Use of Regional Opioids In Post-Operative Pain Management

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Introduction

The identification of opioid receptors in the substantia gelatinosa of the spinal cord has led to new concepts for treatment of acute and chronic pain. Intense and often prolonged analgesia can be produced by the subarachnoid injection of small doses of opioids, which act directly on opioid receptors in the spinal cord, to interrupt pain pathways. Similarly opioids placed in the epidural space diffuse into the subarachnoid space to gain access to the receptors in the spinal cord.

Intra-thecal opioids are reported to inhibit the release of substance P which is believed to be a neurotransmitter for nocioceptive stimuli. Electrophysiological studies have shown that C fiber nocioceptive discharge is more readily blocked than A delta input suggesting that regional opioids relieve dull pain better than sharp pain and would, therefore, not be expected to block intraoperative pain effectively. However, this method of analgesia has been used successfully in the treatment of postoperative pain. In fact postoperative analgesia is the most common indication for the use of intraspinal opioids.

Analgesia produced with this technique is segmental, profound and long lasting. It is not associated with significant sympathetic or motor blockade and therefore, appears to be superior to that produced by epidural and spinal administration of local anaesthetics and intercostal nerve blocks. Intraspinal opioid analgesia has been used to provide postoperative pain relief for thoracic surgery including cardiac surgery, as well as after abdominal and orthopaedic procedures. It has been used in different age groups including children and elderly patients with compromised lung function with excellent results. Grossly obese patients were found to ambulate earlier postoperatively when morphine was given to them epidurally: the risks of pulmonary embolism were thus decreased and hospital stay shortened.

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Drugs Used

A large variety of drugs such as morphine, meperidine, fentanyl, alfentanil, methadone and phenoperidine have been used successfully. Of these morphine seems to be the most popular, having been used in over 80% of epidural and spinal intra-thecal administration. Onset and duration of analgesia appear to be related to lipophilicity of the drug. Thus the onset and duration of analgesia are short with fentanyl, intermediate with meperidine and prolonged with the least lipophilic morphine. The most outstanding feature of epidural morphine is its ability to produce effective segmental and long lasting analgesia with doses that are only 20-40% of the normal intravenous dose. The intrathecal dose is even more potent requiring only 8% of the standard intravenous dose. However, the onset of action of epidural morphine is slow (45 minutes). To again access to the spinal receptors, morphine has to cross several diffusion barriers such as the meninges and spinal tissue. Being hydrophilic, morphine crosses these barriers at a slower rate than the more lipophilic synthetic narcotic fentanyl. However, this hydrophilic characteristic of morphine retards diffusion of the drug away from the receptor site to a much greater extent than is the case for lipophilic substances. This point has been demonstrated by Yaksh and Rudy[5] The factors controlling the duration of analgesia are concentration of the drug at the receptor site and rate of removal. Since in humans CSF and plasma half-lives of morphine are similar, the long duration of analgesia is due to the high concentration of the drug in the vicinity of the opioid receptors. Duration is dose dependent and is reported to last 10-17 hours after an average dose of 4 mg, varying considerably from patient to patient.

The intrathecal route bypasses the meingeal diffusion barriers and consequently smaller doses of morphine are required to produce the same effect as epidural morphine.

Dose and Site of Administration

The doses of epidural morphine have varied from 0.5-20 mg. The results of several studies suggest that doses upto 5mg give adequate analgesia and that larger doses do not appear to improve the quality or duration. Moreover large doses can be expected to increase the incidence of delayed respiratory depression. The accepted dose ratio for intrathecal and epidural doses of morphine is 1:10.

Recent studies have shown that the site of injection is relatively unimportant since lumbar epidural injection has been shown to relieve thoracotomy pain. Thoracic epidurals are technically more complicated so

the lumbar region is the preferred site and the volume of solution injected is 10ml. Addition of epinephrine to the solution does not appear to increase the duration of analgesia but may increase the incidence of side effects such as pruritis, urinary retention and respiratory depression.

Adverse Reactions

Theoretically the binding of opioids to specific receptors should produce selective interruption of pain pathways. However, animal and clinical work have shown that sensations such as light touch, pin prick and temperature are also effected to some degree. A variety of clinically relevant effects such as pruritis, urinary retention, nausea, vomiting, sedation, catatonia and respiratory depression have been reported. The most significant and commonly occuring of these are pruritis, urinary retention and late respiratory depression.

Pruritis

The reported incidence of pruritis is any where from 0-100% and seems to occur with the administration of most opioids including morphine, the incidence appears to be higher with the intrathecal route of administration. In several large series of epidurals, with administration of doses upto 5mg morphine, the incidence of pruritis was reported to be less than 10.0%. Currently it is speculated that pruritis, nausea and vomiting are supraspinal effects secondary to the Rostral spread of opioids injected intrathecally or epidurally.

Urinary Retention

The reported incidence of urinary retention varies but is less in patients undergoing operations as compared to healthy male volunteers. In a study done by Rawal, Mollefors and Axelsson on healthy male volunteers, all subjects receiving epidural morphine showed reduction in detrusor contraction which was not dose related[7]. A corresponding increase in bladder capacity occured which led to urinary retention. These changes were found to be reversed by the administration of intravenous naloxone (opioid antagonist). Furthermore infusion of intravenous naloxone prior to epidural morphine prevented the urodynamic changes. Postoperative urinary retention secondary to epidural morphine has also been successfully treated with naloxone.

Respiratory Depression

Both early and late respiratory depression has been reported with the

use of epidural opioids. Early respiratory depression may occur following administration of large doses of opioids and is believed to be due to vascular absorption of the drug. Plasma levels of morphine after epidural administration have been found to be similar to those occuring after the same dose given intravenously. Delayed respiratory depression occurs several hours after the epidural administration of the drug. It is attributed to the redistribution of the drug through the cerebrospnal fluid to the respiratory centre in the brain stem. This may occur by passive spread or as a result of changes in the cerebrospinal fluid volume secondary to physical activity such as coughing.

The risk of delayed respiratory depression is extremely rare when therapeutic doses (less than 5mg of morphine) are administered epidurally. In 1200 patients receiving 2 mg of morphine by this route, respiratory depression developed in only one patient. In a nation-wide Swedish retrospective study of over 6000 patients receiving opioids epidurally and intrathecally, a low incidence (0.25-0.33%) of respiratory depression was reported. In the majority of these patients other factors could have contributed to the ventilatory depression such as old age, impaired respiratory function and the accompanying parenteral administration of opioids and/or sedatives. The risk of delayed respiratory depression is thought to be many times higher when opioids are given intrathecally. In the nation-wide Swedish study, the incidence of respiratory depression was 5.5% among patients who received intrathecal opioids.

Conclusion

In conclusion the major advantages of regional opioids are:-

Effective and prolonged analgesia with relatively small doses. The therapeutic intrathecal and epidural doses are between 0,5-5 mg of morphine with duration of 10-17 hours compared to 10 mg of intramuscular or intravenous dose lasting 2-4 hours.

Relative lack of respiratory depression with therapeutic doses, making this techbnique a particularly useful one for providing post-operative analgesia in patients with compromised lung function.

Because of the relaxant effect of epidural morphine on the detrusor muscle, it has been used in the treatment of bladder spasm not responding to conventional therapy.

This effect on the detrusor muscle also opens up the possibility of using this technique in the diagnosis and treatment of certain types of uri-

nary incontinence resulting from deterusor hyper-reflexia. This technique, however, is not yet completely safe because of the risk of delayed respiratory depression.

Careful surveillance of all patients receiving regional opioids is recommended. Also intravenous low dose naloxone infusion following epidural opioids will prevent respiratory depression and diminish the risk of other adverse effects while preserving analgesia.

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