Postoperative Patient-Controlled Analgesia in the Elderly
Risks and Benefits of Epidural Versus Intravenous Administration

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Abstract
Postoperative patient-controlled analgesia provided by the intravenous route using morphine (PCA) or by the epidural route using an opioid in combination with a local anaesthetic (patient-controlled epidural analgesia; PCEA) is not yet routinely used in the elderly. However, this modality theoretically provides adequate control of postoperative pain in such patients.

Firstly, an assessment of the level of pain is particularly difficult in the elderly, and patient-controlled techniques that enable the self-administration of analgesic could resolve this problem. Secondly, these techniques provide a fine and controlled titration of analgesic doses. Since analgesic-induced adverse effects increase with age, the risk of overdose is therefore reduced. Thirdly, effective postoperative patient-controlled analgesia may attenuate detrimental physiologic responses, and contribute to improvement in patient outcomes.

In the elderly, PCEA provides better pain relief, particularly for dynamic pain, and improves postoperative recovery with a low incidence of adverse effects compared with PCA. PCA and PCEA techniques have a good safety profile in the elderly only when there is careful preoperative patient selection and strict postoperative monitoring. Standard observation of vital signs, sedation and pain scores and assessment of mental status are required. Patient selection is necessary to identify those patients who may be incapable of using the device (e.g. patients with evidence of cognitive dysfunction or physical disabilities). In addition, caution is required among patients with respiratory, renal or hepatic insufficiency.

PCA and PCEA are particularly useful for elderly patients undergoing major thoraco-abdominal surgery. However, there is a need for further research in elderly patients. In the future, improvements in the management of postoperative pain in the elderly will lead to a greater expansion of self-controlled techniques.

Recent advances in anaesthetic and surgical techniques have substantially improved the perioperative care for patients aged 65 years and older. However, effective postoperative pain control for this vulnerable population remains a topic for discussion. New knowledge has led to the development of better modes of analgesic administration along with improved technology. Postoperative patient-control-
led analgesia can be provided by the intravenous route using morphine (PCA) or by the epidural route using an opioid, either alone or in combination with a local anaesthetic (patient-controlled epidural analgesia; PCEA). These techniques constitute the major recent advance in the management of postoperative pain. Thus, a patient can self-administer small boluses of analgesic, providing better titration and enhancing responsiveness in analgesic requirements. Regarding the effects on postoperative morbidity, it has been suggested that effective patient-controlled analgesia could attenuate detrimental physiologic responses, and contribute to accelerated recovery, but there have been conflicting results on this issue.

Some acute pain therapists are reluctant to offer patient-controlled techniques to older patients since some members of this group are unwilling or unable to use these techniques effectively. Explanations have included a lack of understanding of the technique by elderly patients, different attitudes in elderly patients with regard to pain relief, and patient roles and fears of complications associated with some analgesics, particularly opioids and local anaesthetics. The possibility of differences in pain perception or pain reporting with advancing age has also been considered.

This review examines the clinical evidence from studies that have investigated the effects of postoperative PCA and PCEA techniques, and discusses the advantages in the use of the epidural versus the intravenous route in elderly patients.

1. The Specificities of Pain Management in the Elderly

1.1 Pain Perception and Pain Reporting

Although the threshold of the sensation of pain slightly increases with age in healthy volunteers, no difference has been found during the postoperative period. The techniques for evaluating postoperative pain in the elderly are theoretically based on the same principles as those in the young adult; that is, self-evaluation using a visual analogue or verbal scale. However, therapists consider that postoperative pain is underestimated in elderly patients. Barriers to effective assessment of pain in the elderly have included age-related psychologic and physiologic factors and the attitude of health-care professionals. Elderly patients may appear to be more stoical and less willing to spontaneously express the intensity of their pain. Moreover, elderly patients will have anticipated less postoperative pain than younger patients regardless of previous experience with surgery. Cognitive problems, confusion or even postoperative delirium observed in one out of four patients >60 years of age after major surgery make evaluation of pain difficult. Adequate assessment of pain level in cognitively impaired elderly patients requires the use of specific tools (for instance, a pain intensity scale). This problem of evaluating pain may be complicated by the fact that an overly high dosage of morphine or, on the contrary, pain that is not sufficiently calmed, can contribute to the triggering of postoperative delirium. Finally, during the postoperative period, it is customary for nursing staff to be more preoccupied with the diagnosis and treatment of organ dysfunctions rather than assessing and managing pain.

1.2 Pharmacological Effects

Elderly patients are more sensitive to the effects of analgesics than younger adult patients. In fact, the pharmacokinetic and pharmacodynamic properties of a pharmacological agent change with increasing patient age. In the elderly, total body water and fat-free mass is reduced and peripheral tissue perfusion worsens. This explains why the volume of distribution of hydrophilic drugs in the elderly is reduced. Moreover, the decrease in glomerular filtration and hepatic blood flow in parallel with increasing age causes a reduction in the capacity of excretion of hydrophilic drugs and their metabolites, extending the duration of action of the drug. With parenteral morphine, a hydrophilic opioid, a decrease in plasma clearance and in the volume of distribution and an increase in the elimination half-life have been observed in the elderly.
There is also a relationship, albeit less obvious, between aging and an increase in the intrinsic activity of lipophilic opioids such as fentanyl, alfentanil, sufentanil, and remifentanil. In practice, an analgesic effect is obtained in an elderly patient with half to two-thirds of the opioid dosage that is required to obtain a similar effect in a young patient. Macintyre and Jarvis recommend the use of the following formula to derive an appropriate dose of morphine: average first 24-hour morphine requirement (mg) = 100 – age (years); however, they stress that interpatient variability in morphine doses is large with a difference of up to 10-fold. However, it should be noted that in the short-term postoperative period, Aubrun et al. did not observe any differences between elderly and younger adult patients for morphine requirement to produce an analgesic effect.

The choice of administration route of crucial importance. Indeed, with opioids, the subcutaneous route does not make it possible to obtain a stable plasma concentration. The great variability of systemic reabsorption and the bioavailability of the product administered expose the patient either to the risk of inefficacy owing to a low dosage or to adverse effects owing to a high dosage. This phenomenon, which is more frequent in elderly patients than in young adults, is a strong argument for intravenous administration of opioids with careful titration of doses rather than subcutaneous administration.

Doses of opioids administered by the epidural route must also be reduced to take into account the pharmacological specificities linked to age. The concepts are also valid for local anaesthetics. The concentration of local anaesthetic (lidocaine, bupivacaine or ropivacaine) in plasma depends on the rate of absorption from the administration site, the volume of distribution, and the plasma clearance. There is little or no metabolism of local anaesthetic in the epidural space, nearly all of the dose is absorbed and eliminated primarily by hepatic microsomal metabolism. Liver blood flow and mean clearance of local anaesthetics are reduced by aging.

The key clinical consideration is the possibility that in the elderly, plasma concentrations of local anaesthetics could reach toxic levels during continuous epidural administration. Thus, it is prudent to exercise caution in giving repeated doses to patients >65 years of age. Fortunately, the lower epidural dose required to attain a particular level of block in older patients tends to reduce the likelihood of systemic toxicity. Although local anaesthetic clearance is reduced with increasing age, the clinically relevant epidural dose also declines.

2. Patient-Controlled Intravenous Analgesia (PCA)

In young and middle-aged patients, the benefits of PCA have been studied extensively and discussed widely. Given the specific problems encountered in postoperative pain management in the elderly, PCA could be a useful approach. The principle of PCA is to allow the patient to choose when to administer a bolus of morphine, with the therapist prescribing the bolus dosage and the lockout period between two boluses. This concept therefore resolves both the methodological difficulties of evaluating pain and the pharmacological problems linked to the use of opioids. Indeed, the patient manages his/her pain treatment and is no longer dependent on an evaluation method or the uncertain availability of nursing staff. In addition, PCA corresponds to the principle of continuous intravenous titration of the analgesic doses required for each patient.

Gagliese et al. showed that compared with younger patients (38.5 ± 9.1 years of age), older patients (67.3 ± 7.8 years of age) preferred less information about their healthcare and less direct involvement in their healthcare, but they had similar attitudes toward PCA, similar confidence in their ability to use it successfully and similar satisfaction with the technique. Interestingly, there were no age differences in concerns regarding risks of equipment failure or opioid addiction. Egbert et al. demonstrated that the use of PCA in patients >60 years of age resulted in better pain relief, less confusion and fewer severe pulmonary complications compared with conventional opioid therapy by in-
tramuscular administration. The incidence of clinical confusion was only 2.3% of patients receiving PCA compared with 18% of those given intramuscular analgesia.

According to age-related changes in metabolism and/or the intrinsic activity of opioids, older patients self-administer less opioid than younger patients do for similar levels of pain. In PCA, there is no decisive pharmacological argument for preference of one opioid over another. Herrick et al. showed that the type of opioid (fentanyl or morphine) did not affect the incidence of clinical confusion. Thus, since morphine is an inexpensive drug, it appears to be an obvious choice. Nevertheless, in the patients with renal failure an opioid with no active metabolites, such as fentanyl, might be preferred.

Egbert et al. have proposed that an initial fixed morphine bolus of 0.01 mg/kg with a 10-minute lockout period be regularly adapted according to signs of efficacy or overdosing. Other authors recommended a setting that is equivalent to that used for young adults, that is, a 1–2mg morphine bolus with a 5–8-minute lockout period. The addition of a continuous background infusion of morphine to PCA must be avoided since it has clearly been identified as a factor in respiratory depression. The number of boluses per hour is also an important parameter to evaluate; if it is too high it indicates a poor adaptation to the technique.

Opioid-related respiratory depression constitutes a major concern during the postoperative period. After a single bolus of morphine, respiratory depression is similar in elderly and younger adult patients. However, when the administration of an opioid is repeated, as with PCA, respiratory depression is a more complex problem. Firstly, the incidence of reported severe respiratory depression associated with PCA, usually defined as excessive bradypnea, has been reported as being less than 0.5% during the postoperative period. Nevertheless, patients could experience multiple episodes of hypoxaemia not associated with decrease of respiratory rate. Secondly, multiple factors may contribute to the development of respiratory compromise including background infusion, nurse- or physician-controlled analgesia, concomitant administration of sedatives or hypnotics, renal failure, pre-existing respiratory insufficiency or sleep apnoea syndrome. In the elderly, these problems are frequently observed, but it has not been demonstrated that advanced age is in itself a risk factor for opioid-related respiratory depression.

The aim of using a combination of non-opiate analgesics (e.g. non-steroidal anti-inflammatory drugs) with PCA morphine, within the framework of a multimodal analgesic strategy, is to obtain a morphine-sparing effect. This makes it possible to reduce the incidence of nausea and vomiting and reduce the duration of postoperative ileus after lower abdominal surgery. As with opiate analgesics, it would appear to be preferable to reduce the standard doses of non-opiate analgesics, that are used in young adult patients, for elderly patients. The addition of low doses of droperidol (0.05mg for every 1.0mg of morphine) in the morphine syringe significantly reduces nausea and vomiting in young adults. However, this effect has not been specifically studied in the elderly.

### 3. Patient-Controlled Epidural Analgesia (PCEA)

PCEA is a new, very promising technique with a good safety profile which provides effective management of postoperative pain via the epidural route. Unfortunately, the amount of literature concerning PCEA in the elderly is rather scarce. In order to circumvent this difficulty, this review analysed the recent numerous studies performed in young or middle-aged patients with the aim of specifying the modalities for the optimal use of the PCEA technique in the elderly. This review also describes findings obtained with standardised PCEA protocols in elderly patients.

In young and middle-aged patients, epidural analgesia with a local anaesthetic combined with an opioid provides better pain relief than epidural or systemic opioids and may improve postoperative outcome. However, excessive administration of epidural opioid may result in respiratory depres-
Postoperative Patient-Controlled Analgesia in the Elderly

Table I. Patient-controlled epidural analgesia settings in published studies involving elderly patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean age in years (range)</th>
<th>Analgesic mixture</th>
<th>Bolus dose (mL)</th>
<th>Lockout period (min)</th>
<th>Background infusion (mL/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann et al.</td>
<td>76 (70–89)</td>
<td>Bupivacaine 0.125% Sufentanil 0.5 µg/mL</td>
<td>2–3</td>
<td>12</td>
<td>3–5</td>
</tr>
<tr>
<td>Liu et al.</td>
<td>59 (12–96)</td>
<td>Bupivacaine 0.05% Fentanyl 4 µg/mL</td>
<td>2</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Brodner et al.</td>
<td>&gt;70</td>
<td>Bupivacaine 0.175% or ropivacaine 0.2%</td>
<td>2</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Wigfull et al.</td>
<td>64 (16–95)</td>
<td>Bupivacaine 0.1% Fentanyl 4 µg/mL</td>
<td>2</td>
<td>12</td>
<td>6</td>
</tr>
</tbody>
</table>

Mann et al. have assessed the effect of PCEA on pain management and patient outcomes after abdominal surgery in elderly (>70 years of age) patients. With a standardised protocol (see table I), PCEA provided a very satisfactory analgesic effectiveness without causing serious adverse effects. It is important to stress that by using the same study design in elderly as in younger patients, the authors recorded the same analgesic consumption (median settings of bolus and background infusion were 3mL and 3 mL/h, respectively for both elderly and younger patients). Three recent prospective surveillance studies determining the efficacy and safety of PCEA have enrolled a large population (>1000) of patients, which included elderly patients. Analgesic mixture and PCEA settings (see table I) were similar in young adult and elderly patients except in the study by Brodner et al. which did not add an opioid to the analgesic solution for those aged >70 years. Unfortunately, in these three studies, comparisons of analgesic efficacy and incidence of adverse effects between elderly and young adult populations are not made. However, Liu et al. found that age was not a risk factor for hypotension, sedation or motor block, but they could not take into account the analysis of respiratory depression because of the low incidence (0.3%).

4. PCEA versus PCA

The aim of effective postoperative pain management is to relieve pain so that normal functions, including ventilation, gastrointestinal function, coughing and mobility are minimally impaired. In middle-aged populations, patient-controlled techniques using either intravenous or epidural routes provide effective postoperative analgesia. However,
342  

Mann et al.

the epidural route (with a combination of a local anaesthetic and an opioid) results in better post-operative pain relief,\(^{50,56}\) promotes early mobilisation, improves bowel activity, shortens the duration of hospital stay\(^ {50,54} \) and reduces cardiovascular morbidity\(^ {51} \) compared with the intravenous route. This superiority of epidural analgesia could be explained by the effects of epidural administration of local anaesthetics, the only drugs that totally suppress the stress response after surgical procedures.\(^ {49} \)

For elderly patients, these overall benefits of epidural over parenteral analgesia are especially attractive. However, few studies of analgesia techniques have focused on outcomes in elderly patients. Mann et al.\(^ {37} \) observed that, in elderly patients, PCEA improved postoperative pain relief, mental status and bowel activity but did not reduce postoperative delirium incidence and cardiorespiratory outcome compared with PCA. Nevertheless, it is important to note that in this study, cardiovascular changes and pulmonary complications were without clinical importance. Although the effects of anaesthesia and analgesia on the incidence of postoperative delirium remain controversial,\(^ {113,59} \) PCEA can provide a more rapid recovery of mental status.\(^ {37} \) After abdominal surgery, PCEA contributed to an earlier recovery from postoperative ileus.\(^ {37} \) Experimental and clinical evidence has demonstrated that epidural local anaesthetics can improve bowel activity compared with parenteral analgesia.\(^ {49,60} \) Interestingly, studies in which the epidural catheter was located at the lumbar level and/or the duration of epidural analgesia lasted no more than 24 hours have not found any advantage for epidural analgesia with regard to recovery of bowel function.\(^ {61,62} \) Thus, it is recommended, where possible, to position the catheter at the thoracic level and to provide an effective thoracic sensory blockade.

PCEA has also shown to be superior to PCA in terms of patient satisfaction.\(^ {37,54} \) It is important to emphasise that PCEA techniques are only partly patient-controlled and offer the possibility of setting a background infusion. Firstly, this is particularly useful in confused or not yet totally awake patients who cannot handle the device. Secondly, in contrast with the intravenous route, background infusion by the epidural route improves analgesia achieved by PCEA without further adverse effects.\(^ {63} \) Thirdly, it has been suggested that older patients often prefer to have their analgesics administered by hospital staff, rather than by self-administration.\(^ {64} \) Taken together, these considerations undoubtedly favour PCEA techniques.

5. Limits of PCA and PCEA Techniques

In the elderly, as in young patients, controlled analgesia techniques are indicated for any patient undergoing moderate or very painful surgery. However, as pointed out by Miaskowski et al.,\(^ {65} \) the overall success in using these techniques also relies upon the expertise and knowledge of the supervising therapists. Expert supervision (for instance, from an anaesthesiology-based acute pain service) includes patient selection, patient education about using patient-controlled techniques and close monitoring. Chumbley et al.\(^ {66} \) stated that higher pain ratings are observed if the patient does not receive adequate education about such techniques. Thus, written and/or verbal preoperative instructions for the use of the pump and information on analgesic-related adverse events are required to optimise analgesia.

The efficacy of self-controlled techniques is illusory for patients who cannot handle the device (motor insufficiency or severe arthritis) or who are unable to participate in their own care. In patients >70 years of age, this situation concerns not only those presenting with dementia or a confused state but also those presenting with more general cognitive problems. For example, 17.5% of patients aged >70 years had problems initiating PCA bolus doses on the first day because of mild confusion.\(^ {12} \) Routine perioperative assessment of mental status (e.g. using the Mini Mental State Examination or the Abbreviated Mental Test) is recommended as an effective strategy to identify such patients in order to provide more efficient postoperative pain management in elderly patients.\(^ {37,67} \) On the basis of this assessment, Mann et al.\(^ {37} \) observed that 24% of elderly surgical patients were cognitively impaired.
and thus unable to use patient-controlled techniques effectively. It should be emphasised that for patients who exhibit pre- or postoperative cognitive impairment or physical disabilities, pain management must rely on the judgement of physicians and nurses and requires a conventional analgesia strategy.

Another limitation of PCA and PCEA techniques is their use in patients with, or at risk for, renal and respiratory failure. Although the use of PCA or PCEA should not be completely discounted in such patients, caution should be used and further randomised controlled trials need to be conducted to determine the efficacy and safety of patient-controlled techniques in such patients. In any case, it would seem especially unwise in elderly patients to increase the risk of respiratory depression by using hypnotic or sedative drugs in patients with, or at risk for, renal or respiratory failure. It is essential to adapt management and monitoring procedures of patients perceived to be at increased risk; for instance, systematic supplemental oxygen therapy can reduce the incidence of nocturnal hypoxaemia and monitoring the patient every 2 to 4 hours in an acute pain unit will make it possible to ensure the quality of analgesia, respiratory function and the level of vigilance.

The choice of analgesic technique must also take into account the surgical procedure. After major thoraco-abdominal surgery, PCA and PCEA are considered to be the gold standards of pain management. In contrast after limb surgery, nerve block techniques seem to be the most appropriate strategy. After hip and knee surgery, nervous ‘three-in-one’ block provides comparable pain control but induces less technical problems and adverse effects than do PCA or PCEA.

6. Conclusion

By allowing a more rational use of analgesics, both PCA and PCEA techniques provide effective postoperative pain management. In middle-aged patients, PCEA offers better pain relief, improved mobility and postoperative recovery compared with PCA. Similar benefits of PCEA have been observed in elderly patients, including greater pain relief and patient satisfaction. Both techniques are particularly useful for elderly patients undergoing major thoraco-abdominal surgery. However, there is a need for further research in this patient population.

Both PCA and PCEA techniques have a good safety profile in elderly patients only when there is strict preoperative selection and postoperative monitoring. Elderly patients must be capable of handling the patient-controlled device to be eligible for self administration of analgesics. It is therefore particularly important that patients who are not capable of using the device, such as patients with pre- or postoperative cognitive problems, be identified.

Improvements in the management of postoperative pain in the elderly will lead to a greater expansion of self-controlled techniques. However, further studies should determine the effect of these analgesic strategies on medical care costs and improvements in quality of life.

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