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Chapter

The Utility of Patient-Controlled Analgesia for Managing Acute Pain in the Emergency Department

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Abstract

There is a growing expectation of physicians to treat acute pain more aggressively in the emergency department (ED). This has contributed to an increase in opiate prescribing practices that has resulted in a crisis of medication abuse and misuse. The resultant backlash against physicians has created a void within the realm of acute pain management, as physicians search for a means to treat their patients in a way that is both empathetic and responsible. In an effort to combat this growing epidemic, alternative means of pain control are being explored. Patient-controlled analgesia devices (PCADs) have been used extensively in multiple fields of medicine and have demonstrated significant clinical utility for treating pain postoperatively; however there is a dearth of evidence to support their use within the acute care setting. Due to this lack of evidence, PCADs have not been widely implemented in the ED. Recent studies have shown that the use of PCADs may improve objective pain scores and increase both patient and nurse satisfaction while reducing the likelihood of developing chronic pain. The economic feasibility of this undertaking remains unclear; however there is strong evidence for the clinical utility of this modality to treat acute pain in this population.

Keywords: pain, emergency department, treatment, patient-controlled analgesia, patients-controlled analgesia devices, oligoanalgesia, patient satisfaction, patient autonomy

1. Introduction

Although there are discrepancies in prevalence among different emergency departments (ED), pain is the primary presenting complaint in 45–75% of all ED visits [1]. To put this in perspective, it is important to note just how significantly the landscape of the ED has changed over the last 20 years. Between 1996 and 2015 there was a 46% increase in the utilization of emergency services in the United States with 136 million people seeking emergency care in 2015. This equates to over 100 million patients presenting to the ED in acute pain [2]. As emergency room visits continue to grow every year, so does the need to find effective treatments for patients experiencing such episodes. Currently, the standard of care in most EDs includes the use of intravenous (IV) opiates which are titrated subjectively according to patient complaints; however this is often significantly impacted by outside forces including nursing availability and patient census. Unfortunately, in many

cases a baseline pain score is not adequately established which leads to substantial variations in treatment, with the end result being that patients experience increased pain and less satisfaction with their care. Inadequate pain relief, otherwise known as oligoanalgesia, can lead to a myriad of psychological and physiologic consequences which can extend far beyond the initial injury. Thus, early intervention to treat acute pain is integral to effective patient care.

Current guidelines established by the American Academy of Emergency Medicine Physicians suggest that "parenteral opioids should be titrated regardless of the initial dosing regimen (i.e., weight-based, fixed, or nurse-initiated) at 20–30 minutes intervals until pain is relieved to acceptable levels with frequent re-assessment and evaluation for development of opioid-related adverse effects." [3] Although this schedule may appear ideal, re-dosing of medication at this frequency requires significant time from nursing staff and physicians and may prove difficult given the demanding pace characteristic of most emergency departments. This is problematic from both a practice and administrative standpoint, as increasing patient volumes are taxing our already overburdened EDs. From a clinical perspective this translates into substantial delays in achieving adequate analgesia and prolonged wait times between doses for patients in acute pain. In light of these issues, it is clear that physicians and ED staff must reconsider their current approach to pain management and explore novel methods to improve treatment efficiency without sacrificing quality.

Within the last 20 years, there have been increasing demands placed on ED physicians and staff to aggressively treat acute pain in an effort to improve patient satisfaction, improve outcomes and meet core measures. Consequently, the "Emergency Department Measure Set" was developed by the Centers for Medicare and Medicaid Services (CMS) and has been adopted by The Joint Commission's ORYX program in order to maintain alignment with CMS reporting requirements [4]. These, and many additional factors, have contributed to an increase in opiate prescriptions which has resulted in a crisis of medication abuse and misuse which continues to plague EDs all over the country. The resultant backlash against both physicians and pharmaceutical companies has created a void within the realm of acute pain management, as physicians search for a means to treat their patients in a way that is both empathetic and responsible. Patient-controlled analgesia, which has long been accepted as an appropriate form of pain management in post-surgical care, has shown promising results in its application in the acute care setting and may prove to be an invaluable tool which may be used for effective multimodal pain control.

Patient-controlled analgesia offers multiple benefits to patients in acute pain. The devices themselves are relatively easy to set up, they reduce delays and treatment variability, and provide patients with increased control of their analgesic needs. Delivery of medication via this method also avoids the peaks and troughs in blood levels associated with irregular bolus dosing and allows for a steady-state concentration within the plasma [5]. By controlling both the frequency and quantity of medication being delivered, patients are able to achieve improved levels of analgesia while minimizing the risk of adverse events. Dynamic systems such as this allow for increased patient autonomy and improved personalization of care without the requirement of additional supervision by staff.

2. The risks of undertreating pain

Although many patients achieve full resolution of pain after an acute episode, it has been demonstrated that pain may persist in up to 21% of patients being

discharged from the ED [6, 7]. The precise mechanism for the transition from acute to chronic pain is poorly understood, however, the practical implications of this issue are becoming increasingly apparent as the number of patients experiencing chronic pain has reached epic proportions. Patients experiencing traumatic pain and acute abdominal pain are especially at risk for developing chronic pain and these populations make up a significant amount of ED admissions. In addition to the mechanism of injury there is also a myriad of different symptoms which can predispose individuals to developing persistent pain including age, gender, genetics, pain trajectory and pre-existing anxiety/depression [7]. Although many of these cannot be adequately controlled for in an acute setting, pain trajectory is one of the main factors that can be actively affected by emergency physicians and PCADs have shown increasing effectiveness in this regard. A recent study conducted by Rockett et al., demonstrated that utilization of PCADs in the emergency room significantly decreased the number of patients experiencing persistent pain from non-traumatic abdominal injuries, 6 months post-injury. "The study findings suggest that it may be possible to reduce persistent pain (at least in patients with abdominal pain) by delivering better acute pain management" [7]. Consequently, it appears that increased utilization of patient-controlled analgesia may be a viable alternative to our current practice model which can provide increased comfort to both provider and patient while diminishing the number of patients developing persistent pain.

3. Background on patient-controlled analgesia devices

Patient-controlled analgesia devices were first developed in the 1960s in an effort to allow patients to control their pain without the requirement of frequent nursing intervention [8]. The device itself has gone through significant changes with regards to technology, however its basic purpose remains the same. PCADs generally consist of a volumetric pump which contains opiate medications that may be delivered intravenously once a patient presses the button controlling outflow. The device often contains additional control measures including anti-siphon and anti-reflux valves which allow for precision in the quantity of dosing while minimizing the risk of inadvertent medication administration [9]. Physicians may control several variables including the loading dose, demand/bolus dose, lock-out interval and quantity required for continuous infusions [5]. In the initial stage of treatment a bolus or loading dose is commonly administered to establish a baseline degree of analgesia. Afterwards there is a lock-out period during which the pump does not release any additional medication. Patients may continue to press the release trigger during this period of time but no additional doses are released. A number of demand requests are logged by the device and can help guide physicians when attempting to determine an optimal dosing strategy for each individual patient.

Dosing parameters are generally set by the physician and should reflect the level of pain being experienced by the patient as well as the patient's expected length of stay in the ED, body habitus, and previous use and tolerance to analgesics. An optimal dosing strategy is one that would allow for maximum analgesia while minimizing potential side effects. With traditional dosing methods this is difficult to achieve. To remedy this, several protocols have been developed for use in patient-controlled analgesia which have been demonstrated to be effective in most patients. For instance, a common protocol used in both the US and UK includes a loading dose of 1 mg of morphine followed by a 5 minutes lockout period and subsequent bolus dosing of 1 mg [10]. Lock-out times are an important safety concern among physicians for obvious reasons, however studies show that increments between 5

and 10 minutes are generally considered safe regardless of the type of medication being used [5]. These parameters can be altered in real time in response to patient feedback. This allows for more dynamic analgesic control which has clear benefits for patients presenting to the ED with acute pain.

It is important to note that there are distinct differences between machine programming parameters for postoperative patients versus those in an emergency setting. A prime example of this is the use of background/continuous infusions. Utilization of this setting allows for increased baseline plasma levels of medication and may improve pain control in certain populations [5]. Although the literature supports this type of treatment in post-operative patients, it may not be ideal for the ED as it requires close maintenance by nursing staff. Additionally, research shows that it does not improve pain control significantly in this patient population and may actually lead to increased incidence of adverse events including respiratory depression and sedation [5]. In another study which specifically examined the use of background infusions in the ED it was also found that manipulation of this setting led to an increased rate of pump programming errors. Although the patients involved in this study did not sustain any long-term side effects, there was an increase in the rate of sedation which further supports that this setting is of limited use in the ED [11].

4. General principles in acute pain management

The use of opiate medication in acute pain management has been a staple in most busy emergency departments. They work via blockade of μ-opioid receptor-channels which inhibit the transmission of pain in the central nervous system. In general, pure μ agonists have a high degree of variation in terms of dose-response relationships among individuals and require close monitoring by medical staff [1]. Side effects of medications which target μ-opioid receptors include respiratory depression, sedation, nausea, vomiting and pruritus. The frequency of adverse events associated with opiate administration in an acute care setting is difficult to predict and often, a trial of medication is necessary before sensitivities can be established. The disparities among these patients in regard to appropriate analgesic control is multifactorial and includes differences in opiate tolerance, pain severity, previous opiate use, body habitus, height and weight, dosing quantity and the frequency of administration. Many of these factors are difficult to control in a fast-paced environment such as the emergency room. However, utilization of patient-controlled analgesia may help offset these issues by allowing patients to take a more active role in the management of their pain.

Common opiates used in this setting include morphine, hydromorphone, and fentanyl. They are widely available and physicians are familiar with their general dose-response relationships and safety profiles. Although studies have shown that usage of specific opiates does not necessarily correlate with significant differences in pain scores among patients using PCADs, this does not obfuscate the need for appropriate medication selection [5]. Thus, it is important to take an individualized approach when selecting which medication a patient will receive.

4.1 Opiate selection

4.1.1 Morphine

Morphine is the most commonly used opiate in EDs which is likely due to its intermediate half-life, moderate strength and familiarity among hospital staff.

The average half-life of morphine is 1.5–2 hours with peak intensity usually being established in approximately 90 minutes [12, 13]. This makes it an effective medication for pain control as its effects wear off in a reasonable amount of time and it is generally well tolerated. Analgesic dosing is usually 0.5–3 mg per bolus, with a lockout period of 5–20 minutes [5]. Due to morphine's longer onset of action it could accumulate in the plasma and could result in analgesic stacking if the lockout times are not calibrated appropriately. Although this could theoretically lead to a significant increase in adverse events; it is very rarely seen clinically when administering conventional PCAD level dosages [5]. Additionally, it is important to recall that morphine has a higher degree of histamine release than other opiates in its class. This may preclude it from use in patients that have a history or pruritus or flushing after morphine use. This is, however, only a relative contraindication and may not manifest as readily due to the decreased quantity of medication administered in each dose.

4.1.2 Hydromorphone (Dilaudid)

Hydromorphone is a medication that is both incredibly effective but also increasingly maligned by emergency physicians. It has gained notoriety due to its strength and efficacy in acute pain management and it is widely available in most EDs. Unfortunately, these attributes have also made it a popular drug of abuse among pain seekers and physicians remain wary of regular use. It is seven times more potent than morphine and is broken down into a biologically inactive metabolite which makes it an excellent candidate for patients requiring repeat dosing of opioid medications. It also has an improved side effect profile, including diminished histamine release, which results in less pruritus. The time to peak analgesic effect for hydromorphone is approximately 20 minutes and its dose equivalent when compared to morphine ranges from 4–8 to 1 which can make precise conversions difficult [13]. Although hydromorphone is considerably more potent than morphine studies have demonstrated that PCADs utilizing hydromorphone are equally effective in comparison to morphine PCADs when dosing toward equianalgesia [13]. Typical dosing for hydromorphone is 0.1–0.5 mg followed by a 5–15 minutes lockout interval [5]. A recent study comparing the efficacy of morphine and hydromorphone concluded that the side effect profile is similar between morphine and hydromorphone in terms of opiate-related side effects [13]. Additionally, pain control and patient satisfaction were also equivalent. Thus it appears that prioritization of one medication over another should likely be guided by patient history as each drug has a unique side effect profile which may preclude it from usage in certain groups. Unfortunately, due to the past history of hydromorphone misuse in the ED it will likely remain as a secondary agent.

4.1.3 Fentanyl

Fentanyl has long been a preferred drug in ED for patients in severe acute pain as it reaches peak concentrations quickly within 1–2 minutes and has a short half-life (6 minutes) [14]. This makes it an excellent candidate for patients that require timely analgesia without a lengthy period of sedation. Fentanyl is well suited for use with PCADs as repetitive dosing at appropriate lockout intervals has not been shown to lead to excessive accumulation in the plasma and thus, does not result in analgesic stacking [15]. Intravenous dosing of Fentanyl usually consists of 15–50 μg followed by a 3–10 minutes lockout period. Although intravenous administration of this medication remains popular, novel delivery methods have recently been explored which show promising results. Transdermal Fentanyl is becoming

increasingly popular in the realm of patient-controlled analgesia, as it has been demonstrated to have increased ease of use (i.e. improved confidence/comfort with the device, dosing, and knowledge/understanding) and less technical issues associated with autonomous administration. Although the transdermal route of delivery has been notorious for inconsistencies in medication delivery/absorption it appears as though transdermal Fentanyl produces results in terms of pain control and patient satisfaction which are on par with morphine [16]. Additionally, studies have also demonstrated that it has an improved side effect profile and has less frequent adverse events associated with its use, including hypotension, hypoventilation, nausea, vomiting, pruritus and tachycardia [17]. As such, it may be a viable alternative for patients who have sensitivities to more traditional medications like morphine.

4.1.4 Meperidine (Demerol)

Meperidine is another common opiate that has been studied as an alternative to morphine for use in patient-controlled analgesia, however it has limited utility in the ED. Meperidine has numerous disadvantages, including a short duration of action, a very poor analgesic effect at common doses (25–50 mg), abuse potential, and concerning drug interactions. Meperidine has serotonergic and noradrenergic properties and has the potential to induce serotonin syndrome in patients taking selective serotonin reuptake inhibitors and monoamine oxidase inhibitors [18].

A head-to-head comparison was recently done which evaluated meperidine versus morphine use in patients utilizing patient-controlled analgesia who were chronic opiate users presenting to the emergency room in acute pain. Levels of analgesia among the two groups were similar; however, patients using meperidine had a greater likelihood of experiencing withdrawal symptoms afterwards which was reflected in increased COWS scores [19]. Additionally, meperidine has a less favorable side effect profile when compared to morphine as it is broken down into the biologically active metabolite, normeperidine, which is a neurotoxin that can accumulate in the plasma and increases the risk of seizures, delirium, tremors, myoclonus and restlessness [5, 20]. It is important that patients be closely monitored when receiving this medication. Increased need for staff supervision would likely negate many of the benefits which PCADs provide in an acute care setting. For these reasons, meperidine is a poor choice for acute pain and should be used with caution in the ED [5, 21].

4.2 Additional modes of administration

There are numerous alternative modes of medication administration in patient-controlled analgesia including oral/sublingual, transdermal, intranasal, inhalational, and epidural preparations [22]. Intravenous delivery has remained the most popular route of administration, however, studies have shown promising results for several of these alternatives. Oral/sublingual medication, in particular, may have increased utility in the ED as it has the added benefit of being less invasive than standard IV therapy and may be preferable for some patients who are not candidates for inpatient admission. A meta-analysis of 13 studies demonstrated that sublingual medication administration had less side effects and a statistically significant improvement in global assessment scores (defined as "good" or "excellent") as well as trends which indicated improvements in VAS when compared to both morphine and transdermal Fentanyl [23].

In light of this information, a novel, non-invasive delivery system has recently been developed for the newly FDA approved medication, sufentanil.

This sublingual delivery device has been specifically designed for use in patient-controlled analgesia and has demonstrated excellent titratability and a rapid onset of action which makes it attractive for use in the ED [24]. Phase 3 trials have demonstrated that sublingual Sufentanil has greater efficacy for the treatment of pain than IV medications and has less incidence of oxygen desaturation in the populations being studied [24]. Additionally, a recently conducted prospective, randomized double-blind study has shown that patients receiving sublingual Sufentanil have a higher summed pain intensity difference and improved global assessment scores in comparison to placebo [25]. Although this initial data appears promising, further studies must be done in an acute care setting before this device can be recommended specifically for use in the emergency department.

In additional to oral preparations there may be increased utility for medication delivery via the intranasal or inhalation route as these may also decrease the need for IV insertion and reduce overall cost. Unfortunately there are still significant barriers which must be overcome before these devices become commonplace. Inhalational medication, in particular, offers clear benefits as it is non-invasive, has a rapid onset of action and improved bioavailability [8, 26]. It has not been embraced in its current form; however, due to technical issues with regard to medication delivery, and improper patient compliance. Intranasal administration has been plagued by similar issues; however this may change in the future as technology improves and devices are able to deliver medication more effectively.

For the sake of completeness, epidural preparations should be briefly discussed as they are widely utilized in the perioperative and postoperative setting and have been shown to be more effective at controlling pain than intravenous administration [8, 27]. Epidural delivery of medication allows for targeted placement of opiates adjacent to the spinal afferent pain receptors which may diminish the systemic effects seen with oral and intravenous administration. This would initially appear promising for ED physicians as they are continually searching for ways to reduce the quantities of opiates being prescribed to their patients. Unfortunately this requires placement of an epidural catheter by a trained physician (often an anesthesiologist) which would not be feasible within the scope of the emergency department. Thus, the feasibility of its implementation in this setting is limited.

5. Special populations

5.1 Children

PCAD usage is considered safe for autonomous use in children over 6 who are experiencing acute pain [5]. Studies have demonstrated that PCAD use in this population results in decreased total opiate use, improved analgesia and decreased adverse effects, making it an ideal alternative to standard therapy [28]. One of the main determinants which govern its effective use in this population is the ability of the child to understand how and why the device is being used. The child must be able to understand basic principles regarding their pain as they will be required to follow instructions on how to self-administer medication. Studies have demonstrated that PCAD use in children under 4 is ineffective due to the aforementioned issues; however, children between 4 and 6 may use the device with the caveat that they maintain close nursing oversight. The need for additional monitoring is important for patient safety but this may not be feasible in a busy ED. Parental controlled patient analgesia has been offered as an alternative to this but in order to be effective it requires one-on-one education from nursing staff which also takes

time and cooperation from a third party which may be cumbersome to facilitate. Parental controlled analgesia also has the added detractor that it removes the inherent benefits of patient autonomy which PCADs provide. Thus, it is unlikely to demonstrate a significant benefit over IV morphine for the purposes of acute pain management.

Morphine remains the most commonly used medication for patient-controlled analgesia in the pediatric population [28]. Typical dosing consists of a bolus of 10–20 μg/kg and a lockout period of 7–15 minutes [5]. As with all pain medications there are issues that may arise with prolonged administration of Morphine, which is especially concerning in the pediatric population. Cycling narcotics, especially in children who will be admitted, can help combat some of the sensitivities that are seen in relation to morphine utilization. Switching to medications such as hydromorphone can help decrease side effects like pruritus which may be both uncomfortable and alarming to many children. Hydromorphone, morphine and fentanyl are all considered safe for use in the pediatric population and they may be used interchangeably depending on response to treatment. A recent study found that hydromorphone to morphine switches for patient using PCADS was far more common (88.5% versus 11.5%) than vice versa. The most common reason for switching morphine to hydromorphone in this cohort was due to pruritus and inadequate pain control. Hydromorphone to morphine switches were more commonly due to nausea. Thus, physicians should monitor this population closely and change medications as necessary should any adverse events arise.

5.2 Geriatrics

Acute pain relief in the elderly can be challenging. Elderly patients presenting to the ED frequently have multiple comorbidities and physiologic issues which can affect the way in which analgesics are metabolized. Acute pain control in the geriatric population is an important topic to address because it is integral to their recovery. Studies have shown that unrelieved episodes of acute pain can result in decreased pulmonary function, sympathetic hyperactivity (including tachycardia and hypertension) and central neural sensitization which can lead to the development of chronic pain [29]. PCAD use is well suited for this population as it allows for individualized dosing, decreased fluctuations in opiate plasma concentration and improved pain control [30]. A recent study by Egbert which included 83 high-risk elderly men, demonstrated that PCAD use had improved analgesia without a concomitant increase in adverse events such as sedation. Additionally, the patient-controlled analgesia group reported that the PCAD was easier to use than traditional therapy [30].

Drug choice is important in the elderly as the pharmacokinetics and pharmacodynamic profile of opiate medications changes throughout the aging process. As we age there is an increase in body fat and decrease in total body water which alters drug metabolism. Therefore, fat soluble drugs such as fentanyl and meperidine have a higher volume of distribution and a longer duration of action which make them less attractive for use in this population [29]. Morphine is the most widely used medication for PCADs in the elderly and studies have demonstrated that the optimal loading dose is 1.0–1.5 mg/dose which should be followed by similar bolus dosing after a 5–7 minutes lockout period. It is important to note that water soluble drugs such as morphine have a higher plasma concentration in elderly patients due to their redsuced volume of distribution as well as increased levels of free active drug due to reduced albumin synthesis. As such, continuous infusions are contraindicated in this population as there is an increased frequency of adverse events, namely respiratory depression and hypotension [29].

5.3 Chronic opiate users

Pain control is notoriously difficult in patients who chronically use opiates and they often remain undertreated [31]. Although PCAD use in this population remains controversial, it may prove effective when used selectively [32]. Unlike patients who are opiate naive, bolus dosing in chronic opioid users may necessitate periodic re-adjustments, as larger doses are usually required with shorter lockout periods [31]. By providing these patients with a more uniform dose of medication ED physicians can avoid sedation while also decreasing the propensity for anxiety and cravings that occur frequently with IV therapy. Some physicians may also be worried about the potential for increased medication administration, should patients attempt to tamper with the device. This is usually not possible with standard pumps though, as they contain safety precautions and redundancies within the structure of the device which limit the potential for abuse. It should be noted however, that the "wrist-watch" type of PCAD contains a reservoir which is less secure than standard devices and it has a fixed lockout schedule which makes it less attractive for use in this population [31].

In regards to medication selection, morphine is a commonly used medication which remains effective, albeit at higher concentrations, even in patients that have developed a tolerance. Studies which directly evaluated morphine use in ED patients receiving patient-controlled analgesia are limited but, as noted previously, there is a clear benefit to using morphine over other alternatives for numerous reasons [19]. Hydromorphone is another alternative that might initially seem appealing, however there is a push to limit its use in the ED, especially for chronic opioid users, so it is unlikely that it would gain widespread acceptance. Alternatively, one medication which has shown good efficacy for the treatment of acute pain is oral transmucosal fentanyl. Studies show that this medication is effective in chronic opioid users with breakthrough pain and may be a viable alternative for patients where morphine is initially ineffective or patient sensitivities preclude its use [10].

6. Benefits of patient-controlled analgesia use in the ED

6.1 Opiate utilization

One of the more divisive topics relating to PCAD implementation in the emergency room relates to risk of abuse and reliance on opiates by patients provided with opiate analgesia. Initial systematic reviews regarding this subject demonstrated that patients using PCADs in the postoperative setting required less opiates than those undergoing standard therapy [8]. Unfortunately this does not appear to be the case for patients presenting to the ED. Evaluation of the most current randomized controlled trials for PCAD use in this population have demonstrated that patients receiving this therapy utilize a greater quantity of opiates than those receiving intravenous morphine [11, 33]. A recent study done by Bijur which included 636 patients presenting to the ED in acute pain, demonstrated that patients utilizing a PCAD required significantly more morphine (12.0 mg ± 4.3 versus 6.1 mg ± 2.9; 95% CI: 5.9 [5.2–6.4]) than those in the standard therapy group [11]. This data may seem worrisome at first but, as previously discussed, patients presenting to the ED with acute pain are notoriously undertreated. As such, the increased utilization of opiates in this population may reflect that patients need higher levels of analgesia than provided by standard measures of nurse administered analgesia.

In an effort to mollify this effect, recent studies have evaluated the efficacy of adding non-opiate medications to traditional PCAD formulations, with the

expectation there would be a level of opiate sparing and analgesic synergy. One of the most commonly studied of these additives is the NMDA inhibitor, Ketamine. This medication is of particular interest to emergency physicians as it is widely available and used frequently in both the pediatric and adult populations in procedures such as rapid-sequence intubation and procedural sedation. It has a favorable pharmacokinetic profile in terms of pain management as it has both intrinsic analgesic properties and opiate sparing effects via antagonism of NMDA receptors [5, 34]. Unfortunately, research on this subject has been mixed as some studies have shown that it may not provide a significant reduction in pain scores and has an increased incidence of deleterious side effects [5, 35, 36]. Clonidine has also been used as an additive in PCADs and initially showed some benefits in regard to nausea reduction in certain post-operative patients but this has not been reliably reproduced in subsequent studies [5, 34, 37].

One medication which has shown promise for use with PCADs is dexmedetomidine. This medication is a "highly selective α2-adrenoreceptor agonist, with analgesic, anxiolytic, and sedative properties, but without effects on respiratory function." [5, 38] In a recent study it was shown that adding dexmedetomidine to PCADs with morphine resulted in improved analgesia, decreased nausea and significant morphine sparing, without significantly impacting patients hemodynamic status [5, 39]. Thus, it would appear that this medication would be particularly well-suited for use in the ED. Optimal dosing of this medication has not been definitively established, however the concentration used in this study consisted of 5 μg/mL with the PCAD being programmed to deliver 1 mL per demand bolus followed by a 5-minute lockout period. Formulations such as this are determined by the pharmacokinetic properties of the medication being studied and mixtures of these medications generally require additional assistance by pharmacy staff. This would likely add additional hard costs with regard to medication preparation but this may be a viable option for patients with a labile hemodynamic status (such as the elderly, septic or traumatically injured) where the analgesic benefits of increased dosing may be tempered by the fear of respiratory depression or hypotension. Additionally, these additives would offer a clear benefit for chronic opiate users where opiate sparing may be of increased importance.

6.2 Pain reduction

The perception of pain is highly subjective and varies greatly among individuals and makes it difficult to measure in precise terms. That being said, multiple formal measures have been created to objectively measure reductions in pain, namely the Visual Analogue Scale score (VAS score) and Numeric Rating Scales (NRS). These tools are of primary importance to both patients and physicians in objectifying levels of pain. Studies show that improvement in pain scores are directly correlated with patient satisfaction which can significantly influence the clinical course of patients experiencing an episode of acute pain [40]. Although it is well established that PCADs reduce pain scores in the post-operative setting there has been some controversy as to whether this would hold true for ED patients, as they often do not have as much time to convalesce from injuries. In reviewing the literature it appears that eight randomized controlled trials have been done which specifically examined the effect that patient-controlled analgesia had on pain scores in patients presenting to the ED. Five out of the eight studies in question have shown statistically significant results which favor PCAD use over conventional intravenous therapy. Two of the remaining studies demonstrated a downward trend which favored PCADs (although this did not reach the threshold for statistical significance) and only one study showed no difference [9, 11, 33, 41–46]. Unfortunately there is

significant heterogeneity among these studies and due to the wide range of presenting complaints there are many confounding factors which must be accounted for. That being said, the initial data appears to support the use of PCADs over standard therapy for patients presenting to the ED with acute pain.

6.3 Patient autonomy and patient satisfaction

Patient satisfaction is becoming ever more important in clinical medicine. It is imperative that physicians maximize their ability to take care of patients in an empathetic manner which utilizes principles of patient autonomy and shared decision making. Studies have demonstrated that PCADs are preferred by many patients in comparison with both IV and IM preparations and patient satisfaction with this type of treatment is generally high [5, 9, 11, 33, 41–46]. In a recent systematic review of 21 trials which included 1260 postoperative patients, it was shown that patients had increased satisfaction with PCAD use in all of the studies that were included in the cohort [8]. Additionally, a meta-analysis done on the same group showed that patients preferred PCADs significantly more than standard therapy [8]. Studies which have been conducted that have evaluated patient satisfaction for patients presenting to the emergency room have also shown similar results, with the overwhelming majority of studies showing a clear preference for PCADs [9, 11, 33, 41–46]. This is likely due to several factors including faster time to analgesia, decreased need of nursing assistance and an increased sense of autonomy and control over one's pain [44].

In addition to patient satisfaction it is important to remember that proper implementation of this technology requires cooperation across multiple disciplines. As such, the support of physician extenders, nurses, and hospital pharmacists is integral to patient care and should not be overlooked. Relatively few studies have addressed this issue directly but current evidence shows that PCADs are generally well received by nursing staff. One study in particular demonstrated that patient-controlled analgesia regiments were rated as "good to excellent" more frequently than those utilizing traditional intravenous therapy (69% versus 54%) and the majority of nursing staff would use them again in the future (77%) [41].

7. Drawbacks of patient-controlled analgesia use

The majority of studies which have examined PCAD use in the emergency setting have found that there were similar rates of side effects such as nausea, vomiting, pruritus and drowsiness when compared to those receiving standard therapy [9, 11, 33, 41–46]. However, two studies showed PCADs to have a slightly increased risk of adverse events, including hypotension and hypoventilation, although neither group experienced any long-term sequelae in connection with these events. Additionally, these effects were transient and did not require the use of reversal with naloxone [9, 11]. When evaluating the literature it appears that the preponderance of adverse events associated with PCAD use have been due to factors which are inherent to all sustained opioid use and would likely be minimized with appropriate monitoring by staff. It is important to note that certain subgroups of patients may be prone to respiratory depression with patient-controlled analgesia. Studies have shown that elderly patients, patients with obstructive sleep apnea, and those using concurrent analgesics are at particular risk, and are vulnerable to the sedative effects which occur with repeated dosing [22].

Although it appears that PCADs are safe in this patient population, there are unique characteristics associated with this technology which require special attention

and education for both patients and staff. Programming errors can occur, especially when staff are unfamiliar with the equipment which can lead to over-sedation and respiratory depression. In a large randomized study conducted in the ED by Bijur et al. there were a similar number of adverse events among patients assigned to the PCAD group versus those receiving standard IV therapy. However, the PCAD group had 11 pump programming errors, 10 of which were due to nursing staff unintentionally giving patients background infusions. None of the patients in question were subject to any long-term side effects. Additionally, following staff remediation and education, no additional errors were seen [11]. One way to address this in the ED would be to have special teams which are trained specifically in PCAD usage and implementation. Studies which have examined the effect of using specially trained support staff have demonstrated that there are less adverse events and a greater likelihood of being able to transition to oral opiates (rather than IM) when staff are trained appropriately [5, 47]. Thus, it appears that many of these events may be mitigated by improving education and regular training among providers and support staff.

There are some additional factors relating to patient perceptions which are unique to this modality and may influence its effectiveness in regard to pain control. Chumbley and colleagues found that many patients had reservations about using PCADs with 22% of patients fearing addiction and 30% fearing overdose [44, 48]. The study goes on to explain that lack of education likely played a large role in this and a patient's psychological background and coping abilities were also involved in influencing their response to treatment [44]. Intrinsic issues such as these are more difficult to control for in an acute setting and are largely related to preconceived notions that patients have prior to presenting to the ED. It is likely that these variables could be minimized if providers were to make an effort to first educate the patients regarding PCAD use and set reasonable expectations regarding pain control prior to the initiation of care.

8. Economics

Although patient safety maintains primacy in the hierarchy of prioritization with regard to the implementation of new technology, economic considerations play an important role when determining the feasibility of its widespread clinical utility. With regard to PCADs there are both hard costs, in terms of the device itself, length of stay and medication, as well as soft costs, such as time saved by staff and patient satisfaction, which must be considered when analyzing the cost-effectiveness of this modality. Although current research clearly demonstrates that there are improvements in patient satisfaction and an objective reduction in pain scores in patients receiving patient-controlled analgesia, it is difficult to quantify how these benefits translate in terms of savings. As such, clear cost-benefit ratios remain difficult to establish. Due to this complexity, a multivariate approach must be used when evaluating the benefits that PCADs offer in an acute care setting.

Although device costs vary among distributors it is safe to assume that the cost of obtaining the device and subsequent maintenance would be greater than that of traditional therapy. A study by Pritchard et al., which evaluated specific costs associated with the device including depreciation, electrical testing, calibration/rebuild costs, and servicing demonstrated that the annual costs of a PCAD was approximately $1573 which equates to $4.34 per day [49]. In addition to these initial capital expenditures relating to acquiring the device, there is mounting evidence that patients receiving patient-controlled analgesia in the ED also require a greater quantity of opiates than those receiving IV therapy [9, 33, 42, 44, 46]. These increased costs are also compounded by additional administrative challenges which

require nursing staff, physicians and pharmacy to coordinate care in a novel manner which may be difficult to implement in many EDs.

One factor which clearly favors the use of PCADs in patients experiencing acute pain is the ability of this modality to save valuable staff time. This translates to increased productivity for both nursing staff and physicians which has the propensity to further increase RVUs and improve overall savings. For example, a recent study by Chan et al., demonstrated that PCAD utilization could save an average of 10–13 minutes of treatment time within specific post-operative groups [50]. Literature on costs related to length of stay, on the other hand, appears equivocal. A review of the literature shows that four randomized controlled trials have been done which specifically evaluated length of stay in the ED relative to PCAD use. Two studies reported an increase in length of stay and two reported a reduction [9, 33, 41, 43]. None of the studies reached statistical significance, therefore the question of whether patient-controlled analgesia reduces length of stay remains unanswered.

The PASTIES study was a large scale randomized trial which evaluated the effectiveness of patient-controlled analgesia in the ED for patients suffering from traumatic injuries and non-traumatic abdominal pain [9, 33]. This study evaluated patients presenting to the ED who were subsequently admitted to the hospital, thus, providing important follow-up information on patient outcomes after their initial ED care. Subsequent PASTIES studies have since been published which have evaluated the costs associated with PCAD use in this cohort. These studies are important to this discussion as they are the only studies to date which have specifically evaluated the economic feasibility of patient-controlled analgesia in the ED. According to the study there were significant reductions in pain, particularly in patients with acute abdominal pain, however, this came at increased cost. Patients with traumatic injuries incurred an additional $21.79–$23.10 per 12 hours; and non-traumatic abdominal pain incurred an additional $23.67–$25.09 per 12 hours [49]. Although these costs were significant within the scope of this study, they may be negligible as improvements in patient satisfaction may eventually translate into improved reimbursement. As such, further studies must be done in the future to determine the true financial feasibility of PCAs in this type of setting.

9. Conclusion

Use of patient-controlled analgesia has been demonstrated to be both safe and effective for acute pain management in the ED. It offers a means of pain control which is more patient-centered and allows for a greater degree of shared decision making while simultaneously improving baseline analgesia. Recently, a few small scale studies have shown that the use of patient-controlled analgesia in the acute care setting may improve objective pain scores and increase both patient and nurse satisfaction. However, the economic feasibility for utilization of this modality within the scope of the emergency room remains unclear. As always, medication selection should be guided by clinical presentation and patient response. In conclusion, this technology appears to provide a promising alternative to standard therapy, however, additional studies must be done before more broad recommendations can be made regarding widespread implementation.

Conflict of interest

The authors have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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