

# Safety and efficacy of patient-controlled analgesia

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In a general sense, patient-controlled analgesia (PCA) refers to a process where patients can determine when and how much medication they receive, regardless of analgesic technique. However, the term is more commonly used to describe a method of pain relief which uses disposable or electronic infusion devices and allows patients to self-administer analgesic drugs, usually intravenous (i.v.) opioids, as required. The main focus of this review will be i.v. PCA.

The overall effectiveness of any analgesic technique depends on both the degree of pain relief that can be achieved and the incidence of side effects or complications. Therefore, factors affecting efficacy and safety of PCA are often inextricably linked. This review will consider:

- analgesic efficacy—compared with conventional methods of pain relief in post-operative patients (including pain relief, analgesic use and cost comparisons), when used in non-surgical patients, and with opioid administration by other than the i.v. route;
- patient outcomes—patient satisfaction and post-operative morbidity;
- patient factors that may affect safety and efficacy—including patient age, psychological characteristics, concurrent disorders, opioid tolerance, and inappropriate use of PCA;
- equipment factors that may affect safety and efficacy—including equipment design and malfunction;
- medical and nursing staff factors;
- the PCA ‘prescription’—including programmable variables and drugs used.

## Analgesic efficacy

In 1993, a paper by Ballantyne and colleagues<sup>3</sup> reported on the results of a meta-analysis, which was designed to examine the evidence in published randomized controlled trials comparing clinical outcomes of PCA and conventional

intramuscular (i.m.) analgesia. They included studies comparing i.v. PCA (without a concurrent continuous infusion) with i.m. opioid analgesia ordered 3–4 hourly PRN. Exclusion criteria included studies in special patient populations (e.g. children and elderly patients) and patients who routinely received intensive care post-operatively (e.g. after cardiac surgery). Significantly greater analgesic efficacy was seen with PCA, although the magnitude of the difference was small (just 5.6 on a pain scale of 0–100).

Some of the more recent studies comparing PCA with conventional methods of opioid analgesia, administered as intermittent i.m.,<sup>8 12 16 90</sup> subcutaneous (s.c.)<sup>60</sup> and i.v. injections,<sup>6 93</sup> or by continuous infusion,<sup>34 61</sup> have produced contradictory results. Some show significantly better analgesia with PCA<sup>6 34 90</sup> and others report no difference.<sup>8 12 60 61 93</sup> Colwell and Morris<sup>16</sup> noted better analgesia after i.m. morphine. However, PCA bolus doses used in their study were small, 0.25 or 0.5 mg morphine, while patients in the i.m. group could receive up to 15 mg morphine every 3 h if required. Sample sizes in many of these studies are small and difference, or lack of difference, could be difficult to detect.

Given the continuing popularity of PCA, these results could be seen as surprising. However, it is possible, if analgesia can truly be given ‘on demand’, with doses and appropriate dose intervals tailored to the individual patient, that good results can be obtained regardless of analgesic technique.

Of the studies listed above, in which no difference was found in analgesic efficacy, three<sup>60 61 93</sup> examined pain relief in patients after cardiac surgery. These patients were nursed in intensive care settings where there are usually higher nurse:patient ratios than in general hospital wards. In such settings, it may be easier to provide closer nursing supervision and analgesia when required and with minimal delay. Pettersson and colleagues<sup>71</sup> also compared analgesic efficacies of PCA and nurse-managed i.v. opioids in patients

after cardiac surgery. They found that pain relief using PCA was comparable with that obtained from an infusion while patients were in intensive care (1:1 nurse:patient ratio). However, when the patients were transferred to a general ward, significantly better analgesia was obtained with PCA than with intermittent i.v. bolus doses of opioid.

Whether a study is performed in an intensive care or general ward setting, it is also possible that efficacy may improve because of the study environment. The close interest shown by investigators could lead to greater nursing attention paid to conventional methods of pain relief—the ‘Hawthorn’ effect.<sup>100</sup> In a busy ward setting, the use of an electronically-controlled device may merely facilitate more immediate drug delivery.

In most studies, pain scores are carried out intermittently, often on a 2 or 4 hourly basis and sometimes only once or twice a day, and unrelated to the timing of drug administration. It has been suggested that this could ‘understate the benefit of PCA’<sup>3</sup> as PCA allows a more flexible matching of analgesic delivered and patient need.

### *Analgesic use*

In their meta-analysis, Ballantyne and colleagues<sup>3</sup> reported a non-significant trend towards lower opioid use in PCA patients. In 10 studies looking at differences in use, PCA opioid requirements were significantly higher in one; i.m. requirements were significantly higher in four.

Studies since then have continued to produce conflicting results, with some authors reporting significantly higher opioid use with PCA,<sup>6 34 71</sup> significantly higher use with conventional methods of opioid analgesia,<sup>12 16 90</sup> or no difference.<sup>8 61</sup>

Whether or not there are differences in opioid use, most studies report similar incidences of nausea and vomiting,<sup>3 6 12 16 34 60 61 71</sup> sedation,<sup>3 6 16 34 71</sup> pruritus,<sup>12 60</sup> and bowel function.<sup>6 8 12 16</sup> In view of these findings, total opioid dose may be relatively unimportant.

It is harder to compare the incidence of respiratory depression between PCA and conventional methods of opioid analgesia. This is partly because the risk is small and, therefore, most, if not all, studies would have inadequate numbers of patients in each group to be able to show a significant difference. In addition, the definitions of respiratory depression vary widely. Many authors choose to define respiratory depression as a respiratory rate of less than 8 or 10 breaths min<sup>-1</sup>, even though a decrease in respiratory rate is known to be an unreliable indicator of the presence or absence of respiratory depression.<sup>26 62 101</sup> A better clinical indicator of early respiratory depression is sedation, and many centres routinely monitor patient sedation using sedation scores.<sup>62</sup> Better estimates of the risk of respiratory depression with PCA are obtained from results of larger audits (see later).

### *Cost comparisons*

Costs involved in the provision of analgesia, including the direct costs of drugs, consumables, equipment, and labour, are important when considering whether or not to use a particular method of pain relief, even if it is more effective. Jacox and colleagues<sup>42</sup> reviewed seven studies published from 1984 to 1995 which compared costs related to PCA and i.m. opioid analgesia. They concluded that while PCA may provide superior analgesia and patient satisfaction, it does so at a higher cost. Similar results have been reported by other authors.<sup>12 19</sup> A comparison of the differences in cost across the studies is difficult as they vary with respect to patient population, organization of PCA management, PCA device involved, drugs administered, and methods used to determine expenses.

A significant part of the cost of PCA is the cost of equipment, drugs, and consumables. Nursing time (time involved in the provision of analgesia) is usually much less compared with conventional forms of pain relief.<sup>12 16 19</sup> Therefore, in a busy general hospital ward where the number of appropriately qualified nurses may be limited, it is possible that the use of PCA in some patients may allow more time to attend to other duties, including the more effective provision of other forms of analgesia to patients without PCA.

In view of the current need in most countries to control health care costs, a decrease in average length of stay (ALOS) in hospital also has important implications. However, no difference between PCA and i.m. opioid analgesia was found by Ballantyne and colleagues<sup>3</sup> (although two studies included in this meta-analysis found that PCA was associated with a lower ALOS). Later studies have confirmed this lack of difference.<sup>12 16</sup>

### *Efficacy in non-surgical patients*

PCA is most commonly used in the management of post-operative and post-injury pain. However, it has been shown to be effective in the management of pain from other causes such as sickle cell crises,<sup>98</sup> burns injury,<sup>11</sup> oral mucositis after bone marrow transplantation,<sup>21</sup> cancer pain,<sup>97</sup> extracorporeal shock wave lithotripsy<sup>79</sup> and angina,<sup>59</sup> and as an investigative tool, often used to compare drugs and techniques.

### *Efficacy via non-i.v. routes*

Opioid self-administration has also been shown to be effective using other routes including s.c.<sup>18 95 104</sup>, oral,<sup>87</sup> and intranasal routes<sup>91</sup>. Epidural PCA is discussed by Wheatley and colleagues in their article in this issue of the journal.<sup>102</sup>

Dawson and colleagues<sup>18</sup> compared s.c. and i.v. PCA diamorphine and reported that patients using s.c. PCA experienced significantly less pain and less sleep disturbance. Urquhart and others<sup>95</sup> and White<sup>104</sup> recorded no

significant difference in pain scores using hydromorphone,<sup>95</sup> morphine,<sup>104</sup> or oxymorphone.<sup>104</sup> Interestingly, all three studies reported significantly higher opioid requirements with the use of s.c. PCA compared with i.v. PCA. No difference in nausea and vomiting was found in two of the studies<sup>18 95</sup> while an increased incidence was noted in the other study<sup>103</sup> in association with s.c. PCA.

Oral (using an adapted disposable PCA device)<sup>87</sup> or intranasal<sup>91</sup> PCA appears to be as effective as i.v. PCA.

### *Potential to mask post-operative complications*

Concerns have been expressed by some that PCA may be 'too efficacious' as the patient can self-administer opioid to treat any pain they are experiencing. For example, there have been reports of PCA 'masking' signs of urinary retention,<sup>39</sup> compartment syndrome,<sup>37</sup> pulmonary embolism,<sup>58</sup> and myocardial infarction.<sup>28</sup>

In the case described by Harrington and colleagues,<sup>37</sup> compartment syndrome was not detected until the patient returned for a second operation, 36 h after initial surgery for lower limb trauma. PCA was commenced after the first operation. However, it would appear that the patient was monitored (hourly pain and sedation scores) for the first 6 h only and that these observations were not repeated regularly during the last 30 h of PCA therapy. Despite their concerns about PCA, the authors concluded that this technique might be a 'perfectly acceptable means' of providing post-operative analgesia in patients with lower limb trauma if hourly patient monitoring is continued throughout the duration of therapy.

The concern expressed in these case reports is that PCA allows the patient to increase opioid use to cover any 'new' pain without informing nursing or medical staff. However, in post-operative patients, assessment of pain and opioid use should be regular and frequent. As most PCA treatment regimens incorporate such assessments, often on a 1- or 2-hourly basis, it could be argued that PCA might allow a more accurate measure of pain and increases in opioid dose. Any unexpected change in analgesic use, or the site, severity or character of the pain being treated, warrants careful investigation, as it may signal the development of a new surgical or medical diagnosis.<sup>62</sup>

## **Patient outcomes**

### *Patient satisfaction*

In their meta-analysis, Ballantyne and colleagues<sup>3</sup> concluded that there was 'considerable evidence' of higher patient satisfaction with PCA compared with i.m. opioids. Once again, there have been conflicting results in some of the studies performed since. Both better patient satisfaction with PCA<sup>6</sup> and no difference compared with conventional methods of opioid administration<sup>8 12</sup> have been reported.

Satisfaction ratings are often considered to be an important outcome in health care and an indication of the patients' view of efficacy. However, evaluation of satisfaction is complex and it is known that patient satisfaction surveys tend to produce positive results because patients are reluctant to criticize their treatment.<sup>14</sup>

Although there appears to be a correlation between satisfaction and lower pain intensity,<sup>43 69</sup> many patients who experience quite high levels of pain will also report satisfaction with pain management.<sup>14 15 70</sup> Many patients still expect severe pain after surgery and may be quite pleased to find that it is not as bad as expected.<sup>27</sup>

Other factors that have been shown to have a significant association with higher satisfaction ratings include perceived control,<sup>69</sup> and lower pre-operative anxiety and post-operative depression.<sup>43</sup> A correlation between perceived control and good pain relief has also been reported.<sup>14 69</sup>

As the inverse association between patient satisfaction and pain intensity is small, there must be other additional reasons why satisfaction with PCA is high compared with conventional methods of opioid analgesia. A number of positive aspects about the PCA experience have been identified, in addition to control over pain relief.<sup>14 45</sup> These include not having to wait for pain relief,<sup>14 45 88</sup> not having injections,<sup>14 45</sup> and not having to bother nurses.<sup>14 45 88</sup>

Negative aspects about PCA have also been identified, some of which might constrain the use of PCA and, hence, its effectiveness. Most often the negative remarks relate to inadequate analgesia and/or the presence of side effects,<sup>14 88</sup> but some patients also report not trusting the PCA machine,<sup>14 45</sup> or fearing overdose,<sup>14 45 88</sup> or addiction.<sup>14 45 88</sup> Chumbley and colleagues<sup>14</sup> reported that 22% of patients feared addiction and 30% feared overdose, much higher than the 4 and 11%, respectively, reported by Kluger and Owen.<sup>45</sup> However, 43% of patients in the former study did not receive pre-operative education about PCA (and 24% received no instruction at all at any time during PCA therapy), whereas all patients in the latter study received education about pain management and PCA prior to surgery. Chumbley and colleagues<sup>14</sup> noted that lack of education was associated with higher pain ratings.

### *Effect on post-operative morbidity*

In general, the analgesic technique associated with the greatest improvements in post-operative morbidity, particularly with respect to pulmonary complications,<sup>4</sup> is epidural analgesia, which is discussed in the article by Wheatley in this issue of the journal.<sup>102</sup>

The meta-analysis by Ballantyne and colleagues<sup>3</sup> included three studies that looked at bowel function (time to first flatus or stool) and three that looked at pulmonary function. No differences were found between PCA and i.m. analgesia. Later studies have shown that PCA use, in comparison with conventional methods of opioid administration, may be associated with a lower

incidence of atelectasis,<sup>34</sup> higher VC and FEV<sub>1</sub><sup>6</sup> or no difference in FEV<sub>1</sub>,<sup>93</sup> thus, the evidence is still unconvincing.

Post-operative morbidity related to the side effects of the drugs prescribed is discussed briefly later.

## Patient factors

Patient-related factors, including age, psychological characteristics, concurrent disorders, opioid dependency, and inappropriateness of PCA use, may have a significant influence on the safety and efficacy of PCA.

### Patient age

Although very young and very old patients may be less likely to manage PCA successfully, PCA should not be withheld simply on the basis of age.<sup>27 54</sup> Children as young as 4 yr old<sup>21</sup> to patients in their late 90s<sup>54</sup> have been reported to use PCA effectively.

Egbert and co-workers<sup>25</sup> compared PCA with i.m. morphine analgesia in elderly men. PCA resulted in better pain relief, less confusion and fewer severe pulmonary complications. The incidence of 'significant' confusion was only 2.3% in patients receiving PCA compared with 18% in those given i.m. analgesia. They noted that 17.5% of PCA patients had problems initiating bolus doses on first day because of mild confusion. However, 28% of i.m. patients failed to request injections appropriately for the same reason and, therefore, all elderly patients should be followed closely to ensure that they are getting adequate pain relief.

The successful use of PCA requires reasonably normal cognitive function and patients who have pre-operative evidence of dementia or become confused post-operatively (more likely in the elderly patient<sup>48</sup>) are not suitable candidates for PCA.<sup>25 48</sup>

Post-operative PCA opioid requirements in adults are known to decrease as patient age increases,<sup>53</sup> and it has, therefore, been suggested that a lower PCA bolus dose is prescribed for elderly patients.<sup>27 48 53</sup> Concurrent use of a background infusion is contraindicated in these patients, if they are opioid-naive.<sup>27 48</sup>

### Psychological characteristics

The subjective experience of pain is dependent on a number of factors, including patients' psychological characteristics. These include state anxiety (a transitory state which varies in intensity and over time, and is associated with specific situations involving threat), trait anxiety (a personality disposition which is relatively stable over time), neuroticism, and coping style.<sup>90</sup> These characteristics may affect how well patients make use of PCA and, therefore, its effectiveness, and should be taken into account when patients are considered for this form of pain relief.

Anxiety seems to be the most important psychological measure affecting PCA use<sup>32</sup> and high levels of anxiety are significantly related to higher pain scores in patients using PCA,<sup>32 70 90</sup> although it appears that state rather than trait anxiety may be the better predictor of pain in this circumstance.<sup>70 90</sup> High levels of anxiety may also be associated with more frequent unsuccessful PCA demands, that is, demands during the 'lockout' period, which do not result in increased opioid use.<sup>32 43</sup>

### Concurrent disorders

A number of concurrent patient diseases or conditions may need to be taken into account when PCA is prescribed. For example, renal impairment may affect excretion of the metabolites of morphine, leading to respiratory depression,<sup>74</sup> and pethidine, leading to norpethidine toxicity.<sup>31</sup> Hypovolaemia may also increase the risk of respiratory depression.<sup>26</sup>

Concerns have also been raised about the use of PCA in patients who are morbidly obese or who have obstructive sleep apnoea (OSA).<sup>26 81 96</sup> A near-fatal case of respiratory depression was reported by VanDercar and colleagues<sup>96</sup> associated with PCA use in a patient with OSA. However, the PCA machine was set to deliver a background infusion as well as patient demand doses.

PCA, without a background infusion, has been used safely and effectively for pain relief after abdominal surgery in morbidly obese patients,<sup>10 47 50</sup> up to 40% of whom may have OSA<sup>47</sup>. If patients are known to have OSA, more intensive monitoring and judicious use of PCA (e.g. use of a smaller initial bolus dose) have been suggested.<sup>27 50</sup>

### Opioid-tolerant patients

Patients with a history of opioid consumption (whether legally prescribed or illegally obtained) before admission to hospital may be dependent on these drugs (that is they will exhibit signs of withdrawal if the drug is suddenly stopped or antagonized) and may show signs of tolerance to both their analgesic effects and side effects.<sup>54 62</sup>

Rapp and colleagues<sup>73</sup> compared PCA use after surgery in opioid-tolerant patients (patients with cancer pain, chronic non-cancer pain, and those with an opioid addiction) and in opioid-naive control patients. They concluded that patients with previous exposure to opioids were likely to have higher opioid requirements (total doses averaged three times those of opioid-naive patients), higher pain scores, and fewer emetic and pruritic symptoms. Surprisingly, sedation scores were higher in the opioid-tolerant patients. Although patients in this group were much more likely to be given concurrent anxiolytics, the authors state that this did not correlate with increased sedation. This suggests that if opioid doses can be rapidly increased to levels significantly in excess of pre-admission basal doses, oversedation (a better clinical indicator of early respiratory

depression than a decrease in respiratory rate—see above<sup>62</sup>) may occur in patients who are considered to be tolerant to effects of the drugs.

Significant deviation from ‘standard’ PCA prescriptions may be needed in opioid-tolerant patients if effective analgesia is to be obtained. Background infusions can be used to deliver the equivalent of the patient’s basal opioid dose, if the patient is unable to take their usual opioid.<sup>27 54</sup> The size of the bolus dose will often need to be increased; a dose based on calculated hourly background dose has been suggested.<sup>27 54</sup>

Addiction to opioids was initially thought to be a contraindication to the use of PCA, but it is now recognized to be a useful method of providing pain relief.<sup>62</sup> This may be partly because these patients may have high and unpredictable opioid requirements, and partly because it helps to avoid staff/patient confrontations about dose and dose interval. As these patients are more likely to report high pain scores, a functional assessment of pain relief (e.g. ability to cough, ambulation) may be required in addition to patient self-reports when determining efficacy of analgesia.<sup>73</sup>

### *Inappropriate use of PCA*

The safety of PCA depends on an adequate understanding of the technique by the patient and the fact that unauthorized persons do not press the demand button.

Oversedation with PCA has followed repeated use at the end of every lockout period (patient misunderstanding of pre-operative explanation),<sup>83</sup> mistaking the PCA handset for the nurse-call button,<sup>94</sup> and family,<sup>2 29 81 80</sup> visitor,<sup>9</sup> or unauthorized nurse-activated demands.<sup>29 101</sup>

## **Equipment factors**

Electronic and disposable infusion devices are both used in the provision of PCA. Each type has two components—a reservoir and a patient-control module. Although equipment-related PCA complications are less common than operator-related or drug-related problems, device design and malfunction may affect analgesic efficacy and patient safety. Problems may also arise with PCA-related consumables.

### *Disposable PCA devices*

Disposable PCA devices typically deliver 0.5 ml with each patient demand, take about 6 min for the patient-control module to refill from a reservoir, and deliver no more than 0.5 ml every 6 min, should the demand button be depressed continuously.<sup>75 76</sup> Efficacy and side effects may be comparable with the electronic devices.<sup>75</sup> However, as the device delivers a fixed volume with each demand, the amount of drug delivered in each bolus can only be altered by changing the concentration of drug in the reservoir. In addition, the opioid in the reservoir is much more easily accessible than that in locked electronic infusion devices.

Few significant problems as a result of malfunction have been identified. One of the more potentially serious episodes is that reported by Costigan,<sup>17</sup> where the absence of an ‘O’ ring allowed unrestricted flow of opioid from the reservoir. Fortunately, this was noticed before the device was attached to the patient.

### *Electronic PCA devices*

Electronic PCA devices allow more flexibility in the timing and amount of dose delivered. They can also be programmed to deliver a constant background infusion. They are designed to be ‘tamper proof’, so that access to the drug without using the key is impossible, at least unless the pump is damaged in the attempt. However, successful access has been achieved without machine breakage (unpublished observations). Reports of problems related to the use of electronic PCA devices seem to be more common, although that may reflect usage patterns.

These devices should ‘fail safe’ if any corruption to the program occurs. Reports in the literature describe ‘fail safe’ electrical corruption of the pump program as a result of disconnection from, or reconnection to, mains power.<sup>41 64</sup> In some instances, however, the machines did not ‘fail safe’. This led to spontaneously triggered bolus doses<sup>64</sup> or uncontrolled delivery of the entire syringe contents.<sup>63</sup> Modifications to both hardware and software appear to have overcome these problems in later machines,<sup>41</sup> although a report of repeated spontaneous triggering was published recently.<sup>13</sup>

Problems that allowed uncontrolled syphoning of syringe contents have also been reported, including failure of a damaged drive mechanism to retain the syringe plunger,<sup>46</sup> cracked glass PCA syringes,<sup>23 89</sup> and improperly secured PCA cassettes.<sup>22</sup> In all these instances, the PCA machine was elevated above the patient. Although placing the machine at or below patient heart level may minimize the risk of syphoning occurring,<sup>89</sup> the use of antisiphon valves, as well as antireflux valves, has been suggested.<sup>23 36</sup> The routine use of antireflux valves has been recommended for many years<sup>44</sup> but a respiratory arrest has resulted from a recent failure to use such a valve.<sup>68</sup> Faulty antireflux valves have also been reported.<sup>64 103</sup>

Other causes of equipment-related problems include patient tampering,<sup>2</sup> an excessive dose of opioid being delivered accidentally when tubing from the PCA syringe was not clamped while a new syringe was loaded<sup>103</sup> and the use of pumps close to an MRI machine<sup>49</sup> or in a hyperbaric chamber.<sup>78</sup>

## **Medical and nursing staff factors**

Operator errors have led to oversedation resulting from the programming of incorrect bolus dose size,<sup>103</sup> incorrect drug concentrations (with fatal results),<sup>24</sup> incorrect background infusions<sup>38</sup> and background infusions when none were

ordered.<sup>2</sup> It has been suggested that drug concentrations should be standardized within institutions to reduce the chance of program errors.<sup>42 80</sup>

Operator error is a reasonably common type of safety problem related to PCA use. Lin and colleagues,<sup>51</sup> believing that poorly designed interfaces promote human errors, used a human factors approach (which takes into account human capabilities and limitations) to redesign the user interface of a PCA machine. This resulted in significantly faster programming times and significantly fewer programming errors. They recommended that the task of interfacing with the machine should be made as transparent as possible and that human factors principles should be taken into account in the design and evaluation of medical equipment, as ease of use is just as important as reliability of delivery.

Incorrect checking procedures may lead to the 'wrong' syringe being placed in a PCA pump—for example, a syringe of bupivacaine and fentanyl intended for epidural use, and one of plain fentanyl intended for PCA, have been used for i.v. PCA, when morphine was ordered in both cases (unpublished observations).

The level of knowledge that nursing and medical staff have about PCA may also play a role in its safety and efficacy. The study by Coleman and Booker-Milburn<sup>15</sup> showed that the introduction of an acute pain service (APS) nurse, whose role included staff and patient education, led to improvements in analgesia and patient satisfaction with PCA and an increased use of oral analgesia after PCA therapy was stopped.

A study comparing PCA managed by an APS compared with surgeons in the same hospital but 1 yr later, revealed that patients whose PCA was supervised by the APS used significantly more opioid, were more likely to have adjustments made to the PCA dose in response to complaints about inadequate analgesia or side effects, were more likely to be ordered oral opioid analgesia after PCA rather than i.m. opioids, and had significantly fewer side effects.<sup>84</sup> It would seem that the APS used PCA technology in a different manner to non-APS physicians and was more likely to tailor the PCA 'prescription' to suit individual patients.

Inadequate knowledge about the risks of PCA and prescribing by more than one team (e.g. surgical team as well as the APS), have led to inappropriate prescriptions of supplementary opioids (by other routes) and sedative drugs.<sup>2 26 64 94</sup> This may lead to oversedation and respiratory depression.<sup>2 26 94</sup>

### **The PCA 'prescription'**

The PCA prescription includes the parameters that are programmed into the PCA machine, such as bolus dose, lockout interval, dose limits and background infusion, as well as the drugs used. Each may have some effect on the safety and efficacy of PCA.

### *Bolus dose*

The size of the bolus dose (demand dose) can influence the success or otherwise of PCA. The optimal dose will provide good pain relief with minimal side effects.<sup>65</sup> Owen and colleagues<sup>65</sup> studied the effects of a range of doses of morphine—0.5, 1, and 2 mg—and found that most patients who self-administered 0.5 mg were unable to achieve good pain relief, while patients who received 2 mg with every demand had a high incidence of respiratory depression. They concluded, therefore, that 1 mg was the optimal PCA bolus dose for morphine.

Camu and others<sup>7</sup> studied the effects of three different sized bolus doses of fentanyl—20, 40, and 60 µg—and also found that the larger dose was associated with an increased risk of respiratory depression. They concluded that the optimal dose of fentanyl for use in PCA was 40 µg. This is larger than the dose of fentanyl often used in clinical practice. However, in this study, each dose was infused over 10 min (the time of delivery was counted as the lockout period), which could alter the effect of that dose.

In a further attempt to obtain an optimal PCA dose, Love and colleagues<sup>52</sup> designed a hand piece that allowed patients to choose either a 0.5, 1, or 1.5 mg bolus dose of morphine. They compared the efficacy of this system against the usual PCA machine where dose size can only be altered by staff. No differences were found in pain relief, number of demands made, amount of morphine used, patient satisfaction, sleep, or nausea and vomiting. They concluded that the more complex system offered no advantage.

However, as Etches<sup>27</sup> correctly says, PCA is neither a 'one size fits all' or a 'set and forget' therapy. While it is appropriate to commence most patients with a 'standard' size bolus dose, factors such as patient age or a history of prior opioid use must be taken into account. These initial doses may then need to be altered in the light of subsequent pain reports or the onset of any side effects. When this is done, PCA can be better tailored to the individual patient.

The number of demands a patient makes, including the number of 'unsuccessful' demands, is often used as a guide to adjusting the size of the bolus dose. However, there may be a number of reasons for a high demand rate other than pain, including anxiety, patient confusion, or inappropriate patient use (see earlier). In the study by Owen and co-workers<sup>65</sup> mentioned above, patients who received 0.5 mg bolus doses of morphine and complained of poor pain control averaged only four demands each hour even though they could have made a demand every 5 min. That is, patients cannot be relied upon to increase the demand rate enough if the dose is too small.<sup>52</sup> The number of doses successfully delivered each hour could be used as an indication of the need for a change in bolus dose size. If a patient is uncomfortable and already receiving an average of three or more bolus doses an hour, it may be reasonable to consider an increase in dose.<sup>54</sup>

Post-operative PCA opioid requirements in adult patients are known to decrease as patient age increases.<sup>53</sup> In addition, the risk of respiratory depression with PCA use appears to be higher in the elderly patient,<sup>26</sup> and it has, therefore, been suggested that a lower PCA bolus dose should be used.<sup>27 48 53</sup>

The volume of the bolus dose is also a factor that can affect the safety of PCA. If the line into which the PCA opioid is being delivered becomes occluded, it has been recommended that an alarm should sound within three dose activations.<sup>44</sup> In this way, a maximum of three doses only could accumulate in the tubing in the event of an obstruction. In the PCA machine evaluated by Jackson and colleagues<sup>41</sup> the alarm sounded after three presses at 0.5 ml and two presses at 1 ml. It did not do so until 12 presses at 0.1 ml. Low volume bolus doses should, therefore, be avoided.<sup>41 42</sup>

It should be remembered that PCA is essentially a maintenance therapy and, therefore, a patient's pain should be controlled before PCA is started.<sup>27 54</sup>

### *Lockout interval*

The time from the end of delivery of one dose until the machine will respond to another demand is called the lockout interval. As this interval is seen as one of the safety features of a PCA machine, it should ideally take into account the time taken for the patient to feel the full effect of a dose in order to minimize the risk of side effects.<sup>33</sup> However, lockout periods of between 5 and 10 min are commonly prescribed in clinical practice, regardless of the opioid used, even though the full effect of a dose of i.v. morphine may not be seen for 15 min or more.<sup>33 54</sup> If lockout intervals are too long the effectiveness of PCA could be reduced. Shorter lockout periods are more likely to allow the problems of between-patient (8- to 10-fold<sup>53</sup>) and within-patient (in response to differing pain stimuli) variations in opioid requirements to be overcome.<sup>27</sup>

Ginsberg and co-workers<sup>33</sup> studied the effects of varying lockout intervals (7 or 11 min for morphine; 5 or 8 min for fentanyl) and noticed no difference in analgesia, anxiety, or side effects.

### *Dose limits*

Limits to the maximum amount of opioid that can be delivered over a certain period (commonly hourly or 4-hourly limits) can be programmed into most PCA machines. Dose limits for morphine are commonly set at 10 mg in 1 h or 30 mg in 4 h.

For PCA to be used effectively, a wide range of opioid requirements needs to be tolerated. However, there is no reliable method of determining how much opioid a patient will require for analgesia, far less how much will result in dangerous side effects. The signs of excessive morphine dose can present well before these preset limits are reached

and, to date, there is no good evidence to show that patients have benefited from their inclusion in PCA prescriptions.<sup>27</sup>

So-called 'safety factors', such as lockout intervals and hourly limits, are no substitution for educated and vigilant monitoring of the patient receiving PCA.

### *Background infusions*

Background (or concurrent continuous) infusions can be delivered by most electronic PCA machines. It had been hoped that the use of an infusion, in addition to bolus doses on demand, would improve analgesia and allow patients to sleep better without waking in severe pain. The drawback is that the opioid will continue to be delivered, regardless of the sedation level of the patient.

Most studies comparing PCA with and without a background infusion have been unable to show that the addition of the infusion improved pain relief<sup>20 55 67</sup> or sleep.<sup>67</sup> However, they also report no difference in the number of demands made,<sup>20 55 67</sup> an increase in the total amount of opioid delivered<sup>20 55 67</sup> and an increase in the incidence of side effects, including respiratory depression, when a background infusion is used. Audits of large numbers of adult patients have also shown that the risk of respiratory depression is increased when a background infusion is prescribed.<sup>29 64 81 80</sup> Programming errors may also increase when background infusions are prescribed.<sup>2 67</sup>

In adults, the routine use of a background infusion is, therefore, not recommended. However, relative safety may be improved if a patient's opioid requirements are already known. A background infusion may be suitable in patients who are opioid-tolerant and in opioid-naïve patients who show high opioid requirements or complain of waking in severe pain at night.<sup>27 54</sup>

In children, the use of a background infusion may improve sleep at night,<sup>20</sup> but fails to improve pain relief and may significantly increase the risk of hypoxaemia.<sup>20 57</sup>

PCA devices have been developed that alter the rate of a background infusion according to the demands made by the patient,<sup>40 77</sup> but these devices are not yet in common clinical practice.

### *Opioid drugs used in PCA*

Mather and Woodhouse<sup>55</sup> believe that the success of PCA is independent of the agent used (whether high or low potency, or high or low lipophilicity) and more likely to be affected by the PCA parameters prescribed.

Certainly there is little evidence to suggest major differences in efficacy or side effects between morphine and other commonly used opioids such as pethidine,<sup>85 105</sup> hydromorphone,<sup>72</sup> fentanyl,<sup>105</sup> and oxycodone,<sup>82</sup> although a greater incidence of pruritus may be seen with morphine.<sup>105</sup> Tramadol may have similar analgesic effects to morphine but the incidence of nausea and vomiting may also be greater, while sedation may be decreased.<sup>66</sup>

It should be remembered that these results look across patient populations and it may be that individual responses are highly variable. If drug-related side effects fail to respond to specific treatment, then some patients may experience fewer side effects if a change to another opioid is made.<sup>62</sup>

Any of the opioid-related side effects can occur during PCA therapy but the side effect that causes most concern is respiratory depression. Figures from most audits suggest that the overall incidence in patients using PCA ranges from 0.1 to 0.8%.<sup>2 26 29 64 80 81 101</sup> However, incidences of 1.1 to 3.9% have been found when a concurrent background infusion is used.<sup>29 64 80 81</sup>

Apart from the addition of a background infusion, the risk of respiratory depression with PCA appears to be increased in the elderly patient,<sup>26 80</sup> in patients with OSA,<sup>26 81</sup> when concurrent sedatives or additional opioids are given,<sup>2 26 29</sup> or if patients become hypovolaemic.<sup>26</sup>

Comparison of the risks of respiratory depression with PCA and more conventional opioid analgesic techniques is difficult, as there is a paucity of data relating to the latter methods. The incidence of respiratory depression with conventional methods of opioid administration is probably in the range of 0.2 to 0.9%<sup>5</sup> and an incidence of 1.7% has been reported with continuous i.v. infusions.<sup>80</sup>

Choice of opioid may be more important when there is a need to consider the possible effects of opioid metabolites. In patients with renal failure the use of a drug with no active metabolites, such as fentanyl, might be preferred.<sup>55</sup> Problems resulting from the use of pethidine may occur even in the absence of renal impairment. Norpethidine toxicity, which results in a spectrum of side effects ranging from anxiety and agitation to myoclonic jerks and grand mal seizures (all of which may occur within 24 h of starting therapy) have followed prolonged use and/or high doses of pethidine.<sup>35 56 86</sup>

As the aim of PCA is to allow patients to determine their own opioid requirements, and as the doses required in order to achieve reasonable analgesia are unpredictable and vary enormously between patients, it may be best to avoid the use of pethidine with PCA. If there is no alternative to pethidine, it has been suggested (in patients without renal impairment) that doses be limited to no more than 1000–1200 mg in the first 24 h and that subsequent 24 h doses be lower still.<sup>35 86</sup>

#### *Addition of non-opioid drugs to PCA*

Non-opioid analgesic drugs such as ketamine<sup>1</sup> have been added to the opioid in PCA in attempts to improve analgesia and possibly minimize side effects. There is as yet no clear evidence to suggest any benefit from the combination compared with the independent administration of the same drug. As patient opioid requirements are known to vary widely, the amount of adjuvant drug delivered will also vary. Therefore, the practice of combining drugs in the same syringe could lead to an inadequate effect of the adjuvant drug in some patients, and excessive effect in others.

In attempts to minimize nausea and vomiting associated with PCA opioids, antiemetics such as droperidol<sup>30 92 99</sup> and cyclizine<sup>99</sup> have been added to PCA opioid syringes. Again, because of differing patient opioid requirements, the amount of antiemetic delivered could range from ineffective to excessive. Reporting on the results of a systematic search of trials investigating the effects of adding droperidol to PCA morphine, Tramer and colleagues<sup>92</sup> suggest that the total daily dose of droperidol administered should be kept to less than 4 mg in order to minimize the chance of side effects.

The practice of adding antiemetics is still controversial. As adverse effects of droperidol are dose-dependent, the risk of side effects will increase with increased use of PCA.<sup>106</sup> Cost-effectiveness must also be considered, as the routine addition of an antiemetic to PCA opioid means that all patients receive the drugs even when not all patients need them.<sup>106</sup> Tramer and colleagues<sup>92</sup> concluded that if 100 patients are treated in this manner, 30 will benefit. Gan and others<sup>30</sup> compared the addition of droperidol to PCA morphine with droperidol given separately and found both regimens to be equally as effective.

## **Conclusions**

PCA can be a very effective and safe method of pain relief and may allow easier individualization of therapy compared with conventional methods of opioid analgesia. However, it is not a 'one size fits all' or a 'set and forget' therapy and original prescriptions may need to be adjusted if maximal benefit is to be given to all patients. Efficacy and safety will also be increased if attention is paid to the factors outlined above. Thus, the success or otherwise of PCA lies in how well it is used.

This comment applies equally to conventional techniques for opioid administration. Effective pain relief requires flexibility in dose regimens, the ability to deliver the dose to the patient truly 'on demand' (i.e. 'patient-controlled'), regular monitoring of adequacy of analgesia and of any drug-related side effects, and the use of these parameters to individualize treatment. PCA devices really only facilitate this process. Setting aside patient preference and any arguments about the pros and cons of i.m. or s.c. injections, if similar attention can be given to other methods of opioid administration, conventional methods of analgesia could be as effective as PCA in many patients. However, in many busy hospital wards, staff numbers, time, attitudes, and knowledge may serve to limit the efficacy of nurse-administered pain relief. It is, therefore, likely that the popularity of PCA will continue and that PCA will remain a commonly used method of analgesia.

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