Analgesia in Obstetrics

Analgesieverfahren in der Geburtshilfe

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- delivery
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Abstract

Background: An effective relief of labour pain has become an important part of obstetric medicine. Therefore regional nerve blocks, systemic analgesic and non-pharmacologic techniques are commonly used. This review article gives a summary of pathophysiology and anatomy of labour pain as well as advantages, disadvantages, risks and adverse reactions of analgesic techniques in newborns and parturients.

Methods: We performed a selective literature search in Medline via PubMed using the search-terms "Analgesia" and "Obstetrics". We also included the current guidelines of the German Society for Anesthesiology and Intensive Care Medicine.

Results: PDA and CSE are safe techniques for the relief of labour pain if contraindications are excluded. The risk for instrumental delivery but not for caesarean section is increased under neuraxial analgesia. PDA and CSE should be performed in an early stage of labour using low doses of local anaesthetics if possible. It is not necessary to wait for a defined cervical dilatation before starting neuraxial analgesia. Anesthesiologists and obstetricians should inform patients as soon as possible before the situation of stress during labour. Systemic opioid analgesia is a possible alternative for neuraxial techniques. Because of possible side effects systemic remifentanil analgesia should only be performed under continuous monitoring. Several nonpharmacologic methods can also relieve labour pain, but results of studies about their effectiveness are inconsistent.

Zusammenfassung

Fragestellung: Eine effektive Schmerzbekämpfung ist zu einem wichtigen Bestandteil der geburtshilflichen Medizin geworden. Hierfür stehen Regionalanästhesietechniken, systemische Analgesieverfahren und nicht pharmakologische Methoden zur Verfügung. Die vorliegende Übersichtsarbeit gibt eine Zusammenfassung der anatomischen und (patho-)physiologischen Grundlagen des Geburtsschmerzes sowie der einsetzbaren Analgesieverfahren einschließlich ihrer Vorteile, Auswirkungen auf Mutter und Kind, Risiken und möglichen Komplikationen.

Material und Methoden: Es erfolgte eine selektive Literaturrecherche zu den Stichwörtern Analgesie und Geburtshilfe in Medline via PubMed unter Einbeziehung der aktuellen Empfehlungen der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin.

Ergebnisse: PDA und CSE sind unter Beachtung von Kontraindikationen sichere Verfahren zur Schmerzreduktion unter der Geburt. Die Sectio-Rate ist darunter im Gegensatz zur instrumentellen Entbindungsrate nicht erhöht. Ihr Einsatz sollte möglichst frühzeitig in der Eröffnungsphase und niedrigdosiert erfolgen. Das Abwarten einer definierten Muttermundsweite vor PDA-Anlage wird nicht empfohlen. Der Einsatz einer PDA sollte mit der Patientin schon im Vorfeld und nicht erst in der Stresssituation während der Wehen besprochen werden. Eine systemische Alternative zu PDA/CSE bietet die intravenöse Opioidanalgesie. Wegen möglicher Nebenwirkungen sollte eine systemische Analgesie mit Remifentanil nur unter kontinuierlichem Monitoring durchgeführt werden. Nicht medikamentöse Verfahren können ebenfalls Schmerzen unter der Geburt lindern. Studienergebnisse zu deren Wirksamkeit sind jedoch uneinheitlich.

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Analgesia in Obstetrics

Effective pain relief has become an important part of obstetric medicine. The history of modern analgesia during childbirth can be traced back to 1847 with the application of ether and, later, chloroform. At the beginning of the twentieth century morphine and scopolamine were used to induce a "twilight sleep" [1] and between 1900 and 1930 the first epidural block and pudendal nerve anaesthesia were performed [2]. Further developments in continuous spinal analgesia took place in 1943 [3]. In addition to the long known non-pharmacological methods, today effective regional anaesthesia and systemic analgesic procedures are available for alleviating labour pains. The following review provides a summary of the anatomical and pathophysiological principles involved in labour pain, as well as the analgesic procedures available, including their advantages, effects on mother and child, risks and potential complications.

The pathophysiology of labour pain

Pain impulses from the cervix and lower uterine segment during the first stage of labour are transmitted via the visceral afferent nerve fibres to the spinal cord at the level of T10–L1. Frequently pain is localised in the dermatomes T10–L1. During late first stage and early expulsion stage pain sensations are also caused by pressure on the pelvis and parts of the lumbosacral plexus, often experienced as pain in the thighs, back and legs. Pain during the expulsion stage is mainly somatic, transmitted via the pudendal nerves to spinal segments S2–S4. Particularly strong pain is often experienced in the case of abnormal positioning of the foetus, e.g. occiput posterior position, macrosomic foetus or narrow pelvis.

During the first stage of labour pain is determined mainly by the elongation of the cervix and lower uterine segment. Subsequently, during the expulsion stage, pain is caused by the foetus engaging in the birth canal with increasing pressure on the vaginal and perineal structures. The pain intensity varies greatly from person to person and is higher in first pregnancies than in subsequent pregnancies. The reason for this is that in subsequent pregnancies the cervix is already softened before the start of the labour pains and uterus contractions are less intense at the onset of labour. First pregnancies in older women frequently also result in greater pain than in younger nulliparae. Other factors associated with stronger pain intensity are, for instance, dysmenorrhoea and maternal exhaustion [4].

Psychological factors which can influence the perception of pain during childbirth include anxiety sensitivity [5], the presence of a trusted person [6, 7], cultural factors and preparedness through, for instance, prenatal classes [8].

Besides the subjectively negative experience of pain, labour also has several pathophysiological effects on the mother and child. Pain during labour strongly stimulates breathing, resulting in an increase in breathing minute volume and oxygen during contractions, compensated by hypoventilation between contractions. This can even lead to temporary hypoxia in both mother and child. A respiratory alkalosis caused by hyperventilation can also result from a left shift in the maternal oxygen binding curve leading to reduced O_2 delivery to the foetus and consecutive hypoxia. Stress and pain during labour have been known to cause increased blood pressure, cardiac output and catecholamine concentrations [9] in the plasma. The latter in turn reduces uterine perfusion [10]. Epinephrine is known for its tocolytic effect in this case [11]. Changes in the uteroplacental blood flow are normally tolerated well by healthy foetuses. However, in the case of a pre-existing uteroplacental insufficiency, for instance preeclampsia [12], intrauterine growth retardation or diabetes mellitus may present a risk for the foetus.

A traumatic, excessively painful childbirth may cause serious mental health disorders, possibly resulting in post-natal depression [4] or even post-traumatic stress disorder [13], as well as causing difficulties related to sexuality and mother-child bonding.

Spinal analgesia procedures

Advantages

The advantage of obstetric spinal procedures is good analgesia with no maternal and foetal sedation, allowing the mother to participate actively in the birth and remain conscious. Unfavourable pathophysiological changes and reflexes caused by pain can be reduced. Full anaesthesia via an epidural catheter can be achieved in the event that a Caesarean section is necessary.

Disadvantages, risks and side effects

Results of previous studies, such as the meta-analysis by Liu et al. 2004 [14], suggest a link between obstetric spinal analgesia, in particular in the case of high local anaesthetic concentrations (e.g. Bupivacaine 0.25%), and a prolongation of the second stage of labour (weighted mean difference 15.2 min), as well as a statistically significant, slightly higher instrumental delivery rate (odds ratio 1.63%; 95% confidence interval 1.12–2.37). Excluding induced and elective forceps deliveries, statistical figures indicate an increased but not more significant risk of an instrumental birth in PDA cases (odds ratio 2.11; 95% confidence interval 0.95–4.65). These results may be attributed to the fact that foetal malpositioning or macrosomia, which are more frequent causes for an instrumental birth, lead to increased pain during labour and, therefore, to an increased need for analgesia. The risk of requiring a secondary Caesarean section is not increased with PDA.

Furthermore, a sympathetic block can lead to maternal vasodilation, in particular in the arterial system with consecutive hypotension, reduced cardiac preload and decreased cardiac time volume [12, 15]. Due to failure of the self-regulating mechanism of the blood supply to the uterus, a drop in blood pressure leads to reduced uteroplacental perfusion [16]. Vasopressors, such as ephedrine or phenylephrine, are used to treat hypotensive phases. In literature, the definitions of maternal hypotension requiring intervention differ considerably [17]. Meta-analyses comparing the vasopressors ephedrine and phenylephrine used in spinal anaesthesia for Caesarean sections indicate increased risks of foetal acidosis with the use of ephedrine [18], concluding that phenylephrine is favoured over ephedrine for the treatment of maternal hypotension [19]. Professional bodies (German Society of Anaesthesiology and Intensive Care Medicine, Association of German Anaesthetists, German Society of Gynaecology and Obstetrics) also recommend cafedrine/theodrenaline (Akrinor®) for treating hypotensive phases. A meta-analysis carried out by Mardirosoff et al. [20] indicated that foetal bradycardia was more common after intrathecal opioid administration. Foetal bradycardia can occasionally occur independently of maternal hypotension during the first 15–45 minutes after PDA or CSE, and is possibly associated with a drop in the maternal plasma catecholamine concentrations [10].

One of the most common but harmless and mostly well-tolerated side effects of PDA/CSE is pruritus due to opioid application. The exact mechanism for its occurrence is as yet unknown; however,

it is histamine-independent [21]. In literature, intravenous application of opioid antagonists, such as naloxone or nalbuphine, as well as the administration of diphenhydramine, are indicated as therapeutic interventions for opioid-associated pruritus [22].
Maternal hyperthermia is a further side effect indicated in several studies with a frequency of 1–46% [23]. This has occurred predominantly in extended use of epidural analgesia exceeding six hours [23–25]. Similarly, the mechanism for this occurrence is not yet known; inflammatory causes are suspected. However, studies have shown that neonates of women treated with PDA were more likely to be examined for sepsis and treated with antibiotics [26].
The frequency of nausea and vomiting, provided hypotensive phases can be avoided, appears not to be increased with epidural anaesthesia. However, the frequency of shivering is somewhat increased [27]. The risk of intra and post-partum urinary retention was shown by certain studies to be higher with PDA [28,29].
Complications such as inadvertent dural punctures with the insertion of peridural catheters were recorded in about 1.5% of cases [30]. In 50% of these cases, post-puncture headaches were reported [30]. Conservative therapies, such as increased fluid intake and bed rest, were not effective [31]. Treating post-puncture headaches with an epidural blood patch can potentially be successful. Following inadvertent dura puncture, an intrathecal catheter insertion instead of further epidural puncture attempts can be used as a prophylaxis against headaches related to the dura puncture. The intrathecal catheter should remain in position for 24 hours if possible [32]. Severe unexpected effects such as total spinal anaesthesia, inadvertent intravascular injection with systemic toxicity through local anaesthetics, spinal infections or breathing complications, are rare occurrences. Due to increased congestion of the epidural venous plexus during pregnancy, an intravascular catheter malpositioning occurs relatively often; although this is harmless, a removal of the peridural catheter and a further puncture is necessary.
In literature, the failure rate of spinal analgesia is estimated to be about 12% [33]. In the majority of these cases, good analgesia could still be achieved after one or more catheter re-insertions. However, spinal procedures are contraindicated for patients with blood coagulation disorders or undergoing anti-coagulation therapy (see below).
The results of early, low-dose spinal analgesia (with a cervix dilation of < 4–5 cm) with regard to delivery time, Caesarean section rate and outcomes, have been comparable with those of systemic opioid analgesia [33]. By contrast, patients who received peridural anaesthesia at a later stage (cervix dilation > 5 cm), were more likely to experience vaginal surgical deliveries, poor analgesia and poorer neonate status [34]. This is probably due to an already protracted delivery, as well as maternal issues.

Drugs (bupivacaine/ropivacaine/opioids)

At present spinal analgesia in childbirth is most frequently being used in combination with a low dose of long-lasting local anaesthetics (bupivacaine or ropivacaine) and a lipid-soluble opioid. The opioid component is capable of effectively alleviating visceral pain during the first stage of labour. In combination, the two substances function synergistically [35,36], allowing for the use of lower doses than would be the case in single applications. This contributes to reduced undesirable responses such as a severe motor block through the use of local anaesthetics or significant systemic opioid absorption and effect.
Bupivacaine and ropivacaine are the most commonly used drugs in PDAs during labour. One disadvantage of bupivacaine is a high cardiotoxic potency. Ropivacaine is less cardiotoxic and appears to be less likely to cause motor blocks [37,38]. Clinical studies have found the efficacy of ropivacaine to be comparable with that of bupivacaine [37]. In Germany, the opioid sufentanil is approved for epidural anaesthesia, but not fentanyl.
Internationally, fentanyl and sufentanil are used in conjunction with local anaesthetics during PDA procedures due to their rapid effectiveness of only 5–10 minutes [39,40]. The effects last for 60–90 minutes, thus both opioids are suitable for repeat applications during labour.

Methods (CEI, PCEA, CSE)

The most common spinal analgesia methods used during labour are lumbar peridural anaesthesia (PDA) and combined spinal-epidural analgesia (CSE).
Lumbar PDA can be performed as continuous epidural infusion (CEI) or intermittently as patient-controlled epidural analgesia (PCEA). The PDA catheter is inserted with the patient in sitting position or lying on one side. Once the catheter is fitted, a test dose of a local anaesthetic is applied in order to check for an inadvertent spinal malpositioning. After an initial bolus injection, the analgesia can be controlled by CEI or PCEA, or a combination of these two methods [16].
In the case of CSE, the epidural space is first identified through a puncture with an epidural needle inserted in accordance with standard procedures. An epidural cannula is then used as introducer for a spinal needle. After intrathecal injection, the spinal needle is removed and an epidural catheter inserted [16]. Advantages of the CSE method include the clearly faster analgesic effect of only 2–5 minutes with opioid application, as opposed to 15–20 minutes in the case of a PDA [41]. One disadvantage is a higher incidence of pruritus in comparison with PDA [42,43]. If only one opioid is initially injected intrathecally during CSE, it is possible, as in PDA procedures, to check for a malpositioned intrathecal epidural catheter through the application of a test dose, and thereby avoid an inadvertent intrathecal infusion. Testing is useful only after the intrathecal opioid effect has worn off and immediately before the first delivery via the peridural catheter. During the first stage of labour, an intrathecal opioid injection without local anaesthetic is sufficient to achieve analgesia. Due to the lack of motor block, the patient can still walk around [16]. There are no significant indications that lower umbilical cord pH values and a higher probability of pruritus are more likely with CSE than with low-dosage PDA [42]. With regard to maternal mobility during analgesia, as well as hypotension, maternal outcome (analgesic onset time and kind of delivery) and certain foetal outcome parameters (Apgar scores after 5 min, umbilical venous pH, umbilical pH and need for transfer to paediatric clinic), CSE is comparable with the low-dosage PDA [42].
In both procedures, analgesia can be controlled by continuous epidural infusion or PCEA. PCEA is preferred by professional associations since it yields greater patient satisfaction and reduces the average amount of local anaesthetic used and, therefore, the occurrence of motor blocks [19,44].

Preliminary investigations and prerequisites

The 2009 recommendations of the German Society of Anaesthesiology and Intensive Care Medicine (DGAI), in conjunction with the Association of German Anaesthetists (BDA) and the German Society of Gynaecology and Obstetrics (DGGG), stated that

no routine laboratory investigations were necessary prior to regional anaesthesia in the case of women with unremarkable medical histories of pregnancy and haemorrhaging [19]. The thrombocyte count should be determined in the presence of preeclampsia. In the case of pathological values, a positive medical history of haemorrhaging or HELLP syndrome, thorough coagulation tests should be conducted. However, no definite minimum value has been determined for the thrombocyte count, below which a spinal puncture can no longer be performed. The acute change in thrombocyte count during the hours prior to puncture, as well as a careful risk-benefit assessment by the anaesthetist, are of more crucial importance. A slightly decreased thrombocyte count of 80 000–100 000/µl is not abnormal even in healthy women and increases during pregnancy. An increased coagulation capacity is indicated during the peripartum period.

Optimal application time

A meta-analysis conducted by Marucci et al. in 2007 [34], comparing early (cervix dilation < 4–5 cm) and late (cervix dilation > 4–5 cm) PDA, indicated that early PDA presented no increased risk of a Caesarean section or instrumental delivery. In contrast, an increased risk of an instrumental vaginal delivery, poor quality analgesia and poor neonate outcomes with regard to umbilical arterial pH and the need to administer naloxone, was found in the case of late spinal analgesia and early systemic opioid analgesia. However, significant differences in Apgar scores were not found. According to the current recommendations of the DGAI [19], the American Society of Anesthesiologists and the American College of Obstetricians and Gynecologists [45], waiting for a definite minimum cervix dilation is not necessary for PDA applications.

Non-pharmacological pain therapy, peripheral blocks and systemic analgesia

For the sake of completeness, the following non-pharmacological therapies for intrapartum pain relief should be mentioned: massage, therapeutic hot and cold applications, prenatal classes, aromatherapy, audio therapy, emotional support from, for instance, a specifically trained person (doula), biofeedback, transcutaneous electrical nerve stimulation (TENS), acupuncture, acupressure, hydrotherapy, hypnosis and intradermal water injections [46–55]. In the case of contraindications for PDA/CSE, other regional analgesia methods are available. Bilateral, paracervical Frankenhäuser ganglion block and bilateral, paravertebral sympathetic block are suitable for achieving analgesia during the first stage of labour. In both cases only visceral pain afferences are blocked in the absence of motor block. Possible complications of both methods are foetal bradycardia or inadvertent injection into the head of the foetus with systemic local anaesthetic toxicity [56], as well as systemic toxic effects on the mother in the case of inadvertent intravascular injection.

In order to block somatic pain caused by extension and compression of the vaginal and perineal structures, bilateral pudendus anaesthesia can be applied for transvaginal or transperineal access to the pudendal nerve.

Perineal infiltration anaesthesia can be used in the case of episiotomies or suturing of the perineum.

Opioid analgesia offers a systemic alternative to regional analgesia procedures. Since the early 1940s the most commonly used systemic analgesic has been meperidine (pethidine). Controlled studies indicated better analgesia with PDA than meperidine [57]. The Caesarean section rate with meperidine is comparable to that of PDA [57]. As with all opioids, meperidine crosses the placenta and presents a dose-dependent risk of neonatal respiratory depression and reduction of foetal heart frequency. The mother may suffer from nausea, vomiting, respiratory depression, dysphoria and delayed gastric emptying. In addition to pethidine and piritramide, meptazinole (Meptid) is also one of the most commonly i. v. or i. m. administered opioids in Germany for analgesia during labour [58]. Meptazinole is a partial µ-opioid receptor agonist, with additional central cholinergic properties. In comparison with pethidine, respiratory depression when using Meptazinole is less common in neonates [59]. A new alternative is patient-controlled analgesia with remifentanil, which indicates a substantially shorter half-life compared to meperidine. Remifentanil crosses the placenta but is rapidly eliminated by neonates through metabolic and redistribution processes. A meta-analysis conducted by Leong et al. [60] indicated the superior analgesic effect of remifentanil compared with pethidine within the first hour of administration. Procedures followed by German clinics in the application of remifentanil PCA varied substantially. The doses used for a single bolus varied between 0.25 und 0.7 µg/kg body mass. The lock out time ranged between 1 and 5 minutes [58]. Patients should be informed that remifentanil takes effect only within 30–60 s. A bolus administered at the start of a contraction may take effect when the contraction has already reached its peak. Pain reduction with remifentanil is good within the first hour of administration; however, from the second hour high pain levels can once again be reached [61]. The procedure is currently still the subject of controversy [62]. Administration of remifentanil may result in a drop in oxygen saturation in the blood of the mother, which should be continuously monitored. Effects on the neonate require further investigations [63].

Nitrous gas has been used to relieve pain during childbirth for over 100 years. However, this method has not been as common in Germany as in certain other European countries such as Great Britain. In Germany, nitrous gas is a 50% N_2O und 50% O_2 mixture, marketed under the name of Livopan, while in English-speaking countries it is sold under the brand name Entonox. A meta-analysis conducted in 2002 [64] of the use of nitrous gas during labour indicated that the studies on the analgesic effect of nitrous gas within this context were very inconsistent. Nevertheless, some women benefitted from its use during childbirth. The results obtained with nitrous gas inhalation are not comparable with those of intravenous opioid analgesia using remifentanil [65]. While remifentanil PCA was found to achieve a pain reduction of 1.5 points on the visual analogue scale, nitrous gas only indicated a reduction of 0.5 points. In comparison with this result, PDA reduced pain by 5 points [66]. However, the sedative effect of Remifentanil PCA was also higher than nitrous gas. The maximum analgesic effect of nitrous gas is reached after 50 seconds from start of inhalation. However, a contraction with a duration of 30 seconds would have already reached its peak at that stage.

A review led by the ASA [67] reported on possible undesirable effects of nitrous gas such as respiratory depression, which in combination with maternal hypocapnia during contractions may lead to a drop in oxygen saturation of the blood. This is particularly applicable during the simultaneous use of opioids. The mother may experience drowsiness and occasional loss of consciousness, as well as nausea, vomiting, dizziness, mouth dryness and ringing in the ears [64]. Nitrous gas causes an irreversible oxidation of cobalt atoms in Vitamin B_{12}, which, in the case of long-term use,

can lead to reduced methionine and folic acid synthesis. Since folic acid is needed for DNA synthesis and in particular, in tissues with high cell division functions, bone marrow depression may result [68]. Potential negative effects on the neonate, in particular, on the neuronal development of the child, are still unclear [67].

The inhalation of subanaesthetic concentrations of sevoflurane have also been used in relieving pain during childbirth. A study by Yeo et al. comparing the analgesic quality and side effects of sevoflurane and nitrous gas indicated a better analgesic quality and less nausea with sevoflurane. However, a noticeable sedation effect was reported [69].

Conclusion

With due consideration of possible contraindications, PDA and CSE are safe methods of pain reduction during childbirth. The rate of Caesarean sections for these two procedures is lower than the rate of instrumental deliveries. PDA and CSE should be applied as soon as possible during the first stage of labour and in low doses. A definite minimum cervix dilation is not required for PDA application. It is recommended that the use of PDA be discussed in advance with the patient and not during the stressful process of labour.

Conflict of Interest

None.

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