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Update in Obstetric Anaesthesia

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Abstract
We present a review of four major topics in obstetric anaesthesia, including obstetric outcomes, analgesia for labor and anaesthesia for caesarean section.

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I. Introduction

Obstetric anaesthesia has positioned itself as a fundamental pillar during the peripartum period of women. Numerous advances have been made in the last decades and although its practice is carried out daily in numerous centers around the world, there still are controversies regarding its application, safety and potential relationship with obstetric outcomes. The objective of this review is to integrate the available information on ten multiple-choice questions that cover different areas of interest in obstetric anaesthesia in a simple, practical and evidence-based way to try to unravel the main current controversies of this practice. We have divided this review into four main topics, including obstetric outcomes, analgesia for labor, anaesthesia for caesarean section and miscellaneous ones. In this unusual and didactic way, we intend to cover most of the relevant aspects of each area, with an evidence-based review supporting the best answer.

Effects of Epidural Analgesia on Obstetrical Outcomes

It is mandatory to describe the risks and benefits of medical treatment to patients so that they can make free and informed choices [1]. Nowadays, pregnant patients demand information, so it is important to recognize aspects that may affect their outcome. Neuraxial obstetric analgesia could interfere at multiple levels with relevant outcomes such as duration of labor, forceps delivery and cesarean section rates. It is important to note that there has been an evolution in anaesthesia techniques, with results that have changed over time. If we consider modern obstetric analgesia techniques, its relationship with different outcomes are:

Duration of labor: a recent meta-analysis showed that neuraxial analgesia compared to systemic analgesia prolong first stage of labor (cervical dilation) by nearly 30 minutes [95% confidence interval (95%CI): 18-46 min], and second stage of labor by 15 minutes [95%CI: 9-22] [2, 3]. Although these values may be clinically unimportant, we cannot ignore them. Certainly, work should be done to reduce this risk by using low doses and concentrations of local anesthetics, decreasing the risk of motor blockade, which could be responsible for this outcome, although this is still controversial [4].

Instrumental delivery (forceps): its relationship with the obstetric outcome is still a matter of debate. There seems to be an increased risk of forceps-assisted deliveries in those patients who have received neuraxial analgesia [2]. It is difficult to isolate confounders that determine the use of forceps. Some of them include depth of neuraxial block in the second stage of labor (higher blockade, greater risk of forceps delivery) and the obstetric practice at each center (greater tendency in forceps delivery in patients with effective analgesia and in teaching hospitals, which is precisely where the studies are carried out) [5]. Most importantly, studies including modern neuraxial analgesia techniques (after 2005), have not been able to demonstrate this association [2].

Cesarean delivery: this outcome has been most consistently unrelated to neuraxial analgesia. It has been shown that there is no relationship between the incidence of cesarean sections when comparing neuraxial analgesia versus systemic analgesia, both in nulliparas in spontaneous and induced labor, nor in early initiation of neuraxial analgesia (before four centimeters of cervical dilation) versus late administration [6-8]. However, there is a relationship between protracted labor and a higher risk of cesarean sections, which concomitantly translates into a higher consumption rate of anesthetics [9].

In summary, epidural analgesia can reduce labor pain more effectively than any other analgesic strategy and can increase maternal satisfaction with pain relief, at the cost of a discrete prolongation of the duration of labor. In turn, some women who receive epidural drugs instead of systemic opioids may be more prone to have an assisted vaginal delivery (forceps); however, this finding probably reflects the use of higher

concentrations of traditionally used local anesthetics instead of low concentrations of modern neuraxial techniques and, therefore, this effect is less likely to occur today.

The traditional epidural technique remains the gold standard for the management of labor pain. Although it is a blind technique, there are multiple methods to rule out that the final location of the epidural catheter is in an unwanted position, such as the intrathecal space (after a wet tap) or intravascular space (red tap). Diagnostic tests to rule out abnormal catheter positions include the use of fractional doses, use of the minimum effective dose (for the patient's stage in labor), intermittent aspiration of the catheter between doses and use of a test dose. The latter was designed to rule out the catheter being in the intrathecal space (by using lidocaine 45 mg), as well as one to rule out being in the intravascular space (by using epinephrine 15 ug), all in the same mixture [10]. Unfortunately, this test has low specificity in the pregnant patient (a painful contraction that induces tachycardia can be falsely confused with the effect of intravascular epinephrine), and has been replaced by the concept that each therapeutic dose should be a test dose itself ("every dose is a test dose") [11].

The combined spinal-epidural technique is a widely used technique since its analgesic effect is very fast, homogeneous and provides better sacral analgesic coverage than the traditional epidural [12]. However, there is a reasonable doubt that it could affect the obstetric outcome. In a recent meta-analysis, Hattler *et al*. suggested that combined spinal–epidural labor analgesia may be associated with a higher risk of non-reassuring fetal heart rate tracings than epidural analgesia alone [13].

We believe that combined spinal-epidural analgesia should be used with caution, especially in patients in whom the obstetric outcome could be influenced, leading to unfavorable outcomes (for example, patients with placental insufficiency). More studies are warranted to adequately determine the doses of the intrathecal and epidural component in order to have more homogeneous results and thus give an evidence-based recommendation. For the moment, in general, the clinical benefits of the combined spinal-epidural technique outweigh its risks.

The dural puncture epidural technique (DPE) has been positioned as an intermediate option between the traditional epidural and the combined spinal-epidural technique. In a recent study, Chau *et al*. were able to demonstrate benefits of the new DPE technique, characterized by a reduction in the incidence of uterine tachysystole, hypertonia and conversion of category I to II fetal heart rate tracings, which was greater in the group that received a combined spinal-epidural technique and with no differences with the traditional epidural technique [14]. DPE technique is apparently effective when using a 26G needle or thicker (the technique with a 27G needle apparently is not) [15].

The continuous spinal technique allows titration of analgesia and, eventually spinal anaesthesia, in a controlled and progressive manner. This is highly desirable in patients for whom slow-onset anaesthesia is desired, but with optimal coverage and quality, such as in cardiac pregnant patients. The problem with the technique is its high risk of post-dural puncture headache, which makes it prohibitive as a routine technique, but it can certainly be considered for special cases [16].

Analgesia for Labor

Initial experiences with this methodology allowed comparing drugs or situations, mainly determining the effect in 50% of the studied population. Although this outcome is useful, much of the rest of the dose-response curve (between 50% and 100%) could only be estimated, with a high degree of uncertainty. The advantages of the method were that it is simple to do, few patients are required, and could be used as a guide for formal dose-response studies. Considering the aforementioned caveats, the MLAC of bupivacaine was studied during labor and the influence of the stage of labor on anesthetic requirements. It is known that the pain of labor.

Labor pain is constantly evolving in type (from visceral it evolves to somatic), location (from abdominal and dorsal to perineal) and especially with respect to intensity, which increases along with labor. Capogna *et al*. determined that epidural analgesia requirements are three times higher in patients in the second stage of labor than in the first stage [18]. This is explained by the structures and pain pathways they use. For the dilation stage, the pain of uterine contractions and cervical dilation is mainly integrated at the level of the spinal segments T10 to L1, while during the second stage of labor, they will do so through the thick sacral S2-S4 nervous roots, with somatic characteristics which are more challenging to anesthetize.

The "Up-Down" technique evolved and has allowed to determine other values in the dose-response continuum. Thus, it was used to determine the 90% effective dose of oxytocin for the prevention of bleeding after the elective caesarean or after failed labor. The method is essentially the same, except that the desired outcome (in this case, an adequate uterine contraction) will determine the dose required by the next patient with a probability of 1:9, allowing the median dose to be grouped around 90% of successes in this case. Under these conditions, authors were able to determine that the ED90 of oxytocin for the prevention of bleeding after the elective caesarean section was 16 IU/h [95% CI: 13.1-19.3], while post-labor was 44 IU/h [95% CI, 33.8-55.6] [19]. Not only could they determine a value that may be clinically useful but described a down-regulation effect of oxytocin in the myometrial tissue, which has been shown in vitro and represents desensitization of oxytocin receptors after prolonged exposure, as is labor [20].

On the other hand, the use of adjuvants to neuraxial local anesthetics have been studied with this methodology. Fentanyl is a lipid-soluble opioid, which favors its systemic absorption when administered in the epidural space. Its clinical behaviour in the obstetric population is explained by a systemic effect, but mainly by its effect on the spinal cord. Polley *et al*. compared the MLAC of epidural bupivacaine when co-administered with fentanyl, versus a group dosed with intravenous fentanyl. They demonstrated a reduction of more than 50% in the dose of the local anesthetic in the first stage of labor when it was associated with epidural fentanyl [21]. This strongly supports the concept that its effect is primarily at the spinal level, supporting its use as a neuraxial analgesia in obstetric anaesthesia.

The relationship between the anthropometric characteristics and the epidural analgesic requirements of local anesthetics in labor is something that the method has also allowed us to study. Panni *et al*. evaluated the analgesic requirements of obese and non-obese patients in labor. They found that the former will require a third of the bupivacaine dose of a non-obese patient [22]. It is likely that the increase in body fat tissue, including that of the epidural space, favors this clinical effect by compressing the dural sac, decreasing the relative volume of cerebrospinal fluid where the anesthetic is injected, increasing its performance. In the case of spinal anaesthesia for caesarean section, when a standard spinal dose is administered to obese patients, the anesthetic reaches a more cephalad spinal level (T2 vs T4, 95%CI: 0-2 dermatomes) and the duration of the anesthetic effect increases by 20 minutes [95%CI difference: 3.8-36.2 min] [23].

Combined spinal-epidural anesthetic technique refers to the intrathecal administration of opioids, local anesthetics or a mixture of both, to achieve a rapid onset of action with high efficacy associated with a small amount of drug. The technique then includes the insertion of a catheter in the epidural space allowing maintenance of analgesia as the effect of the initial intrathecal dose fades [24-26].

Successful analgesia has been described with the administration of opioids such as sufentanyl 5-10 ug or fentanyl 25-30 ug for the spinal component of the technique during the first stage of labor, lasting for approximately 90 min. When associating local anesthetics, bupivacaine 2.5 mg is generally used, which prolongs analgesia by approximately 30 more minutes [24].

Multiple authors agree that these dose ranges were arbitrarily established [26-28]. Subsequently, studies have been carried out to determine the dose-response of both local anesthetics and opioids. Van de Velde *et al*. determined the ED95 of bupivacaine, levobupivacaine and ropivacaine (associated with sufentanyl 1.5 ug): 3.3 mg, 4.8 mg and 5 mg, respectively [26]. This study also reveals that the sensitive block is proportional to the dose used, with a duration of 60 versus 100 minutes for bupivacaine 1 mg and 3.5 mg, respectively. Stocks *et al*. compared the effect of bupivacaine associated with different doses of fentanyl and the role of the latter as a local anesthetic dose sparer. Fentanyl doses greater than 5 ug did not provide a greater effect in terms of sparing local anesthetic doses, but they were associated with a longer duration of analgesia together with a higher incidence of pruritus [28]. In terms of hemodynamic side effects, patients receiving CSE with a dose of bupivacaine 2.5 mg and fentanyl 25 ug will develop arterial hypotension in 8%, defined as a decrease greater than 20% of baseline systolic blood pressure [29]. Others have reported arterial hypotension in a range of 0-13% [30].

Anaesthesia for Cesarean Section

Pregnant patients have lower intrathecal local anesthetic requirements when compared to the general population due to a lower relative volume of cerebrospinal fluid, associated with greater sensitivity of nerve fibers to local anesthetics during pregnancy [25].

The local anesthetic of choice for this technique is bupivacaine, which provides a dense and long-lasting blockade. Levobupivacaine and ropivacaine have not been shown to be superior to bupivacaine in spinal anaesthesia and have not been approved by the Food and Drug Administration (FDA) for intrathecal administration. Studies carried out with bupivacaine in doses ranging between 12 and 15 mg have determined that age, height, weight and length of the spine do not affect the outcome of the neuraxial block [31]. The required dose of local anesthetic and the need for supplementary analgesia are reduced by using fat-soluble opioids as adjuvants, improving the quality and duration of the blockade [31-33].

The main adverse effects described for the spinal technique are arterial hypotension, nausea, and vomiting. Maternal arterial hypotension can cause deterioration of uteroplacental perfusion, resulting in fetal hypoxia, acidosis, neonatal depression, and neurological damage. Severe hypotension can worsen maternal outcomes such as compromising consciousness, increasing the risk of aspiration of gastric contents, favoring apnea and cardiac arrest [25]. In order to lower the risk of arterial hypotension and intraoperative vasopressor drug requirements, a reduction in the dose of intrathecal local anesthetics has been used. Ben-David *et al*. and Choi *et al*. have proposed bupivacaine doses between 5 to 8 mg, associated with opioids (10-25 ug fentanyl) with which a cesarean section could be carried out successfully [33, 34].

Ginosar *et al*. determined that the ED50 and ED95 for hyperbaric bupivacaine associated with opioids (fentanyl 10 ug + morphine 200 ug) in cesarean section correspond to 7.6 mg and 11.2 mg respectively, values much higher than the low doses previously suggested, increasing the risk of insufficient intraoperative analgesia [35]. In a systematic review by Arzola *et al*., they compared the efficacy of low-dose spinal bupivacaine (≤8 mg) and conventional-dose (> 8 mg) for elective caesarean section. The low-dose group had a significantly

greater need for supplemental intraoperative analgesia than with conventional doses (relative risk (RR) = 3.76, 95%CI: 2.38–5.92), determining that the number needed to detect a case of intraoperative pain was only four patients (number needed to harm: (NNTH)=4; 95%CI: 2-7) [36].

The use of low doses of spinal bupivacaine for cesarean section, due to its high risk of insufficient analgesia during the intraoperative period and the requirement for supplementary analgesia and/or conversion to general anaesthesia, is not justified considering the available prevention and management strategies for arterial hypotension. Low dose regimens can be used safely in the context of a catheter-based technique, such as the CSE technique.

For a patient in labor with an epidural catheter in place, there are three alternatives to provide anaesthesia for an emergency cesarean section: epidural anaesthesia, spinal anaesthesia and general anaesthesia. The decision of which alternative to use will depend on the type of emergency, the performance of the epidural catheter during labor, the patient's preferences, and the experience of the anesthesiologist in charge, among others.

Regarding urgency categories for caesarean section, these have been classified into 4 types: Grade 1 (Emergency): there is immediate fetal and/or maternal risk; Grade 2 (Urgency): there is maternal or fetal compromise, but without immediate risk; Grade 3 (Scheduled): it is necessary to perform a prompt cesarean section but there is no fetal or maternal compromise, and Grade 4 (Elective): cesarean section can be performed according to the preferences of the mother and the obstetric team [37]. In the proposed case, there is fetal compromise without imminent risk, constituting a Grade 2 urgency, allowing to choose the most appropriate anesthetic alternative. Historically, general anaesthesia is considered to be the fastest alternative for Grade 1 obstetric emergencies, with studies showing that is almost eight minutes faster than regional anaesthesia (7.9 min, CI95%: 4.2-11.6 min) [38].

Additional unscheduled boluses of epidural analgesia to treat pain during labor has been found to be one of the most important risk factors for catheter failure. Indeed, a meta-analysis showed a three-fold greater probability of catheter failure in patients who required additional boluses compared to those who did not (conversion failure of 16.4% versus 4.6% respectively, odds ratio (OR): 3,2; 95%CI: 1.8-5.5) [39]. Two other risk factors associated with epidural catheter failure are the insertion of an epidural catheter by non-obstetric anesthesiologists and the urgency of cesarean section [40]. Other factors studied such as the use of CSE versus traditional epidural, duration of labor, cervical dilation, and patient weight, do not appear to be relevant risk factors according to the current evidence [39].

The quality of analgesia (evidenced by the need for additional boluses) is a relevant factor in the success of eventual conversion to surgical anaesthesia, however, it does not ensure success since there are other associated factors. In addition, the conversion failure will depend on the way we define it, since we can consider a failure when it is required to convert to general anaesthesia, or when the patient requires systemic analgesic supplementation. From this last perspective, the "conversion failure" would range from 0% to 21% [40]. On the other hand, a 2012 systematic review showed that the incidence of conversion to general anaesthesia in patients with an epidural catheter is approximately 5% [39]. In this way and as with any anesthetic technique, we cannot ensure complete efficacy; however, it is possible to predict and estimate the probability of failure based on risk factors.

The alternative of performing a spinal technique after suspecting a dysfunctional epidural catheter is controversial since it is uncertain the dose necessary to achieve adequate anaesthesia without exceeding the sensitive level that may eventually result in high or total spinal anaesthesia. The SCORE (Serious Complication Repository) project in 2014 identified that more than 50% of high spinal anaesthesia cases were due to a spinal technique performed after the failure of epidural conversion [41]. It is important to mention that cases of high spinal anaesthesia have been reported both in patients who have received recent epidural boluses prior to the spinal technique and also in those who have not [40]. Thus, it is recommended to proceed with caution and make a detailed evaluation before executing a spinal technique in a patient with an epidural catheter that has been used recently. Some authors have estimated that it is reasonably safe to provide spinal anaesthesia after at least thirty minutes from the last bolus administered and decreasing the doses of local anesthetics by 10-20%, finding no cases of total spinal anaesthesia in the series [42].

Postoperative analgesia management after cesarean section performed under general anaesthesia should be more aggressive than under neuraxial techniques since the rate of persistent pain in the former is significantly higher [43, 44]. After neuraxial anesthetic techniques, we have the possibility of combining intrathecal or epidural water-soluble opioids (such as morphine) to obtain high-quality analgesia. In contrast, when caesarean section is performed under general anaesthesia, a multimodal approach is necessary for pain control. The combination of systemic morphine or TAP block associated with paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) provide an analgesia quality similar to that achieved by neuraxial techniques [44].

Neuraxial morphine is a postoperative analgesic technique recognized for its effectiveness in the management of postoperative pain after cesarean section [45]. However, it´s not free of adverse effects, where

respiratory depression is one of the most feared. Recently, the Society of Obstetric Anaesthesia and Perinatology (SOAP), published guidelines for patients using neuraxial morphine, which is based on the baseline risk of the patient and the dose of morphine used. In patients without risk factors for opioid respiratory depression (body mass index> 40 kg/m2, obstructive sleep apnea/hypopnea syndrome (OSAHS), chronic opioid use/abuse or use of magnesium sulfate) and using ultra-low doses of morphine (intrathecal morphine <50 ug or epidural morphine <1 mg), no additional sedation monitoring or respiratory rate is required. For low doses (intrathecal morphine 50 to 150 ug or epidural morphine 1-3 mg) it is recommended to monitor these variables every 3 hours for 12 hours. If high doses are used (intrathecal morphine >150 ug or epidural morphine >3 mg) or the patient has some of the mentioned risk factors, monitoring is recommended according to the ASA guidelines: every 1 hour for 12 hours and then every 2 hours for the next 12 hours [46].

Regarding additional analgesic techniques (such as TAP block), patients using intrathecal morphine, it does not add greater analgesic benefit, while in patients who have not received it, is an effective technique that must be considered, taking into account that it is not better than the use of intrathecal morphine and therefore does not replace it [47]. In addition, TAP block has been shown to reach potentially toxic local anesthetic blood levels in some patients undergoing cesarean section, and also reports of local anesthetic systemic toxicity (LAST), making it advisable to adjust the doses and add epinephrine to minimize the absorption of local anesthetic, maintaining the same efficacy [48-51]. Thus, it is mandatory to weigh the risks and benefits of analgesic alternatives in each patient.

Although there is a variety of reported intrathecal morphine doses (spinal morphine 50 to 250 ug) and adverse effects will depend on it, analgesia quality will be similar except for analgesia duration, which will range from approximately 14 to 36 hours [43]. Doses over 100 ug (up to 250 ug) will extend the time to the first analgesic requirement by 4.5 hours compared to doses between 50 and 100 ug [52]. It is also important to consider other common adverse effects of opioids: after intrathecal morphine 100 ug, 43% will experience pruritus, 12% will have vomiting and 10% will have postoperative nausea [45].

Arterial hypotension is the most frequent complication of spinal anaesthesia for cesarean section. The sensory block needed for anaesthesia during a cesarean section is T4-T6. It implies an extensive sympathetic blockade, causing decreased systemic vascular resistance and venous return. The sympathetic blockade, in addition to a variable degree of inferior vena cava compression, causes arterial hypotension in 70 to 80% of elective cesarean deliveries [53]. There are three main interventions to prevent this adverse effect: use of intravenous fluids, use of vasoactive agents and patient positioning. A recent systematic review assessed the effects of multiple prophylactic interventions, concluding that various of them can reduce the incidence, but none have been shown to eliminate the need to treat maternal hypotension [54].

Intravenous fluids use has been extensively studied. Protocols of prehydration (fluid load immediately before spinal anaesthesia) and cohydration (fluid load concomitant with spinal anaesthesia) with crystalloids and colloids have been tested. In brief, the use of crystalloids is superior to non-fluid load, and cohydration has proven greater effectiveness over prehydration (RR 0,70, IC95% 0,59–0,83) [53]. Regarding pharmacologic interventions, ephedrine and phenylephrine are the main vasoactive drugs studied. They are both effective at reducing arterial hypotension following spinal anaesthesia, however, phenylephrine has been positioned as the drug of choice because of its lower incidence of fetal acidemia, lower transplacental passage (median umbilical venous/maternal arterial plasma concentration ratio 0.17 vs 1.13) and faster onset [53, 55-57].

Norepinephrine is a sympathomimetic catecholamine approximately 15 times more potent than phenylephrine [58]. It is an attractive alternative in the management of arterial hypotension following spinal anaesthesia due to its alpha and beta-adrenergic effect, unlike phenylephrine, which is a pure alpha agonist. Norepinephrine appears to cause less cardiovascular depression than phenylephrine, expressed in higher cardiac output associated with a lower incidence of maternal bradycardia [58]. A recent study reaffirms the effectiveness of norepinephrine, with a good maternal hemodynamic profile and without adverse neonatal effects [59]. It is likely that this drug will replace phenylephrine in the near future. However, it seems reasonable to wait for accumulated evidence of doses, dilutions, transplacental passage, and neonatal outcomes before generalizing its use. In conclusion, crystalloid cohydration associated with an alpha agonist vasopressor seems to be the best option to prevent arterial hypotension following spinal anaesthesia for cesarean section [60-62].

Despite the fact that neuraxial analgesia and anaesthesia techniques are quite safe, they are not exempt from the occurrence of adverse events. Epidural hematoma is an uncommon complication that can cause permanent neurological damage, generally associated with bleeding disorders [63-65]. Approximately 10% of pregnant patients have thrombocytopenia, which accounts as the main coagulation disorder in this population [66]. However, routine intrapartum coagulation testing is not recommended. There is no evidence to support the routine use of platelet count as a predictor of anesthetic complications in healthy parturients. According to the American Society of Anesthesiologists (ASA) recommendations, the decision to request laboratory tests should be made on individual bases, considering the clinical history and physical examination [67].

Ruppen *et al*. estimated the incidence of epidural hematoma in women after epidural analgesia during labor, with an overall rate of 1 in 183,000 women or 5 per million [64]. Thrombocytopenia, depending on its

severity, has been considered a relative or even absolute contraindication to neuraxial techniques, given its increased risk of epidural hematoma. The minimum platelet count at which it is safe to perform a neuraxial technique is unknown [63]. Traditionally, a platelet counts greater than 100,000 platelets/ml was recommended. Multiple authors have studied the risk of epidural hematoma in patients undergoing neuraxial techniques during labor with lower platelet counts and have suggested that they would be safe above 75,000 platelets/ml, in the absence of a clinical history of coagulopathy or a decrease prior to the procedure [63, 68, 69].

In multiple retrospective studies performed in term pregnant women with platelet counts less than 100,000 platelets/ml who received neuraxial analgesia during labor, no cases of neuraxial hematoma were reported [63, 69-71]. Goodier *et al*. and Bernstein *et al*. [69, 70]. combined their data with other case series, determining that the upper limit of the 95% CI of epidural hematoma was 0.4 to 0.6% in this population. Given the small number of cases in the lower platelet count range, a stratified risk analysis was not possible. Lee *et al*. published a multicenter retrospective cohort study in 2017, identifying 1,524 women who received neuraxial techniques in labor with platelet counts less than 100,000 platelets/ml. There were no cases of epidural hematoma requiring surgical decompression [65]. According to their results, the upper limit of the 95% CI of risk for epidural hematoma with platelet count from 0 to 49,000 platelets/ml was 11%, from 50,000 to 70,000 platelets/ml 3% and from 70,000 to 100,000 platelets/ml 0.2%. They conclude that the risk of epidural hematoma with platelet count below 70,000 platelets/ml remains uncertain because of the limited number of cases in these groups.

Therefore, in a healthy parturient without clinical coagulopathy and without evidence of a rapidly progressive decrease in the platelet count, it would be safe to perform a neuraxial technique for analgesia or anaesthesia during labor with a platelet count greater than 70,000 platelets/ml. In patients with a lower count, it will be necessary to evaluate the risk-benefit ratio of the intervention for each case, taking into account the symptoms, evolution of the platelet count, coagulation status and thrombocytopenia etiology.

General anaesthesia for cesarean section is a technique that is usually reserved for emergency cases, when neuraxial anaesthesia fails or is contraindicated. General anaesthesia-related maternal mortality has decreased in recent decades (from 16.8 to 6.5 deaths per million deliveries), approaching to neuraxial anaesthesia risk (3.8 deaths per million deliveries), meaning that the risk of general anaesthesia mortality decreased from 16.7 to 1.7 (95% CI: 0.6-4.6); therefore, differences in anesthetic methods no longer influence mortality rates [44, 72]. However, there are still controversies related to this practice.

Airway management is one of the most relevant issues. Given the physiological changes of pregnancy, the risk of difficult airway increases approximately eight times compared to the general population [73]. In addition, there is a new perception of decreased risk of gastric content aspiration for this population and less invasive alternatives have begun to be used to control the airway, such as supraglottic devices, where laryngeal mask stands out. Some studies have shown the effectiveness and potential safety of its use in elective caesarean sections [74-77]. However, these studies were carried out in healthy, non-obese, fasting patients, and in an elective setting, therefore, results cannot be extrapolated to emergency cases and non-fasting patients. Today, its use is restricted to cases in which the trachea cannot be intubated during an emergency cesarean section, favoring adequate lung oxygenation over a potential regurgitation and aspiration of gastric content risk.

Awareness is a recognized complication after cesarean section performed under general anaesthesia, with an incidence thirty times higher than the average (1:670 versus 1:19,600 procedures) [78]. Two-thirds of cases occur at induction and awakening of anaesthesia, while the remaining third occurs during maintenance. In emergency cesarean section, anaesthesia induction constitutes a critical moment due to the convergence of many identified risk factors: use of thiopental, use of neuromuscular relaxants, rapid sequence induction technique and omission of opioids [74].

The concentration of inhaled anesthetics should be decreased during surgery to limit transplacental passage and to reduce the risk of uterine atony when using doses greater than 1 minimum alveolar concentration (MAC) [25]. However, despite the fact that during pregnancy, MAC of inhaled anesthetics decrease by 25-40%, it may not correlate with their hypnotic potency. A study carried out in 2010 showed through an electroencephalographic study that, although pregnancy reduces the analgesic requirement of inhaled anesthetics, the hypnotic effect does not decrease compared to non-pregnant patients. Therefore, a decrease in MAC during pregnancy does not mean an enhanced volatile anesthetic effect on the brain [79].

Opioid use is one of the most controversial issues in general anaesthesia for cesarean section, mainly due to neonatal respiratory depression that would produce its transplacental passage just before birth. However, in pre-eclamptic patients there is an increased risk of haemorrhagic stroke when general anaesthesia is compared to regional anaesthesia, probably due to hemodynamic derangements when performing a rapid sequence induction and tracheal intubation and not using systemic opioids [74, 80]. Remifentanil has emerged as an attractive option due to its rapid onset of action and metabolism. Although it crosses the uteroplacental barrier, it doesn´t affect neonatal outcomes [81]. However, a higher incidence of transient respiratory depression has been seen in a prospective study [82]. Considering all evidences, opioids (preferably remifentanil) should be used during the induction of all patients undergoing general anaesthesia to decrease the hemodynamic response to

laryngoscopy and tracheal intubation and the risk of stroke, especially in patients with cardiac or neurological comorbidity [74]. Its use in healthy patients is controversial, but it still has benefits of reducing the risk of intraoperative awareness. Whatever the case, it is imperative to notify the neonatology team of its use.

II. Conclusion

Multiple advances have been achieved in obstetric anaesthesia during the last decades, including areas such as obstetric outcomes, labor analgesia, anaesthesia for cesarean section and other specific topics such as obstetric emergencies, anesthetic complications, and postpartum pain management, among others. Numerous clinical trials on classic controversial topics, as well as on future projections have been carried out in order to get the best information and finally provide us with guidelines for giving medical care to our patients. This didactic way of presenting current information may aid the clinician in achieving up to date knowledge.

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