



ELSEVIER

Best Practice & Research Clinical Anaesthesiology

Vol. 21, No. 1, pp. 99–107, 2007

doi:10.1016/j.bpa.2006.12.007

available online at <http://www.sciencedirect.com>



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Postoperative pain management and outcome after surgery

Francis Bonnet*

Professor and Chairman

Emmanuel Marret MD, PhD

Assistant Professor

*Département d'Anesthésie Réanimation, Hôpital Tenon, Université Pierre et Marie Curie,
4 rue de la Chine, 75970 Paris cedex, France*

Postoperative pain management aims not only to decrease pain intensity but also to increase patient comfort and to improve postoperative outcome. Better pain control is achieved through a multimodal combination of regional analgesic techniques and systemic administration of analgesic agents. To guarantee uneventful follow-up and unnecessary prolongation of hospital stay, it is important to avoid side-effects of analgesic agents, especially those of opioids which are dose-related, by decreasing opioid demand through combination with non-opioid agents. Epidural analgesia not only has the advantage of providing potent and effective analgesia but also of hastening recovery of bowel function and facilitating physiotherapy and rehabilitation. Unfortunately, a reduction in postoperative morbidity and mortality by epidural analgesia has not actually been demonstrated. Inclusion of postoperative pain treatment in a multimodal approach of patient rehabilitation may improve recovery and shorten hospital stay. Effective treatment of postoperative pain is also likely to prevent chronic pain syndrome after surgery, but further studies are needed to support this hypothesis.

Key words: postoperative analgesia; epidural analgesia; postoperative morbidity; opioids; non-opioid analgesics.

The concept of pain treatment has evolved over the past year from the objective of reducing pain intensity to the optimization of patient comfort. This means not only a decrease in pain scores but also a reduction in analgesic-agent-related side-effects. Avoiding side-effects such as nausea, vomiting, urinary retention and sedation may indeed facilitate patient recovery and is likely to shorten hospital stay. For years it

* Corresponding author. Tel.: +33 156016571; Fax: +33 156017007.

E-mail address: francis.bonnet@tnn.aphp.fr (F. Bonnet).

has been speculated that treatment of pain could avoid postoperative complications and consequently decrease in-hospital morbidity. Studies aiming to demonstrate this theory have focused on the effect of epidural analgesia.¹ More recently, it appears that postoperative analgesia has to be integrated into a global process that improves patient rehabilitation, shortens hospital stay, and potentially decreases postoperative complications.^{2,3} This include pre- and postoperative measures such as information of patients, preoperative nutritional support, minimally aggressive surgery avoiding drains and nasogastric tubes, the use of short-acting anaesthetic agents, preservation of patient homeostasis during surgery, early oral feeding and deambulation, and active physiotherapy. Effective pain treatment is not only a part of this process but also a necessary condition for applying most of the other postoperative measures. Thus postoperative pain treatment may significantly change postoperative outcome. In addition, recent studies have suggested that effective pain treatment may avoid the development of chronic pain syndromes, although further studies are needed to support this hypothesis.⁴

IS POSTOPERATIVE PAIN TREATMENT EFFECTIVE?

Postoperative pain can be defined as a complication of surgery. Thus, avoiding postoperative pain rarely impairs postoperative outcome, but it remains a challenge. There is indeed a discrepancy between the results of many epidemiological surveys that still report persistent pain in a significant proportion of postoperative patients and the fact that very effective analgesic tools are available to treat postoperative pain.⁵ The reason is probably related to the lack of organization of pain treatments in many institutions, despite the development of acute pain services. A recent survey in the United Kingdom documented that acute pain services are struggling to survive.⁶ In the same survey, physicians agreed on the need for a better organizational approach rather than new treatments and delivery techniques. It is clear that analgesic techniques and protocols allow a complete control of postoperative pain, but analgesic efficacy varies according to the technique and to the surgical procedure. A meta-analysis demonstrates that epidural analgesia with local anaesthetics provides better pain control than intravenous morphine patient-controlled analgesia (PCA) during the first 2 postoperative days after surgery, meaning that it is worth using this technique after major surgery during the first 2 days, but that the benefit vanishes thereafter.⁷ Multimodal analgesia, defined as the combination of analgesic agents in order to reinforce pain control while decreasing side-effects, is claimed to be the rule for postoperative pain treatment.⁸ Surprisingly, owing to the fact that combination of analgesic agents is common in daily practice, there are not so many studies that examine the benefit from such association in terms of pain control. Most of them assess a combination of opioid and non-opioid agents, while in clinical practice more than two different agents and/or techniques are commonly used. Moreover, a combination of agents is sometimes only as effective as each agent used separately; for example, the combination of paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) is not more effective than NSAIDs alone.^{9,10} Analgesic agents are not equally effective in all instances, and a more specific approach based on each surgical procedure is required.¹¹ To include a given analgesic agent in guidelines requires that this agent has been demonstrated to be effective in the setting of a specific surgical procedure, bearing in mind that difference may be noted. For example, paracetamol is more effective after dental surgery than after orthopaedic surgery¹¹; epidural analgesia is effective

after colon surgery but does not bring further pain control after abdominal hysterectomy compared to systemic analgesia.^{12,13} In addition, the cost–benefit analysis of the same technique may vary: for example, epidural analgesia is worth performing after major abdominal surgery, but despite its efficacy it is too risky to be performed after cholecystectomy. Thus, guidelines for postoperative pain treatment for the most common surgical procedures should be developed on the basis of evidence from the literature.

CAN WE AVOID POSTOPERATIVE SIDE-EFFECTS OF ANALGESIC AGENTS?

Decreasing analgesic side-effects is an issue, especially in the case of opioids. While physicians have focused on the risk of respiratory depression for years, such a complication is fortunately rare, although it requires appropriate monitoring of patients who receive opioids. Conversely, side-effects such as nausea, vomiting, pruritus, urinary retention and prolongation of postoperative ileus are extremely frequent, although underestimated.¹⁴ These side-effects have a significant impact on hospital stay which may be prolonged by persisting problems, such as the lack of recovery of bowel function, that interfere with patient oral nutrition. In ambulatory surgery, opioid side-effects are probably the second leading cause for re-hospitalization of patients after incomplete pain relief.¹⁵

Morphine side-effects are related to morphine dose.^{16,17} Reducing the morphine (or morphine equivalent) dose consequently results in a decrease in the incidence of side-effects. This has been demonstrated for the combination of NSAIDs or cyclooxygenase-2 inhibitors with intravenous PCA morphine; the combination significantly reduces the incidence of sedation, nausea, and vomiting.^{15,18} Other analgesic agents such as paracetamol are not powerful enough to achieve this goal because their opioid-sparing effect is weak.¹⁹

Alternately, morphine side-effects could be prevented or treated specifically. Nausea and vomiting are prevented by droperidol, dexamethasone, and setrons given — alone or in combination — according to the number of risk factors in a given patient, administration of opioid being one of those risk factors.²⁰ In contrast, nasogastric suction is poorly effective (NNT = 20 for prevention of vomiting) and carries a risk of inhalation pneumonia.²¹

Concerning postoperative ileus, beside the use of specific opioid receptor antagonists that do not cross the gut barrier (alvimopan) or the blood–brain barrier (methylnaltrexone)^{22,23}, the best alternative is provided by epidural analgesia with local anaesthetics. Evidence demonstrates that epidural analgesia significantly shortens the duration of postoperative ileus²⁴ without increasing the risk of bowel anastomotic fistulae.²⁵ Combination of epidural opioid with local anaesthetics impairs their effect on bowel function. The effect of accelerating recovery of bowel function on hospital discharge is less clear, probably due to the fact that factors other than those depending on medical care interfere with the potential benefit that results from the use of epidural analgesia.²⁶ Combining opioid and non-opioid analgesic agents also results in a decrease in the duration of postoperative ileus.²⁷

Patients receiving non-opioid agents such as NSAIDs experience side-effects, including an increased risk of bleeding (haemorrhage at the operative site or gastrointestinal haemorrhage) and complications such as acute renal failure, worsening of cardiac failure or bronchospasm. The risk of surgical bleeding could be a concern

because of the location of the operative site. Bleeding risk is increased in patients receiving NSAIDs after tonsillectomy, breast surgery and pelvic surgery.^{27,28} In these cases the use of a COXib is a favourable alternative.^{29,30} On the other hand COXibs increase the occurrence of cardiovascular complications in patients scheduled for coronary artery bypass surgery, leading to myocardial infarction or stroke.³¹ Evidence can be inferred to contraindicate COXibs in postoperative patients at risk of cardiovascular complications (e.g. patients scheduled for aortic surgery). However, in a population of patients scheduled for orthopaedic or abdominal major surgery, including aged patients, no increased risk in cardiovascular complications has been demonstrated so far.¹⁸

Epidural analgesia is responsible for side-effects of its own (i.e. hypotension, paraesthesia, muscle weakness, urinary retention). Since one of the aims of using epidural analgesia is to facilitate deambulation, it is critical to prevent the occurrence of orthostatic hypotension or lower-limb muscle weakness. This is best achieved by reducing the concentration of local anaesthetic solutions and using ropivacaine that is less inclined to induce motor blockade than bupivacaine. On the other hand, local anaesthetic solution that is too diluted may fail to achieve significant pain relief if not associated with systemic analgesics as recommended above.

DOES POSTOPERATIVE PAIN TREATMENT DECREASE HOSPITAL STAY AND THE INCIDENCE OF POSTOPERATIVE COMPLICATIONS?

This is the most controversial issue that has been addressed for many years in the anaesthetic literature. Most of the literature concerning this problem is dedicated to the effect of epidural analgesia. A meta-analysis of 141 studies performed over a 20-year period concluded that epidural analgesia prevented postoperative major complications and decreased postoperative mortality.¹ These results and conclusions have been extensively criticized, one of the reasons being that one cannot compare or mix together studies that have been performed at intervals of many years because of the evolution of medical practice over this period of time. Others have reported that epidural anaesthesia may selectively prevent the occurrence of respiratory or cardiovascular complications.^{32–34} Unfortunately, the most recent prospective trials, including a significant number of patients, have failed to confirm the beneficial effect of epidural anaesthesia on postoperative morbidity and mortality after major abdominal or orthopaedic surgery most of the time.^{35–46} Such a discrepancy may result from the improvements in postoperative medical care. For example, epidural analgesia is supposed to decrease the risk of deep vein thrombosis by 50%. This effect was demonstrated in the 1980s.⁴⁷ At this time thromboprophylaxis by low-molecular-weight heparin (LMWH) was not in use, knowing that LMWH decreases the risk of deep vein thrombosis by more than 80%. Consequently, in patients receiving LMWH, no further reduction in deep vein thrombosis is noted with epidural analgesia. Similarly, the preventive effect of epidural analgesia on postoperative pulmonary complications is mainly demonstrated in old studies, where this risk is especially elevated. Nowadays, due to prophylactic antibiotic therapy, active physiotherapy and other means of prevention, the incidence of pneumonia has dramatically decreased after abdominal surgery, and the preventive effect of epidural analgesia is probably less important.

The impact of epidural analgesia on postoperative outcome should be assessed based on the surgical procedure. Postoperative complications are different after

orthopaedic, thoracic, and abdominal surgery. After orthopaedic surgery, trials and meta-analyses have failed to document a decrease in the incidence of cognitive dysfunction or respiratory and cardiovascular complications in patients receiving epidural analgesia^{35–37}. In the specific settings of cardiac surgery, epidural analgesia does not really decrease postoperative morbidity, except for respiratory complications, and carries a risk of epidural haematoma that makes many staff reluctant to use it.³⁸

After abdominal aortic surgery, several studies have tried to highlight a reduction in cardiovascular complications in patients treated by epidural analgesia pre- and/or postoperatively, but they have failed to achieve this goal.^{39–44} Nevertheless, in a selected subgroup of patients scheduled for abdominal aortic surgery, epidural analgesia may occasionally reduce postoperative morbidity through a reduction in respiratory and cardiac complications, as stressed above.⁴⁸ Finally, a qualitative analysis and three recent large multicentre trials dedicated to abdominal surgery did not document that patients receiving epidural analgesia benefitted from a more rapid hospital discharge.^{26,45,46,48} Consequently, one is obliged to consider that epidural analgesia has no effect per se on postoperative morbidity, but as part of a multimodal rehabilitation process it may facilitate recovery from surgery. This has been demonstrated by Basse et al in colon surgery.⁴⁹ Combining epidural analgesia with a local anaesthetic, general anaesthesia with short-acting agents, restriction of intravenous fluid administration during surgery, careful and as least damaging as possible surgical dissection, prevention of postoperative nausea and vomiting, lack or restricted use of nasogastric tube, drains and bladder catheters, oral feeding with complementary protein intake and early mobilization, they were capable of managing patients in hospital over less than 2 days after uncomplicated colon resection. The superior quality of pain relief provided by epidural analgesia combined with parenteral analgesia does indeed have a positive impact on out-of-bed mobilization, bowel function and consequently food intake that results in a significant improvement in postoperative quality of life.⁵⁰

In orthopaedic surgery, regional analgesia may also provide a functional benefit, allowing better physiotherapy. This may result in a significant shortening of convalescence after total knee replacement.⁵¹

DOES POSTOPERATIVE PAIN TREATMENT PREVENT THE OCCURRENCE OF POSTOPERATIVE CHRONIC PAIN SYNDROMES?

Chronic pain after surgery is not a new syndrome, but this issue has been addressed in recent reviews.⁴ Typically, preoperative pain-free patients experience a prolongation of postoperative pain that persists during at least 2 months without relapse or pain-free interval. Chronic pain syndromes have been described after breast surgery, hernia repair, cholecystectomy, thoracic surgery, cardiac surgery, and limb or organ amputation.⁴ Almost 5% of patients who have undergone hernia repair complain of severe pain 1 year after surgery.⁵² In this setting, chronic pain depends on the surgical procedure, being less frequent after mesh placement than after direct repair of the hernia.⁵³ In patients having thoracotomy, the incidence of a chronic pain syndrome is as high as 60% at 6 months after surgery.⁵⁴ After breast surgery, different kinds of pain syndromes have been described, such as phantom pain and postmastectomy syndrome.⁵⁵

Risk factors are difficult to identify, but patients who experience severe pain and, above all, persistence of postoperative pain several days after the expected duration,

are prone to develop a chronic pain syndrome.^{56,57} On the basis of this it was worth trying to demonstrate that good postoperative pain control could prevent the occurrence of chronic pain syndromes. This has been done in thoracic surgery, where epidural analgesia compared to intravenous PCA morphine tends to decrease the incidence of chronic pain syndrome.⁵⁸

Another approach consists in substances that may prevent the occurrence of allodynia and hyperalgesia postoperatively. Indeed, during surgery tissue damage induces release of free fatty acids and cytokines and induction of cyclo-oxygenase-2 that results in prostaglandin synthesis.⁵⁹ Prostaglandins are thought to promote transmission of nociceptive stimulation both at nerve endings and at the level of the dorsal horn of the spinal cord.⁶⁰ Through activation of NMDA receptors, changes in NO synthase activity promote synthesis of transcriptional proteins and new glutamate receptor expression. A complex sensitization phenomenon is responsible for allodynia and hyperalgesia that is documented after surgery and could be worsened by the administration of opioids.⁶¹ Ketamine used in low doses (0.1–0.5 mg/kg) provides the opportunity to block NMDA receptors. Postoperative administration of ketamine has been documented to not only decrease opioid consumption and improve postoperative pain control but also decrease the incidence of chronic pain syndromes several months after surgery.^{62,63} Other analgesic agents could potentially reduce or prevent postoperative hyperalgesia and consequently could avoid the occurrence of chronic pain. Among these drugs α_2 adrenergic agents⁶⁴ could be cited, but also COXibs and local anaesthetic agents that have been demonstrated to prevent inflammatory processes after tissue damage.^{65,66} The administration of gabapentin, which induces suppression of sodium channel, calcium channel and glutamate receptor activity at peripheral, spinal and supraspinal sites, markedly decreases postoperative opioid consumption when given at the time of anaesthetic induction.⁶⁷ Promising results have been obtained in the reduction of chronic pain after breast surgery with gabapentin, EMLA, and a combination of the two, but also with venlafaxine, a tricyclic antidepressant.⁶⁸ Further evaluations for treatments of neuropathic pain at the earliest stage of the postoperative pain period are worth performing.

Practice points

- begin administration of analgesic agents before the end of anaesthesia
- combine NSAIDs with opioids to reduce opioid demand
- give dexamethasone (4–8 mg) during anaesthetic induction, and/or droperidol (1.25 mg) or ondansetron (4 mg) before the end of anaesthesia, to prevent nausea and vomiting in patients with more than two risk factors
- avoid systematic use of nasogastric tube, bladder catheter and drains
- use, in combination with systemic analgesia, epidural analgesia with ropivacaine 2 mg/mL in continuous infusion or on demand, to control pain after abdominal or thoracic surgery and to facilitate recovery of bowel function
- use low doses (0.1–0.5 mg/kg) ketamine or gabapentin (1200 mg) in patients susceptible to developing chronic pain syndromes after surgery
- provide (in the wards and the recovery room) written analgesic protocols dedicated to the most frequent surgical procedures encountered in the institution

Research agenda

- postoperative pain management needs to be evaluated per surgical procedure; for each analgesic protocol a balance between advantages and drawbacks should be determined
- combinations of analgesic agents should be more systematically compared to individual agents to assess their benefit
- further research is warranted to evaluate the impact of postoperative pain treatment on chronic pain syndrome after surgery

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