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REVIEW

A Review of Current and Emerging Approaches to Pain Management in the Emergency Department

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ABSTRACT

Introduction: Pain is the most common symptom prompting an emergency department visit and emergency physicians are responsible for managing both acute pain and acute exacerbations of chronic pain resulting from a broad range of illnesses and injuries. The responsibility to treat must be balanced by the duty to limit harm resulting from analgesics. In recent years, opioid-related adverse effects, including overdose and deaths, have increased dramatically in the USA. In response to the US opioid crisis, emergency physicians have broadened their analgesic armamentarium to include a variety of non-opioid approaches. For some of these therapies, sparse evidence exists to support their efficacy for emergency department use. The purpose of this paper is to review historical trends and emerging approaches to emergency department analgesia, with a particular focus on the USA and Canada.

Methods: We conducted a qualitative review of past and current descriptive studies of emergency department pain practice, as well as clinical trials of emerging pain treatment modalities. The review considers the increasing use of non-opioid and multimodal analgesic therapies, including migraine therapies, regional anesthesia, subdissociative-dose ketamine, nitrous oxide, intravenous lidocaine and gabapentinoids, as well as broad programmatic initiatives promoting the use of non-opioid analgesics and nonpharmacologic interventions.

Results: While migraine therapies, regional anesthesia, nitrous oxide and subdissociative-dose ketamine are supported by a relatively robust evidence base, data supporting the emergency department use of intravenous lidocaine, gabapentinoids and various non-pharmacologic analgesic interventions remain sparse.

Conclusion: Additional research on the relative safety and efficacy of non-opioid approaches to emergency department analgesia is needed. Despite a limited research base, it is likely that non-opioid analgesic modalities will be employed with increasing frequency. A new generation of emergency physicians is seeking additional training in pain medicine and increasing dialogue between emergency medicine and pain medicine researchers, educators and clinicians could contribute to better management of emergency department pain.

Keywords: Acute pain; Emergency medicine; Gabapentinoids; Ketamine; Lidocaine; Nitrous

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oxide; Non-opioid analgesics pain; Pain medicine; Regional anesthesia

INTRODUCTION

Pain is the most common reason for seeking emergency department (ED) care and, as a presenting complaint, pain accounts for up to seventy percent of ED visits [1]. Descriptive studies of ED pain practice began appearing in the 1990s and many of these investigators discovered that specific patient subgroups were at risk for inadequate pain treatment. Those at risk included the very young, older adults and members of minority ethnic groups [2–9]. A number of efforts to increase awareness of unmet pain treatment needs, both in the ED and other settings, originated in the USA and Canada in the mid-1990s [10]. Educational campaigns to promote pain treatment became widespread throughout the healthcare system and, in particular, an increased emphasis on standardized pain assessment was promulgated by the Joint Commission on the Accreditation of Healthcare Organizations, soon to be renamed The Joint Commission [11].

As a consequence of these efforts, and in part due to industry marketing, pharmacologic approaches to pain treatment (particularly the use of opioids) became more aggressive. The opioid-centric nature of this change in practice soon became apparent, as the number of opioids prescribed by all healthcare providers increased dramatically over the following decade. US opioid prescribing peaked in 2010 at 782 morphine milligram equivalents (MME) per capita. As of 2015, this volume had decreased to 640 MME per capita, but remained three times higher than levels in 1999 [12].

Importantly, the USA ranks number one in the consumption of prescription opioids globally, with a per capita consumption rate two to three times that of European countries [13]. Recent studies of prescription opioid misuse and abuse in Canada and Australia suggest increasing levels of harm while countries of the European Union report disparate rates of prescription opioid abuse [14–16]. The reasons for these cross-national consumption disparities are no doubt complex, related to multiple cultural and pharmaceutical marketing differences, and beyond the scope of this review.

In this paper, we present a qualitative review of past and current descriptive studies of ED pain practice, as well as clinical trials of emerging pain treatment modalities. Our purpose is to review historical trends and emerging approaches to ED analgesia, with a particular focus on the USA and Canada. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

CURRENT STANDARD TREATMENTS AND APPROACHES

A prospective, multicenter study published in 2007 provides a snapshot of US and Canadian ED practice at perhaps the height of an opioid-centric analgesic approach to pain treatment [17]. Investigators enrolled 842 patients age 8 years or older presenting to the ED with moderate to severe pain (> 3 on an 11-point numerical rating scale) to one of 20 EDs. Contrary to common belief that most ED pain results from injury or trauma, only 32% presented with pain of traumatic etiology (Table 1). Common nontraumatic diagnostic groups included neck and back pain, abdominal pain, headache, noncardiac chest pain and upper respiratory infection.

Pain intensity ratings on arrival ranged from 4 to 10 with a median pain score of 8. Only 50% of patients had a 2-point or greater reduction in numeric rating scale (NRS) pain intensity scores during the ED stay. Almost three quarters of patients were discharged in moderate pain (45%; NRS, 4–7) or severe pain (29%; NRS, 8–10).

Overall, 589 of 842 subjects (70%) expressed a desire for analgesics, and 506 of these (86%) received them. The median time interval from triage to analgesic administration was 90 min, and fewer than one third of patients received analgesics within 1 hour of arrival (Fig. 1). A total of 735 doses of 24 different analgesics were administered in the ED. The majority of analgesics administered were opioids (59%):

Table 1 Major etiologies of pain. Reprinted from Todd et al. [17], with permission from Elsevier

	N (%)
Wound, abrasion or contusion	91 (11)
Sprain or strain	90 (11)
Back or neck pain	85 (10)
Abdominal pain	71 (9)
Fracture or dislocation	48 (6)
Headache	47 (6)
Chest pain (noncardiac)	40 (5)
Upper respiratory infection	30 (4)
Abscess or cellulitis	25 (3)
Toothache	19 (2)
Urinary tract infection	16 (2)
Renal colic	14 (2)
Other diagnoses	243 (30)
Total with ICD-9 diagnosis	819 (100)

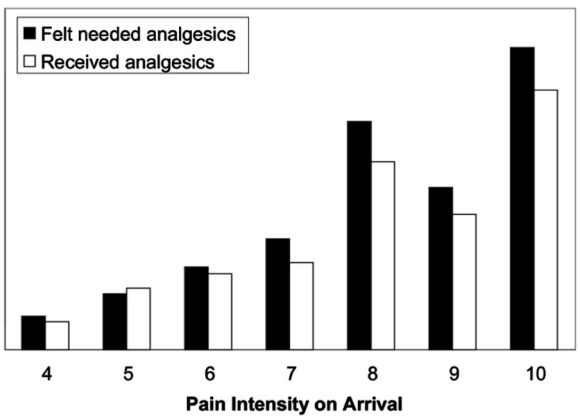

Fig. 1 Patient perceived need for, and administration of, analgesics. Reprinted from Todd et al. [17], with permission from Elsevier

Table 2 Analgesics administered in the ED. Reprinted from Todd et al. [17], with permission from Elsevier

Analgesics administered in the ED (735 doses given to 506 patients)	*N* (%)
Morphine	148 (20.1)
Ibuprofen	127 (17.3)
Hydrocodone/acetaminophen	93 (12.7)
Oxycodone/acetaminophen	83 (11.3)
Ketorolac	60 (8.2)
Acetaminophen	53 (7.2)
Hydromorphone	36 (4.9)
Antacid	26 (3.5)
Meperidine	24 (3.3)
Fentanyl	23 (3.1)
Metoclopramide	13 (1.8)
Codeine/acetaminophen	12 (1.6)
Oxycodone	10 (1.4)
Naproxen	9 (1.2)
Other	18 (2.4)
Total	735 (100)

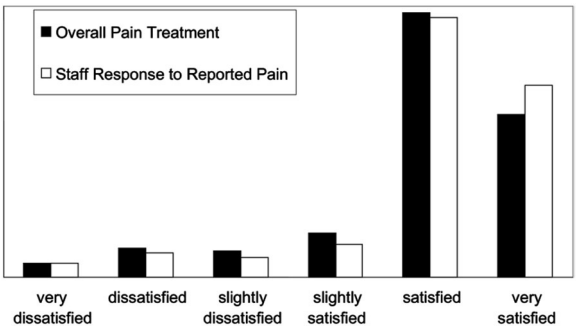

Fig. 2 Patient satisfaction. Reprinted from Todd et al. [17], with permission from Elsevier

morphine was the single most commonly administered analgesic (20%), followed by ibuprofen (17%; Table 2). Despite rather small reductions in pain intensity, patients expressed relatively high satisfaction with both overall pain treatment and staff responses to reports of pain (median scores of 5 on a 6-point scale; Fig. 2).

Over the first decade of the current century, evidence of prescription opioid-related harm, including overdose and death, became painfully obvious in the USA. Since 1999, overdose deaths

involving prescription opioids, as well as total sales of prescription opioids, have quadrupled [18].

While it is difficult to estimate the precise contribution of ED opioid prescribing to the rise in prescription opioid harm in the USA, recent studies suggest that the contribution of emergency medicine is limited. In 2012, emergency medicine as a specialty accounted for only four percent of US opioid prescriptions, ranking behind dentists, surgeons, internists and family physicians [19]. The number of doses per prescription suggests an even smaller role for the specialty. In a study of 19 US EDs, 17% of patients received opioid prescriptions at discharge with an average of only 15 pills per prescription [20].

Nonetheless, over the last decade, initiatives to increase scrutiny of those seeking pain treatment in the ED, including widespread use of prescription drug monitoring programs, have become widespread [21]. Professional societies, regulatory bodies and individual EDs have created guidelines to limit and standardize opioid prescribing [22, 23]. As a result of these efforts, emergency physician opioid-prescribing rates dropped by almost ten percent between 2007 and 2012 [19]. With increasing frequency, emergency physicians are incorporating non-opioid alternatives and multimodal analgesic options into practice [24].

EMERGING TREATMENTS AND APPROACHES

In the remainder of this review, we consider the increasing use of non-opioid and multimodal analgesic therapies, as well as the need for additional research and quality improvement activities to promote safe and effective ED pain management.

For treatment of some common ED pain presentations, such as benign headache, robust evidence exists to support non-opioid and migraine-specific modalities. Despite well-accepted evidence, progress toward standardizing US and Canadian ED headache treatment and giving primacy to non-opioid interventions of known efficacy (i.e., dopamine agonists, serotonin agonists) has been remarkably slow [25]. Almost 20 years after the Canadian Association of Emergency Physicians published guidelines for the acute management of migraine headaches [26], evidence reviews reveal that opioids remain the first line of treatment for large proportions of US and Canadian ED patients with benign headaches [27–30]. While opioid administration is less common in non-North American EDs [31, 32], migraine-specific therapies are likely underutilized in ED settings worldwide. The crisis of prescription opioid harm in the USA provides additional stimulus to harmonize rational migraine therapy across national boundaries.

Emergency physician-administered regional anesthesia is another modality that is well supported by the literature and appears ripe for expansion. Fostered by the ubiquity of emergency medicine training programs in ultrasound, local and regional nerve blockade are increasingly employed for a large variety of painful injuries and illnesses [33–36].

A recent multicenter randomized controlled trial of regional nerve blockade for elderly patients with hip fractures illustrates the evolving role of emergency physicians in the delivery of regional anesthesia and the teamwork between emergency medicine and anesthesiology required to achieve optimal pain control and functional outcome for these often frail patients [37]. In this study, 161 ED patients with acute hip fractures from three New York City hospitals were randomized to receive either an ultrasound-guided, single-injection femoral nerve block administered by emergency physicians followed by placement of a continuous fascia iliaca block by anesthesiologists within 24 h, or opioid analgesics alone. Although both arms allowed opioids as needed, pain scores in the ED favored the intervention group over controls, as did pain scores on post-operative day 3 (Figs. 3, 4). Intervention subjects required one third fewer morphine milligram equivalents and reported fewer opioid adverse effects. Perhaps more surprisingly, intervention subjects reported superior functional status, including walking and stair climbing ability, up to 6 weeks after their initial fracture.

Intravenous subdissociative-dose ketamine has also been the subject of a number of recent

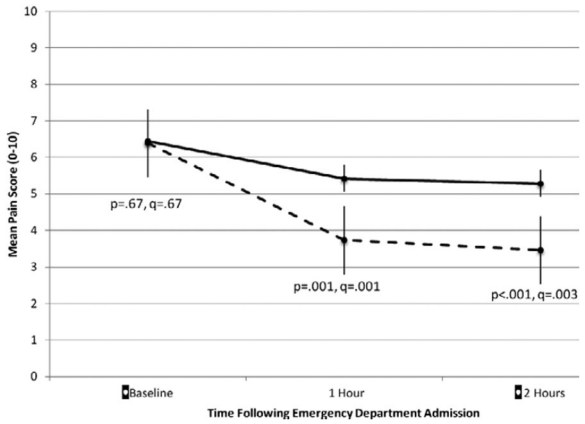

Fig. 3 Mean pain scores with standard errors for pain at ED admission (baseline) and 1 and 2 h after admission for control (solid lines) and intervention (dashed lines). Reproduced with permission from Morrison et al. [37]

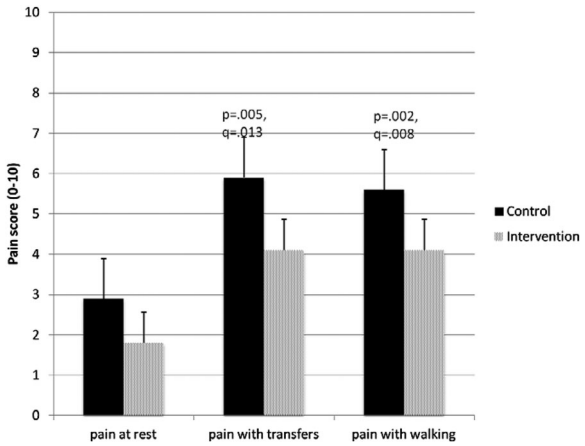

Fig. 4 Mean pain scores for pain at rest, with transfer out of bed, and with walking for control (shaded) and intervention (hashed) subjects on postoperative day 3. Reproduced with permission from Morrison et al. [37]

ED studies. Perhaps because ketamine has long been used for procedural sedation and as an induction agent for rapid sequence intubation, subdissociative-dose ketamine (0.1–0.4 mg/kg) as monotherapy or adjunctive therapy has become more rapidly adopted for use than other non-opioid analgesics.

In a recent position paper from the American Academy of Emergency Medicine, subdissociative-dose ketamine was judged safe and effective both as a single agent and in combination with opioids for the treatment of acute pain [38]. Although ketamine is well known to cause troubling neuropsychiatric adverse effects (emergence phenomena), in subdissociative doses these adverse effects appear to be minor and short-lived. Eight supportive studies of subdissociative-dose ketamine pertinent to pre-hospital and ED settings have been published over the last 10 years [39–46]. Another recent study examined adverse effects and analgesic efficacy of ketamine administered as either a single intravenous push (IVP) or a short infusion over 15 min [47]. Using a double-dummy design, the investigators reported similar analgesic efficacy with fewer reports of adverse effects for when ketamine was infused over a 15-min infusion period.

While subdissociative-dose ketamine, as either monotherapy or multimodal therapy, is generally supported by published evidence to date, emergency physicians should inform patients about potential side effects and avoid ketamine for patients with underlying psychiatric disorders or substance abuse-induced transient psychosis. Ketamine should be administered in accordance with established departmental policies and procedures.

Nitrous oxide has a long history of use as both an anxiolytic and analgesic among pediatric ED patients. Administered as a 50%–70% nitrous oxide vapor, it is used for children undergoing a number of procedures, including venipuncture, laceration repair, fracture reduction as well as incision and drainage of abscesses. Its use has been limited by the need for proper ventilation and scavenging equipment as well as the documented potential for staff recreational use [48]. Nitrous oxide has seen less use among adult ED patients. In a recent non-controlled pilot study of self-administered nitrous oxide among 85 ED patients with abscesses or orthopedic injuries, nitrous oxide appeared to be safe and well tolerated. Given the current emphasis on decreasing opioid use in the ED, it is likely that nitrous oxide use will increase over time [49].

In contrast to the modalities discussed above, a number of non-opioid analgesics for which there is less robust evidence are receiving increased attention. Analgesic therapies such as intravenous lidocaine, gabapentinoids, trigger

point injections and even acupuncture, mind–body approaches and music therapy have recently been promoted for ED use [50].

Intravenous lidocaine has demonstrated efficacy for central pain syndromes and neuropathic pain, as well as opioid-sparing effects in the post-operative setting. Two Iranian research groups recently published studies of intravenous lidocaine for ED the treatment of renal colic. The first studied intravenous lidocaine as an adjuvant to opioid therapy in 110 patients presenting to the ED with typical renal colic symptoms [51]. The investigators reported that those treated with a combination of lidocaine and morphine reported fewer episodes of nausea and more rapid resolution of both pain and nausea than those treated with morphine alone. A second study of 240 patients with renal colic directly compared monotherapy with intravenous lidocaine to morphine [52]. Pain reduction was reported to be greater over the first 30 min for those treated with lidocaine. In another US study comparing intravenous lidocaine to intravenous ketorolac for ED patients with acute radicular back pain, lidocaine was less impressive, failing to reach a clinically significant reduction in reported pain intensity over 60 min [53].

While intravenous lidocaine has thus far received limited investigation in the ED, other non-opioid and nonpharmacologic approaches, such as the use of gabapentinoids, trigger point injections and even acupuncture, mind–body therapies and music therapy, have received little rigorous study. Perhaps the most ambitious ED program encouraging non-opioid analgesic therapies as well as a variety of nonpharmacologic therapies is the Alternatives to Opiates Program (ALTO) developed by St. Joseph's Regional Medical Center in Patterson, New Jersey, USA [54]. Initiated formally in January 2016, ALTO encourages multimodal treatments for five specific conditions: acute low back pain, lumbar radiculopathy, renal colic, migraine and extremity fracture/dislocation. Condition-specific multimodal therapeutic protocols include a variety of non-opioid analgesics, specifically non-steroidal anti-inflammatory agents, ketamine, lidocaine/ropivacaine, benzodiazepines, corticosteroids, gabapentinoids and nitrous oxide. Ultrasound-guided regional anesthesia is advised for appropriate extremity fractures and dislocations. Although opioids are allowed as rescue analgesics in these protocols, alternatives to opioids are administered when possible. The program encourages discussions with patients of opioid adverse effects and addiction risks, and program goals include the incorporation of medically assisted treatment of opioid addiction, acupuncture and mind–body modalities. Although published data is limited, the program claims to have reduced opioid administration for selected conditions by almost 50%.

While this review concentrates on ED analgesics, the sole focus on pharmacologic intervention risks overlooking nonpharmacologic measures that can be employed effectively in the ED. Given the adverse effects associated with many opioid (and non-opioid) analgesics, it is important to understand and employ such treatments, including patient-centered communication techniques, physical interventions and relaxation techniques.

Additionally, for complaints such as pain, the emergency physician often lacks obvious confirmatory evidence of an inciting factor (e.g., migraine, low back pain). Those in pain often present with co-morbid anxiety and depression, or exhibit low self-efficacy, catastrophizing ideation or behaviors typical of chemical coping. Such patients may be perceived as "difficult" and challenge our professional competence and ability to maintain a positive therapeutic stance [55]. Negative stereotypes or stigmatization of those in pain impair the patient-physician relationship and predictably result in inadequate clinical care [56].

Particularly in the context of an ongoing national crisis of opioid harm, it is important that emergency physicians display empathy in treating patients who may (or may not) be at risk for opioid abuse. The concept of empathy for those in pain involves cognitive (the ability to envision standing in another's shoes), affective (the appreciation of another's emotional state) and action (patient-centered communication) elements. The ability to display empathy and provide patient-centered communication are core competencies for

emergency physicians [57]. Patient-physician interactions characterized by empathy and trust are more likely to lead to optimal outcomes [58]. Although we lack sufficient ED research into the phenomenon, such "empathetic attention" has the potential reduce analgesic needs, particularly for patients with high levels of anxiety, and should be considered an integral tool in our therapeutic armamentarium [59].

Clinicians who successfully integrate these skills into practice will likely realize higher levels of patient satisfaction, enhanced treatment compliance and better clinical outcomes. To the extent that these practices promote patient self-efficacy and self-management of pain, healthcare costs related to unnecessary diagnostic imaging and adverse effects of inappropriate prescribing may also be reduced [60]. Finally, enhancing emergency physician empathy for those in pain has the potential to reduce career burnout [61, 62], increase physician well-being [63] and lower medicolegal risk [64].

RECENT DEVELOPMENTS AND CONCLUSION

A number of recent developments are encouraging to those promoting excellence in ED pain management. After many years of discussion, emergency medicine residency training has become an accepted pathway into US pain medicine fellowships and a small but growing number of emergency physicians are now dual-certified in both specialties. Emergency physicians seeking dual certification will be more likely to pursue academic careers and promote a higher level of scholarship in pain-related emergency medicine, including the conduct of analgesic clinical trials pertinent to the ED. The recent publication of consensus-based recommendations for an emergency medicine pain management curriculum signals an increased interest in standardizing and enhancing the role of pain medicine in emergency medicine residency training [65]. Finally, the American College of Emergency Physicians has established a new Pain Management Section, with an inaugural meeting scheduled for late 2017. The Section's goals are to promote further development of the subspecialty of pain medicine within emergency medicine, encourage additional research and education around the ED management of acute and chronic pain and ultimately develop an emergency medicine pain management fellowship with official recognition by the Accreditation Council for Graduate Medical Education (ACGME).

Although the management of ED pain continues to challenge emergency physicians and our practice patterns evolve slowly, these are encouraging trends within our specialty that bode well for the future growth of a new subdiscipline of emergency medicine focused on the perennial problem of pain.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

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