Unplanned cesarean section in parturients with an epidural catheter in-situ: how to obtain surgical anesthesia?

E. DEPUYDT and M. VAN DE VELEN

Abstract: Epidural analgesia is frequently used for labor. Several authors advocate its use when parturient women are at increased risk for emergency Cesarean delivery. Hereby, the time needed to achieve adequate surgical anesthesia may be shortened and general anesthesia may be avoided. Starting from epidural labor analgesia, the most predominant anesthetic technique for unplanned Cesarean surgery is to top-up the existing epidural catheter. Little consensus can be found in literature about the nature of local anesthetic solution to be used to provide rapid onset and high quality anesthesia for the entire duration of surgery. Women, whose epidural analgesia extension fails either receive a new neuraxial blockade, or receive general anesthesia. We reviewed the medical literature to better define the best methods and choice of products at providing a rapid and adequate surgical anesthesia in parturient women with an epidural catheter in-situ.

Key words: Unplanned C-section; labor epidural; top-up solutions; epidural failure.

With an increasing trend of secondary Cesarean sections (CS) rate, there is a need for a standardized approach in these situations. Sixty-nine percent of parturient women in Flanders (Belgium) receives epidural analgesia, when considering all delivery types. The frequency of epidural analgesia in patients undergoing secondary Cesarean sections (defined as sections after unsuccessful labor) is 92.1%. The secondary CS rate for singleton pregnancies is 8.6%, and 20.4% for multiple pregnancies (1). Both for the future mother and the obstetric anesthesiologist, regional anesthesia is the preferable method for Cesarean delivery. Hereafter, we will discuss the clinical highlights of a sudden CS, the number and causes of failed epidural catheters, some key principles and most effective anesthetic solutions for epidural top-up, alternative neuraxial techniques, and finally a few remarks on general anesthesia. As a summary, we will provide a practical flowchart on how to act in the situation of an unplanned Cesarean section in women with an epidural catheter in-situ.

Indication and communication in unplanned Cesarean section

The reasons of unplanned CS include failed progress of labor or failed instrumental delivery, signs of impaired fetal well-being, cord prolapse, maternal medical conditions, antepartum hemorrhage, ruptured uterus, placental abruption, and placenta praevia (2, 3, 4). The obese parturient, defined by the WHO (World Health Organization, United Nations system) as having a pre-pregnant BMI > 30 kg/m², is at higher risk of developing complications during labor. These are in turn highly predictive of the need for abdominal delivery (5, 6).

Not every non-elective Cesarean section is an emergency. Multidisciplinary teams now use the four-category classification system widely. It was first described by Lucas et al. to enhance communication and data collection on the urgency of Cesarean delivery (7, 8). Category one implies an immediate threat to woman or fetus life. In category two, there is maternal or fetal compromise, which is not immediately life threatening. Cases classified as category three need early delivery but maternal or fetal compromise is absent. In category four, the delivery is timed to suit the mother and maternity team. Categories 1 to 3 are declining urgencies, category 4 is considered elective. Related to these CS categories, the Royal College of Anaesthetists proposed a standard for best practice on regional anesthesia (RA), intra-operative pain and conversion to general anesthesia (GA) (9) (Table 1).

Based on a variety of maternal and neonatal outcome measures, the NICE (National Institute for
Failure of epidural labor analgesia

Definition of failure

In the literature, we found several different definitions for epidural analgesia failure (Table 2). These include failure to site, high VAS (Visual Analogue Scale) or VPS (Verbal Pain Scale) scores 30 minutes after initiation of epidural pain relief, need for an additional dose administration of local anesthetic agent within the first 30 minutes, replacement of an ineffective epidural catheter, and failure to provide effective anesthesia if topped up for CS, or a combination of these definitions (9, 11). When considering extension of epidural labor analgesia failure for CS, definitions may be inadequate neuraxial blockade despite adequate time for onset of epidural anesthesia, inadequate anesthesia necessitating replacement of an epidural catheter or conversion to an alternative anesthetic technique, block failing to provide satisfactory anesthesia despite adjustment of epidural solution or catheter manipulation, and pain during surgery requiring parenteral or inhalational anesthetic agents (2, 12, 13, 14) (Table 2). Sometimes, failed epidural analgesia is only defined as the need to convert to general anesthesia (15) (Table 2).

Failure rate

We reviewed some large studies published over the past years to determine and compare failure rates of epidural labor catheters (Table 2). In a large prospective analysis on complications in obstetric epidural anesthesia, Paech and colleagues reported that only 1.7% of their patients had inadequate epidural anesthesia for CS. Half a percent of them required intra-operative conversion to GA due to inadequate block, and 0.7% was converted to GA intra-operatively, despite an adequate block. However, only 28% of the epidural catheters used at CS were originally placed for labor analgesia (14). pan et al. found that 7.1% of pre-existing labor epidural catheters failed for CS. Among them, 4.3% required conversion to general anesthesia, 1.3% had an epidural catheter replacement, and 1.5% had conversion to spinal anesthesia (13). A more recent study reported a total failure rate of 5.9%, with a similar 4.1% general anesthesia rate for CS in parturient women with pre-existing labor epidural analgesia. Seventy-one percent of the latter occurred intra-operatively. Epidural catheter replacement occurred in 0.2% of parturient women, 1.2% had a conversion to spinal anesthesia, and 0.4% to CSE (16). The 10 fold larger audit by Kinsella showed a 13.7% rate of pain during CS with epidural top-up anesthesia. The general anesthesia conversion rate for epidural top-up anesthesia was 8% for emergency CS. The overall conversion rate of regional to general anesthesia was 4.9% in unplanned CS, and 20% in category 1 CS (2). A study of lee et al. showed a failed epidural extension rate of 1.7%. This low failure rate, however, may be explained by the very frequent use of CSE analgesia and early replacement of uncertain catheters during labor analgesia (12). Overall, Campbell and colleagues had an epidural labor analgesia to GA conversion rate of 4.4% for intrapartum Cesarean delivery over a 3-year review period, with rate of 1.2% for subspecialist obstetric

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Category 4 CS</th>
<th>Category 1-3 CS</th>
<th>Category 1CS</th>
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</thead>
<tbody>
<tr>
<td>CS under RA</td>
<td>&gt; 95%</td>
<td>&gt; 85%</td>
<td>&gt; 50%</td>
</tr>
<tr>
<td>RA to GA conversion</td>
<td>&lt; 1%</td>
<td>&lt; 5%</td>
<td>&lt; 15%</td>
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<tr>
<td>Intra-operative pain</td>
<td>&lt; 5%</td>
<td>&lt; 15%</td>
<td>&lt; 20%</td>
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</table>
### Table 2

Failure of labor epidurals and RA for CS in large studies

<table>
<thead>
<tr>
<th>Study &amp; year of publication</th>
<th>Pro-/retrospective &amp; studied period</th>
<th>n</th>
<th>Type of RA</th>
<th>Definition of labor epidural failure</th>
<th>Failure rate</th>
<th>GA conversion rate</th>
<th>Remarks</th>
<th>Elective vs. emergency CS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paech et al., 1998 (14)</td>
<td>Prospective, 5 years</td>
<td>4624</td>
<td>All epidurals</td>
<td>Inadequate block for CS</td>
<td>1.7% of all epidurals</td>
<td>1.2%</td>
<td>Only 28% had pre-existing labor epidural at CS</td>
<td>No</td>
</tr>
<tr>
<td>Pan et al., 2004 (13)</td>
<td>Retrospective, 3 years</td>
<td>4190</td>
<td>63% epidurals, 37% CSE</td>
<td>Inadequate anesthesia necessitating replacement of epidural or conversion to another anesthetic technique for CS</td>
<td>7.1% of pre-existing labor epidurals</td>
<td>4.3%</td>
<td>41% had pre-existing labor epidural</td>
<td>No</td>
</tr>
<tr>
<td>Halpren et al., 2009 (16)</td>
<td>Prospective, 16 months</td>
<td>501</td>
<td>94% epidurals, 6% CSE</td>
<td>Primary: GA conversion rate, secondary: conversion to another anesthetic form or replacement of epidural in theatre</td>
<td>5.9%</td>
<td>4.1%</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Kissella, 2008 (2)</td>
<td>Prospective, 5 years</td>
<td>5080</td>
<td>26% epidurals, 63% spinals, 5% CSE</td>
<td>Pre-operative: conversion to another anesthetic or failure to achieve a satisfactory block, intra-operative: unsatisfactory anesthesia requiring analgesia</td>
<td>GA conversion rate see next box, 13.7% rate of pain during CS with epidural top-up anesthesia</td>
<td>8% (6.2) for epidural top-ups, 4.9% (4.1) for overall RA and 20% (14) for overall RA in cat. 1 CS</td>
<td>GA given in presence of labor epidural not topped up counted as converted RA rather than as primary GA. If these cases would have been counted as primary GA, then rates between brackets would be correct</td>
<td>Yes (only emergency considered)</td>
</tr>
<tr>
<td>Lie et al., 2009 (12)</td>
<td>Retrospective, 18 months</td>
<td>1025</td>
<td>12% epidurals, 88% CSE</td>
<td>Inadequate neuraxial blockade for CS in the presence of adequate time for onset of epidural anesthesia</td>
<td>1.7%</td>
<td>1.7%</td>
<td>Frequent use of CSE and early replacement of ‘uncertain’ catheters in labor, repeat neuraxial anesthesia was not used, cases excluded when epidural injection-skin incision interval less than 15 min</td>
<td>No</td>
</tr>
<tr>
<td>Campbell and Tran, 2009 (17)</td>
<td>Retrospective, 3 years</td>
<td>895</td>
<td>All epidurals</td>
<td>Unsuccessful epidural top-up for CS utilizing surgical anesthetic concentrations of local anesthetics or no attempted top-up</td>
<td>13.4% inadequate epidural anesthesia -&gt; 10.9% after catheter pulled back 1 cm</td>
<td>4.4% (5.5% in general anesthesiologists, 1.2% in subspecialist obstetric anesthesiologists)</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Rau et al., 2010 (19)</td>
<td>Prospective, 4 years</td>
<td>2273</td>
<td>Epidural + spinal (ratio unknown)</td>
<td>RA to GA conversion rate</td>
<td>See next box on GA conversion rate</td>
<td>4.8%, 8.1% for cat. 1 CS</td>
<td></td>
<td>Yes (only emergency considered)</td>
</tr>
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</table>
anesthesiologists, and 5.5% for general anesthesiologists. This was the first study making a discrimination between anesthesiologists with different levels of expertise in obstetric anesthesia (17).

The Royal College of Anaesthetists suggested, in their 2006 compendium, that the conversion rate from regional to general anesthesia should be lower than 1% in elective, and lower than 3% in emergency Cesarean sections (18). Through a 4-year prospective study, Rahi et al. demonstrated improved rates for successful neuraxial anesthesia in emergency CS, and a reduced need for conversion to general anesthesia (varying from 2.7 to 7.8%, with an overall rate of 4.8%) in all but category 1 CS (overall rate of 8.1%). They suggested that the Royal College standards might need to become category-specific. A previous unpublished 5-year retrospective study in their unit found a 9.4% conversion rate to GA for CS among women with epidural catheters in-situ (19). In the 2012 Compendium of the Royal College, the proposed target for best practice in RA to GA conversion became more category-specific, stating a rate lower than 1% for category 4, lower than 5% for categories 1-3, and lower than 15% for category 1 (9) (Table 1).

**Determinants of failure**

Labor epidural analgesia providing inadequate pain relief may fail to produce effective anesthesia when topped up for operative delivery. Several studies have identified factors associated with inadequate labor epidural analgesia and risk factors for failure to extend in case of CS. These determinants of failure can be listed into three groups, according to their anesthetic, maternal and obstetric nature. Anesthetic risk factors include lack of a dedicated obstetric anesthesiologist, no ready availability of consultant backup for trainees, epidural anesthesia technique (conventional epidural technique compared to CSE), drug regimens, history of opioid tolerance (recent regular user), inappropriate block assessment, previous failed epidural analgesia, inadequacy of pre-operative anesthetic block, number of clinician top-ups during labor, higher VAS scores during the 2 pre-operative hours, 2 or more episodes of breakthrough pain (VAS equal or higher than 3) during labor, prolonged duration of epidural labor analgesia, incorrect primary epidural placement, secondary migration of a catheter after correct initial placement, and suboptimal dosing of local anesthetic drugs (2, 5, 9, 11, 12, 15, 16, 17, 20, 21). The GA conversion rate is also significantly lower for subspecialists in obstetric anesthesia than for general anesthesiologists (1.2% and 5.5% respectively) (17). Equipment problems such as single-orifice catheters, manufacturing errors, debris, disconnection, air lock in the bacterial filter, and knotting of the catheter causing obstruction may also be responsible for epidural failure, and can also be seen as anesthetic factors (20).

Maternal factors associated with inadequate labor epidural analgesia and with failure of extension for CS include higher BMI, concomitant comorbidity, higher height, and younger age (2, 5, 15, 16).

Obstetric determinants related to higher failure rates are high degree emergency for operative delivery, cervical dilatation larger than 7cm, no previous CS, acute fetal distress as the indication for CS, duration of surgery, higher gestational age, and obstetric preference to GA (2, 9, 11, 15, 16).

Using random-effects meta-analysis, Bauer and colleagues only identified a limited number of risk factors for failure of converting labor epidural analgesia to anesthesia. They included the number of clinician-administered boluses during labor, high degree emergency for Cesarean delivery, and care being provided by non-obstetric anesthesiologists. In this recent systematic review, the evidence was not strong enough to entail CSE as compared to a standard epidural technique, duration of epidural analgesia, cervical dilatation at the time of epidural placement, and BMI or weight as risk factors (22).

**Regional anesthetic techniques for emergency CS**

Women having CS should be offered neuraxial anesthesia as frequently as possible, because it is safer and results in less maternal and neonatal morbidity than general anesthesia. Campbell and colleagues showed that an initial successful conversion rate of epidural labor analgesia to epidural surgical anesthesia of 85.4% can be increased to 92.7% when pulling the catheter approximately 1 cm back before the incremental administration of additional surgical concentrations of local anesthesia. Replacing the remaining unsuccessful catheters by single shot spinal anesthesia brings the total regional anesthesia success rate to 98.8% (17). This ideal example of appropriate management of (initially failed) epidural catheters by a subspecialist obstetric anesthesiologist shows that best standards for epidural and neuraxial anesthesia can be reached, hereby reducing GA conversion to a minimum (Fig. 1).
Testing the sensory block

One of the difficulties of using neuraxial blocks for CS is a total lack of block assessment standardization. Several possibilities exist, and vary according to the tested sensory modality, method of stimulus application, and duration of stimulus. In addition, formulation of questions to the patient is important. Whatever the testing modality/method, it is generally accepted that the rostral end of a neuraxial block is a differential block. When testing caudally from the rostral end of the block, the first dermatome displays loss of cold sensation only, while the following dermatome displays complete loss of both pinprick and light touch sensation. It might even be that the loss of touch sensation is 1 or 2 dermatomes more caudal than loss of pinprick. The use of cold is more specific but less sensitive than touch (23, 24).

More importantly, testing the sacral roots is imperative, because they provide the sensibility of perineum and labia. The upper block level differs amongst studies, but it is generally accepted that it reaches at least the T5 dermatomal level. In our center, bilateral block to cold at the level of T4 is used. In many studies, the onset of surgical block is assessed using more than one sensory modality or sought at different dermatomal levels. Most of the studies use loss of cold sensation at the T4 level, but also loss of touch sensation at the T4, T5 or T7 level. In his best practice audit, Levy stated that blockade of light touch sensation from S5 to T5
should avoid the need for supplementation or conversion to GA (25). However, this assertion is currently questioned by renown practitioners, who still rely on loss of cold sensation at least at the T4 level!

**Extending epidural analgesia**

A well-functioning epidural analgesia can be quickly extended to provide surgical anesthesia by administering a top-up dose of local anesthetic solution. Decision-to-delivery time can be as fast for a top-up as for general anesthesia (26). High-risk (anesthetic, maternal, as well as obstetric) parturient women should therefore be encouraged to have a well-functioning epidural catheter early during labor, in order to use it for top-up in case of urgent Cesarean delivery (3, 5, 26).

**Test dose**

The role of a formal epidural test-dose to determine correct placement of the catheter is now questioned. However, it is imperative to confirm that no blood is aspirated from the catheter before preforming the top-up, to ensure proper monitoring of mother and fetus throughout labor, and to verify the appropriate functioning of the epidural catheter (5). A test-dose is given with the main objective of detecting intrathecal or intravascular catheter placement. For parturient women, a test dose with epinephrine to detect intravascular placement is usually not recommended due to lack of sensitivity and specificity and potential side effects. However, in the setting of a top-up for Cesarean section where larger doses of local anesthetics are given, and where the consequences of a significant intravascular injection may be worst, it is corresponds to routine practice of many anesthesiologists. Regarding the use of fentanyl instead of epinephrine in parturient women, there is reasonable evidence though no consensus. A lidocaine test dose to detect intrathecal catheter misplacement is not proven effective, and can have serious adverse effects. The incidence of undetected intravascular or intrathecal misplacement is infrequent, again rendering the use of a test dose in parturient women controversial (27). Moreover, the epidural catheter has already been used to provide analgesia, and a test dose should have been administered as part of the initial establishment of the epidural blockade. Intrathecal and intravascular migration of the catheter have been described, but are rare. In that case, the efficacy of a further test dose in improving safety is far from being established. It also needs to be balanced against the delay in establishing blockade, which in a true emergency setting may not be acceptable (28). However, slow administration of the top-up dose and incremental dosing is advised for both intravascular and intrathecal placement recognition.

**Delivery room or operating theatre?**

The place to initiate the epidural top-up depends on a variety of factors, including the emergency degree for delivery, local logistical factors, and layout of the individual unit. Ravi et al. recommended starting the top-up in the labor room, after ensuring adequate venous access. The main reason was to allow more time for anesthesia installation (19). The recent ‘Saving Mothers’ Lives’ report also recommends to top-up the epidural catheter in the delivery room, provided that an anesthesiologist and suitable equipment are present at all times. Epidural analgesia that has been working well during labor should be topped up to provide full surgical anesthesia without delay, once the decision to perform an emergency operative delivery has been made (6). A survey of Regan et al. on current UK practice revealed that, in 68% of surveyed maternity units, anesthesiologists give the full dose of the local anesthetic mixture in the delivery room, 12.5% initiate the top-up in the delivery room, and terminate in the operating theatre, while 15% of them transfer the woman to theatre before commencing anesthesia. Of those who commence anesthesia in the delivery room, only 25% employ any form of monitoring during transfer to theatre, while 87% have ephedrine immediately available. The authors suggest that a safer alternative would be to immediately transfer the patient to the theater once decision of a category 1 CS has been made by the obstetrician, while, at the same time, arranging for the anesthesiologist, theatre staff and pediatrician to proceed to theatre (28, 29). Audits indeed revealed that the longest delay in the decision-to-delivery interval is the time needed to transfer the mother to the operating theatre, and the time needed to assemble the staff (5). Levy stated that topping up in the delivery room might offer time gain, but at the cost of suboptimal maternal monitoring when the risk of high block or systemic local anesthetic toxicity is greatest. Waiting for arrival in theatre before starting to top-up can however invoke obstetrician impatience, and a call for GA. The suggested compromise is to administer a small initial dose in the delivery room, and the incremental doses in the theatre (25).
Epidural top-up solutions

There is no high-level evidence supporting an optimal top-up solution to convert labor epidural analgesia to surgical anesthesia for Cesarean delivery. It is very difficult to extrapolate from one study to another, because of differences between epidural regimens during labor, differences in mode of epidural top-up administration (i.e. volume and speed of injection), differences in onset time measurement methods, in onset time endpoints (i.e. dermatomal level and sensory modality), and in study populations.

According to a survey on UK about epidural blockade extension practice for emergency CS, 13 combinations of local anesthetic agents and adjuncts were used. Bupivacaine 0.5% was the most commonly used agent, followed by lidocaine 2%, either used as a sole agent or combined. Epinephrine was added to the chosen local anesthetic by 23.5% of practitioners, while 12% of them added bicarbonate. Levobupivacaine and ropivacaine were used as a sole agent by less of the respondents. However, it is likely, currently, a great number of anesthesiologists are using either one of those in place of bupivacaine (28). Mixtures containing lidocaine or chloroprocaine with or without additives are the most frequently used solutions for epidural top-up in category 1 CS (26).

Levobupivacaine, the S-enantiomer of bupivacaine, has a greater safety margin for cardiotoxicity than racemic bupivacaine in the event of accidental intravascular injection. Consequently, some practitioners recommend it as the agent of choice for emergency extension of epidural analgesia (25).

Lidocaine, due to its lower pKa, is believed to have a faster onset time than bupivacaine. Indeed, a greater proportion of unionized drug is available at body pH to cross the neuronal membrane. Lidocaine is less cardiotoxic than bupivacaine, levobupiva- caine or ropivacaine (30). Because commercial preparations of lidocaine are acidic, increasing the pH towards the physiological range can theoretically increase the speed of onset. Alkalinization of local anesthetic solutions towards their pKa value increases the unionized drug fraction, thereby increasing the available amount of lipid-soluble base to cross the neuronal membrane. It is possible that the addition of bicarbonate also increases lipid solubility of fentanyl, and thus facilitates its penetration through lipid-soluble membranes into the spinal cord and systemic circulation (31). Alkalinization should not be attempted with ropivacaine, levobupivacaine or bupivacaine, as precipitation may result (32, 33, 34).

Adding epinephrine to local anesthetic solutions may reduce systemic absorption of local anesthetic agent from the extradural space, thereby reducing plasma levels and potential toxicity, and improving speed of onset and quality of block. However, there is little evidence to support this in an emergency situation. For epidural top-up anesthesia, the use of epinephrine was associated with less pre- and intra-operative failure (2). Addition of adjuvants, especially opioids and epinephrine, may substantially increase the success rate of epidural analgesia (20). Hereafter, we will see whether the literature provides us with clues to identify the ‘best’ local anesthetic solution for topping up epidurals for unplanned CS (Table 3).

Lucas and colleagues compared bupivacaine 0.5% with a 50/50 mixture of bupivacaine 0.5% and lidocaine 2% with epinephrine, and with lidocaine 2% alone with epinephrine. They were not able to evidence any significant difference in onset time between groups. The addition of epinephrine to epidural bupivacaine 0.5% has been shown to improve the quality of block for elective CS, but not when an existing epidural is extended for emergency CS (33).

Although Goring-Morris and colleagues were unable to demonstrate a significant difference in neither onset time nor intra-operative supplementation when comparing bupivacaine 0.5% with a lidocaine 2% - epinephrine solution containing 100 μg of fentanyl (LEF) (35) in a prematurely stopped study, Balaji et al. later on compared levobupivacaine 0.5% with the same LEF mixture in women who had received epidural fentanyl during labor. They found that the freshly prepared LEF mixture provided a 50% faster onset and superior quality of block than levobupivacaine alone. The LEF speed of onset was significantly faster, even when taking account of the time needed for drug preparation. In a category 1 CS, a gain of 3 minutes could make the difference between being able to proceed under epidural anesthesia, and having to induce general anesthesia. Moreover, in the levobupivacaine group, and before the beginning of surgery, the need for additional doses for achieving the block was significantly higher (36).

In a study of Malhotra et al., women receiving fentanyl containing labor epidural analgesia were randomly allocated to receive levobupivacaine 0.5% with either fentanyl 75 μg in 1.5 ml or the same 1.5 ml volume of saline. There were no significant differences in onset times or intra-operative supplementation between groups, but the incidence of intra-operative nausea/vomiting was significantly higher in patients having received epidural fentanyl.

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### Table 3

Epidural top-up solutions in patients for unplanned CS

<table>
<thead>
<tr>
<th>Study &amp; year of publication</th>
<th>n</th>
<th>Epidural top-up solutions compared</th>
<th>Sensory block</th>
<th>Conclusion</th>
<th>Remarks</th>
</tr>
</thead>
</table>
| GUERER et al., 1998 (4)     | 30  | A: pH-adjusted lidocaine 1.5% with epinephrine  
                              |              | B: pH-adjusted 2-chloroprocaine 3%  
                              | Loss of cold to T4  
                              | Mean onset time significantly shorter in chloroprocaine group  
                              | (A 4.4, B 3.1 min)  
                              | No major differences in neonatal outcome. |
| LUCAS et al., 1999 (33)     | 90  | A: bupivacaine 0.5%  
                              |              | B: 50:50 mixture of bupivacaine 0.5% :  
                              | Loss of cold to T4  
                              | Lidocaine 2% with epinephrine  
                              | No statistically significant difference in onset time  
                              | Without alkanilization. |
| LAM et al., 2001 (31)      | 40  | A: lidocaine 2% with epinephrine and fentanyl  
                              |              | (LEF) with saline  
                              | Loss of pinprick to T6  
                              | LEFB’s onset time almost twice as fast as for LEF (A 9.7, B  
                              | 5.2 min)  
                              | Preparation times not taken into account.  
                              | Maternal side effects and neonatal outcomes were similar. |
| SANDERS et al., 2004 (40)  | 45  | A: ropivacaine 0.75%  
                              |              | B: ropivacaine 0.5%  
                              | Loss of cold to T4  
                              | No statistically significant difference in onset time.  
                              | Study was stopped prematurely. |
| GERING-MORRIS et al., 2006 (35)| 68  | A: bupivacaine 0.5%  
                              |              | B: Lidocaine 2% with epinephrine and fentanyl  
                              | Loss of touch to T7  
                              | No clear statistically significant benefit in onset time  
                              | Study was stopped prematurely. |
| MALHITRA et al., 2007 (37) | 112 | A: levobupivacaine 0.5% with fentanyl  
                              |              | (LEF) with saline  
                              | Loss of cold to T4  
                              | No statistically significant for onset times or quality of block.  
                              | Patients received fentanyl containing labor epidural solution.  
                              | Study was stopped prematurely. |
| ALLAM et al., 2008 (39)    | 40  | A: lidocaine 1.8% with epinephrine and  
                              |              | bicarbonate (LEB)  
                              | Loss of cold to T4  
                              | LEF’s onset time significantly faster (T5 and T4 resp A 7 and  
                              | and of touch to T5  
                              | 7, B 14 and 11 min)  
                              | Pre- and intra-operative supplementation, maternal side  
                              | effects and neonatal outcomes were similar.  
                              | Intra-operative supplementation/pain in LEB group was 19%.  
                              | Study was stopped when primary outcome reached statistical  
                              | significance. |
| BALASH et al., 2009 (36)   | 100 | A: levobupivacaine 0.5%  
                              |              | B: Lidocaine 2% with epinephrine and fentanyl  
                              | Loss of touch to T7  
                              | LEF statistically faster onset time (A 15, B 10 min,  
                              | preparation times included 18 and 15 min) and superior  
                              | Patients received fentanyl containing labor epidural  
                              | quality of block.  
                              | solution. |
| HONG et al., 2010 (38)    | 61  | A: lidocaine 2% with epinephrine and fentanyl  
                              |              | B: Lidocaine 2% with epinephrine and saline  
                              | Loss of cold and pinprick to T4  
                              | No statistically significant differences in onset time to T4.  
                              | Patients received fentanyl containing labor epidural  
                              | Maximum levels of sensory block significantly higher in the  
                              | solution.  
                              | LEF group.  
                              | Intra-operative nausea more frequent in the saline group.  
                              | Failure rate of top-up was 1.6%.  
                              | Preparation times not compared. |
They speculated that repeated administration of epidural fentanyl during labor leads to a near-maximal effect such that further dosing produces no extra benefit. The study was stopped prematurely (37).

Comparing the top-up effect of lidocaïne 2% - epinephrine - fentanyl solution with sodium bicarbonate was almost half that of the lidocaïne 2% - epinephrine - saline for the extension of a fentanyl containing epidural labor analgesia, HONG et al. also concluded that the addition of fentanyl offers no advantage with respect to speed of onset. However, it did improve the quality of the block with fewer side effects in emergency CS (38).

LAM et al. demonstrated in their RCT that the median onset time of a lidocaïne 2% - epinephrine - fentanyl solution with saline. They did not take account of preparation times. Maternal side effects and neonatal outcomes were similar between groups (31).

ALLAM et al. conducted a RCT to compare the speed of onset and reliability of the epidural block when using a lidocaïne – epinephrine - bicarbonate (LEB) solution or a levobupivacaine 0.5% solution. Median onset times were significantly shorter for LEB. Pre- and intra-operative supplementation, maternal side effects and neonatal outcomes were similar between groups. Intra-operative maternal sedation was deeper with LEB than with levobupivacaine, but the difference did not reach statistical significance. The study was stopped when the primary outcome reached statistical significance. This can have resulted in conclusion errors regarding the other outcomes (39).

The ester local anesthetic 2% chloroprocaine 3% is the fastest for achieving efficient epidural top up, but this agent is still uncommon outside North America (5). Epidural top-up with chloroprocaine is rapid and does not require any additives, even though the addition of bicarbonate would result in an even shorter latency.

GAISER et al. compared pH-adjusted lidocaïne 1.5% with epinephrine and pH-adjusted 2% chloroprocaine 3%. They found that the mean onset time was significantly shorter in the chloroprocaine than in the lidocaïne-epinephrine group. There were no major differences in neonatal outcome between groups (4).

According to a study of SANDERS et al., there was no significant difference in onset times between ropivacaine 0.75% and bupivacaine 0.5% when used for top-up. Analgesic supplementation, though, was significantly less frequent in the ropivacaine than in the bupivacaine group (8.7 and 42.9%, respectively). Ropivacaine would also have a more predictable onset time (40). SNG et al. compared lidocaïne 2% - epinephrine - fentanyl (LEF) with ropivacaine 0.75% and with levobupivacaine 0.5%. They did not find a significant difference in time to surgical readiness either. However, the parturients of this study had received epidural analgesia through a CSE technique, which largely methodologically differs from all other mentioned studies, where labor analgesia was provided by an epidural catheter solely (41).

In their recent meta-analysis of 11 RCTs, HILLYARD et al. identified the best epidural solutions for emergency CS anesthesia (30). A lidocaïne 2% - epinephrine mixture with or without fentanyl (LE ± F) results in a significantly faster onset of sensory block than bupivacaine 0.5%, levobupivacaine 0.5% or ropivacaine 0.75%. Adding fentanyl 50-75 μg results in a significantly faster onset, but does not affect the need for intra-operative supplementation. When epidural block quality is considered, ropivacaine 0.75% seems to perform best. Bupivacaine or levobupivacaine are the least effective with respect to both speed of onset and quality of block. Analysis of secondary outcomes could not show any differences between solutions. Drawing conclusions from this meta-analysis is complicated by the diversity of protocols and endpoints, this being most apparent for onset time. In all included trials, LE ± F solutions showed median onset times shorter than 15 minutes. With such a technique, the time needed for surgical readiness is comparable with general anesthesia, which is at higher risk of serious complications. The onset time shortening appears more pronounced when bicarbonate is added, even though only one trial compares lidocaïne – epinephrine - bicarbonate (LEB) with levobupivacaine, bupivacaine or ropivacaine (39). For that reason, the authors could not add weight to this claim by including it in their meta-analysis (30). Furthermore, in that study, 19% of women receiving LEB required intra-operative supplementation (39). MAJHOTRA et al., by contrast, recommend the routine use of LEB to top up. This recommendation is based on the results of previous work, and on the observation, in their unit, of a half reduced GA conversion rate during the year after its introduction. They also stated that comparison between studies is hardly possible because of the large number of involved variables, especially when those are so crucial to the main outcomes (29). Another possible criticism to the meta-analysis of HILLYARD et al. is the absence of trials evaluating 2% chloroprocaine 3% (30).
Anesthesiologists may long continue to argue about the best epidural analgesia extension agent for CS, and particularly for category 1 CS. In practice, the agent or mixture used will probably be chosen to suit the needs, staffing levels, and geography of any particular obstetric unit (29).

We believe that organizational and logistical factors are more important than the actual local anesthetic solution used. However, it seems that chloroprocaine 3%, ropivacaine 0.75% and LEF are the solutions of choice. Bupivacaine and levobupivacaine should no longer be recommended.

Neuraxial alternatives when epidural catheter fails

Replacement of the epidural anesthesia

Pulling the failed epidural catheter out and replacing it by a new one has become less popular. In the literature, the frequency of such varies between 1.7 to 19% (13, 17). Problems include possible local anesthetic toxicity, prolonged time to establish a block, and subsequent block reliability and quality (42). More and more frequently, spinal anesthesia or at least the spinal component of a CSE is used to ensure pain relief during surgery. Women where the epidural catheter is replaced to insure operative anesthesia will be managed according to the same principles as those described above for patients with epidural top-up, but with reduced doses.

Single-shot spinal anesthesia

In this technique, the subarachnoid space is punctured and a shot of local anesthetic is injected. The L3-L4 interspace or below should be used to avoid the risk of spinal cord trauma (32). The aim is to provide anesthesia for the entire duration of surgery with a single intrathecal administration. A subarachnoid block provides fast and reliable anesthesia, and allows the anesthesiologist co-administering other agents for post-operative analgesia. The speed of onset may be advantageous when the fetus needs to be delivered urgently. A disadvantage is the inability to extend the block when anesthesia is inadequate. Hypotension is the most common complication of spinal anesthesia for Cesarean delivery and can have adverse consequences for both the mother and the fetus – it is, for example, linked to a higher risk of fetal acidosis. For hypotension treatment, phenylephrine is currently the first choice (5, 43). Intravenous fluid pre- or co-loading may also be used to reduce the frequency of maternal hypotension. Initiation of spinal anesthesia should however not be delayed to administer a fixed volume of intravenous fluid (3). The suitability of single-shot spinal (SSS) anesthesia in obese patients is arguable, because exaggerated spread of local anesthetics and subsequent unpredictable block level, and technical placement difficulties (3, 5).

Large analyses reveal that 20 to 59% of failed epidurals at CS are converted to spinal anesthesia (13). The 59% spinal anesthesia conversion rate found in the audit of Campbell et al. was successful in 83%. This observation is clinically significant as it indicates that subarachnoid block is a viable option when faced with inadequate epidural anesthesia. However, the success rate is much lower than that observed with elective CS. It does not support the “routine” practice of removing all epidural catheters failing to provide adequate epidural surgical anesthesia, while performing a single shot subarachnoid block immediately. Pulling the epidural catheter 1 cm back, followed by the incremental administration of surgical top-up solution, should be considered prior to undertaking spinal anesthesia (17) (Fig. 1). As an alternative to GA, Kinsella and colleagues proposed a rapid sequence spinal anesthesia for category 1 CS, with pre-oxygenation during attempt, ‘no touch’ technique, addition of fentanyl 25 μg or, alternatively, a higher dose of hyperbaric bupivacaine 0.5%, single attempt, and, if necessary, start of surgery when the block reaches T10 or higher, and is still ascending. During that sequence, the anesthesiologist should always be prepared to convert to GA. Diamorphine 300-400 μg can also be used for spinal anesthesia for CS. However, it presents in the form of a powder. A rapid sequence induction does not allow time for diluting the medication, and, therefore, fentanyl is often preferred (44).

The use of spinal diamorphine has been associated with less failure according to Kinsella’s study (2). Data from this large audit indicate that, if spinal anesthesia is to be used in the presence of an epidural, the epidural should not have been topped up for surgery, to avoid high blocks (2). Sia et al. also recommend prudently modulating spinal anesthetic dose in the presence of a partially effective epidural block. Not doing so could lead to excessively high blocks with cardio-respiratory compromise (5). For a spinal block (using SSS or CSE) after a failed epidural, it is recommended to decrease the dose of local anesthesia by 20-30%, and use additive opioids. A normal dose can be given if there is no documented block, or if more than 30 minutes passed since the last epidural dose (26, 45). Carvalho made a stand against SSS anesthesia following a failed epidural top-up. The reason was...
that the adequate intrathecal dose of local anesthetic agent is difficult, if not impossible, to predict in this setting. Either too small or too large doses are harmful (42). To prevent spinal-induced hypotension, low-dose bupivacaine is often recommended in the literature. In that case, low-dose spinal anesthesia as part of a CSE or SSS technique has been found to be a valuable method (45, 46, 47). However, a recent systematic review with meta-analysis demonstrates that these techniques compromise anesthetic efficacy in elective CS (48). In skilled hands, a SSS technique can be as fast or almost as fast as GA and it has a low failure rate. The drug of choice still seems to be bupivacaine. The addition of a lipophilic opioid such as fentanyl or sufentanil would further reduce the need of local anesthetic and shorten the time to surgical readiness (26, 49).

The dose and effect of baricity and posture for parturients are not identical as for non-obstetric patients. Because of vena cava compression, with engorgement of the epidural venous plexus, turning a parturient to the supine position causes bulk movement, hyperbaric solutions will redistribute because of gravity, while isobaric solutions mix with CSF, and further spread is limited. Block height is more easily controllable with hyperbaric solutions. This is important, in order to avoid high or total spinal blocks.

CSE anesthesia

If epidural top-up fails to provide a sensory block from S5 to T5, a combined spinal-epidural technique with a small intrathecal dose of local anesthetic is a useful approach. This technique allows the clinician reducing the initial intrathecal local anesthetic dose to minimize the potential for a high or total spinal block, and to reduce maternal side effects such as hypotension and nausea. The epidural catheter can then serve to facilitate additional dosing, and prevent subsequent anesthetic failure (42). Using a dose that is appropriate for a de novo spinal is not an inherently safe option because of the risk of excessively high block. A prudent and conservative spinal dose might well suffice, and can be safely augmented by subsequent increments of epidural local anesthetic agent (25, see also previous section on SSS). Various techniques use a volume of either a local anesthetic agent or NaCl 0.9% in the epidural space to extend the low-dose spinal anesthesia. Hereby, it is possible to adjust the level of anesthesia very accurately. This epidural volume expansion (EVE) technique is especially useful in high-risk cardiac patients, because it reduces the required dose of intrathecal local anesthetic substantially. For stat emergencies, the sequential CSE is not recommended, due to the extra time consumption (26). Hyperbaric bupivacaine, with or without the addition of fentanyl is also the solution of choice for the spinal component. Insofar as CSE is extendable, and can easily be used for the management of post-operative pain, this regional technique is widely accepted. The reported incidence of overall failure is lower in women receiving CSE versus epidural analgesia (12, 13). However, the epidural block functionality cannot be tested or proved at induction of spinal anesthesia. At the time of extension, one should expect a larger block spread (5).

General anaesthesia for emergency CS

The physiologic changes of pregnancy place pregnant women at high risk of morbidity and mortality when GA is administered for CS instead of regional anesthesia. The risk of a severe life threatening complication with regional anesthesia increases when the probability of a conversion to general anesthesia increases (21). Targets for best practice suggested by the Royal College of Anaesthetists depend on category-specific RA to GA conversion rates (9) (Table 1). General anesthesia remains a significant risk to obese women undergoing CS, because of a high incidence of difficult airway or failed intubation. This may lead to a significant reduced maternal oxygen reserve and a high risk of regurgitation and aspiration, while causing significant maternal morbidity or mortality (5, 6, 16, 17). Tracheal intubation after rapid sequence induction remains the approach to airway management during GA, although it is often challenging to visualize the larynx during laryngoscopy. Mask ventilation is difficult and pregnant women are prone to rapid oxygen desaturation upon induction of general anesthesia. Use of the laryngeal mask airway can be a rescue in the situation of failed intubation (5).

Emergency of delivery, failure of regional anesthesia, and anticipated large blood loss are the main indications of GA (2, 9, 12, 19, 21). General anesthesia for unplanned CS should include pre-oxygenation, cricoid pressure, and rapid sequence induction to reduce the risk of aspiration. Intravenous ephedrine or phenylephrine should be used for managing hypotension during CS. Each maternity unit should have a protocol for difficult airway management, and failed intubation during obstetric anesthesia (5, 10).
According to a recent UK national survey, 93% of respondents used thiopental for induction (most common reasons were historical, a reduced risk of awareness and concerns about neonatal effects), while 7% used propofol (58% of respondents who use thiopental would support a change to propofol for induction, in the USA the latter is also the first line induction agent in most large obstetric centers), 15% use opioids during rapid-sequence induction, 85% use nitrous oxide (main reasons are for reducing the risk of awareness, lowering concentrations of halogenated anesthetic agents, and for its analgesic properties), and 52% use sevoflurane [followed by isoflurane (46%) and desflurane (2%), respectively] for maintenance of anesthesia (51).

The regimen of thiopental, succinylcholine and nitrous oxide/oxygen without vapors for CS was first introduced 50 years ago (52). Until recently, it was common clinical practice to avoid opioids for the induction of general anesthesia, because of the potential respiratory depression in the neonate. Remifentanil – a short-acting lipophilic μ-receptor agonist – has a rapid onset with a maximum effect at 1 to 3 minutes. It is rapidly degraded by nonspecific blood and tissue esterases in both the mother and neonate, resulting in a half-life of a few minutes. It crosses the placenta, but is rapidly cleared from neonatal plasma. Following a study comparing thiopental-succinylcholine with or without the addition of remifentanil (bolus of 1 μg/kg given immediately before induction), Ngan Kee and colleagues stated that remifentanil might offer a new and promising way to maintain cardiovascular stability after induction and tracheal intubation, with having little effect on the neonate. It should however be used for clear maternal indications, when adequate facilities for neonatal resuscitation are available, as it does have the potential to cause a certain degree of neonatal respiratory depression (53). In a meta-analysis by Heesen et al., remifentanil was found to attenuate the maternal circulatory response to endotracheal intubation and surgery during CS under general anesthesia. Base excess was significantly higher in infants of remifentanil-treated mothers (54). Levy stated that induction and maintenance doses of drugs for GA should not be reduced in the belief that the baby will be harmed. In the event of severe hypovolemia, anesthesia can be induced and maintained with intravenous ketamine, which has a useful sympathomimetic effect (25). Although thiopental (at a dose of 5 to 7 mg/kg) is still regarded as the induction agent of choice for CS, etomidate, propofol, ketamine and midazolam have all proved to be well tolerated by the mother and the neonate. Ketamine 1 mg/kg and etomidate 0.3 mg/kg are useful in women with hemodynamic instability. Rapid sequence induction with thiopental and succinylcholine, and maintenance with halogenated inhalation agents (the latter reducing the risk of awareness together with neuro-monitoring) is still the choice for most anesthesiologists, when GA has to be performed in emergency situations (26). End-tidal vapor concentrations higher than 0.75 MAC, with 50% of inhaled nitrous oxide has been recommended to maintain BIS values below 60, and hence to obtain adequate depth of anesthesia for CS (51). At the present time, succinylcholine may be replaced by a high-dose of rocuronium (0.9 mg/kg or higher), and the backup solution of a rapid reversal by sugammadex in case of intubation difficulties, or at the end of the procedure. Sugammadex is a cyclodextrin that can chelate or encapsulate rocuronium, enabling rapid reversal of profound rocuronium blockade. It has been used safely in category 1 CS that were performed for fetal indications (52, 55).

**Conclusion**

We reviewed the medical literature to suggest how anesthesia can be safely and quickly provided in unexpected obstetric surgery. In case of an unplanned CS in women with a well-functioning labor epidural catheter, epidural top-up with either ropivacaine 0.75% for a block of good quality, or a lidocaine 2% – epinephrine – fentanyl solution for a fast onset time, should be recommended. Alkalization of the latter solution would further enhance onset times, though preparation times should also be taken into account. Mixing drugs takes longer, increases the risk of drug dilution errors, and the risk of bacterial contamination. Chloroprocaine 3% seems to have the fastest onset time, but is not available on the European market. The possible dangers of a general anesthesia technique in pregnant women are avoided by using regional anesthesia. It is important for the anesthesiologist to test for the functionality of the epidural catheter quickly after its insertion, especially in parturient women at higher risk of CS. Noteworthy, in addition to the speed of onset of the top-up solution, organizational and logistical factors also determine surgical readiness. In terms of sensory block, bilateral loss of cold to dermatome T4 should be reached before incision. Epidural failure rates and determinants of failure have been widely observed and vary among studies. If labor epidural analgesia fails, pulling the catheter one centimeter back, and follow this maneuver by the
administration of incremental doses of local anesthetic agents at concentrations that are compatible with surgery, can often be successful. If not, the degree of CS emergency will help to choose the fastest and most reliable technique to obtain surgical anesthesia. In CS category one or two, general anesthesia or single-shot spinal anesthesia are the most frequently used techniques. In category three or four, CSE or replacement of the epidural catheter can also be envisaged. As discussed above, dose modulation can be necessary when applying another neuraxial technique. A flowchart summarizes this management sequence in Figure 1. The regional to general anesthesia conversion rate varies from 1.2% to 8.1% in the literature. This rate attains 20% in case of category one CS.

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