Safe IV Opioid Titration in Patients With Severe Acute Pain

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Providing Effective Pain Control

Providing effective pain control while minimizing opioid-induced adverse effects in patients with severe acute pain presents special challenges for clinicians who work in PACUs, outpatient surgery settings, emergency departments (EDs), and intensive care units (ICUs) because they must also deal with the additional central nervous system depression caused by the sedative and anesthetic agents that are administered intraoperatively, and sometimes throughout care. Rapid analgesia must be provided to patients who are in a nonsteady state, and that adds to the complexity of titration.1 (Steady state is achieved when the rate of excretion of a drug equals the rate at which the drug enters the system.) Furthermore, many of these patients are opioid-naïve, which places them at greater risk for adverse opioid-induced effects, particularly excessive sedation and respiratory depression.

Less difficulty is experienced when a multimodality approach is used in patients with acute pain.2,3 Combinations of analgesics improve pain relief with lower analgesic doses, and lower doses can result in fewer adverse effects. If a nonsteroidal anti-inflammatory drug (NSAID) has not already been given and is not relatively contraindicated, it can be started on admission. Epidural opioids are usually combined with local anesthetics to reduce the opioid dose. Acetaminophen may be added to any treatment plan.3

Opioid Selection for Initial Titration in Patients With Acute Pain

The mu-agonist opioids—morphine, hydromorphone, and fentanyl—are most commonly used for initial titration in patients with severe acute pain, but nurses often ask which opioid is the best choice. Important patient characteristics to consider when selecting an opioid for titration include previous exposure to and tolerance of opioids, current organ function, and hemodynamic stability. For example, fentanyl is favored in patients with any type of end-organ failure.3 It also produces minimal hemodynamic effects, which adds to its appeal for patients with an unstable blood pressure.

In addition to patient characteristics, the pharmacokinetics of the opioids and the goals of treatment are considered when deciding which opioid is best for titration.3 Morphine is hydrophilic (readily absorbed in aqueous solution) and requires several minutes to yield peak effects after intravenous (IV) administration; the more lipophilic (readily absorbed in fatty tissue) opioids such as fentanyl produce peak effects almost immediately when given intravenously. Hydromorphone is less hydrophilic than morphine and less lipophilic than fentanyl and has an intermediate effect. For patients who have undergone major surgery, some PACU nurses like to administer a few doses of fentanyl, and then follow with either hydromorphone or morphine for longer lasting analgesia. Although it makes sense to use a fast-onset opioid such as fentanyl in patients presenting with severe, escalating pain, it may not be necessary and can complicate the assessment process in those with less severe pain. When opioids are combined and adverse effects occur in this situation, it is difficult to interpret which opioid might be the culprit. Therefore, a general principle of initial titration in patients with acute pain is to keep in mind the

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ongoing pain treatment plan. As an example, consider the patient who is admitted to the PACU and will have hydromorphone IV patient-controlled analgesia (PCA) for ongoing postoperative pain management. Unless the patient has severe, rapidly escalating pain on admission, it makes sense to begin titration with hydromorphone so that the effects (both pain relief and adverse effects) of the drug that will be used for the next day or so can be evaluated more easily.3

**Titration Protocols for Severe Acute Pain**

Some studies have shown that standard practices related to titration in patients with acute pain may lead to undertreated pain. Although opioid-induced adverse effects are dose-related and have been identified as a limiting factor during titration in postoperative patients,1 some researchers suggest that the customary doses used to manage immediate postoperative pain are well tolerated and that an exaggerated fear of adverse effects may pose the greater threat.4 A placebo-controlled study of 88 patients after abdominal hysterectomy or prostatectomy found that a single IV bolus dose of 7.5 mg of morphine did not cause any clinically significant cardiovascular or respiratory adverse effects but provided only slight relief of moderate to severe pain in the PACU.5 Nevertheless, single large IV boluses are associated with high peak effects and must be administered with caution and careful assessment for adverse effects.3

A large prospective, nonrandomized study illustrated the challenges of finding a balance between comfort and adverse effects in the immediate postoperative period by evaluating four different dosing regimens.6 Each regimen consisted of administering 2 to 3 mg IV morphine boluses until patients experienced pain relief or adverse effects. The regimens were: Group 1—boluses given every 10 minutes to a limit of five boluses (N = 400); group 2—boluses given every 5 minutes to a limit of five boluses (N = 400); and groups 3 and 4—boluses given in unlimited numbers every 5 minutes (N = 400 each group). Groups 1, 2, and 3 received subcutaneous morphine 4 hours after IV titration, and group 4 received subcutaneous morphine 2 hours after IV titration. Group 4 had the highest percentage of pain relief (73%) at the end of the PACU period, but sedation was dose-related and was highest in groups 3 (62%) and 4 (61%), both of which received an unlimited number of IV boluses compared with group 1 (27%), which received the more conservative regimen of IV boluses every 10 minutes up to a maximum of five boluses.6

Although weight is not recommended for the calculation of opioid doses in adults,3 most guidelines for titration in patients with severe pain in the ED setting call for a starting opioid dose based on weight, ie, 0.1 mg/kg of IV morphine (approximately 7 mg in a 150-lb person) followed by titration until adequate pain relief is achieved; however, a prospective study of 119 patients showed that this starting dose resulted in 67% of the patients’ experiencing less than 50% pain relief within 30 minutes; no patient required an opioid antagonist (eg, naloxone).8 A later randomized controlled study (N = 280) found that 0.15 mg/kg (approximately 10 mg in a 150-lb person) provided pain relief superior to 0.1 mg/kg in the ED.9 This higher dose was supported in another study of 621 patients with severe pain in the ED; 3-mg increment doses of IV morphine (2 mg in older patients) were administered every 5 minutes to comfort or “sleep” and resulted in adequate pain relief in 82% of the patients.10 The mean morphine dose administered was 10.5 mg (0.16 mg/kg), the median time of titration was 15 minutes, and the median number of boluses was three. Nausea and vomiting were the most common adverse effects (4.2%), and mild respiratory depression occurred in 2.6%. These researchers stressed the need to use flexible rather than fixed (mg/kg) dosing during titration. Although no serious adverse events were reported in this study, it is likely that “sleep” during titration might have actually been excessive sedation. This type of rapid dosing always carries the risk for excessive sedation and respiratory depression, and these parameters must be watched closely during titration and for at least 3 hours after the peak of the last opioid dose administered.11

A patient-driven titration procedure dubbed the “1 + 1 hydromorphone protocol” may provide an alternative to traditional procedures. The protocol involved the administration of 1 mg of hydromorphone to 223 patients in the ED who had severe pain. That was followed by assessment and the offer of another 1-mg dose 15 minutes later.12 This led to adequate analgesia in 95% of the patients. A follow-up study (N = 224)
comparing this protocol with physician-driven management, which was described as being reflective of current practice and consisted of the administration of an IV opioid dose with no offer of additional analgesia, found that 94% of the patients in the 1 + 1 group achieved adequate analgesia within 60 minutes of protocol initiation and had significantly greater decreases in pain than did the physician-driven group. Just 10% of the patients in the physician-driven group were given a follow-up dose of analgesia. Adverse effects were similar in the groups, and no one required naloxone.

Another protocol, which called for the administration of 2 mg of IV hydromorphone over 2 to 3 minutes, relieved pain effectively and rapidly (within 5 minutes) in the ED but resulted in one or more periods of desaturation in 26% of the patients in one prospective study. The researchers appropriately concluded that 2 mg of IV hydromorphone is too much opioid to be given routinely to opioid-naive patients as a single initial dose.

Titration in Older Adults With Severe Acute Pain

Age is an important consideration during opioid titration, and a common recommendation is to reduce the initial dose in older patients; however, one study (N = 224; 68% young adults, 32% older adults) showed that the dose of IV morphine required during postoperative titration to achieve adequate pain relief was not significantly different in older (0.14 mg/kg) compared with younger (0.15 mg/kg) patients. Higher pain intensity was associated with higher morphine requirements; no patients required naloxone. It is important to note that the lack of difference noted in this research was assessed after normalizing for body weight, which was lower in the older patients. An earlier study (N = 875 young adults, 175 old adults) also found no differences in morphine requirements in age groups after doses were normalized for body weight.

Nevertheless, conservative initial opioid doses, along with careful monitoring during titration, continue to be recommended in the older adult population; doses should be increased based on patients’ responses rather than specific age. An observational study (N = 418) demonstrated the safety of a postoperative protocol for patients older than age 65 in whom IV morphine was started at a dose one-third less than for younger patients. This method was found to be as safe and efficacious for the older patients at the lower dose (2 mg) as for younger patients at the higher dose (3 mg).

Patients Who Have Severe Pain and Are Sedated Excessively

The presence of sedation does not necessarily mean that patients are comfortable, and despite being excessively sedated, some patients will report pain. Further, sleep during opioid titration is not normal sleep but primarily the result of the sedative effects of the opioid. Sedation must be monitored closely during opioid titration, and opioid doses should not be increased (titration should be stopped) in patients who are sedated excessively. To prevent clinically significant opioid-induced respiratory depression, nurses must advocate for adding or increasing the dose of nonopioid analgesics (local anesthetics or full doses of acetaminophen or an NSAID) rather than administering increased opioid doses to a patient who is both sedated excessively and in severe pain. Ensuring safe pain management is a primary objective.

Dosing to a Specific Pain Intensity

Research has shown that the relationship between visual analog scale (VAS) pain intensity scores and dose requirement during and after titration is not linear, suggesting that many factors influence pain and its relief and that there is no specific dose that will relieve pain of a specific intensity. Pain was assessed in a study of more than 3,000 patients admitted consecutively to the PACU, and those with a 0 to 100 VAS score above 30 were titrated with 3 mg of IV morphine every 5 minutes until their VAS scores were below 30. The mean morphine requirement to obtain pain relief was 12 mg. A VAS score of 70 or higher was indicative of severe pain based on the need for a morphine dose of more than 0.15 mg/kg, which corresponds with the 10-mg morphine dose suggested by other research as being appropriate for some patients with severe pain. However, when VAS scores were analyzed, a sigmoid rather than linear relationship between morphine requirement and pain intensity was noted, as demonstrated by pain intensities that
changed little with initial doses and then decreased rapidly with the final incremental dose. Although this study has noted limitations, it underscores the importance of individualized selection of analgesic doses and systematic assessment of response during and after titration.

An interesting prospective, observational study evaluated patients’ desire for pain medication in 104 patients with acute pain and found that no single pain intensity can reliably predict a given patient’s analgesic requirements or desire for additional analgesia. Dosing to a specific pain intensity (eg, IV morphine 2 mg for pain ratings of 1–3 [on a scale of 0–10], 4 mg for pain ratings of 4 to 6, and 6 mg for pain ratings of 7 to 10) can be dangerous and is strongly discouraged. Numerous other factors, such as patient comorbidities; previous opioid exposure; desire for pain medication; and the presence of adverse effects, particularly excessive sedation and respiratory depression, must be considered when selecting an opioid dose.

Transfer of Care: Hand-off Communication

The patient’s pain control is an important consideration when transferring care from one area to another. Some EDs, short-stay units, outpatient surgery units, and PACUs establish a pain rating goal (also called comfort-function goal) of at least 4 (on a scale of 0–10) before discharge; however, the expectation that all patients must be discharged from these areas with pain ratings below an arbitrary number can lead to the unsafe administration of further opioid doses to patients who are excessively sedated, and the practice is widely discouraged. All team members must appreciate that it may take time after transfer to the clinical unit to establish optimal pain control in patients who had severe pain on admission to an area like the PACU or ED, and that achieving optimal pain relief is best viewed on a continuum, with the primary objective being to provide both effective and safe analgesia. Optimal pain relief is the responsibility of every member of the health care team and begins with analgesic titration, for example, in the PACU or ED followed by continued prompt assessment and analgesic administration after discharge to the clinical unit to achieve pain ratings that allow patients to meet their functional goals with relative ease.

Although it is not always possible to achieve a patient’s comfort-function goal within the short time the patient is an area like the PACU or ED, the goal provides direction for ongoing care. Important information to give to the nurse assuming care of the patient is the patient’s comfort-function goal, how close the patient is to achieving it, what has been done thus far to achieve it (analgesics, doses, and times of administration), and how well the patient has tolerated the administration of analgesics (adverse effects).

References


