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INVITED REVIEW ARTICLE

Controversies in obstetric anesthesia

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Abstract Obstetric anesthesia has become a widely evidence-based practice, with an increasing number of specialized anesthesiologists and a permanent research production. We believe that with the review of commonly discussed and controversial points the reader will be able to incorporate an evidence-based practice into their routine and offer to parturients and their babies a safe, reliable and consistent anesthesia care.

Keywords Anesthesia · Obstetric · Epidural · Spinal · Labor · Cesarean

Introduction

In 1847, the Scottish obstetrician James Young Simpson administered for the first time anesthesia to a woman during labor. Still amazed by the effects of the inhalation of ether on labor pain, he expressed concerns and doubts about the anesthetic intervention: "It will be necessary to ascertain anesthesia's precise effect, both upon the action of the uterus and on the assistant abdominal muscles; its influence, if any, upon the child; whether it has a tendency to hemorrhage or other complications" [1]. Interestingly, the questions brought by Simpson so long ago are still some of the ones currently debated. Obstetric anesthesia is seen in many cultures as a detrimental intervention [2] and myths related to pain relief, even in developed societies, are present among health providers. The lack of knowledge and the strong behavioral and cultural influences are important reasons for so much controversy regarding anesthesia for labor and delivery.

Considering a world population of 6,928,198,253 and global birth rate of 19.15 births/1,000 population in 2011 [3], we can estimate that 132.6 million births occur annually. Differently from United States where 58 % of all births utilize neuraxial anesthesia [4], in Japan, a small percent of deliveries have the participation of anesthesiologists. However, a recent study showed that a Japanese community in the United States has an epidural rate of 63 % [2].

The aim of this review article is to bring out the most recent evidence-based discussion regarding current topics in obstetric anesthesia.

Controversies related to neuraxial labor analgesia

Neuraxial anesthesia has been used for labor since the 1930s [5] but it is still challenged as a safe practice for the mother and baby. The historical and cultural background, when it was believed that the woman should feel pain during labor, as part of a punishment, inflicted for breaking divine law [6], is not anymore a reason for this skepticism. In modern evidence-based medicine, the reluctance concerning neuraxial anesthesia comes from studies done in the late 1980s and 1990s. During that period, the results suggested undesired delivery outcomes associated with neuraxial analgesia, such as prolonged labor, increased rates of cesarean delivery (CD) and assisted second stage.

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Appropriate cervical dilation for neuraxial analgesia

In a controversial statement based on studies with questionable methodology [7–9], in 2002, the American College of Obstetricians and Gynecologists (ACOG) suggested that neuraxial analgesia in nulliparous women should be delayed until a cervical dilation of 4–5 cm [10]. According to the authors, this cervical dilation was necessary to avoid prolonged labor, instrumented or cesarean deliveries, and that other forms of analgesia should be used for pain relief until the parturient achieved the desired dilation. Surprisingly, the ACOG statement was published even with consistent data available proving the harmless effect of regional anesthesia on obstetric outcome. Chestnut and colleagues performed two important studies to assess the effect of early epidural analgesia in nulliparous parturients. Pregnant women in labor, at term, with cervical dilation of 3–4 cm who requested analgesia, were randomized to receive epidural analgesia at the request time or intravenous nalbuphine until a cervical dilation was equal or over 5 cm, when they received the epidural analgesia. In the first study just parturients in spontaneous labor were enrolled [11], while the second one involved parturients on intravenous oxytocin for induction or augmentation of labor [12]. In both studies there were no increased rates of CD, oxytocin augmentation or vertex malposition at delivery.

In a prospective randomized trial, Wong et al. [13] assigned nulliparous women, at term, in spontaneous labor or with spontaneous rupture of membranes, with cervical dilation less than 4 cm, to receive intrathecal fentanyl or systemic hydromorphone. The epidural analgesia was initiated in the intrathecal group upon request and in the systemic group at a cervical dilatation of 4.0 cm or greater. The rate of CD was not significantly different between groups and early neuraxial analgesia was related to shorter duration of labor and delivery.

In 2006, the ACOG document was revised and, currently, it states that early neuraxial analgesia does not increase the risk of CD compared to neuraxial analgesia administered later in labor [14].

The American Society of Anesthesiologists (ASA) published in 2007 guidelines for obstetric anesthesia recommending that patients in early labor (i.e., less than 5 cm dilation) should have the option of neuraxial analgesia and it should not be withheld on the basis of achieving an arbitrary cervical dilation [15]. According to a joint statement on pain relief during labor from ASA and ACOG, a specific cervical dilation is not necessary and "*In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labor*" [16].

A systematic review, including 3,320 parturients, assessed the effects of early neuraxial analgesia in nulliparous women and found no increased risk of operative delivery [17]. On the other hand, parturients receiving early parenteral opioid and late epidural analgesia had a higher risk of instrumental vaginal delivery for nonreassuring fetal heart rate, lower quality of analgesia and also worse indices of neonatal wellness.

Wong et al. [18] showed that early combined spinal-epidural (CSE) labor analgesia in nulliparas, at term, in induction of labor is not related to increased rates of CD compared to epidural administered later in labor and the patients who received early CSE had shorter labor. Wang et al. [19] published the largest prospective randomized study so far, with 12,793 nulliparous parturients in spontaneous labor. There were no differences in cesarean or instrumented delivery rates, indications of CD, percentages of labors augmented with oxytocin, or maximal oxytocin dose. In both studies there was no difference in maternal fever rate between groups, even with the early neuraxial group having the epidural for a longer period.

Labor analgesia and instrumented deliveries

In 1987, Kaminski et al. [20], in a retrospective study, showed that the frequency of instrumental delivery among women receiving epidural analgesia was increased when compared to parturients without epidural. However, retrospective studies are subject to selection bias and instrumental deliveries in academic hospitals could have been performed for teaching proposes, especially if the obstetric team knew that the patient was confortable under epidural analgesia [21].

Still in the late 1980s, Chestnut et al. [22] developed a series of prospective randomized controlled trials studying different epidural analgesia schemes with different local anesthetic concentrations, addition of fentanyl [23], and maintenance of epidural analgesia during second stage [24], differently from the usual practice at that time. These studies showed the importance of local anesthetic concentration in labor outcome during epidural analgesia and also demonstrated that the association of diluted local anesthetic with fentanyl improves pain relief without significant motor block or increased incidence of instrumental vaginal delivery [25].

Corroborating with these findings, Wong et al. [13] showed that CSE technique with intrathecal fentanyl at 25 μg, followed by epidural diluted local anesthetic, either with or without fentanyl, was not associated with increased rates of instrumented vaginal delivery. Tsen et al. [26], in 1999, had already showed that when comparing CSE and epidural analgesia for labor, the mode of delivery does not change between groups. However, when comparing regular epidural analgesia with intravenous meperidine for term nulliparous in spontaneous labor, a randomized trial

demonstrated a clear difference in forceps deliveries rates between groups. Twelve percent of women receiving epidural analgesia had forceps deliveries compared to 3 % in the meperidine group [27], but it is not clear in the study why it happened. Apparently, the obstetric providers were not blinded to the anesthetic technique and it can be one of the reasons for the higher rate of assisted deliveries in the epidural group. A recent study shows that, regardless of the use or not of epidural analgesia, neonates delivered with vacuum-assistance have significant lower Apgar scores and umbilical arterial pH [28]. The clinical significance of those findings still need to be determined with further studies.

A recent Cochrane review of 38 studies involving 9,658 women [29] found that just five studies compared epidural analgesia with systemic opioids. The authors demonstrated that epidural labor analgesia is associated with increased risk of assisted vaginal delivery but has no impact on CD.

From high concentration, in the 1980s, to diluted local anesthetic combined or not with opioids, the epidural analgesia options have changed during the last two decades. Thus, it is important to note that comparing different studies within a long time frame can be challenging and extrapolating findings from over 20 years ago might be inappropriate.

Neuraxial analgesia and cesarean delivery

Parturients in pain impose ethical and clinical challenges, which lead to methodology flaws even in prospective studies. One example is the woman that does not have satisfactory pain control and migrates from her original assigned study group. It generates cross over between groups and protocol failures. However, well-designed and controlled studies are able to minimize those biases using intention-to-treat analysis and generate reliable results. If a retrospective analysis is used, selection bias can occur and a high incidence of CD [30] might be identified in patients with dysfunctional and painful labor [31].

Another way to access the correlation of labor epidural analgesia and CD is the application of studies of sentinel events. This type of study compares the rates of a determined outcome before and after the sudden implementation of an intervention in a controlled environment, for example a hospital. Thus, we consider that confounding factors such as patient population, teamwork, obstetrician practice and other internal variables are stable and unchanged before and after the intervention. The rates of CD associated with the introduction of epidural analgesia in those institutions have not shown significant changes [32, 33]. Methodologic limitations apply to sentinel event studies, especially because subgroups of the population are not individually analyzed and changes in practice of the providers working in that institutions can occur in the period studied.

Studies have compared conventional epidural analgesia, low-dose epidural analgesia and CSE. No difference in the mode of delivery and CD rates were found according to those studies [34–37]. The same has been demonstrated when comparing CSE and systemic analgesia [13].

Neuraxial analgesia and labor progress

Prolongation of labor related to neuraxial analgesia is commonly questioned by parturients. Based on evidence, it can be addressed in several ways. First, not every neuraxial anesthesia works in the same way; second, the anesthesiologist can use different drugs, concentrations and doses; and third, nulliparous parturients have a labor and delivery pattern that differs from multiparas.

Studies comparing epidural analgesia and systemic opioid for nulliparous women in spontaneous labor, have demonstrated that epidural analgesia prolongs the overall length of labor. In the study of Sharma et al. [27], epidural analgesia with an initial bolus of bupivacaine 0.25 % followed by a continuous infusion of bupivacaine 0.0625 % with fentanyl 2 μg/mL prolonged the length of the first and second stages of labor by 40 and 10 min, respectively. However, the prolongation of labor did not affect fetal outcome, assessed by Apgar score and umbilical artery blood analysis.

The CSE has been compared to both conventional epidural and systemic opioid analgesia. Tsen et al. [26] hypothesized that neuraxial anesthetic technique may influence the rate of cervical dilation and compared the effects of CSE with those of conventional epidural analgesia. They concluded that in healthy nulliparas in early labor, CSE analgesia was associated with faster cervical dilation. The duration of second stage and mode of delivery did not differ between groups. The authors attributed the findings to a possible reduction in local anesthetic exposure in the CSE group when compared to the epidural analgesia group, which could affect the uterine activity. Moreover, the rapid analgesia onset with the intrathecal medication may allow for sudden change in maternal catecholamine profile that could increase uterine activity.

Wong et al. [13] compared CSE and systemic hydromorphone in nulliparous women in spontaneous labor with cervical dilation less than 4 cm. The spinal component of the CSE used was fentanyl 25 μg without local anesthetic. As a secondary outcome, the authors found that CSE resulted in a shorter duration of labor, with a mean length of 90 and 81 min shorter for first and second stages, respectively.

CSE and fetal heart tracing abnormalities

Changes in fetal heart tracing (FHT) immediately after CSE technique can occur and is a common cause for

skepticism. The mechanism responsible for these changes is not totally clear. It is speculated that the spinal opioid can generate an imbalance between levels of circulating norepinephrine and epinephrine, with the first overcoming the second. It would generate uterine vasoconstriction and hyperactivity that, ultimately, may promote FHT abnormalities [38, 39]. Maternal hypotension is not the apparent reason for nonreassuring FHT. In a retrospective study, Van de Velde et al. [40] reviewed 1,293 charts and concluded that intrathecal sufentanil 7.5 μg was related with more nonreassuring FHT and uterine hyperactivity than other techniques. However, changes in FHT were not associated with higher rates of CD or neonatal acidosis when compared to the control group.

Management of the accidental dural puncture (ADP) during epidural placement

Various approaches may be used when an ADP happens [41]. One should assess risks and benefits of inserting the epidural catheter in the intrathecal space or to replace it in the epidural space at another vertebral interspace. The intrathecal catheter has the advantage of fast onset of action, less local anesthetic requirement, higher quality analgesia and a controversial benefit of reducing the risk of post-dural puncture headache (PDPH). On the other hand, the intrathecal catheters are related to increased risk of CNS infection, spinal cord trauma, neurotoxicity and the unrecognized injection of wrong medication. When an epidural catheter is replaced, the down-side is the potential risk of unexpected high-block due to the prior large dural-puncture hole and the higher risk of PDPH because one dural puncture has already happened and there is a chance of a second one occurring.

Some studies demonstrated that in patients undergoing CD, the use of intrathecal catheters for over 24 h after ADP reduces the incidence of PDPH [42, 43]. Russell, in a prospective controlled study [44], concluded that the insertion of an intrathecal catheter after ADP for labor analgesia did not reduce the incidence of PDPH or epidural blood patch when compared to repeat epidural catheter placement. According to the author, the most significant factor for PDPH and blood patch is the diameter of the needle used, when comparing 16-gauge and 18-gauge needles.

Risk of intrathecal catheter migration after uncomplicated CSE

One can say that after the voluntary creation of a needle hole in the dura-mater with a spinal needle, the introduction of the epidural catheter could facilitate its migration from the epidural into the intrathecal space.

Holmström et al. [45] in a percutaneous epiduroscopy study in fresh cadavers demonstrated that it was impossible to force an 18-gauge epidural catheter through the dural hole made by a 25-gauge spinal needle. After dural puncture with a 16 or 18-gauge Tuohy needle, the epidural catheter penetrated the dural hole in nine of 20 cases. The conclusion from this study is that, in an uncomplicated CSE technique, the risk of epidural catheter migration is extremely small, which was confirmed applying an interesting laboratory model with cadaver dura [46].

Apparently, the concern of intrathecal catheter migration during uneventful CSE does not justify the avoidance of this technique.

Ultrasound guided neuraxial anesthesia

The use of ultrasound (US) to determine the distance from the skin to the ligament flavum was first reported in 1980 [47]. However, just after 2000 US has gained popularity for clinical use in both obstetric and non-obstetric fields, but its applicability is still controversial. Differently from peripheral nerve blocks, where the anatomy is easily identified by US (called sonoanatomy), the epidural lumbar space is localized in a deep area surrounded by bone. The transducer necessary to assess the lumbar spine has low frequency (2.5–5.0 MHz) and consequently lower quality image, which makes the learning of the technique more challenging. Despite possible technical limitations, many studies demonstrate that the distance of the epidural space from the skin can be reliably estimated in obstetric patients, including obese ones [48, 49]. Another advantage of the US is the correct finding of the vertebral midline and interspace that is frequently underestimated by anesthesiologists [50, 51]. When applied for teaching, the US can improve the learning curve with higher success rates and less complications [52, 53]. However, it is criticized for being unnecessary for a safe and cost-efficient epidural technique and for being time consuming [54].

Spinal anesthesia for cesarean delivery

The CD rate worldwide has increased significantly despite the effort of health agencies to reduce it. Currently, CD is the most common surgery performed in United States, with over 1 million procedures per year [55]. In Asia, the global rate of CD is 27.3 % and in Japan it accounts for 19.8 % of the deliveries [56]. Small differences in outcomes become huge numbers when dealing with a very common procedure. Thus, we aim to discuss how to approach critical points during anesthesia for CD and also highlight recent changes in the scope of this practice.

Perioperative fasting in obstetric setting

The physiologic changes induced by pregnancy lead to a particular condition of the parturient that increases the rates of potential morbidities, such as respiratory complications from pulmonary aspiration of gastric contents. The reduced lower esophageal sphincter tone, dislocation of the stomach to an upper position and increased abdominal pressure make the pregnant woman to be considered to have a full stomach. However, it has been demonstrated, using acetaminophen absorption rates and antrum cross-sectional area measured by ultrasound, that the gastric emptying is preserved in parturients not in labor [57, 58].

Parturients in active labor receiving epidural analgesia with local anesthetic (LA) and opioids have slower intestinal transit when compared to patients with epidural analgesia just with LA [59].

Prolonged fasting promotes endocrine-metabolic response, delayed gastric emptying, increased gastric residual volume and risk of pulmonary aspiration [60]. The last ASA obstetric anesthesia guideline [61] recommends 6–8 h fasting for solids, depending on the fat content, and suggests that clear liquids may be used in modest amounts up to 2 h before elective CD. The most recent guidelines have changed the recommendations and the European Society of Anaesthesiology (ESA) guideline from 2011 [62] encourages patients to keep drinking clear liquids up to 2 h before surgical procedure. It would reduce the discomfort of prolonged fasting and improve well-being. Recently, Itou et al. [63] published a prospective randomized multicenter study demonstrating the safety of oral intake of clear liquids until 2 h prior to the surgical procedure. Their clinical trial included non-pregnant, low risk patients going for different surgical interventions. The results showed no difference between groups regarding gastric fluid volume and pH.

Chewing gum

Chewing gum in the perioperative period is still controversial. The most recent data suggest that if not beneficial, at least, chewing gum is not harmful to the patient, once there are no increased rates of pulmonary aspiration or nausea and vomiting described [64].

Interestingly, recent studies have demonstrated the benefits of gum chewing after surgery. In 2008, Purkayastha et al. [65] showed in a meta-analysis with randomized studies that gum chewing enhanced recovery after colectomy. Studies in the obstetric subpopulation have confirmed the previous findings and demonstrated that gum chewing stimulates early bowel activity following CD. While one study demonstrated statistically significant shorter hospitalization in the gum chewing group [66], it was not replicated in a similar trial [67], but patients requested less medication for nausea in the chewing group. Apparently, chewing gum in the postoperative period is a simple, cheap and safe method that can generate patient well-being and cost reduction due to early hospital discharge.

Antibiotic prophylaxis for cesarean delivery

Antibiotic prophylaxis for CD has been, traditionally, given after the procedure has started and the umbilical cord is clamped. The explanation for this unusual prophylaxis is based on the premises that the antibiotic would be harmful to the newborn and could either produce resistant microorganisms or mask neonatal infections. Nevertheless, in 2007, Sullivan et al. [68] demonstrated that the use of antibiotic before skin incision for CD was related to less serious infectious (i.e., endometritis) and did not increase infection rates or severity of infections in neonates. The American College of Obstetricians and Gynecologists (ACOG) [69] and others [70] ratified those results. Although a Cochrane meta-analysis could not demonstrate a difference between different classes of antibiotic regarding maternal infections after CD [71], the current data suggest that cephalosporins of the first generation such as cefazolin 1–2 g within 1 h prior to skin incision would be adequate for a non-obese patient. According to a recent study, the concentrations of cefazolin in the adipose tissue of patients with BMI over 30 kg/m^2 can be less than the appropriate inhibitory concentration [72]. In our institution, patients over 100 kg receive cefazolin 3 grams IV within 30 min prior to the skin incision.

How to optimize fluid loading during cesarean delivery?

Crystalloid preload

Crystalloid preloading has been used with the objective of reducing hypotension after neuraxial block. This practice has not been recommended since the 1990s when Rout et al. [73] demonstrated that the use of IV crystalloid 20 mL/kg prior to spinal anesthesia for CD did not change the rates of severe hypotension nor ephedrine consumption. Those findings were replicated by others and the lack of benefit of crystalloid preload has now been widely accepted.

Colloid preload

Owing to the failure of crystalloid to reduce maternal hypotension, the interest shifted to the use of colloids. There appears to be a clear benefit of using colloids up to 1,000 mL IV prior to the spinal anesthesia [74, 75].

Ueyama et al. [74] assessed blood volume and cardiac output of pregnant women and showed that the augmentation of blood volume with preloading must be large enough to result in a significant increase in cardiac output for effective prevention of hypotension. These findings can be justified by the short duration of crystalloids in the IV space when compared to colloids. It can be even more accentuated in parturients, who have pregnancy-induced reduction in colloid-osmotic pressure.

Crystalloid coload

If apparently the key-point for IV fluid management is the infusion start time and its pharmacokinetics, it seems adequate to study the difference in results when using crystalloids before or during the spinal anesthesia, defined as pre and co-load, respectively. Dyer et al. [76], even with a small number of patients, demonstrated that the hypotension rates and the vasopressor consumption were lower when lactate Ringer's 20 mL/kg was used as coload compared to preload technique. In 2005, Ngan Kee et al. [77] compared one group receiving 2 L of IV lactate Ringer's coload to a control with no pre or coload. Both groups received, after the spinal anesthesia, IV phenylephrine in continuous infusion targeted to maintain the blood pressure near baseline values. The authors demonstrated that, even with vasopressor infusion, IV fluid is an essential part of the anesthetic management of parturients going for CD and that the combination of crystalloid coload with IV vasopressor reduces significantly the hypotension rate and phenylephrine requirements. Differently, a meta-analysis not including the Ngan Kee et al. study [77], found no difference in rates of hypotension, nausea or vomiting when comparing pre or co-loading IV fluids for elective spinal anesthesia for CD [78].

Colloid coload

Considering the prolonged half-life of colloids in the IV space, it is understandable that studies comparing pre and coload using colloids solutions found no significant difference in hypotension between groups [79–82].

A recent publication regarding fluid therapy in the context of CD compares colloid coload versus crystalloid coload. Theoretically, both fluids would be able to sustain maternal blood pressure along with vasopressor. In this study, McDonald et al. [83] allocated patients to receive a rapid 1 L IV coload of 6 % hydroxyethyl starch solution or crystalloid solution and a phenylephrine infusion was used to maintain the maternal baseline systolic blood pressure (BP) in both groups. The authors used a suprasternal Doppler flow technique to measure maternal cardiac output (CO) as primary outcome and the secondary outcomes were phenylephrine doses, maternal hemodynamic and fetal outcome. No significant differences in the CO variables and in the total vasopressor dose between groups were found and the authors concluded that there is no advantage in using colloid over crystalloid when in combination with phenylephrine infusion. This study evaluated hemodynamic variables just for the initial 20 min after the spinal anesthesia. A longer evaluation may have shown significant changes, considering the different redistribution patterns for colloids and crystalloids.

Vasopressors during cesarean delivery

The use of spinal anesthesia for CD can produce hypotension due to sudden sympatectomy, reduced preload and supine hypotension. Despite the anesthesiologists' effort, the rates of hypotension can be as high as 83 % [84]. The most important steps to minimize the hemodynamic changes from spinal anesthesia are left uterine displacement, IV fluid coload and IV vasopressors.

Until the decade of 1990, the vasopressor of choice for obstetric anesthesia was ephedrine. Phenylephrine used to be considered a harmful medication for fetuses. More recently, studies comparing umbilical cord blood gases have shown that neonates born to mothers who received ephedrine had more acidotic pH when compared to ones whose blood pressure was controlled with phenylephrine [85]. However, laboratory findings did not correlate with clinical presentation of the newborns, as with the Apgar score. Currently, several centers use phenylephrine in continuous infusion to maintain the maternal BP stable [86]. Although phenylephrine can be an ideal vasopressor, its pharmacodynamics can produce undesirable effects. Phenylephrine is a direct acting selective α_1-agonist that can fast increase the systemic vascular resistance (SVR), improve BP and ultimately produce reflex bradycardia. It has been shown that, in patients in phenylephrine infusion, the BP is inversely proportional to HR and CO [87, 88]. Thereby, The improvement in maternal BP can, in reality, mask an accentuated depression in CO that is directly proportional to maternal bradycardia [88]. In the absence of CO monitoring, the anesthesiologist can use the maternal HR as a surrogate indicator of CO [88]: low HR would mean low CO and normal HR would correspond to normal/high CO.

Ephedrine is a sympathomimetic drug with a direct and indirect α and β-agonist effect that increases maternal BP, SVR and HR. It can easily cross the placental barrier and, in the fetus in distress, ephedrine can increase catabolism and HR, which might decrease fetal pH and wellbeing. These metabolic effects have not been proven to change fetal outcome in the short or long-term.

Cesarean delivery and oxytocin use

Oxytocin is an endogenous hormone and its synthetic form was developed in 1953, by the Nobel awarded researcher Du Vigneaud. Oxytocin's central mechanism of action is binding to G-proteins at the uterine myocyte and ultimately generating cellular calcium release and uterine contraction [89].

It is structurally similar to antidiuretic hormone (ADH) and can produce water retention and hyponatremia, especially if used with hypotonic IV solutions. Other potential adverse effects of oxytocin are hypotension, cardiac dysrhythmias and ischemia, flushing, headache, nausea and vomiting.

Oxytocin is used for induction and augmentation of labor and for postpartum maintenance of uterine contractility. However, its use can be harmful for both parturients and fetus, especially when used in high doses, rapid IV infusions or mistakenly administered due to labeling issues—as highlighted by health agencies in warning notes [90, 91].

The management of a patient after CD following augmented labor differs completely from an elective case. Parturients going for surgical delivery due to failure to progress tend to need increased doses of oxytocin and also to have failed initial treatment with oxytocin as single agent. Balki et al. [92] showed that the ED90 of oxytocin in cases of arrested labor is 3.0 IU, while in cases of elective CD in uncomplicated parturients it is 0.95 IU [93]. Moreover, according to an in vitro study, the oxytocin receptors desensitization occurs independently of the exposition time [94], i.e., the period that the gravid uterus is exposed to oxytocin.

The reports of cardiovascular collapse following administration of IV oxytocin during CD [95, 96] have stimulated obstetric anesthesiologists to change their practice. In an editorial, Tsen and Balki [97] urge the necessity of better protocols when administering such a potentially harmful drug and propose the "rule of threes" to initiate oxytocin in the operating room. The authors suggest to start with 3 IU oxytocin IV slow loading dose, wait 3 min for assessment interval and use up to two repeat doses (total of three). In case of uterine hypotonia, three pharmacologic options (ergonovine, carboprost and misoprostol) should be available to use. This comprehensive protocol would be appropriate for most of the clinical scenarios and would consider the oxytocin half-life of approximately 3 min [98] and ED90 of 3 IU for patients in arrested labor.

Post-cesarean delivery analgesia

Pain after CD can interfere with the mothers' ability to breastfeed and interact with their babies. It might also potentially increase venous thromboembolism risk in case of immobilization [99] as a consequence of uncontrolled pain.

Spinal morphine has been used for post-cesarean analgesia since the decade of the 1980s and became the most reliable and consistent way to provide effective analgesia in the obstetric population. Intrathecal morphine (ITM) can be related to respiratory depression, although this is a rare complication. The exact incidence of respiratory depression is unknown, with a lack of definition between several studies. A review article showed an incidence of respiratory depression of 0.26–3 % after ITM in doses ranging from 0.15–0.8 mg [100]. Palmer et al. [101] demonstrated that intrathecal doses of morphine over 0.1 mg do not increase analgesia and the pruritus rate is directly proportional to the morphine dose, differently of nausea and vomiting incidences. The same group showed that the analgesia provided by epidural morphine improves when the dose is increased up to 3.75 mg, but beyond this dose a ceiling effect apparently occurs. Except for the placebo group, the incidence and intensity of pruritus did not differ between groups (1.25, 2.5, 3.75 or 5 mg) [102].

Neuraxial morphine, despite being a great analgesic, has the disadvantage of provoking pruritus, nausea, vomiting and also the necessity of monitoring respiratory rate for up to 18–24 h. Recently, other analgesic options such as IV ketamine, gabapentin and ropivacaine infusion at the incisional wound have been tried [103–105]. Transversus abdominis plane (TAP) block can be an option when there are contra-indications to neuraxial morphine or neuraxial techniques. In these cases, TAP block reduces the postoperative narcotic consumption and improves pain scores [106, 107]. However, many studies, including one meta-analysis have demonstrated that when compared to ITM, the TAP block has inferior analgesic effects [108–110]. In studies comparing one group with ITM (control) with another group receiving ITM plus TAP block, it did not provide significant additional analgesia [111, 112]. In conclusion, TAP block has the advantage of minimizing side effects related to opioids and is a feasible option when ITM is contra-indicated, but it has no additional benefit when ITM is used.

In our hospital, for elective CD, we use ITM 0.1–0.2 mg, intrathecal fentanyl 10–20 μg and IV ketorolac 30 mg. The TAP block is reserved for cases of contra-indications to neuraxial technique and specific clinical scenarios where we think the parturient can benefit from it in, for example, patients with history of opioid abuse.

Conclusion

Obstetric anesthesia has become a widely evidence-based practice, with an increasing number of specialized

anesthesiologists and a permanent research production. We believe that, with the review of commonly discussed and controversial points, the reader will be able to incorporate an evidence-based practice into her/his routine and offer to parturients and their babies a safe, reliable and consistent anesthesia care.

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