



## Strategies for postoperative pain management

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Despite advances in our understanding of the neurobiology of nociception, postoperative pain continues to be undertreated. There are many modalities that may provide effective postoperative analgesia, including systemic (e.g. opioids, non-steroidal anti-inflammatory agents) and regional analgesic options. The particular modality or modalities utilized for a particular patient will depend on the risk-benefit profile and patient preferences. Ideally, analgesic options should be incorporated into a multimodal approach to facilitate patient recovery after surgery.

**Key words:** postoperative pain; epidural; opioid; non-steroid anti-inflammatory agent; patient-controlled analgesia.

Recent history has heralded the advent of the vocal public in the medical field. With the formalization of patient rights, the profession faces new challenges in the effort to provide medical care that recognizes the patient as a participating entity. This evolution has gained particular prominence in the arena of pain management. Fear of inadequate pain management abounds in surveys of surgical hospital populations. Such fear reflects hesitancy by the medical profession to treat pain aggressively in an environment compromised by concerns of addictive potential and federal sanction for inappropriate prescription. However, our expanding knowledge of pain perception and propagation presents the opportunity to revolutionize care. An evidence-based strategy for postoperative pain management will incorporate the latest systematic information for analgesic options individually tailored to each patient's needs. We review the major

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modalities available for postoperative pain management, focusing on evidence obtained from randomized controlled trials and meta-analyses.

## **PATHOPHYSIOLOGY OF POSTOPERATIVE PAIN**

The study of the neurobiology of pain has produced a remarkable understanding of the role of nociception in the perioperative period. We now recognize that pain is not a 'hard-wired' system but a dynamic arrangement of multiple nociceptive and descending modulatory inputs. Surgical incision is a traumatic event triggering profound sympathetic and inflammatory responses. The inflammatory response activates peripheral nociceptors that transmit nociceptive signals centrally and initiate a larger inflammatory process, amplifying that transmission and potentially altering subsequent 'pain' sensation through central sensitization. With a resultant increase in catecholamine release and metabolic oxygen consumption, the neuroendocrine stress response amplifies metabolic activity, induces the sympathoadrenal axis, and imposes an increased burden on many organ systems with an associated impact on patient morbidity and mortality. Poorly controlled postoperative pain limits patient mobilization, compromising pulmonary function and possibly increasing patient morbidity.

Indeed, it is possible to envision how these acute events may result in long-term consequences. Poorly controlled postoperative pain may result in the development of chronic pain after surgery.<sup>1,2</sup> Whether postoperative pain is a causal predictor of chronic pain is unclear; however, there is increasing recognition that long-term neurobiological changes occur much more quickly than previously anticipated, and chronic pain after surgery is common following procedures such as thoracotomy (up to 67%), breast surgery (up to 57%), limb amputation (up to 83%), sternotomy (27%), and gallbladder surgery (up to 56%), with the severity of postoperative pain suggested as an important predictor for development of chronic pain.<sup>1</sup>

Current evidence suggests that continued peripheral nociceptive input may maintain central sensitization, amplify postoperative pain, and contribute to chronic pain. Preemptive analgesia attempts to prevent the development of central sensitization and incidence of chronic pain by administration of analgesics in the perioperative period to prevent the establishment of incisional (intraoperative) and inflammatory (postoperative) injuries.<sup>2-4</sup> Despite the fact that experimental studies indicate that preemptive analgesia would decrease postoperative pain, clinical trials are equivocal in the benefits of preemptive analgesia as there are many methodological and study design issues that may complicate the question of whether preemptive analgesia is clinically relevant.<sup>4,5</sup> Since both incisional and inflammatory injuries are important in initiating and maintaining central sensitization, maximum clinical benefit is observed when there is a complete blockade of noxious stimuli with extension of this block into the postoperative period.<sup>6</sup>

## **SYSTEMIC ANALGESIC THERAPY**

### **Non-steroidal anti-inflammatory agents (NSAIDs)**

NSAIDs are a major systemic pharmacological option, providing analgesia without the potential for dependence or addiction but limited by a therapeutic ceiling. These agents

inhibit central and peripheral cyclo-oxygenase (COX) and production of prostaglandins, resulting in attenuation of inflammation and a decrease in the mediators of nociception. The discovery of two COX isoforms with different functions (COX-1: constitutive, causing platelet aggregation, haemostasis and gastric mucosal protection; COX-2: inducible, causing pain, inflammation and fever) has resulted in the development of selective COX-2 inhibitors, which differ from traditional NSAIDs that block both COX-1 and COX-2. COX-2 inhibitors may confer advantages of the analgesic efficacy of a traditional NSAID with decreased gastrointestinal haemorrhage and minimal effects on haemostasis. Acetaminophen also does not appear to inhibit platelet function and has minimal bleeding risk. Although the precise mechanism by which acetaminophen acts is unclear, the discovery of a 'COX-3' isoform may represent the central mechanism by which acetaminophen decreases pain and fever.<sup>7</sup>

Independently, NSAIDs provide adequate analgesia for mild to moderate pain, although some recent data suggest that NSAIDs may be more efficacious as analgesics than previously recognized (see Table 1). Recent quantitative systematic reviews suggest that NSAIDs may be as efficacious as opioids alone.<sup>8-17</sup> When used as an

**Table 1.** Relative efficacy of single-dose analgesics to provide >50% pain relief for moderate to severe postoperative pain.

Drug	Mean NNT	95% CI
<i>Codeine 60 mg</i>		
+ Acetaminophen PO 1000 mg <sup>8</sup>	2.2	1.7-2.9
Didofenac PO 50 mg <sup>9</sup>	2.3	2.0-2.7
Rofecoxib PO 50 mg <sup>10</sup>	2.3	2.0-2.6
Ibuprofen PO 600 mg <sup>9</sup>	2.4	1.9-3.3
Oxycodone PO 15 mg <sup>11</sup>	2.4	1.5-4.9
<i>Oxycodone 5 mg</i>		
+ Acetaminophen PO 325 mg <sup>11</sup>	2.5	2.0-3.2
Ketorolac PO 10 mg <sup>12</sup>	2.6	2.3-3.1
Ibuprofen PO 400 mg <sup>9</sup>	2.7	2.5-3.0
Meperidine IM 100 mg <sup>12</sup>	2.9	2.3-3.9
Morphine IM 10 mg <sup>13</sup>	2.9	2.6-3.6
Ketorolac IM 30 mg <sup>12</sup>	3.4	2.5-4.9
<i>Codeine 60 mg</i>		
+ Acetaminophen PO 600/650 mg <sup>14</sup>	3.6	2.9-4.5
Acetaminophen PO 1000 mg <sup>10</sup>	3.8	3.4-4.4
Aspirin PO 1000 mg <sup>15</sup>	4.0	3.2-5.4
Aspirin PO 600/650 mg <sup>15</sup>	4.4	4.0-4.9
<i>Dextropropoxyphene 65 mg</i>		
+ Acetaminophen PO 650 mg <sup>16</sup>	4.4	3.5-5.6
Tramadol PO 100 mg <sup>17</sup>	4.8	3.4-8.2
Acetaminophen PO 600/650 mg <sup>14</sup>	5.3	4.1-7.2
Tramadol PO 50 mg <sup>17</sup>	7.1	4.6-18
Dextropropoxyphene PO 65 mg <sup>16</sup>	7.7	4.6-22
Dihydrocodeine PO 30 mg <sup>11</sup>	8.1	4.1-54.0
Codeine PO 60 mg <sup>17</sup>	9.1	6.0-23.4

CI, confidence interval; IM, intramuscular; NNT, number needed to treat; PO, oral administration. Data compiled from several systematic reviews as referenced. NNT in this case refers to the number of patients who must be treated to obtain >50% pain relief for moderate to severe postoperative pain.

adjunct to opioids, NSAIDs may improve postoperative analgesia, reduce opioid requirements, facilitate return of gastrointestinal function, reduce nausea, decrease respiratory depression and improve patient satisfaction.

NSAIDs are associated with a number of side-effects, including decreased haemostasis, renal dysfunction, gastrointestinal haemorrhage, and adverse effects on bone healing. NSAID-induced platelet dysfunction and inhibition of thromboxane-A<sub>2</sub> causes decreased haemostasis, although the evidence of NSAIDs as a major source of perioperative bleeding is equivocal; a large observational study of perioperative ketorolac did not demonstrate any significant increase in bleeding at the operative site.<sup>18</sup> Patients with hypovolaemia, abnormal renal function or serum electrolytes may be at higher risk for developing NSAID-induced renal dysfunction. A meta-analysis of postoperative patients receiving NSAIDs did not demonstrate any significant reduction in urine volume or cases of postoperative renal failure in euvolaemic patients with normal renal function.<sup>19</sup> NSAIDs are also associated with a higher incidence of gastrointestinal bleeding<sup>18</sup> and may have an adverse effect on bone healing.<sup>20</sup> Intravenous formulations of COX-2 inhibitors may even prove to be more efficacious in the postoperative period as these agents are associated with a lower incidence of gastrointestinal complications and exhibit minimal platelet inhibition even when administered in supratherapeutic doses.<sup>21</sup> It is unclear whether COX-2 inhibitors will reduce the incidence of renal complications compared to traditional non-selective NSAIDs.

### Opioids

Opioids remain a central option in the management of perioperative pain. Opioids inhibit  $\mu$  receptors, which are distributed both centrally and peripherally, and accordingly account for both the analgesic efficacy and side-effects associated with these medications. A ceiling effect is not seen, but the dose that can be administered is generally limited by side-effects, including respiratory depression, pruritis, nausea and vomiting.

Parenteral opioids are typically administered for the treatment of moderate to severe postoperative pain and will provide reliable onset of analgesic action, although intramuscular (IM) administration may result in a wider variability in serum drug concentrations than intravenous (IV) administration. Although oral opioids are traditionally prescribed on an as-needed (PRN) basis postoperatively, some recent evidence suggests that there may be a role for sustained-release oral opioids in providing superior postoperative analgesia in certain populations.<sup>22</sup>

### Intravenous patient-controlled analgesia

The introduction of patient-controlled analgesia (PCA) has provided a useful tool for adjusting opioid dosage to the varied analgesic needs of each patient while mitigating side-effects. Patients may self-administer a set dose on a PRN basis to maintain a therapeutic serum level while minimizing complications. PCA is based on the premise that a negative feedback loop exists where analgesic medication is self-administered when pain is present. When this negative feedback loop is violated, side-effects—including excessive sedation or respiratory depression—may occur.<sup>23</sup>

Available evidence suggests that the optimal demand dose for morphine is 1 mg, and that for fentanyl is 40  $\mu$ g with a lower dose (10–20  $\mu$ g) more common in actual clinical practice.<sup>23–25</sup> Typical lockout intervals range from 5 to 10 minutes, and varying

the interval within this range appears to have no effect on analgesia efficacy.<sup>23</sup> Routine use of a background infusion in an opioid-naïve patient is discouraged as this only increases the dose used and incidence of side-effects such as respiratory depression.<sup>26</sup>

IV PCA may provide many benefits, including superior postoperative analgesia, improved patient satisfaction, and decreased risk of pulmonary complications, compared to traditional PRN analgesic regimens. A meta-analysis of 15 randomized trials demonstrated that IV PCA provided significantly greater analgesic efficacy.<sup>27</sup> A more recent systematic review also demonstrated that IV PCA improves analgesia and decreases the risk of pulmonary complications, although there were no differences in cumulative opioid consumption, duration of hospital stay or opioid-related side-effects compared to PRN systemic opioids.<sup>28</sup> The incidence of opioid-related side-effects—including respiratory depression (<0.5%)—from IV PCA does not appear to differ significantly from that administered neuraxially or systemically.<sup>26,28,29</sup>

### Other non-opioid analgesics

#### *Ketamine*

Widely used as an anaesthetic agent, ketamine may be useful as an analgesic agent as it inhibits N-methyl-D-aspartate (NMDA) receptor activity, and therefore may prevent central sensitization.<sup>30</sup> Parameters for perioperative dosing are unclear, although the use of low-dose ketamine infusion for postoperative analgesia has been reported and eventually may be a valuable adjunct in a multimodal analgesic regimen by enhancing analgesia and reducing opioid-related side-effects.<sup>30</sup> Despite the fact that ketamine has been reported to be administered neuraxially<sup>31,32</sup>, the routine use of neuraxial ketamine is discouraged until the neurotoxicity of ketamine can be further delineated.

#### *Tramadol*

As a synthetic opioid which exhibits weak  $\mu$ -agonist activity, tramadol exerts its analgesic effects by inhibiting the central reuptake of serotonin and norepinephrine and may also exhibit peripheral local anaesthetic properties.<sup>33</sup> With relatively less respiratory depression, major organ toxicity, depression of gastrointestinal motility and abuse potential compared to traditional opioids, tramadol has been shown to be an efficacious analgesic agent for the treatment of moderate postoperative pain.<sup>34,35</sup> Dizziness, drowsiness, sweating, nausea, vomiting, dry mouth and headache are commonly reported side-effects.<sup>34,35</sup>

## REGIONAL ANALGESIC TECHNIQUES

### Neuraxial opioids

Use of a single dose of opioid may provide effective postoperative analgesia. Hydrophilic opioids (e.g. morphine and hydromorphone) tend to remain within the cerebrospinal fluid (CSF) and produce a delayed but prolonged duration of analgesia, whereas lipophilic opioids (e.g. fentanyl and sufentanil) tend to provide rapid onset of analgesia with rapid clearance from the CSF.<sup>36</sup> The differences between lipophilic and hydrophilic opioids will affect the choice of opioid for a particular clinical situation. Single-dose intrathecal administration of a lipophilic opioid may be useful when rapid analgesic onset combined with a moderate duration of analgesia is applicable, whereas single-dose hydrophilic

opioid administration may be useful in patients who will be monitored on an inpatient basis and require a longer duration of analgesia. Although the site of analgesic action for hydrophilic opioids is predominantly spinal, the primary site of action for single-dose neuraxial lipophilic opioids is unclear.<sup>37,38</sup> A single epidural bolus of a lipophilic opioid like fentanyl, diluted in at least 10 ml of preservative-free normal saline, will provide rapid postoperative analgesia.<sup>39</sup> With lower doses required for elderly patients and thoracic catheter sites, single-dose epidural hydrophilic opioid may provide effective prolonged postoperative analgesia and is useful in situations where epidural catheter location is not congruent.<sup>40,41</sup>

### **Epidural analgesia**

Epidural catheter techniques capture the benefits of targeted delivery and allow for prolonged analgesia with the ability to titrate the degree of analgesia to the particular patient needs during the perioperative period. Intraoperative use of higher doses and concentrations of local anaesthetics provide a profound sympathetic, motor and sensory block capable of facilitating a complete surgical anaesthetic. Lower doses and concentrations of local anaesthetics in the postoperative period can then provide an adequate sensory block after surgery without mitigating motor function while facilitating mobilization. Responsive analgesia has been developed further with the advent of the patient-controlled epidural analgesia (PCEA). Compared to that seen from systemic opioids, postoperative epidural analgesia provides superior analgesia<sup>42,43</sup>, and intraoperative use of the epidural catheter as part of a combined epidural-general anaesthetic technique will facilitate patient recovery immediately after surgery<sup>44</sup>; however, it is important to realize that 'epidural analgesia' is not a generic term but incorporates a range of variables including the choice of analgesic agents, location of catheter placement, and onset and duration of perioperative use.<sup>45</sup>

### **Analgesic agent**

#### *Local anaesthetics*

Epidural infusions of local anaesthetic alone do not seem to be commonly used for postoperative epidural infusions due to a significant failure rate from inadequate analgesia and relatively high incidence of motor block and hypotension.<sup>45</sup> In addition, epidural infusions of local anaesthetic alone do not appear to be as effective as local anaesthetic–opioid regimens in controlling postoperative pain.<sup>45,46</sup> Local anaesthetics administered in the epidural space may act at the spinal nerve roots, dorsal root ganglion (DRG), or spinal cord itself<sup>38</sup>, although some anatomic studies suggest that the initial site of epidural local anaesthetic block is at the nerve root sheath and DRG.<sup>47</sup> Epidural infusions of local anaesthetic alone may be used to avoid opioid-related side-effects.

#### *Opioids*

Opioids used alone for postoperative analgesia do not cause motor block or hypotension.<sup>45</sup> There are many different choices for continuous epidural infusions of opioids, with differences between lipophilic and hydrophilic opioids. The analgesic site of action for continuous hydrophilic opioid infusions is primarily spinal.<sup>48</sup> Continuous epidural infusions of a hydrophilic opioid may be used when the epidural catheter insertion site is not congruent with that of surgery or when local anaesthetic side-effects

are difficult to manage. Continuous infusions (versus intermittent boluses) of an epidural hydrophilic opioid results in superior analgesia with fewer side-effects<sup>48,49</sup> and will provide superior analgesia versus PRN administration of systemic opioids.<sup>50</sup> The site of action for continuous epidural infusions of lipophilic opioids appears to be systemic<sup>51</sup>, with no differences in plasma concentrations, side-effects, or pain scores between IV or epidural infusions of fentanyl.<sup>51,52</sup>

#### *Local anaesthetic–opioid combinations*

The combination of a local anaesthetic and opioid results in superior postoperative analgesia and possibly decreases the dose of local anaesthetic administered.<sup>45,46,53</sup> Compared to IV PCA, continuous epidural infusions of a local anaesthetic–opioid combination provides superior analgesia.<sup>43</sup> Although the choice of local anaesthetic varies, bupivacaine ( $\leq 0.125\%$ ), ropivacaine ( $\leq 0.2\%$ ) or levobupivacaine ( $\leq 0.125\%$ ) are typically used for their preferential sensory blockade and minimal impairment of motor function.<sup>54,55</sup> In addition, a lipophilic opioid is often added to allow for rapid titration of analgesia<sup>45,48</sup>, although addition of a hydrophilic opioid to the local anaesthetic regimen will also provide effective analgesia.<sup>48</sup>

#### *Adjuvant agents*

There are many adjuvants that may be added to epidural infusions, but none are universally used routinely in the clinical setting. Two of the more studied adjuvants are clonidine and epinephrine. The epidural dose of clonidine typically used is in the range of 5–20  $\mu\text{g}/\text{hour}$ <sup>56,57</sup>; however, the clinical use of clonidine is limited by the presence of hypotension, bradycardia and sedation.<sup>57</sup> Epinephrine may improve postoperative pain control and increase sensory block.<sup>58</sup> Experimental epidural administration of ketamine may attenuate central sensitization and potentiate the analgesic effect of epidural opioids<sup>31</sup>, but the routine clinical use of ketamine is discouraged until additional safety and analgesic data become available.<sup>59</sup>

#### **Location of catheter insertion**

'Catheter-incision congruent analgesia'—that is, insertion of the epidural catheter congruent to the incisional dermatome—results in superior postoperative analgesia, decreased side-effects and decreased patient morbidity.<sup>45,60</sup> Catheter-incision incongruent epidural analgesia results in poor pain control with subsequent early removal of the epidural catheter.<sup>61</sup> Thoracic epidural analgesia for abdominal/thoracic surgery results in a low incidence of urinary retention and routine bladder catheterization.<sup>62</sup> Catheter-incision incongruent analgesia may result in an increased incidence of side-effects as there is a higher incidence of lower extremity motor block with use of lumbar epidural catheters.<sup>63,64</sup> The decrease in morbidity in patients undergoing abdominal and thoracic surgery is seen only with thoracic (congruent) but not lumbar (incongruent) epidural catheter placement.<sup>65</sup>

#### **Patient-controlled epidural analgesia (PCEA)**

The administration of epidural analgesia via a patient-controlled device (PCEA) has become more common and, like IV PCA, allows for individualization of postoperative analgesic requirements and may lower drug use, improve patient satisfaction,

and provide superior analgesia.<sup>43,66,67</sup> Over 90% of patients with PCEA receive adequate analgesia, with median pain scores of 1 (out of a possible 10) at rest and 4 with activity.<sup>68,69</sup> The incidences of side-effects for PCEA are comparable with those from continuous epidural infusions: 1.8–16.7% for pruritus, 3.8–14.8% for nausea, 13.2% for sedation, 4.3–6.8% for hypotension, 0.1–2.0% for motor block, and 0.2–0.3% for respiratory depression.<sup>68,69</sup> Although the optimal PCEA analgesic solution and delivery parameters are unclear, most clinicians use a variety of low-concentration local anaesthetic–opioid combinations in an attempt to improve analgesia while minimizing side-effects. A lipophilic opioid like fentanyl is generally more appropriate for use with PCEA due to its more rapid analgesic effect and shorter duration of action.<sup>68</sup>

### Benefits and risks of epidural analgesia

Although the overall superiority of intraoperative regional versus general anaesthesia is still somewhat controversial, despite a recent large meta-analysis demonstrating a reduction in overall mortality with use of neuraxial anaesthesia<sup>70</sup>, use of an appropriately sited catheter and optimized epidural analgesic technique may be important in attenuating and decreasing postoperative morbidity/mortality. Compared to analgesia with systemic opioids, postoperative epidural analgesia is associated with a reduction in mortality/morbidity<sup>70–73</sup> and may specifically decrease the incidence of postoperative gastrointestinal, pulmonary and cardiac complications.<sup>60,71</sup>

Many of the clinical benefits of epidural analgesia are related to the provision of superior analgesia, inhibition of sympathetic outflow, and some direct and indirect effects of the epidural local anaesthetics. For instance, perioperative thoracic epidural analgesia with a local anaesthetic-based solution will inhibit sympathetic outflow, reduce opioid consumption and attenuate spinal reflex inhibition of the gastrointestinal tract<sup>71</sup>, which ultimately will facilitate return of gastrointestinal motility without contributing to anastomatic bowel dehiscence.<sup>53,67,74</sup> Patients undergoing abdominal surgery who receive a local anaesthetic-based epidural analgesic regimen will have an earlier return of gastrointestinal motility compared to those who receive epidural opioids. The provision of superior analgesia and attenuation of the spinal reflex inhibition of diaphragmatic function by a local anaesthetic-based epidural analgesic regimen will result in a decrease in postoperative pulmonary complications.<sup>71–73</sup> Use of an appropriately sited catheter to optimize the physiological benefits<sup>60,71</sup> may result in a decrease in the incidence of postoperative myocardial infarction<sup>65</sup> as thoracic epidural analgesia may attenuate the stress response and hypercoagulability, improve postoperative analgesia, and provide a favourable redistribution of coronary blood flow.<sup>75,76</sup> Catheter-incision congruent epidural analgesia results in a reduction in drug administered and incidence of drug-induced side-effects.<sup>68,77</sup> Postoperative epidural analgesia is also associated with an improvement in patient-oriented outcomes such as patient satisfaction<sup>78</sup> and quality of life.<sup>79</sup>

Although postoperative epidural analgesia may improve analgesia and decrease certain morbidity, the benefits of postoperative epidural analgesia are not as clear for other areas. Postoperative epidural analgesia has not consistently been shown to be superior to systemic opioids in the areas of postoperative coagulation, cognitive dysfunction<sup>80</sup> and immune function.<sup>81</sup> By attenuating perioperative hypercoagulability, intraoperative epidural and spinal anaesthesia and analgesia may also reduce the incidence of coagulation-related events<sup>70</sup>; however, a reduction in the incidence of hypercoagulable-related events by postoperative epidural analgesia per se has not been consistently demonstrated.



One of the most contentious issues has been the concurrent use of anti-coagulants and epidural analgesia.<sup>82</sup> The incidence of spinal haematoma is estimated at approximately 1:150 000 for epidural block and 1:220 000 for spinal blocks<sup>83</sup>; however, the incidence of spinal haematoma increased to 1:40 800 for spinal anaesthetics and 1:6600 for epidural anaesthetics with the introduction of low-molecular-weight heparin in North America.<sup>84</sup> The available data also suggest that epidural catheter removal is a traumatic event, although this is still a relatively controversial issue.<sup>85,86</sup> There are different recommendations for the timing of neuraxial techniques in the presence of various anti-coagulants.<sup>87</sup>

Timing of epidural  
C LMWH

Infectious complications with epidural analgesia is relatively uncommon, with an incidence of less than 1:10 000.<sup>88</sup> Patients who develop epidural abscesses often have other underlying predisposing factors (e.g. prolonged duration of epidural analgesia, malignancy, or trauma).<sup>45,88</sup> Despite the fact that there may be a relatively high incidence of superficial inflammation (4–14%) and epidural catheter colonization (20–35%)<sup>89,90</sup>, these appear to be poor surrogate endpoints for epidural space infection<sup>90</sup> as the typical use of epidural analgesia is generally not associated with abscess formation.<sup>68,69</sup>

A final, often overlooked 'complication' of epidural analgesia is accidental epidural catheter migration out of the epidural space. The overall 'failure' rate for postoperative epidural analgesia has been reported to be anywhere from 6 to 25%, with many centres reporting a rate between 10 and 20%; however, the actual incidence of epidural catheter dislodgment is probably lower (5.7%)<sup>64,68,69,91</sup> as there may be other reasons contributing to epidural 'failure' (e.g. medication-related side-effects).

### Peripheral nerve blocks

When compared to systemic opioids, peripheral regional analgesic techniques<sup>92,93</sup> appear to provide superior postoperative analgesia and can be used as either a single injection or continuous infusion. Peripheral regional analgesia may decrease opioid-related side-effects, improve patient satisfaction when compared to systemic opioids, and may be more appropriate than neuraxial techniques when there is an increased risk of epidural haematoma with systemic anti-coagulation.<sup>92,94</sup> Although the overall benefits of peripheral nerve analgesia on patient outcomes is unclear, some data suggest that peripheral regional analgesic techniques may improve certain patient outcomes.<sup>78,94</sup>

Peripheral regional analgesia includes a wide range of techniques such as wound infiltration and peripheral nerve blocks. A variety of analgesic agents may be used; however, local anaesthetics appear to be the most common and effective analgesic agents. Although a single peripheral regional injection of local anaesthetic may be used to supplement intraoperative anaesthesia, the duration of postoperative analgesia from the single peripheral injection of local anaesthetic may last up to 24 hours in certain instances.<sup>95</sup> Continuous infusions of a local anaesthetic-based regimen can provide effective postoperative analgesia when administered through peripheral nerve catheters. As with a single injection, continuous peripheral regional infusions using a local anaesthetic-based solution will provide superior analgesia, a decrease in opioid-related side-effects and greater patient satisfaction compared to systemic opioids.<sup>78</sup> Outpatient/home use of peripheral regional analgesia can be successfully achieved with a high degree of patient acceptance and low complication rate.<sup>96</sup> The optimal parameters (e.g. local anaesthetic, adjuvants, continuous versus PCA) for peripheral analgesia are unclear. Peripheral regional analgesic techniques, in combination with systemic adjuvants (e.g. acetaminophen and ketorolac), may be

used to provide an opioid-free postoperative analgesic regimen.<sup>97</sup> Finally, a single injection or continuous infusion of local anaesthetics may also provide effective wound infiltration analgesia.

### **Intraarticular analgesics**

Intraarticular injection of analgesic agents may provide effective postoperative analgesia.<sup>98–100</sup> Although a wide variety of agents have been examined, the most commonly used agents are local anaesthetics and opioids. Several systematic reviews have evaluated the analgesic efficacy of these agents, particularly with intraarticular administration after knee arthroscopic surgery. It appears that intraarticular injection of morphine may provide up to 24 hours of pain relief postoperatively, especially when the intensity of postoperative pain is moderate to severe.<sup>98,99</sup> Although the analgesic effect is presumed to be due to a local effect on peripheral opioids receptors, a systemic effect of morphine cannot be excluded.<sup>98</sup> Intraarticular injection of local anaesthetics may also provide postoperative pain relief; however, the duration of the analgesia may be limited.<sup>100</sup>

## **MULTIMODAL APPROACH TO POSTOPERATIVE CONVALESCENCE**

Despite the analgesic and physiological benefits of superior analgesia, whether it be through systemic or regional analgesia, it is unclear whether pain control per se will lead to an improvement in patient outcomes. More likely, patient recovery after surgery is optimized when the benefits of superior postoperative pain control are integrated into a multimodal approach to patient convalescence<sup>101</sup>, which includes aggressive control of postoperative pain to allow early patient mobilization, early enteral nutrition, education, and attenuation of the perioperative stress response through the use of regional anaesthetic techniques and a combination of analgesic agents (i.e. multimodal analgesia).

The available data indicate that a multimodal approach to patient convalescence will facilitate patient recovery and decrease length of hospital stay.<sup>101</sup> Compared to routine perioperative care, patients undergoing major surgery who participated in a perioperative multimodal approach to patient convalescence demonstrated a decrease in markers of the neuroendocrine stress response, including preservation of total body protein, lower pain scores, earlier return of bowel function, and earlier fulfillment of intensive care unit discharge criteria.<sup>102</sup> Although a multimodal approach to patient convalescence appears to hold great promise in decreasing perioperative morbidity and length of stay without compromising patient safety, ultimate success of this approach necessitates multidisciplinary collaboration, with a change in traditional principles of postoperative care.<sup>101</sup> Traditional acute pain services with these pain specialists who have the expertise in pharmacology and regional anaesthetic techniques are logical starting points for the development of these programmes.

## **SUMMARY**

Management of the perioperative pain period is uniquely within the realm of anaesthesiology practice, in that these practitioners are intimately involved with

mitigating patient response to the trauma of surgery. Our understanding of the neurobiology of nociception suggests that attenuating central sensitization will result in diminished pain both in the immediate postoperative period and at distant time points, potentially preventing chronic pain development. There are many effective modalities and techniques to manage postoperative pain. The integration of these modalities and techniques into a multimodal model of patient recovery will facilitate postoperative convalescence.

#### Practice points

- uncontrolled postoperative pain may result in detrimental acute and chronic sequelae
- epidural analgesia is not a generic term: analgesic regimen, catheter-incision congruency, and duration of analgesia will affect the efficacy of epidural analgesia
- the clinician should weigh the risks and benefits of each technique (along with patient preferences) in the management of postoperative pain
- a multimodal approach to convalescence optimizes the physiological and analgesic benefits of epidural analgesia

#### Research agenda

- further examination of the patient preferences and utility of each analgesic modality and technique
- further define the role of postoperative epidural analgesia per se on patient outcomes
- further evaluation of cost-effectiveness of each analgesic modality and technique

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