for Caesarean delivery was 1.04 (95% CI 0.81–1.34).[25] The results of these studies suggest that the administration of neuraxial analgesia, by itself, does not increase the risk of Caesarean delivery.

Dose–response studies have been performed to determine if the concentration of local anaesthetic impacts Caesarean delivery rates. The COMET study investigated this association by randomizing more than 1000 women to one of three labour analgesia regimens: (i) 'high-dose' epidural (intermittent boluses of bupivacaine 0.25%); (ii) 'low-dose' epidural (continuous infusion of bupivacaine 0.1% and fentanyl 2 μg ml^{-1}); or (iii) 'low-dose' CSE (intrathecal bupivacaine 2.5 mg/fentanyl 25 μg, followed by intermittent boluses of bupivacaine 0.1% and fentanyl 2 μg ml^{-1}).[26] The investigators found no difference in the Caesarean delivery rate among the three groups. Similarly, three other randomized controlled trials found no difference between groups in terms of Caesarean delivery rates despite differences in local anaesthetic concentrations.[27–29] These results suggest that 'high-dose' neuraxial analgesia does not result in a higher risk for Caesarean delivery compared with 'low-dose' analgesia. Additionally, as several of these studies compared CSE *vs* epidural analgesia, these results imply that the mode of neuraxial analgesia does not affect the risk of Caesarean delivery.

Timing of initiation of neuraxial analgesia

Data from observational studies suggest an association between Caesarean delivery and the initiation of neuraxial analgesia during early labour (usually defined as cervical dilation less than 4–5 cm).[30 31] Based on these observations, the American College of Obstetricians and Gynecologists (ACOG) recommended for many years that women delay requesting epidural analgesia, 'when feasible, until the cervix is dilated to 4–5 cm.'[32] However, similar to the cause-and-effect question raised regarding the association of neuraxial analgesia with the risk of Caesarean delivery, the question arises as to whether early initiation of neuraxial labour analgesia is directly responsible for adverse labour outcomes, or is merely associated with an increased risk of Caesarean delivery.

Randomized controlled trials have addressed this issue by comparing early-labour neuraxial analgesia to systemic opioid analgesia followed by neuraxial analgesia at a cervical dilation of 4–5 cm.[33–37] Two studies by Chestnut and colleagues[33,34] randomized nulliparous women in spontaneous labour or those receiving oxytocin augmentation to one of the two groups: early epidural analgesia or early i.v. nalbuphine analgesia followed by epidural analgesia when cervical dilation reached 5 cm. Although the investigators found no difference in Caesarean delivery rates between groups, the median cervical dilation at the time of initiation of analgesia was 3.5 cm in spontaneous women and 4.0 cm in women receiving oxytocin augmentation. Therefore, the external validity of the results is limited, as women, especially those undergoing an induction of labour or those with premature rupture of membranes, often request analgesia at cervical dilations less than 3 cm.

Consequently, two randomized trials—one by Wong and colleagues[37] and the other by Ohel and colleagues[36]—compared the initiation of early-labour neuraxial analgesia with systemic opioid analgesia in women whose median cervical dilation at initiation of analgesia was 2 cm. Similar to the results of the studies by Chestnut, neither was there a difference in the rate of Caesarean delivery in the two groups, nor was there a difference in the rate of instrumental vaginal delivery. As a result of these latter studies, in 2006 the ACOG published an updated Committee Opinion entitled *Analgesia and Caesarean Delivery Rates*, stating that:

> 'In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labour. The fear of unnecessary cesarean delivery should not influence the method of pain relief that women can choose during labour.' [38]

Similarly, a 2007 joint statement by the Royal College of Obstetricians and Gynaecologists, the Royal College of Midwives, the Royal College of Anaesthetists, and the Royal College of Paediatrics and Child Health stated:

> 'When women chose epidural analgesia for pain relief in labour, they should be able to receive it in a reasonable time. This means that obstetric units should be able to provide regional analgesia on request at all times.'[39]

The results of these studies have been further confirmed by two more recent randomized controlled trials. A 2009 trial by Wang and colleagues[40] over a 5-yr period involving more than 12 000 nulliparas demonstrated no increase in Caesarean delivery rates in parturients randomized to receive epidural analgesia in the latent phase when compared with active phase of labour (23.2% *vs* 22.8%, $P=0.51$). Similarly, in women undergoing induction of labour, Wong and colleagues[41] found no difference in Caesarean delivery rates between parturients randomized to receive neuraxial analgesia early in labour (cervical dilation <4 cm) *vs* later in labour (32.7% *vs* 31.5%, $P=0.65$). Finally, a meta-analysis of eight randomized controlled trials and cohort studies of early-labour *vs* late-labour initiation of neuraxial analgesia ($n=3320$) demonstrated that early initiation of neuraxial analgesia does not increase the rate of Caesarean delivery.[42]

The effect of neuraxial anaesthesia on instrumental vaginal delivery rates

Observational data suggest an association between neuraxial labour analgesia and instrumental vaginal delivery, i.e. forceps delivery or vacuum extraction. Similar to the data of studies investigating the effect of neuraxial analgesia on Caesarean delivery rates, interpretation of these data is difficult owing to the presence of multiple confounding factors (e.g. maternal pain and the urge to bear down, neuraxial analgesia-induced motor blockade, and position of the fetal vertex and station). The contribution and interaction of these factors to the mode of vaginal delivery are not only poorly understood, but have also not been well controlled in many studies. Although assessed as a secondary outcome in numerous trials, no randomized clinical trial has assessed the effect of neuraxial analgesia on the mode of vaginal delivery as its primary outcome.

Many impact studies have observed no difference in the instrumental vaginal delivery rate before and after the availability of neuraxial analgesia. At Tripler Army Hospital, the rate of instrumental vaginal delivery did not change (11.1% *vs* 11.9%) despite a large increase in the rate of epidural analgesia.[11] Similarly, the rate of instrumental vaginal delivery at the National Maternity Hospital in Dublin remained unchanged despite a greater than five-fold increase in epidural rate.[12] These findings were confirmed in a systematic review of seven impact studies involving more than 28 000 parturients, which showed no difference in instrumental vaginal delivery rates (mean change, 0.76%; 95% CI −1.2 to 2.8).[18]

In contrast, systematic reviews of randomized controlled trials of neuraxial compared with systemic opioid analgesia, in which rate of Caesarean delivery was the primary outcome, have concluded that neuraxial analgesia is associated with an increased risk of instrumental vaginal delivery. For example, in the meta-analysis of 17 studies by Halpern and Leighton,[19] the OR for instrumental vaginal delivery in women randomized to receive epidural analgesia *vs* systemic opioid analgesia was 1.92 (95% CI 1.52–2.42) (Fig. 3). Similarly, in both the individual patient meta-analysis reported by Sharma and colleagues[25] and a 2004 meta-analysis by Liu and colleagues,[43] the adjusted ORs for instrumental vaginal delivery were 1.86 (95% CI 1.43–2.40) and 1.63 (95% CI 1.12–2.37), respectively.

These conflicting results emphasize the potential impact of multiple confounding factors on data interpretation regarding this topic. One such confounding factor is the density of neuraxial analgesia during the second stage of labour. Relaxation of the abdominal wall musculature secondary to epidural local anaesthetic could result in decreased effectiveness of maternal expulsive efforts. Dense sensory blockade of the uterus and birth canal might also decrease maternal ability to coordinate expulsive efforts with uterine contractions. Additionally, high concentrations of neuraxial local anaesthetic might relax pelvic floor musculature and interfere with fetal rotation during descent. Obstetricians might be more likely to perform instrumental vaginal deliveries in parturients with effective second-stage analgesia than in parturients without analgesia. Finally, randomized controlled trials are usually performed in teaching institutions, which have an obligation to teach obstetric trainees how to perform instrumental vaginal deliveries, whereas impact studies are frequently performed in non-teaching institutions.

Adding more confusion to the topic is the fact that the degree of neuraxial analgesia is, in turn, influenced by several other factors (e.g. specific analgesic technique, local anaesthetic concentration, total dose of local anaesthetic) that overlap and are difficult to study. Several randomized studies have investigated the effect of bupivacaine concentration on the rate of instrumental vaginal delivery, with conflicting outcomes.[26 28 29 44] For example, James and colleagues[44] noted that women randomly assigned to receive epidural bupivacaine 0.1% with fentanyl 2 μg ml^{-1} had a lower incidence of instrumental vaginal delivery than women who received epidural bupivacaine 0.25% (6% *vs* 24%, $P=0.03$). Similarly, in a larger study by Olofsson and colleagues,[29] women randomized to 'low-dose' bupivacaine 0.125% with sufentanil had a lower instrumental vaginal delivery rate compared with those who received 'high-dose' bupivacaine 0.25% with epinephrine.

Adding further uncertainty to the picture is the fact that the method of maintenance of epidural analgesia has also been shown to affect the density of the neuraxial blockade. In general, continuous infusion techniques result in higher total doses of bupivacaine (and, thus a greater degree of motor blockade) when compared with intermittent bolus techniques. However, the relationship between motor blockade and instrumental vaginal delivery is inconsistent. A small, randomized trial ($n=57$) by Smedstad and Morison[45] demonstrated a higher incidence of instrumental vaginal delivery when bupivacaine 0.25% was administered as a continuous epidural infusion when compared with intermittent bolus injections. However, two later studies (a 2006 study by Wong and colleagues[46] and the COMET

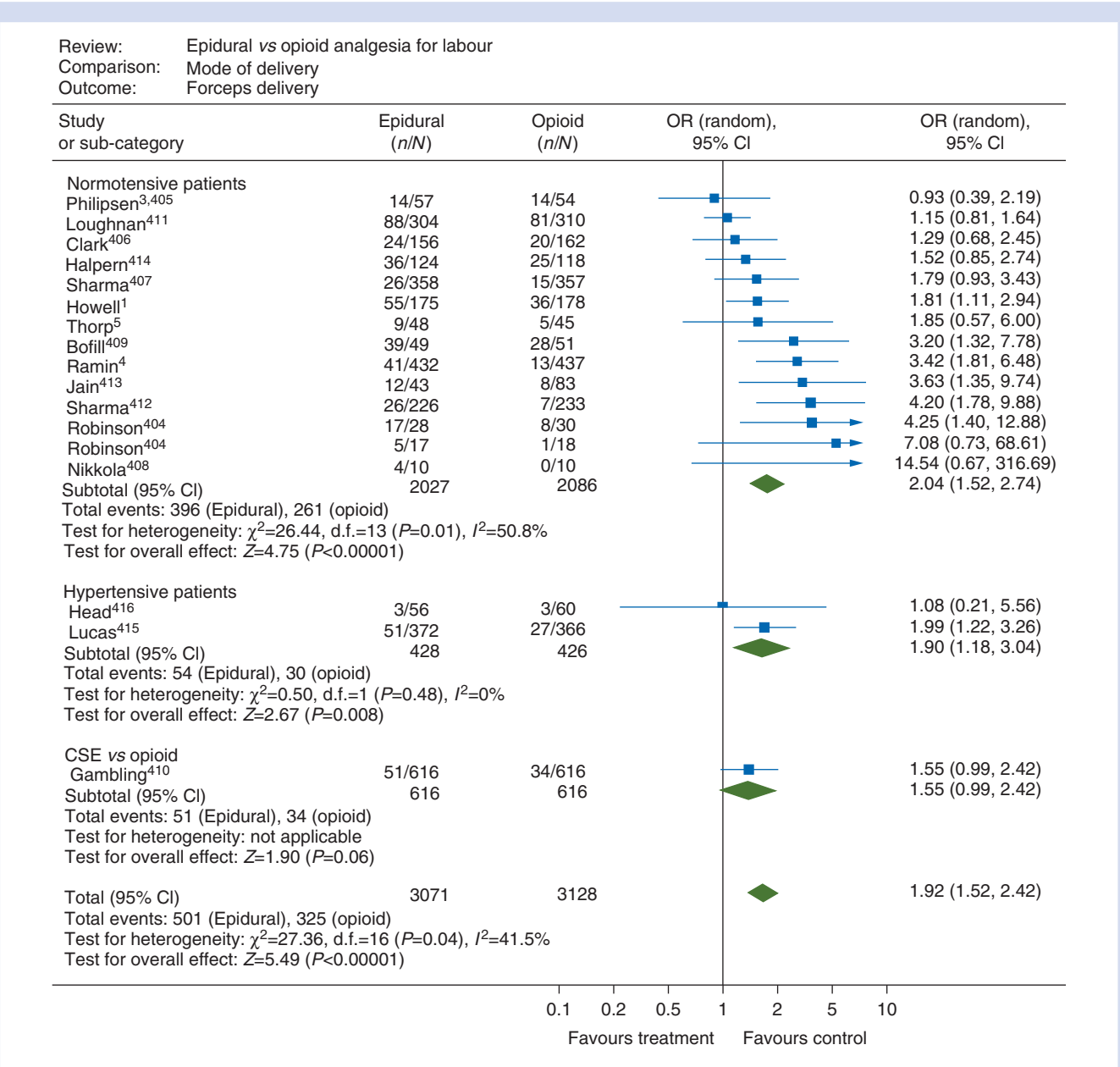

Fig 3 Meta-analysis of instrumental vaginal delivery rate in women randomized to neuraxial *vs* systemic opioid analgesia. The number of women who had instrumental vaginal delivery, the OR, and 95% CI of the OR (random effects model) are shown for each study. The size of the box is proportional to the weight of the study in the meta-analysis. The scale is logarithmic. Reprinted from Halpern and Leighton,[19] © (2005) with permission from John Wiley and Sons, Inc.

study[26]) detected no difference in the instrumental vaginal delivery rate between groups who received 'low-dose' bupivacaine/fentanyl by either intermittent bolus or continuous infusions. Furthermore, a meta-analysis comparing patient-controlled epidural analgesia (PCEA) without background infusions to continuous epidural infusions found lower dosages of bupivacaine and degree of motor blockade in the PCEA group, but no difference in the rate of instrumental vaginal delivery.[47] These inconsistent results might be explained by the differences in bupivacaine dosages (0.25% and 0.125% *vs* 0.125% and 0.0625%) and degree of motor blockade.

Finally, several studies have investigated the impact of specific neuraxial techniques (i.e. CSE *vs* epidural) on instrumental vaginal delivery rates, with conflicting results. Collis and colleagues[27] found no difference in instrumental vaginal delivery rates between parturients randomized to receive 'low-dose' CSE (intrathecal bupivacaine/fentanyl followed by intermittent boluses of epidural bupivacaine 0.1%/fentanyl 2 μg ml^{-1}) *vs* traditional 'high-dose' epidural

(0.25% bupivacaine). In contrast, Nageotte and colleagues[28] demonstrated a lower rate of instrumental vaginal delivery in parturients randomly assigned to receive CSE *vs* 'traditional' high-dose epidural analgesia. Similarly, the COMET study[26] reported a lower rate of instrumental vaginal delivery in the groups randomized to either low-dose epidural or CSE techniques than in the high-dose epidural group. However, in this study, the total bupivacaine dose in the high-dose epidural group did not differ from the low-dose epidural group as the former was given by intermittent injection and the latter by continuous infusion. In contrast, the total bupivacaine dose in the CSE group was significantly lower than the other two groups.

These conflicting findings highlight the fact that the impact of specific neuraxial technique on the degree of neuraxial blockade, and therefore the incidence of instrumental vaginal delivery, is not well understood. Cappiello and colleagues[48] reported, as a secondary outcome, a higher incidence of instrumental vaginal delivery in parturients who received a dural puncture with a 25-gauge spinal needle without intrathecal medication before epidural drug administration when compared with parturients who received epidural analgesia without a dural puncture. Although the total dosage of bupivacaine between the two groups was not different, the authors suggested that the potentially higher intrathecal exposure to local anaesthetics might have contributed to this result. However, a recent prospective randomized trial by Kamiya and colleagues[49] demonstrated that lidocaine concentrations in cerebrospinal fluid were similar with or without prior dura-arachnoid puncture when the cerebrospinal fluid collection site was only one interspace from the epidural administration site. These results suggest that, while a small amount of local anaesthetic does cross through a dural hole during epidural administration, the amount is trivial when compared with the amount crossing through the intact dura-arachnoid. Moreover, the results of the COMET study demonstrate no difference in instrumental delivery rates between the 'low-dose' epidural infusion group and CSE group, also suggesting that the presence of a dura-arachnoid puncture might not play a significant role.[26] Further studies are needed to determine if the presence of a dural puncture, as is seen with a CSE technique, influences the rate of instrumental vaginal delivery.

Despite this confusing picture, the overall available evidence suggests that effective neuraxial analgesia in the second stage of labour results in an increased risk of instrumental vaginal delivery. Increased rates of instrumental vaginal delivery are important to all obstetric anaesthesia providers as the use of instrumental delivery increases the risk of significant maternal perineal trauma,[50] and in cases of difficult midforceps delivery increases the risk of adverse neonatal outcomes.[51–54] As such, minimizing the risk of instrumental vaginal delivery while maximizing patient comfort is an art and a science, requiring diligence by the anaesthesia provider to the individual needs of each parturient.

The effect of neuraxial analgesia on the duration of labour

First stage of labour

Similar to studies addressing the impact of neuraxial labour analgesia on instrumental delivery rates, no randomized controlled trial has yet investigated the effect of neuraxial analgesia on the duration of the first stage of labour as a primary outcome. Studies that have assessed this parameter as a secondary outcome have conflicting results. Two meta-analyses (one involving nine studies by Halpern and Leighton,[19] and a 2005 Cochrane review[1]) reported no difference in the duration of the first stage of labour among women receiving epidural labour analgesia and those receiving systemic opioid analgesia or no analgesia. However, the individual meta-analysis of studies conducted at the Parkland Hospital[25] demonstrated prolongation of the first stage of labour by approximately 30 min in nulliparous women who received epidural analgesia.

Interestingly, in their trials examining the impact of early-labour neuraxial analgesia administration, both Wong[37 41] and Ohel[36] found that the duration of the first stage of labour was significantly shorter in women randomized to receive early-labour neuraxial analgesia (CSE techniques in the Wong studies, epidural technique in the Ohel study) when compared with systemic opioid analgesia. Similarly, studies investigating the impact of specific neuraxial anaesthetic techniques on the duration of the first stage of labour are conflicting. Tsen and colleagues[55] demonstrated a faster rate of cervical dilation in women randomized to receive CSE analgesia compared with those who received epidural analgesia (2.3 *vs* 1.3 cm h^{-1}, respectively; $P=0.015$). However, several other randomized controlled trials comparing CSE with epidural analgesia found no difference in the duration of the first stage of labour.[26 28 56 57]

The differences in outcomes among these studies are likely owing to variations in study design and the impact of confounding factors influencing uterine activity. One such variation in study design is the method by which authors assess the duration of the first stage of labour. Although the definition of the end-time of the first stage of labour is clearly defined at a cervical dilation of 10 cm, the definition of the start time varies among studies (but is usually consistent between groups within a study). Determination of complete cervical dilation can influence a study's results owing to variations in study protocol regarding frequency of cervical examinations. Most studies do not require regular cervical examinations, or if they do the intervals are usually far apart. Full cervical dilation is diagnosed with a cervical examination only when the parturient complains of rectal pressure, which is likely to be at a later time in women with effective neuraxial analgesia compared with women with systemic opioid analgesia. Therefore, the duration of the first stage of labour might be artificially prolonged simply owing to the presence of effective labour analgesia.

Changes in uterine activity are known to significantly impact the duration of the first stage of labour. Studies

have observed increases and decreases in uterine activity with neuraxial labour analgesia. However, there are several confounding factors that can increase or decrease uterine activity. Two studies, one by Cheek and colleagues[58] and the other by Zamoroa and colleagues,[59] demonstrated decreased uterine activity after the i.v. administration of 1 litre crystalloid solution, but not after infusion of 0.5 litre. One hypothesis explaining this observation is that a fluid bolus inhibits the release of antidiuretic hormone, which in turn transiently decreases the production of oxytocin, as both hormones are released by the posterior pituitary gland. As fluid boluses are routinely administered during neuraxial analgesia placement, this could partially explain the transient decrease in uterine activity often observed after initiation of neuraxial analgesia.

Additionally, epidural analgesia has been suggested to cause a decrease in concentrations of hormones known to augment uterine activity. Behrens and colleagues[60] observed that women who received epidural analgesia during the first stage of labour had a decrease in the release of prostaglandin $F_{2\alpha,}$ a hormone known to increase uterine activity. In a prospective, non-randomized study, Rahm and colleagues[61] demonstrated lower plasma oxytocin concentrations 60 min after initiation of epidural analgesia (bupivacaine with sufentanil) compared with parturients without epidural analgesia.

Yet, many reports and studies demonstrate an *increase* in uterine activity after initiation of neuraxial analgesia, a phenomenon attributed to an acute decrease in plasma epinephrine concentrations.[62–65] Epinephrine causes tocolysis owing to its effects on β-adrenergic receptors. Initiation of neuraxial analgesia is associated with a rapid decrease in maternal plasma concentrations of epinephrine owing to sympatholysis and acute pain relief.[8] This acute decrease in maternal epinephrine concentrations, in turn, is thought to result in increased uterine activity secondary to decreased β-adrenergic receptor activation.[63] In a 2009 randomized double-blinded controlled trial by Abráo and colleagues,[62] parturients who received CSE analgesia for labour had a higher incidence of uterine tachysystole (hypertonus) when compared with women who received traditional epidural analgesia. Although maternal plasma epinephrine concentrations were not obtained in this study, the authors proposed that faster onset of pain relief and sympatholysis in the CSE group caused a more precipitous decrease in maternal epinephrine concentrations, resulting in uterine tachysystole. Van de Velde and colleagues[65] demonstrated a higher incidence of uterine hypertonus in parturients randomized to receive intrathecal sufentanil 7.5 μg (as part of a CSE technique) compared with parturients who received either intrathecal bupivacaine 2.5 mg/sufentanil 1.5 μg/epinephrine 2.5 μg, or epidural analgesia with bupivacaine 12.5 mg/sufentanil 7.5 μg/epinephrine 12.5 μg. However, similar to the study by Abráo and colleagues,[62] plasma epinephrine concentrations were not measured. As neither study assessed the duration of the first stage of labour as an outcome, one cannot conclude that this increase in uterine activity has any impact on the duration of the first stage of labour.

The available evidence suggests that neuraxial labour analgesia has a variable effect on the duration of the first stage of labour: it might prolong it in some parturients, while shortening it in others. These inconsistent results are probably a result of the influence of several factors known to affect uterine activity and duration of the first state of labour. In those studies in which neuraxial analgesia was associated with prolongation of the first stage of labour, there was no increase in adverse maternal or neonatal outcomes owing to increased labour time. Further investigations that control for potential confounding factors are needed to elucidate the true impact of neuraxial analgesia on the duration of the first stage of labour.

Second stage of labour

It is widely agreed that *effective* neuraxial analgesia prolongs the second stage of labour. Meta-analyses of randomized controlled trials comparing neuraxial *vs* systemic opioid analgesia support this consensus opinion, demonstrating a second stage duration approximately 15 min longer in women receiving neuraxial analgesia.[19 25] As such, the ACOG has incorporated the presence or absence of neuraxial analgesia into their definition of second-stage dystocia, and states that the need for intervention (instrumental or surgical) should not be mandated solely based on second stage duration, especially if progress is being made. [66] In fact, several studies suggest that a prolonged second stage of labour does not result in adverse maternal or fetal outcomes provided that fetal status is reassuring, the mother is well hydrated and has adequate analgesia, and there is progress in fetal head descent.[67–69] Paterson and colleagues[70] evaluated the second stage of labour in more than 25 000 women who spontaneously delivered an infant ≥37 weeks gestation with vertex presentation. They concluded that there was no clear-cut point for expectation of spontaneous delivery for parous women with epidural analgesia. Similarly, the authors determined that there was no clear-cut point predicting unsuccessful spontaneous vaginal delivery in nulliparous women, as this patient population continued to give birth at a steady rate over several hours.

A potential factor influencing the length and outcome of the second stage of labour is the timing of the initiation of pushing, or immediate *vs* 'delayed' pushing. Data from several studies investigating the impact of immediate and delayed pushing on second-stage labour duration and outcomes in women with neuraxial analgesia are conflicting. In a randomized multi-centre controlled trial (n=1862), the Pushing Early or Pushing Late with Epidural (PEOPLE) study,[71] the rate of spontaneous vaginal delivery was higher, duration of pushing shorter, and rate of mid-rotational forceps lower in women randomized to delayed pushing compared with immediate pushing. In contrast, a 2004 meta-analysis of nine studies (n=3000),[72] which included the PEOPLE study,[71] concluded that delayed

pushing did not decrease the rate of instrumental vaginal delivery (RR 0.92; 95% CI 0.84–1.01) or Caesarean delivery, but did decrease the rate of midpelvic rotational forceps delivery (RR 0.69; 95% CI 0.55–0.87). The duration of the second stage of labour in the delayed pushing group was longer, but there were no differences in neonatal outcomes. It appears that delayed pushing does not impart any major neonatal or maternal benefits, although it seems reasonable to delay pushing until the fetus has descended to a lower fetal station to avoid maternal exhaustion.

Association between labour pain and mode of delivery

Multiple observational studies have noted an association between labour analgesia and Caesarean delivery, hence the belief for many years that neuraxial analgesia increased the risk of operative delivery. However, the association between analgesia and operative delivery is explained by the finding that women at increased risk for prolonged labour and operative delivery are more likely to experience severe labour pain, and therefore request neuraxial labour analgesia, compared with women with rapid, uncomplicated labours. Wuitchik and colleagues[73] observed that women who experienced higher levels of pain during the latent phase of labour not only experienced longer latent and active phases, but also were twice as likely to require instrumental delivery. Hess and colleagues[74] found a similar relationship: women who experienced more breakthrough pain during low-dose bupivacaine/fentanyl epidural analgesia were more than twice as likely to undergo Caesarean delivery than those with less breakthrough pain (OR 2.62; 95% CI 2.01–3.43). Similarly, Alexander and colleagues[75] found a significantly higher rate of Caesarean delivery in women who self-administered $>$50 mg h^{-1} of patient-controlled i.v. meperidine analgesia (PCIA) than women who self-administered $<$50 mg h^{-1} (14% *vs* 1.4%). Finally, a retrospective study of more than 2000 parturients demonstrated that women who experienced breakthrough pain during the first stage of labour were more likely to undergo instrumental vaginal delivery.[76] Taken together, these studies suggest that the early onset of severe pain and higher labour analgesia requirements increase the risk of abnormal labour and operative delivery, possibly explaining the observed association between neuraxial analgesia and operative delivery.

Conclusions

Neuraxial labour analgesia has the potential to impact the course, duration, and outcome of labour. Considerable data support the notion that neuraxial labour analgesia does not increase the risk of Caesarean delivery compared with systemic analgesia. Additionally, initiation of neuraxial analgesia in the latent phase of labour does not increase the rate of Caesarean delivery or prolong the duration of labour. Yet, effective neuraxial analgesia can prolong the second stage of labour and, possibly, increase the rate of instrumental vaginal delivery. The effects of neuraxial analgesia on the outcome and progress of labour are summarized in Table 1.

Table 1 Summary of impact of neuraxial analgesia on labour outcomes: available evidence

Labour outcome	Evidence
Incidence of Caesarean delivery	Neuraxial analgesia does not increase the risk of Caesarean delivery. Initiation of neuraxial analgesia in the latent phase of labour (cervical dilation $<$ 4 cm) does not increase the risk of Caesarean delivery
Incidence of instrumental vaginal delivery	Conflicting evidence; not assessed as primary outcome in any trial. Overall evidence suggests increased rate of instrumental vaginal delivery in women receiving neuraxial labour analgesia. Results affected by multiple confounding factors (e.g. degree of analgesia during second stage of labour, local anaesthetic concentration, method of epidural analgesia maintenance, neuraxial analgesic technique, obstetric factors)
Duration of first stage of labour	Conflicting evidence; overall evidence suggests no difference in the duration of the first stage of labour
Duration of second stage of labour	*Effective* neuraxial analgesia increases duration of second stage of labour

No single, universal method of managing labour pain exists that fits all circumstances and parturient needs. Multiple obstetric and anaesthetic factors exist that require individual tailoring of anaesthetic management of labour pain. Ultimately, it is each anaesthetic provider's responsibility to take these factors into account in order to provide safe and effective labour analgesia for each parturient.

Conflict of interest

None declared.

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