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Review

Use of nerve block techniques for postoperative analgesia

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Introduction

The innervation of the operative would area may be easily blocked by infiltration of local anesthetic. However, a subcutaneous and subfascial local anesthetic block will rarely suffice to prevent postoperative pain sensations completely, because pain from different sites and tissue layers may be transmitted via different conductive pathways. The partial pain relief provided by local anesthetic infiltration of the would will usually last no longer than the effect of the local anesthetic, i.e., for a few hours [1]. Although intermittent blocks of intercostal nerves have been found effective in relieving pain after thoracotomy, thereby improving ventilatory function, it is most impractical for both patient and physician to carry out multiple blocks every 4–6 h for a period of at least 48 h. Therefore, continuous nerve blocks, either as intermittent administration through catheters or as infusions, have become more and more popular. Due to the fact that usually several, and anatomically separate afferent nervous routes are involved in the transmission of painful impulses from the surgical site, the continuous blocks are preferably applied at a proximal level, close to or at the spinal cord level. Typical examples are continuous brachial plexus blocks after hand or arm surgery, and continuous epidural analgesia after surgery of the trunk or the lower part of the body.

Bupivacaine and ropivacaine—the local anesthetics of choice for analgesic blocks

Today, bupivacaine is still the local anesthetic most often used for postoperative continuous analgesic blocks. In epidural analgesia, in particular, low concentrations of bupivacaine (0.06%–0.25%) will provide effective block of "pain nerve fibers" (A-delta- and C-fibers) with minimal effect on motor nerve fibers (large A-fibers). This phenomenon has been called "clinical differential blockade," and its usefulness is appreciated most in the provision of obstetric analgesia, and analgesia after major operations of the abdomen and the chest. The patient retains motor function, i.e., he/she is able to move about while relieved of pain.

The newest amide-type local anesthetic, ropivacaine (the *S*(−)-enantiomer of 1-propyl-2′,6′-pipecoloxylidide, seems to have even better differential pain fiber/motor fiber block properties than bupivacaine [2,3], and it may therefore succeed bupivacaine as the agent of choice for, e.g., epidural analgesia, quite soon. However, in clinical practice it may be difficult to distinguish between differential nerve blocking properties of ropivacaine and bupivacaine because, to achieve adequate analgesia, ropivacaine has to be administered at a slightly higher concentration than that of bupivacaine. Furthemore, the modern practice of combining low concentrations of local anesthetics with low concentrations of opioids seems to have eliminated a clinically distinguishable separation of the various nerve block components, and the analgesic efficacy may be more attributable to the opioid in the epidural drug mixture.

Central blocks

Epidural analgesia

The advantage of using epidural analgesia for the control of postoperative pain are obvious both from a practical and a clinical point of view. It is practical to be able to continue with the analgesic treatment via the epidural route in cases where epidural anesthesia, or epidural analgesia combined with general anesthesia, has been used for surgery. The need for intramuscular or intrave-

nous opioids, and the risk of opioid-related side effects, will decrease when a local anesthetic is included in the epidural analgesia regimen. Some studies have shown a clear improvement in the quality of postoperative analgesia if the patients have had an adequate epidural anesthesia for surgery [4,5]. If, on the other hand, the analgesic dosage of bupivacaine and morphine cannot be regarded as sufficient for surgical anesthesia, there does not seem to be a difference in the quality of postoperative analgesia whether the epidural therapy is started before or after surgery [6].

Although the greatest benefit of epidural anesthesia in comparison with general anesthesia is associated with an attenuation of a generalized stress response to surgery [7,8], some other factors, partly related to the stress response, can be modified in the postoperative period as well. For instance, an adequate circulation [9] and bowel motility [10,11] may be maintained by the continuation of the administration of epidural local anesthetics in the postoperative period. Epidural infusion of morphine alone does not augment bowel function postoperatively [10,12], and epidural buprenorphine may delay bowel function after surgery [13].

Epidural administration of local anesthetic in the postoperative period may be difficult to balance regarding the blockade of different nerve fiber categories (differential block). An epidural block, even with very low local anesthetic concentration and dosage, also always involves a significant autonomic nerve block (B-fibers). Therefore, cardiovascular instability may occur during the period of thoracic epidural analgesia, and micturition problems are often seen during both lumbar and thoracic continuous epidural analgesic blocks [14]. Motor block cannot be totally avoided even with dilute ropivacaine infusions [15], and this may delay the mobilization of the patient.

The discovery of spinal opioid receptors and the first clinical trials of pain therapy with epidural or subarachnoid morphine [16,17] marked the start of a new era in the clinical use of epidural analgesia for the control of postoperative pain. Probably all clinically available opioids have been tried for epidural analgesia. However, morphine is still one of the most commonly used opioids for spinal regional analgesia in postoperative patients [18,19]. Its usefulness is particulary evident in long-term therapy, e.g., in cancer pain, due to the fact that morphine-6-glucuronide, a major metabolite of morphine, has a great affinity to opioid μ-receptors [20], and is analgesically quite potent [21].

A large portion of an epidurally administered opioid dose is rapidly absorbed into the blood and, therefore, part of the analgesic effect can be ascribed a systemic opioid action. This seems to be the case, at least with the more lipid soluble opioids fentanyl [22], alfentanil [23], and sufentanil [24]. In the case of fentanyl, it has been demonstrated that epidural and intravenous administration are equally effective when the epidural catheter is at the lumbar level [22]. On the other hand, fentanyl administered into the thoracic epidural space seems to be more effective than intravenous administration in the control of postthoracotomy pain [25]. The discrepancy between these two studies may be explained by anatomical differences between the lumbar and the thoracic epidural space, e.g., in dimensions, fat contents, and vascularity, which may influence the systemic uptake of the drug.

Spinal (epidural or subarachnoid) opioids have a synergistic antinociceptive effect with spinal local anesthetics [19,26]. An interesting exception has been demonstrated in the case of 2-chloroprocaine, which has an antagonistic effect on epidural opioid analgesia [27]. Various mixtures of dilute local anesthetic solutions and low doses (concentrations) of opioids have been shown to relieve labor pain better than the opioid alone, e.g., lidocaine and butorphanol [28], bupivacaine and fentanyl [29], bupivacaine and meperidine [30], and bupivacaine and sufentanil [31]. The latter combination has also been shown to be superior to sufentanil alone in the control of postthoracotomy pain [32]. In patients having undergone major abdominal surgery, the combination of bupivacaine and morphine epidurally was superior to morphine alone, also when analgesia was assessed during exercise and coughing [33].

Spinal alpha$_2$-adrenergic agonism by clonidine exerts quite modest postoperative analgesia [34], but it prolongs significantly the analgesic action of subarachnoid bupivacaine [35] and epidural bupivacaine [36]. The addition of clonidine, or other alpha$_2$-adrenergic agonists, to an epidural analgesic drug mixture may not be advisable because of the risk of hypotension and bradycardia [34,37,38].

Subarachnoid analgesia

Intrathecal (subarachnoid) morphine produces intense and prolonged analgesia by stimulating opioid receptors in the substantia gelatinosa of the posterior horn of the spinal cord. The single-dose injection of morphine is simple, reliable, and produces predictable pharmacologic effects [39]. In adults, doses as low as 0.2–0.4 mg seem to provide adequate analgesia after major hip or knee surgery [40,41]. Larger single doses of intrathecal morphine have been used in coronary artery graft patients under close monitoring and supervision. Even after a preoperative dose of 4 mg, the time to extubation of the trachea in the postoperative intensive care unit was not delayed [42]. In myasthenia gravis patients who underwent thymectomy, a preoperative intrathecal morphine dose of 10 μg/kg did not cause any respiratory depression postoperatively [43].

Despite the use of small doses of opioids for intrathecal analgesia, there is still a potential for the drug to migrate within the cerebrospinal fluid to the brainstem level. In a Swedish survey [44], it was estimated that delayed respiratory depression had occurred in 1 in 300 patients following subarachnoid morphine administration. Therefore, it has been emphasized repeatedly that the lowest effective opioid dose should be chosen for subarachnoid analgesia; 0.1–0.3 mg may suffice for postoperative analgesia in adults after surgery of the lower part of the body.

In the treatment of acute, e.g., postoperative, pain and also of longer-lasting pain, repeated subarachnoid injections would not be practical. The development of thin spinal catheters for use in continuous spinal anesthesia and analgesia at the beginning of the 1990s [45,46] initiated a great interest in this technique all over the world. However, quite soon after a promising start, the thin catheters attained a negative reputation, first because of catheter breakage [45], and then because of the occurrence of several cases of cauda equina syndrome when hyperbaric local anesthetic solutions had been injected [47,48]. In the United States, therefore, the Food and Drug Administration forbid the use of spinal catheters of the diameter of 27-gauge or thinner (FDA Safety Alert, May 29, 1992). It is quite obvious that it is not the catheter, but the strong local anesthetic in a hyperbaric solution, which is the true cause of intrathecal neurotoxicity. However, it is also apparent that occasionally the catheter aids in maldistributing the local anesthetic solution to the most caudal part of the subarachnoid space [47,49]. Continuous spinal catheters are still in use; in Europe the thinnest commercial catheter is of the size 28-gauge, and in the United States, 22-gauge and 24-gauge catheters are in use, mainly in elderly patients.

In addition to preservative-free morphine, fentanyl may be another commonly used intrathecal opioid. Single subarachnoid doses of fentanyl in the range of 0.25 to 0.75 μg/kg have been found to produce good but short-lasting analgesia after cesarean section [50]. Opioid-related side effects, such as pruritus, nausea, and micturition difficulties, seem to become greater with higher doses. A continuous intrathecal infusion of fentanyl 5 $\mu g \cdot h^{-1}$ has been found inadequate for analgesia after hip or knee arthroplasties [51].

Meperidine has been shown to produce analgesia sufficient for surgery [52], but its safety for the neural tissue has still to be documented. In animal experiments, intrathecal administration of butorphanol and sufentanil appear to be neurotoxic [53].

Continuous intrathecal infusion of low doses of local anesthetics for the control of postoperative pain has also been tried [54,55]. Adequate analgesia after hip or knee arthroplasties can be achieved with the continuous infusion of bupivacaine 2 $mg \cdot h^{-1}$ [54]. However, arterial hypotension and reinstitution of the spinal block have been disturbing side effects. By combining bupivacaine 1 $mg \cdot h^{-1}$ with morphine 8 $\mu g \cdot h^{-1}$ in the intrathecal infusion, analgesia was as good as that with bupivacaine 2 $mg \cdot h^{-1}$ [56]. After hip or knee operations performed under spinal anesthesia, postoperative nausea and vomiting are still disturbingly frequent, both when bupivacaine alone or bupivacaine with morphine is administered.

$Alpha_2$-adrenergic agonists act synergistically with both local anesthetics [35] and opioids [57] in the dorsal horn of the spinal cord. Clinically, a significant prolongation of bupivacaine spinal anesthesia has been observed when 150 μg [35] or 3 $\mu g \cdot kg^{-1}$ clonidine [58] has been added to the local anesthetic solution. Another, also rather nonspecific $alpha_2$-adrenergic agonist, dexmedetomidine, has been shown to produce effective spinal antinociception in rats [59]. Its use in humans may not be justified, because more targeted and subtype-selective $alpha_2$-adrenergic agonists are already under development.

Peripheral nerve blocks

Brachial plexus blocks

Continuous brachial plexus block, with its various modifications, has become a popular postoperative pain control technique. Thin plexus catheters, specially designed, or epidural catheters, may be inserted after the identification of the nerve trunks or nerves by a nerve stimulator or, alternatively, by searching for paresthesia. To prevent displacement of the catheter tip form the vicinity of the plexus in the perivascular space, firm fixation of the catheter is mandatory (suture preferred) [59,60]. For practical reasons, i.e., patients are mobile and some are discharged the following day after surgery, catheters are usually not kept for longer than 48 h.

Bupivacaine 0.125%–0.25% (occasionally 0.5%) is used for continuous infusions, and in adults the dosage of 0.25 $mg \cdot kg^{-1} \cdot h^{-1}$ has provided good postoperative analgesia without any signs of bupivacaine toxicity [60]. From the beginning of 1996, ropivacaine 0.2%–0.375% has become more and more popular, and the infusion rates in adult patients have varied from 5 to 10 $ml \cdot h^{-1}$. Until now there have been no studies on the pharmacokinetics of continuous brachial plexus blocks with ropivacaine.

The more proximal brachial plexus block techniques, the supraclavicular ones, invariably also cause a block of the ipsilateral phrenic nerve, which will paralyze the corresponding hemidiaphragm [62,63]. During continuous infusion, even with low doses of local anesthetic the

diaphragmatic motility remains reduced [63,64]. It is obvious that bilateral supraclavicular brachial plexus blocks should not be performed. Careful monitoring of respiration and oxygenation is mandatory when patients with chronic respiratory diseases are given such blocks.

Prolongation of the postoperative analgesic period from a brachial plexus block has been accomplished by adding opioids to the local anesthetic solution [65]. On the other hand, fentanyl (15–27 $\mu g \cdot h^{-1}$) added to a continuous interscalene brachial plexus infusion of 0.125% bupivacaine did not produce better postoperative analgesia after shoulder surgery than 0.125% bupivacaine infusion alone [64].

In addition to providing analgesia with continuous brachial plexus blocks, the concomitant block of the sympathetic innervation to the arm produces vasodilation, which may be beneficial in most circumstances.

Intercostal nerve block

Block of the intercostal nerves T5–T11 with 3 ml of 0.5% bupivacaine with epinephrine (5 $\mu g \cdot ml^{-1}$) just before the start of subcostal cholecystectomy clearly postponed the postoperative demand of analgesia, and decreased the amount of analgesics needed in the postoperative period [66]. Continuous intercostal block through a single catheter has been found to be effective in controlling pain after subcostal cholecystectomy [67]. This seems to be in accordance with experiments with cadavers, which show that ink injected into one intercostal space will spread subpleurally to at least four adjacent intercostal spaces and to the paravertebral region [68]. The more posterior, i.e., the closer to the vertebral column, the intercostal block is performed, the greater the diffusion of the local anesthetic to the sympathetic nerve trunk, as well as to the parietal nerve endings [66].

Before the closure of the thoracotomy wound, the surgeon can freeze the intercostal nerves with a cryoprobe for long-lasting postoperative analgesia [69]. This technique has not become very popular because the safety of it has not been documented, and because presently, the continuous thoracic epidural block for the control of thoracotomy pain appears to be both efficacious and safe [70,71].

Paravertebral nerve block

Injection of local anesthetic through a single paravertebrally inserted needle or catheter can affect the sensory innervation of at least four adjacent dermatomes [72]. If, after thoracotomy, the pleural drainage tube is brought through the skin several dermatomes lower that the thoracotomy incision, two paravertebral block catheters would probably be needed for adequate postoperative analgesia. When a catheter is placed by the surgeon under the parietal pleura, near the paravertebral area, before closing the thoracotomy wound, partial postoperative analgesia can be achieved by an infusion of 0.25% bupivacaine at a rate of 4–8 $ml \cdot h^{-1}$ [73]. However, in that study [73], as well as in another study with thoracotomy patients [74], the paravertebral technique was not superior to a continuous thoracic epidural technique.

Interpleural regional analgesia

The mechanism of action of interpleural analgesia has been much debated, but it seems to include at least a blockade of sympathetic nervous structures (splanchnic nerves, paravertebral sympathetic trunk) within the thoracic region, and a block of a varying number and of varying degree of intercostal nerves [75]. Other nervous structures in this region, e.g., parietal pleural nerve endings and phrenic nerve endings, may also be affected. The efficacy of the technique is strongly dependent on the posture of the patient during the instillation of the local anesthetic solution into the pleural cavity [76]. Therefore, the best and most consistent quality of analgesia has been achieved after subcostal cholecystectomy and nephrectomy [77,78]. On the other hand, continuous infusion or intermittent administration of local anesthetics through interpleural catheters after thoractotomy in adult patients is less efficacious [79,80].

The prominent sympathetic blockade involving also the splanchnic nerves, produced by instillation of large volumes (25–30 ml) of 0.5% bupivacaine, has been found useful in the treatment of both visceral pain in the splanchnic region [81,82], and complex regional pain syndrome (reflex sympathetic dystrophy) [83]. Controlled studies comparing interpleural regional analgesia (sympathetic blockade) with other sympathetic nerve-blocking techniques or with sympatholytic techniques in the management of certain chronic pain syndromes have not been performed.

Intraperitoneal regional analgesia

Instillation of large volumes (100–200 ml) of 0.15% lidocaine or 0.1% bupivacaine intraperitoneally may provide satisfactory, but short-lasting analgesia after abdominal surgery [84]. After colonic surgery, intraperitoneal bupivacaine, 2 $mg \cdot kg^{-1}$, shortened the duration of postoperative colonic motility inhibition [85], but this therapy did not influence postoperative analgesia after upper abdominal surgery [86].

The intensity of shoulder pain, typical after gynecological laparoscopy, has been found to be reduced by

presurgical instillation of 0.5% lidocaine or 0.125% bupivacaine [87]. After laparoscopic cholecystectomy, instillation of a small dose of bupivacaine had only a short-lasting, or no analgesic effect [88,89]. However, when the dose of bupivacaine has been larger and instilled intraperitoneally both prior to and at the end of laparoscopic cholecystectomy, the analgesic efficacy has been improved [90]. Since local anesthetics have an antiinflammatory effect [91] and an antimicrobial effect [92], and no toxic symptoms seem to occur even after intraperitoneal doses as high as 200 mg bupivacaine [93], intraperitoneal analgesia with local anesthetics (bupivacaine) can be recommended for the control of pain after laparoscopic cholecystectomy.

An interesting modification of intraperitoneal application of local anesthetics was presented by Iwama and co-workers in this journal in 1994 [94]. In cases of open cholecystectomy, a catheter was placed into the omental sac through the epiploic foramen, and 10 ml of 2% lidocaine was injected. Analgesia was found to be good or excellent in six of eight patients, while there was no analgesia in two patients. At the present this technique may not be considered a real alternative to other established analgesic techniques.

Intraarticular regional analgesia

Stein and co-workers [95] were the first to report a short-lived postoperative analgesia after arthroscopic knee surgery when 0.5 or 1 mg of morphine had been injected into the knee joint at the end of surgery. This regional analgesic technique, which has been confirmed by others [96–98], seems to require the presence of inflammation in the knee joint.

In patients receiving an intraarticular injection consisting of bupivacaine and morphine, the analgesic effect was found to last longer than after morphine alone [97]. This might indicate a synergistic action of local anesthetics and opioids also in intraarticular analgesia, since bupivacaine alone provides only a very short-lasting (few hours) analgesia [99]. Others have been unable to show any postoperative analgesia after intraarticular bupivacaine [100].

The reasons for a prolonged duration of action of intraarticularly applied morphine are not completely clear. Possible explanations include low blood flow to, and therefore low clearance from, the knee joint, low lipid solubility of morphine, and slow absorption of morphine into the circulation. In addition, the anti-inflammatory action of the opioid [101] may preempt or delay the establishment of central sensitization, and result in prolonged analgesia [102].

In contrast to opioids, nonsteroidal antiinflammatory drugs (NSAIDs) have principal effects peripherally, and local application to the site of injury should produce analgesia while minimizing systemic side effects. Intraarticular ketorolac has been shown to have an analgesic effect equivalent to that of intraarticular local anesthetic and morphine [103,104]. Intraarticular tenoxicam at the end of knee arthroscopy reduced the need for supplemental analgesics postoperatively [105,106], but the patients' perception of pain was not different from those patients who had received intraarticular bupivacaine or saline [106].

Local infiltration of the wound

Although the infiltration of the wound with local anesthetic is a simple matter and can provide some postoperative analgesia at least as long as the local anesthetic acts, this technique is surprisingly little used. The infiltration of the surgical wound with bupivacaine by the surgeon may provide postoperative pain relief for several hours, and it can delay the time to the demand of intramuscular opioids [107,108]. In patients who have undergone abdominal surgery, visceral pain cannot be relieved by this superficial block technique. In spite of this, preincisional infiltration with bupivacaine before hysterectomy has been found clearly to reduce the need for postoperative opioid medication [109]. These particular patients were premedicated with an NSAID and an opioid was given during general anesthesia which, probably, aided in the provision of beneficial postoperative analgesia. Preincisional infiltration of the inguinal herniotomy wound area with lidocaine has been claimed to be more effective in reducing postoperative analgesic requirement than postsurgical infiltration of the wound with a similar amount of lidocaine [110]. Another study, however, showed that there was no difference in postoperative analgesia during the first 24 h, whether the herniotomy wound area had been infiltrated with local anesthetic before incision or at the end of surgery [111]. The perioperative use of intravenous opioids, as part of the general anesthesia regimen, may have been a confounding factor. It is also possible that the relatively mild pain associated with herniotomy makes it difficult to demonstrate clear statistically significant differences in pain scores and postoperative analgesic requirement.

Wound perfusion through thin plastic catheters with local anesthetic has been found effective in reducing postoperative pain after laparotomy [112]. Interestingly, wound perfusion with saline also had some analgesic effect, suggesting that "washing" of the wound or diluting the concentration of inflammatory and nociceptive chemical substances may be the explanation. Wound healing does not seem to be impaired by low concentrations of local anesthetics, and the antimicrobial effect of local anesthetics [92] may provide some protection against infection.

Other blocks

Almost any peripheral nerve block may be used to provide pain relief in the postoperative period. Usually, such single nerve conduction blocks are not true alternatives to the established pain-relieving techniques. They are effective supplements when regional pain intensity increases temporarily and, e.g., when an additional dose of intravenous or intramuscular opioid imposes a risk of respiratory depression.

Although the lumbar plexus block ("3-in-1" block) has been shown to produce good postoperative analgesia after major knee surgery [113], postoperative pain is usually better, and technically more easily, controlled by epidural or intrathecal analgesia techniques. However, the continuous lumbar plexus block technique can be utilized favorably to relieve pain before surgery in patients with femoral neck fracture.

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