TURKISH JOURNAL OF EMERGENCY MEDICINE

Invited Review Article

Access this article online

Quick Response Code:

Website: https://turkjemergmed.com/

DOI: 10.4103/tjem.tjem_141_25

Emergency department pain management in special populations

Katherine Vlasica[1], Amanda Hall[1], Mohammad Anzal Rehman[2], George Notas[3], Christina Shenvi[4], Sergey Motov[5]*

[1]Department of Emergency Medicine, St. Joseph's Health, Paterson, NJ, USA, [2]Department of Emergency Medicine, Mediclinic City Hospital, Dubai, UAE, [3]Department of Emergency Medicine, University Hospital of Heraklion, Crete, Greece, [4]Department of Emergency Medicine, University North Carolina Hospitals, Chapel Hill, NC, [5]Department of Emergency Medicine, Maimonides Medical Center, Brooklyn, NY, USA
**Corresponding author*

Abstract:

Pain is a leading cause of emergency department (ED) visits globally, yet certain patient populations experience persistent disparities in their pain management due to physiological complexities, comorbidities, and gaps in evidence-based guidelines. This clinical review focuses on individualized, evidence-based approaches to ED pain management in four vulnerable groups: pregnant and breastfeeding patients, patients with sickle cell disease, geriatric populations, and patients with cancer pain and requiring palliative care. The practical recommendations presented in this review for optimal ED pain management in these special populations call for timely, effective, and multimodal analgesia; prioritization of nonpharmacologic and pain syndrome-targeted techniques; awareness of drug-disease and drug-drug interactions; interdisciplinary coordination; and education to mitigate ED clinicians' biases. This review emphasizes the importance of tailoring pain strategies to population-specific needs to improve outcomes, reduce harm, and advance equity in emergency care delivery.

Keywords:

Analgesia, emergency department, pain management

Introduction

Pain is a common presenting complaint in emergency departments (EDs) worldwide, with up to 78% of ED visits involving pain as a primary or secondary symptom.[1,2] Despite advances in ED pain management, certain patient populations present unique challenges requiring individualized, pain syndrome-specific approach to achieve optimal analgesia while minimizing adverse outcomes. Pregnant women, people with sickle cell disease (SCD), geriatric patients, and patients with cancer pain or palliative care represent vulnerable populations whose pain management needs often diverge significantly from standard protocols, necessitating evidence-based, population-specific interventions.[3-6]

The management of pain in these special populations is complicated due to altered pharmacokinetics, comorbidities, physiological vulnerabilities, refractoriness to conventional therapeutic approaches, and concerns about medication safety that frequently translate into inadequate pain control in the ED. This focused clinical review aims to provide emergency physicians with evidence-based approaches to pain management in these challenging populations.

Submitted: 21-04-2025
Revised: 06-05-2025
Accepted: 08-05-2025
Published: 01-07-2025

ORCID:
KV: 0009-0000-9763-7144
AH: 0009-0001-8984-7050
MAR: 0000-0003-0081-7013
GN: 0000-0002-2506-5252
CS: 0000-0003-2944-8581
SM: 0000-0002-9668-216X

Address for correspondence:
Prof. Sergey Motov, Department of Emergency Medicine, Maimonides Medical Center, NY, USA. E-mail: smotov@gmail.com

How to cite this article: Vlasica K, Hall A, Rehman MA, Notas G, Shenvi C, Motov S. Emergency department pain management in special populations. Turk J Emerg Med 2025;25:159-77.

Pain Management of Pregnant and Breastfeeding Patients in the Emergency Department

Acute pain is common in pregnancy, with analgesics being the third-most-prescribed medication class after antiemetics and antibiotics.[7] Managing pain in pregnancy and breastfeeding requires a tailored and multifaceted approach that balances pharmacologic and nonpharmacologic options with fetal safety risks. However, evidence-based guidelines remain limited due to the historical exclusion of pregnant women from clinical trials, leaving clinicians to navigate treatment with incomplete data. Physiological changes in pregnancy (altered drug metabolism, hepatic and renal clearance, volume distribution changes, and placental transfer) further complicate drug pharmacokinetics and fetal exposure risks.[8]

ED clinicians must assess the risks of untreated illness and potential adverse effects of pharmacotherapy on pregnancy and breastfeeding and unfavorable perinatal and infant outcomes such as miscarriage, major congenital disabilities, preterm birth, stillbirth, neonatal adaptation signs, and behavioral and developmental effects.[7,9] Table 1 lists commonly used analgesics (dosing and routes) in pregnant and breastfeeding patients.

Commonly used analgesics in pregnancy and breastfeeding

Acetaminophen (Paracetamol, APAP)

Acetaminophen is used in 40%–70% of pregnancies and is the only pain medication considered safe during pregnancy and compatible with breastfeeding.[7,10] Its use has no clear evidence linking it to fetal developmental issues.[7,10,11] Oral, intravenous (IV), and rectal formulations are available with a maximum of 4000 mg per day with IV single infusion of 1000 mg not exceeding 15 min. A large population-based study of 185,909 children found no significant link to autism, ADHD, or intellectual disabilities.[12] A systematic review and meta-analysis also found no association with preterm birth or low birth weight, though data on dosage and frequency were limited.[13,14]

Nonsteroidal anti-inflammatory drugs

NSAIDs, including their parenteral, oral, and topical forms, are generally considered safe in pregnant and lactating women and are commonly used for musculoskeletal (MSK) pain, headaches, and renal colic.[7,15] However, their use during pregnancy requires caution due to potential embryo-fetal risks based on specific NSAID, gestational timing, and duration of use.[7,15] NSAIDs are contraindicated in the third trimester due to risks of premature ductus arteriosus closure and uteroplacental vasoconstriction.[16]

Beyond 20 weeks, NSAID use has been linked to fetal nephrotoxicity and oligohydramnios, prompting FDA recommendations to minimize use after 20 weeks and avoid it entirely after 30 weeks.[17] NSAIDs can be used cautiously in the first and second trimesters with the lowest effective dose and shortest course when benefits outweigh the risks, as courses longer than 10 days may adversely affect fetal health.[18]

Opioids

Opioids are widely used for pain management during pregnancy via IV, oral (PO), sublingual (SL), and intranasal (IN) routes. Frequent titration and the use of the lowest effective dose for the shortest duration are recommended to minimize complications.[19,20] Opioids increase the risk of Neonatal Opioid Withdrawal Syndrome (NOWS) with stronger opioid agonists (e.g., oxycodone, methadone, hydromorphone, and morphine) posing a higher NOWS risk.[20,21]

Pregnant women with opioid use disorder (OUD) face higher risks of inadequate prenatal care, fetal growth restriction, preterm labor, and NOWS.[20,21] Methadone or buprenorphine should be initiated promptly, as both improve maternal and fetal outcomes. Buprenorphine has been associated with reduced neonatal withdrawal and increased birth weight, making it the preferred option for OUD treatment during pregnancy.[20]

Despite the relative infant dose of opioids in breast milk being in the range of 1%–5% of the mother's therapeutic dose, there are significant risks associated with continued breastfeeding while on opioids.[21] The around-the-clock use of opioids by the mother during breastfeeding should be limited to 2–3 days,[22] Tramadol and codeine should be avoided due to the risk of life-threatening respiratory depression in infants of mothers with the ultra-rapid CYP2D6 metabolizer phenotype.[23]

Steroids

Corticosteroids administered as a short course orally, topically, or intravenously are generally considered safe for treating radicular back pain, joint pain, and inflammatory pain during pregnancy.[19] Prolonged or chronic use has been linked to cataracts, fetal growth restriction, both maternal and fetal immunosuppression, and adrenal insufficiency.[24] Rheumatological guidelines recommend the use of nonfluorinated glucocorticoids, such as prednisone and prednisolone, as they do not cross the placenta.[8,25] Maternal exposure to topical corticosteroids without exceeding the recommended dose revealed no causal association with fetal orofacial clefts, preterm delivery, or low Apgar score.[26]

Magnesium

Magnesium is commonly used in obstetrics and has been well tolerated by both the mother and baby in the treatment of acute and chronic painful syndromes.[16,27,28]

Table 1: Commonly used analgesics in pregnancy and lactation

Medication	Route	Dose	Maternal risk	Fetal risk	Safety/nursing/RID	Comments
Acetaminophen (Paracetamol)	PO PR IV	325–1000 mg Q4–6 h	None	None	Safe for nursing RID: 1.1–1.8%	
NSAIDs Ibuprofen Naproxen Ketorolac Diclofenac Ketoprofen Dexketoprofen	PO IV	Ibuprofen 400 mg Q4 h Naproxen 220 mg Q12 h Ketorolac 10 mg Q6 h Diclofenac 50 mg Q6 h Ketoprofen 60 mg Q6 Dexketoprofen 12.5 mg Q6 h	Use in 1st and 2nd trimester Prolonged gestation/ labor, anemia, blood loss in labor	Bleeding, premature closure ductus arteriosus (third trimester) pulmonary hypertension Naproxen- cardiovascular defects	Safe for nursing: Ibuprofen <1% Naproxen 2.8% Ketorolac 0.18% Ketoprofen 0.31%	Cautious use in the first and second trimesters Contraindicated in the third trimester
NSAID Diclofenac	Topical	2–4 g Q6	Absorption is minimal, generally safe in the first trimester	One case of premature closure of ductus arteriosus	Safe for nursing	
Opioids Oxycodone (IR) Morphine (IR) Fentanyl Hydromorphone Hydrocodone/ acetaminophen Codeine	PO, IV, IM, IN, SQ	Varies	Constipation, increased maternal sensitivity Nausea Vomiting Pruritus CNS depression Respiratory depression Medication dependence Overdose/OUD	NOWS IUGR No known significant malformations	Safe for short-term only (2–3 days)	Codeine to be avoided due to potential for ultrarapid metabolism (CYP2D6) and the risk of fatal respiratory depression in infants (b)
Buprenorphine (first line opioid)	Transdermal SL PO IM IV	Varies	Constipation	NOWS	Use with caution as first-line opioid	Partial agonist – lower maternal and fetal risk
Methadone	IM, PO	Varies	Constipation, Respiratory/CNS depression	NOWS	Safe	Second-line opioid if buprenorphine is contraindicated
Tramadol	PO	25–100 mg Q6		Increased risk for cardiac septal defect and pes equinovarus (49)	Not safe	To be avoided due to the potential for ultrarapid metabolism (CYP2D6) and the risk of fatal respiratory depression in infants (b)
Steroids	PO, IV, topical	Varies	Adrenal insufficiency Hyperglycemia	Oral cleft palate formation- small studies Multiple courses IUGR/low birth weight neonatal sepsis	Safe for nursing	Prednisone/ prednisolone does not cross the placenta
Magnesium	PO, IV		Diarrhea, muscle weakness	None known	Safe for nursing	

Contd...

Table 1: Contd...

Medication	Route	Dose	Maternal risk	Fetal risk	Safety/nursing/RID	Comments
Nitrous oxide Inhaled 50%–70%	INH	Varies	Increased nausea, vomiting Avoid due to risk of air entrapment (bowel obstruction, pneumothorax, pneumomediastinum)	Avoid in the first trimester		Limited data in the second trimester, use in the third trimester
Topicals Lidocaine 5% Capsaicin Steroids	Topical	Varies	Skin irritation	None	Safe for nursing	
Gabapentin	PO	100–300 mg single dose followed by titration	Minimal	Possible cardiac defects, preterm birth, SGA	Safe for nursing	

RID: Relative infant dose, NSAIDs: Nonsteroidal anti-inflammatory drugs, PO: Oral, PR: Rectal, IV: Intravenous, IN: Intranasal, IM: Intramuscular, SQ: Subcutaneous, NOWS: Neonatal opioid withdrawal syndrome, IUGR: Intrauterine growth retardation, CNS: Central nervous system, OUD: Opioid use disorder, SL: Sublingual, SGA: Small for gestational age, INH: Inhalation

Several randomized controlled trials (RCTs) have shown that magnesium supplementation can help relieve muscle cramps, improve general comfort, and promote better sleep during pregnancy.[29] For migraine headaches, magnesium is often used in combination with other medications.[30]

Anticonvulsants (gabapentin and pregabalin)

Gabapentin and pregabalin are commonly used for postherpetic neuralgia, diabetic neuropathy, and radicular back pain in pregnant patients and are generally safe in breastfeeding. A large population-based study of 4642 pregnancies with early gabapentin exposure did not demonstrate an association with major congenital malformations. However, maternal gabapentin use in late pregnancy was associated with a 20%–30% increased risk of preterm birth, a 30%–40% increased risk of small-for-gestational-age infants, and a 35% increased likelihood of neonatal intensive care unit admission.[31] Research related to pregabalin in pregnancy is even more sparse, suggesting no teratogenicity, but its unpredictable absorption may cause maternal sedation.[32]

Local anesthetics and targeted analgesia

Targeted analgesic techniques such as topical, local, and regional anesthesia offer rapid pain relief with minimal systemic effects to pregnant and lactating patients.[16,17,19] In addition, existing research of large observational studies demonstrates no evidence of teratogenicity of local anesthetic administered topically, locally, or regionally.[33-35] Very small amounts of local anesthetics are secreted into the breast milk of lactating mothers, with ropivacaine having the lowest transmission rate compared to lidocaine and bupivacaine.[15]

Antidopaminergics

Antidopaminergics (metoclopramide, prochlorperazine, droperidol, and haloperidol) are frequently used for the management of intractable nausea/vomiting, primary headache, and intractable abdominal pain in the ED. While generally safe in pregnancy and breastfeeding, the use of metoclopramide might be associated with maternal extrapyramidal symptoms. The use of phenothiazines rarely leads to the development of cleft palate, skeletal, limb, and cardiac abnormalities, as well as neonatal respiratory depression during pregnancy. The administration of droperidol or haloperidol is often avoided due to concerns about maternal prolonged QTc.[36]

Muscle relaxants

The use of central muscle relaxants such as baclofen, methocarbamol, chlorzoxazone, cyclobenzaprine, tizanidine, and thiocolchicoside should be generally avoided in pregnant patients as numerous animal studies demonstrated teratogenicity of such medications and human data is severely limited.[37,38]

Nitrous oxide

The use of nitrous oxide during pregnancy, particularly for short-term procedures and labor pain management, appears to be safe with no significant adverse effects on the fetus. However, long-term exposure to high concentrations of nitrous oxide, such as in occupational or recreational settings, may negatively impact fertility and fetal outcomes. Additionally, there are concerns regarding its use in the first trimester, where the inactivation of Vitamin B12 disrupts the folate metabolism.[39] Further research is needed to fully understand the implications of nitrous oxide use, especially in preterm pregnancies.[39-43]

Ketamine

Ketamine is frequently used in the ED for procedural sedation and analgesia, intubation, and pain management. Ketamine readily crosses the placenta and preferentially distributes in neuronal tissue, raising concerns about

its neurotoxic effects in the developing brain.[44-46] Additionally, animal models of prenatal exposure to ketamine demonstrated long-term behavioral and cognitive deficits, including hyperactivity, disinhibition, social withdrawal, anxiety, depression, and aggression in adulthood.[47,48] While direct human evidence is lacking, these data raise significant concerns about potential neurotoxic effects of ketamine on a developing fetus and its use should be generally avoided in pregnancy.[49]

Complementary and alternative therapies

Exercise and physical therapy have been associated with reduced pain intensity, decreased disability, and improved quality of life in pregnancy-related MSK and back pain.[20,50,51] Osteopathic manipulative treatment was shown to decrease low back pain intensity and improve functional status in pregnancy.[50,51] Transcutaneous electrical nerve stimulation has been found to be safe in all trimesters, demonstrating efficacy in lumbar pain and a small but measurable benefit for labor pain.[20,50-53] Additionally, pelvic belts have been shown to be quite effective in the treatment of symphyseal and pelvic girdle pain, outperforming exercise therapy alone.[20] Acupuncture has been investigated for pregnancy-related back pain and labor analgesia, with some studies demonstrating significant pain relief, though methodological limitations remain.[54,55]

Breastfeeding

Breastfeeding-all drugs under 1000 kDa transfer into breast milk. A quantitative estimate of how much medication is transferred to the nursing infant is expressed as a relative infant dose (RID). For most drugs, a RID of 10% or less is considered relatively safe; caution is required for drugs excreted in dosages of 10%–25% of the maternal dosage; and those few drugs excreted in dosages over 25% of the maternal dosage are considered unacceptable.[56]

Take-home pearls

- Prescribe at the lowest effective dose, quantity, and duration of treatment to minimize in utero exposure to medications
- Prioritize topicals and nonpharmacological therapies over systemic treatments
- Use targeted analgesia whenever possible
- Collaborate with patients to establish treatment goals.

Management of Pain in Patients with Sickle Cell Disease in the Emergency Department

SCD is an autosomal recessive disorder characterized by disrupted morphology (sickling) that affects close to 8 million people globally and results in painful crises, hemolytic anemia, splenic sequestration, infections, and stroke.[57] The most common presenting symptom for patients in the ED is pain associated with vaso-occlusive crisis (VOC) due to organ ischemia and neurogenic inflammation.[58] National estimates in the United States (U. S.) found that nearly 75% of all SCD patients presenting to the ED had a primary complaint of pain,[59] with a significant increase in utilization of opioid-based analgesia.[60]

The best practice guidelines by the American Society of Hematology (ASH) and the American College of Emergency Physicians recommend assessing all patients presenting with acute VOC to the ED as high-risk, administering appropriate analgesia within 1 h of arrival with pain reassessment every 30–60 min, and individualizing the plans of care for each patient based on their history of analgesic use and effective dosage and route for pain relief in the past. The goal of analgesia in VOC is to provide appropriate relief for patient discomfort in a safe and effective manner while evaluating patients for underlying complications of SCD.[61] Table 2 lists common therapeutic modalities with their dosing and routes for pain control in patients with SCD.

Therapeutic modalities

Paracetamol (acetaminophen, APAP)

Paracetamol's mechanism of action for pain reduction seems to primarily involve its central inhibition of cyclooxygenase (COX), without a significant anti-inflammatory effect. The use of IV acetaminophen (with its debatable analgesic superiority over oral form[62] in combination with opioids for VOC has been associated with pain reduction and opioid sparing in one trial,[63] and an absence of such effects in another.[64] As a single analgesic, IV acetaminophen was found to be superior to IV diclofenac for skeletal VOC in pediatric patients.[65]

To date, no published RCTs have examined IV APAP's clinical efficacy, either as a single agent or as an adjunct to opioids for VOC treatment in adults. Recommended dosing is 10–15 mg/kg per dose in children (500–1000 mg per dose in adults), with a maximum dose of 75 mg/kg/day in children (4 g in adults). Adverse effects include nausea and vomiting, with hepatic insufficiency being one of the major contraindications and lack of titratability as a major limitation.

Nonsteroidal antiinflammatory drugs

Nonsteroidal antiinflammatory drugs (NSAIDs) act by reducing both pain and inflammation through the inhibition of COX enzymes, thereby decreasing prostaglandin production. As a part of multimodal analgesia, ibuprofen, ketorolac, diclofenac, ketoprofen,

Table 2: Summary of analgesic options in the treatment of acute pain in vaso-occlusive crisis in sickle-cell disease patients

Medication class	Commonly used drugs	Common routes of administration	Suggested initial dosage	Notes
APAP	Acetaminophen Paracetamol	IV, PO, PR	Pediatric: 10–15 mg/kg (maximum 1000 mg) Adults: 500–1000 mg	Risk of hepatotoxicity in supra-analgesic dosages, avoid use in hepatic impairment
NSAID	Ketorolac Diclofenac Ketoprofen Dexketoprofen	IV, IM, IN IV, IM, PR, PO IV, IM, PO IV, IM, PO	Pediatric: 0.5 mg/kg IV (maximum 10 mg), 1 mg/kg IM (maximum 30 mg) Adults: 10 mg IV, 30 mg IM, 31.5 mg IN Pediatric: 0.3 mg/kg IV, 0.5 mg/kg PR, 1 mg/kg PO Adults: 50 mg PO, 75 mg IV/IM Adults: 25–50 mg PO, 50 mg IM/IV Adults: 25 mg PO, 50 mg IV/IM	Use with caution in pediatric patients. Avoid use in renal impairment, or in patients with full-dose anticoagulation
Opioids	Morphine Fentanyl Hydromorphone	IV, SQ, IM, oral IV, IN, SL, buccal IV/IM, IN, PO	0.1 mg/kg: IV/IM/SQ (maximum single dose 10 mg), 15–30 mg immediate-release (MSIR) tablet PO Pediatric: 1–1.5 µg/kg IV and 1.5 µg/kg IN (maximum 100 µg) Adults: 50–100 µg IV/IN, 100 µg SL/buccal Pediatric: 0.015 mg/kg IV, 0.03–0.06 mg/kg IN Adults: 0.75–1.5 mg IV, 4–8 mg IN, 4–8 mg PO	Avoid Codeine and Tramadol due to unreliable CYP2D6 metabolism. Use morphine with caution in renal impairment. Increased risk of acute chest syndrome with morphine use
NMDA antagonist	Ketamine Lidocaine	IV, IM, IN, SQ, Inhalation IV	0.15–0.3 mg/kg IV, 0.5 mg/kg: IN/SQ, 0.75 mg/kg Nebulization 1–1.5 mg/kg IV	Consider slow infusion of ketamine over 15 min to avoid emergence Consider slow infusions of 15–30 min and watch for neurologic signs (perioral numbness, dizziness) or hemodynamic instability (local anesthetic systemic toxicity)

IV: Intravenous, PO: Oral, PR: Rectal, IN: Intranasal, IM: Intramuscular, SL: Sublingual, SQ: Subcutaneous, NEB: Nebulized, NMDA: N-methyl-D-aspartate, NSAIDs: Nonsteroidal anti-inflammatory drugs, APAP: Acetaminophen, Paracetamol (N-acetyl-p-aminophenol), MSIR: Morphine sulfate immediate release

and dexketoprofen were found to be beneficial in reducing pain and overall opioid consumption.[66] Despite demonstrated equianalgesia to morphine in some studies,[67,68] the Cochrane database systematic review found the evidence of insufficient quantity and quality to reliably confirm significant efficacy of NSAIDs for acute pain in sickle-cell patients.[69] NSAIDs should be administered in the safest doses, not exceeding accepted analgesic ceilings, and for the shortest period to avoid complications, such as renal dysfunction and peptic ulcer disease.[70]

Opioids

Opioids remain the cornerstone of management of pain in VOC. Commonly used mu-receptor agonists (morphine, hydromorphone, and fentanyl) decrease afferent nociceptive signals, thereby reducing pain sensation. Parenteral formulations must be titrated to optimal analgesic effect, and only immediate-release and short-acting opioids should be used in the ED for VOC treatment. Opioid administration should target achievement of a "therapeutic window,' where optimal analgesia is achieved with the least amount of side effects, which could include nausea/vomiting, itching, dizziness, somnolence, and even respiratory depression. The factors affecting this "therapeutic window" in patients with VOC include renal and hepatic function, drug metabolism, prior pain events, and amount and duration of opioid use in the past.[71,72]

Numerous clinical trials support the use of IN administration of hydromorphone and fentanyl for sickle cell patients in the ED, demonstrating similar analgesic efficacy to their parenteral counterparts. Similarly, SL administration of fentanyl, sufentanil, and buprenorphine resulted in significant pain relief of acute pain of VOC.[73] The subcutaneous route is a suboptimal choice for such patients due to the delay in the onset of analgesia, and the intramuscular route should be avoided due to severe pain on injection, unpredictable absorption, and the development of myofibrosis.[73,74]

Once optimal analgesia is achieved, those patients admitted for subsequent pain management could benefit from patient-controlled analgesia (PCA) infusions or intermittent boluses. The use of PCA in the ED may also have a positive impact on patient satisfaction and reduced need for additional analgesics, provided adequate training and experience with this modality is maintained amongst ED providers.[75]

Opioid tolerance, which is associated with a reduction in analgesic effect following repeated or prolonged opioid use, and opioid-induced hyperalgesia (OIH)-a

paradoxical nociceptive sensitization leading to a hyper response to acute noxious stimuli in the setting of opioid therapy-are frequently present in sickle cell patients.[76] Given the considerable variability in dosage and response for patients receiving opioids, the approach to optimal analgesia, including choice of drug, dose, and route, should be individualized based on each patient's severity of pain and level of reduction following opioid administration.[72]

Finally, the metabolism of tramadol and codeine is dependent on the hepatic CYP2D6 enzyme, which affects the amount of available active metabolite due to gene polymorphism in sickle-cell patients, thus warranting avoidance of these opioids in these patients.[77]

Adjunctive therapies

Ketamine is a noncompetitive antagonist of N-methyl-D-aspartate and plays a role in the reduction of pain through central sensitization. Two RCTs demonstrated similar analgesic efficacy of sub-dissociative dose ketamine to opioid-based therapy and opioid-sparing effect, illustrating its potential as an adjunct in pain management for VOC.[78,79] Continuous infusions of ketamine in sub-dissociative doses coupled with opioids are recommended for sickle cell patients in order to reduce dysphoria, nausea, and vomiting.[66,80]

Systemic IV administration of lidocaine, an amide local anesthetic, has been found to reduce pain and provide opioid-sparing in patients with VOC. However, the data is based on retrospective case series and reports showing a variability in outcome measures and dosing. In general, both ketamine and lidocaine, while limited by current evidence, still hold potential benefits as adjuncts to opioid medication, potentially reducing the amount of opioids used to effectively manage acute pain in SCD patients.[81-83] Ultrasound-guided regional analgesia targeting specific regions of acute pain in SCD patients with the potential to reduce pain warrants a future investigation for use in VOC in the ED.[84]

Nonpharmacologic options

A review of nonpharmacologic options for pain relief in sickle cell patients, including distraction therapy, cognitive–behavioral therapy, hypnosis, biofeedback, and massage, demonstrated significant reduction in pain and anxiety and improvements in patients' satisfaction.[85] While underutilized in the ED, their inclusion as part of a multimodal analgesia regimen warrants further investigation. In addition, the involvement of a multidisciplinary team will enable optimal management of social, neuropsychiatric, surgical, and pain-related outcomes.[86]

Pitfalls in emergency department pain management

Frequent use of high dosages of opioids in patients with SCD is frequently met with negative provider attitude and bias as well as fear of dependence and/or addiction, leading to delayed and ineffective pain management.[87] Contrary to popular belief, the prevalence of opioid dependence and addiction in sickle-cell disease patients is approximately 0.5%–8%.[88] Improved education about disease pathology and guideline-based management may reduce negative provider attitudes and stigmas and improve strategies to enhance patient safety, timely administration of appropriate pain relief, and optimization of subsequent care for SCD patients.[89,90]

Take-home pearls

- ED clinicians should attempt to create and utilize patient-specific pain management pathways that improve pain management and throughput in the ED
- ED clinicians should use opioids in a safe and effective manner by frequent titration and balancing pain relief and adverse effects
- ED clinicians should utilize nonopioid analgesics and adjuncts in a judicious and effective manner for the control of acute pain
- ED clinicians should collaborate with an interdisciplinary team to ensure effective pain management in the ED and continuation of care upon discharge from the ED.

Pain Management in Cancer/Palliative Care Patients in the Emergency Department

ED's visits of cancer patients for breakthrough pain, inadequate baseline analgesia, or serious complications are challenging due to limited initial clinical information.[91,92] Pain management varies based on cancer type, stage, treatment phase, and overall health status. Cancer and treatment-related organ dysfunction alter drugs' pharmacokinetics, complicating the analgesic response. The absence of standardized protocols and concerns about opioid overprescription can make emergency clinicians hesitant to provide optimum analgesia.[93-95] When evaluating patients with cancer pain in the ED, emergency clinicians should focus on the following elements [summarized in Table 3]: Presenting symptoms (cancer or treatment related),[91,96,97] risk stratifications (age, comorbidities),[98,99] presence of breakthrough pain,[98,99] OIH,[100] neuropathic pain as a distinct modality either from the cancer itself or as a result of chemotherapy, radiation, or surgery,[96,97,101] as well as anxiety, depression, fear, and distress.[98,101] Table 4 summarizes therapeutic approaches (dosing and routes) for the management of cancer pain.

Table 3: General approach to cancer pain in the emergency department

Pain-related reason for ED visits	Approach in the ED
Acute complications from underlying cancer or cancer-related therapy (infection or adverse effects)	Use a personalized, patient-specific approach based on history (current/recent therapies and complications if available) and clinical findings
	Avoid availability and anchoring biases
Acute painful conditions unrelated to underlying cancer (preventing "cancer pain bias" and ensuring effective treatment of other painful syndromes)	Assess and evaluate existing comorbidities
Breakthrough pain (disease progression or increasing tolerance to opioids)	Evaluate breakthrough pain in a timely and effective manner, although it can be challenging at times
OIH	Understand the challenges of identifying and treating (OIH) in the ED
	Consider optimization of pain relief with nonopioid analgesia, opioid reduction, opioid rotation
Neuropathic pain	May responds to opioids
	Anticonvulsants and antidepressants may help reduce opioid use, but their long-term effectiveness cannot be evaluated in the ED
Anxiety, depression, stress, and distress	Exercise empathy
	Adequate anxiolytics should be included in the plan

OIH: Opioid-induced hyperalgesia, ED: Emergency department

Therapeutic approaches

Nonpharmacologic measures

Communication and shared decision-making with patients and their families regarding pain management goals, expectations, and adverse effects are essential for timely and effective pain, stress, and anxiety control in the ED.[102] Heat and cold packs might be considered for the initial management of myalgias, arthralgias, and neuropathic pain in patients with active cancer.[103,104] Similarly, positioning and immobilization for acute pathologic fractures reduce pain exacerbation, and "position of comfort" can significantly reduce pain in patients with pleural metastases.[103,104] The efficacy of music therapy and virtual reality for breakthrough cancer pain in the ED remains largely unstudied.[103] Guided imagery, breathing exercises, and cognitive behavioral techniques might reduce pain and anxiety and should be a part of a multidisciplinary approach in the ED.[103,104]

Pharmacologic approaches [Table 4]

Opioid analgesics

Opioids are the most studied analgesics for cancer pain. Most cancer patients with breakthrough pain develop tolerance, requiring higher doses for satisfactory analgesia.[100,101,105] Morphine and fentanyl are available in parenteral, oral, IN, and rectal (morphine) forms and remain the first-line option for severe cancer pain in the ED, with morphine having a longer-lasting effect and fentanyl having fewer complications in patients with renal impairment.[101,105]

Hydromorphone administered in parenteral, oral, and rectal forms is equally effective for managing chronic cancer pain, but its metabolites may accumulate in patients with renal or hepatic impairment.[101,105] Although less effective than the above-mentioned opioids, tramadol is frequently used for cancer pain.[106,107] Tramadol's opioid activity is dependent on CYP2D6 metabolism, leading to significant variability in humans and a less favorable safety profile.[105-107] For patients with acute pathologic fractures, hyperalgesia, and opioid tolerance, methadone can be beneficial when other opioids are ineffective or intolerable.[108,109]

A Cochrane review demonstrated equal or even superior efficacy of transdermal buprenorphine in comparison to other opioids in cancer patients.[110,111] EPs should calculate the current daily and equivalent dosages and provide a bolus dose of an opioid equivalent to 10%–20% of the patient's current daily dose[101,105] [Table 5]. If discharged, patients should be provided with "breakthrough doses" of opioids, preferably in a nonparenteral formulation (e.g., buccal or SL drops, tablets, or films).[101,105]

Nonopioid analgesics

Paracetamol (acetaminophen) is not considered a first-line therapy for cancer pain.[112,113] The Cochrane systematic review found insufficient evidence to support or refute its use either alone or in combination with codeine or dihydrocodeine in neuropathic pain.[112-114] Furthermore, there is evidence for paracetamol's ineffectiveness in reducing the need for opioids and reducing pain in cancer patients receiving potent opioids.[113,114]

NSAIDs are found to be effective in managing cancer pain in the ED when administered alone or in combination with opioids, enhancing analgesic efficacy and reducing the need for opioids.[102,115] However, high-quality evidence is lacking regarding the analgesic efficacy of NSAIDs in cancer pain.[116] It is important to consider the potential side effects and contraindications associated with NSAID use, such as gastrointestinal and renal

Table 4: Commonly used analgesics with routes and dosing regimens in the emergency department

Medication	Route	Initial dose (opioid-naïve)	Dosing interval	Notes
Morphine	PO	5–15 mg (immediate release)	Every 4 h	Common first-line agent
		15–30 mg (controlled release)	Every 12 h	For stable pain
	IV	2–8 mg	Every 4 h or as needed	3:1 oral to IV conversion
		0.8–10 mg/h (continuous)	Continuous	For severe pain
	SC	2–8 mg	Every 4 h	Similar potency to IV
		0.8–10 mg/h (continuous)	Continuous	Common in-home care
	PR	10–20 mg	Every 4 h	Alternative when oral unavailable
Hydromorphone	PO	2–4 mg (immediate-release)	Every 4–6 h	5x more potent than oral morphine
		8–12 mg (controlled-release)	Every 12–24 h	For stable pain
	IV	0.5–1 mg	Every 3–4 h	High potency option, severely euphorigenic
		0.2–1.0 mg/h (continuous)	Continuous	For severe pain
	SC	0.5–1 mg	Every 4 h	Similar potency to IV
		0.2–1.0 mg/h (continuous)	Continuous	Good for home care
Fentanyl	TD	12–25 µg/h patch with a gradual increase up to 400 µg/h	Every 72 h	Ideal for outpatient use
	IV	25–50 µg	Every 1–2 h prn	Very rapid onset (1–2 min)
		25–100 µg/h (continuous)	Continuous	High potency
	IN	50–100 µg	Every 1–4 h prn	Rapid onset for breakthrough pain
	SL/Buccal	100–200 µg	Every 2–4 h prn	Rapid absorption
	INH	100–400 µg	Every 1–4 h prn	Limited usage in cancer pain
Oxycodone	PO	5–10 mg (immediate-release)	Every 4–6 h	1.5 × more potent than oral morphine
	PO	10–20 mg (controlled-release)	Every 12 h	Good option when morphine is poorly tolerated
	PR	5–10 mg	Every 4–6 h	Alternative when oral unavailable
Methadone	PO	2.5–5 mg	Every 8–12 h	Complex pharmacokinetics. Requires expertise; long half-life
	IV	2.5–5 mg	Every 8–12 h	Limited use in acute settings
	SC	2.5–5 mg	Every 8–12 h	Limited data on SC administration
Buprenorphine	TD	5–10 µg/h patch	Every 7 days	Partial agonist with ceiling effect
	SL	0.2–0.4 mg	Every 6–8 h	Limited use in cancer pain
Tramadol	PO-IR	50–100 mg	Every 4–6 h (maximum 4 times daily)	Unstable analgesic effect due to genetic differences in CYP2D6. Adjust in renal/hepatic impairment
	PO-ER	100–200 mg	Every 24 h	Maximum 300 mg/day. Once-daily dosing
	IV	50–100 mg	Every 6 h	Slow IV push. Limited cancer pain use
	SC	50–100 mg	Every 6 h	Less common route. Limited clinical data
	IM	50–100 mg	Every 6 h	Rarely used. Painful injection site
Ketamine	IV	0.1–0.5 mg/kg	Intermittent doses	Refractory pain. Adjuvant for opioid-resistant pain
	IV	Low-dose: 0.05–0.5 µg/kg/h	Continuous	Chronic pain. Potential opioid-sparing effect
	SC	0.1–0.5 mg/kg	Every 4–6 h	Breakthrough pain. Less studied than the IV route
	PO	0.2–0.5 mg/kg/dose	Every 6–8 h	Limited use. Poor bioavailability
	IN	50–100 mg	As needed	Breakthrough pain. Rapid onset, alternative route. Rapid onset, alternative route
Lidocaine	IV	1–2 mg/kg/h	Continuous infusion	Neuropathic pain. Requires cardiac monitoring
	IV	Low dose: 20–50 mg/h	Continuous	Chronic pain. Potential anti-inflammatory effect
	SC	1% solution	Continuous or intermittent	Localized pain. Limited systemic absorption
	Topical	5% patch	Applied for 12 h/day	Localized neuropathic pain. Targeted nerve pain relief
	TM	2%–4% viscous solution	As needed	Oral/pharyngeal pain. Local anesthetic effect
Ibuprofen	PO	400–800 mg	Every 6–8 h	Maximum daily dose: 2400 mg. Take with food to reduce GI side effects
Diclofenac	PO, IM, PR, topical	50 mg (oral)	Every 8–12 h	Maximum daily dose: 150 mg. Higher risk of cardiovascular events compared to some other NSAIDs. Available as enteric-coated tablets

Contd...

Table 4: Contd...

Medication	Route	Initial dose (opioid-naïve)	Dosing interval	Notes
Naproxen	PO	250–500 mg	Every 12 h	Longer half-life than ibuprofen. Maximum daily dose: 1500 mg. Lower cardiovascular risk compared to some other NSAIDs
Ketoprofen	PO, IM, topical	50–100 mg	Every 6–8 h	Maximum daily dose: 300 mg. Available as extended-release formulation
Etoricoxib	PO	60–120 mg	Once daily	COX-2 selective inhibitor. Contraindicated cardiovascular disease, cerebrovascular disease, and peripheral arterial disease
Nimesulide	PO	100 mg	Every 12 h	Maximum daily dose: 200 mg. Restricted/banned in some countries due to hepatotoxicity concerns. Limited duration of use recommended (max 15 days)
Meloxicam	PO	7.5–15 mg	Once daily	Preferential COX-2 inhibitor. Longer half-life requiring once-daily dosing
Indomethacin	IV, PO, PR	25–50 mg	Every 8–12 h	Maximum daily dose: 200 mg. Higher incidence of adverse effects, especially CNS (headache, dizziness)
Piroxicam	PO	20 mg	Once daily	Long half-life. Higher risk of GI side effects. Not recommended as first-line therapy, especially in elderly
Paracetamol (acetaminophen)	IV, PO, PR	500–1000 mg	Every 4–6 h	Not an NSAID. Maximum daily dose: 4000 mg (lower in hepatic impairment/elderly). No anti-inflammatory effects. Less GI toxicity but risk of hepatotoxicity at high doses

All initial doses should be titrated based on patient response and tolerability. The doses listed are general starting points for opioid-naïve adults. For breakthrough Pain: Prescribe 10%–15% of the 24-h opioid dose as needed. Reduce doses and extend intervals for patients with renal/hepatic impairment. Start with lower doses (approximately 25%–50% of the standard dose) in elderly patients. Consider concurrent use of adjuvant analgesics (NSAIDs, anticonvulsants, antidepressants) to improve pain control. When using opioids, consider implementing a bowel regimen to prevent constipation. IV: Intravenous, SL: Sublingual, IN: Intranasal, IM: Intramuscular, INH: Inhalation, PO: Oral, PR: Rectal, SQ: Subcutaneous, SL: Sublingual, TD: Transdermal, TM: Transmucosal, IR: Immediate release, ER: Extended release, CNS: Central nervous system, NSAID: Nonsteroidal anti-inflammatory drug, GI: Gastrointestinal

Table 5: Oral and parenteral equivalent doses of opioids and conversion ratios

Opioid	Equianalgesic oral dose	Equivalent IV dose	Conversion ratio
Morphine	Reference dose (30 mg)	10 mg	3:1 (IV: Oral)
Fentanyl	Not recommended for direct oral conversion	100 µg	
Hydromorphone	7.5 mg	1.5 mg	5:1 (IV: Oral)
Hydrocodone	30 mg	30 mg	1:1 oral morphine equivalent
Tramadol	300 mg	100 mg	3:1 (IV: Oral)
Codeine	200 mg		
Oxycodone	20 mg		
Methadone	10 mg		

Fentanyl patch strength (µg/h)	Approximate daily oral morphine equivalent (mg)
12	25
25	50
50	100
75	150

Conversions should consider potential complex interactions with other medications and potential patient variability. It is recommended to titrate slowly and monitor for side effects, IV: Intravenous

toxicity, and to provide appropriate gastrointestinal prophylaxis when necessary.[116,117]

Sub-dissociative doses of ketamine can be helpful in the treatment of opioid-tolerant and refractory cancer pain.[118-120] Both intermittent and continuous IV infusions were found to reduce opioid requirements in cancer patients.[118] IN ketamine demonstrated a significant reduction in breakthrough cancer pain not controlled by opioids, with higher doses providing more significant pain relief without major side effects.[119] Oral ketamine can also be an effective adjuvant to morphine for managing refractory neuropathic cancer pain.[103,115] Several systematic reviews and guidelines showed that ketamine significantly reduces pain intensity in cancer patients and recommend considering it for refractory cancer pain.[108,120]

A single-phase II study supported the efficacy and safety of IV lidocaine in refractory cancer pain.[121] Although a retrospective case series reported that cardiac monitoring is not required, it should be applied in patients with

cardiac disease. If the initial bolus (1–1.5 mg/kg) is effective and well tolerated, it is followed by an infusion for prolonged symptom relief.[115,122]

Adjunctive agents

Although benzodiazepines do not have a direct analgesic effect, small boluses of midazolam (1–2 mg IV) are effective in reducing anxiety and muscle spasms.[103,115,122] Benzodiazepine use should be cautious when opioids are used concurrently due to the risk of respiratory depression.

Corticosteroids, despite limited efficacy, are commonly used as adjuvant analgesics in cancer pain management, particularly for neuropathic pain, bone metastasis, and pain associated with inflammation or edema.[123-125] Dexamethasone is preferred for most oncologic emergencies. Significant hyperglycemic effects should be anticipated in diabetic patients.

Anticonvulsants such as gabapentin and pregabalin can be helpful adjuncts for neuropathic types of cancer pain. The initiation of gabapentin or pregabalin in the ED for compression or chemotherapy-induced neuropathies may be considered, although these therapeutics are not expected to provide immediate relief[126-128] and may worsen opioid-induced respiratory depression.[128]

There is strong evidence from several RCT that antiemetics should be considered early for co-administration with opioids to prevent nausea/vomiting.[129,130] Ondansetron (4–8 mg IV) is regarded as the first-line treatment, with metoclopramide (10 mg IV) as an alternative.[115,129,130]

Nerve blocks

Ultrasound-guided nerve blocks are an excellent therapeutic modality for cancer patients who present to the ED with properly localized acute pain.[115,131,132] Numerous RCTs support their efficacy and safety in such patients, with intercostal blocks for rib metastases and femoral nerve blocks for pathologic hip fractures being commonly used in the ED.[131,132] While cryo-neurolysis has been more commonly applied to conditions like rib fractures and postsurgical pain, its principles and efficacy in neuropathic pain management also make it a suitable option for cancer-related pain in the emergency department.[133-135]

Common pitfalls in cancer pain management in the emergency department

Although the list of potential pitfalls in cancer pain management is vast, they can be categorized into assessment issues, treatment-related issues, opioid-related pitfalls, system gaps, and psychosocial and patient-related factors [Table 6]. EPs commonly encounter one or more of these pitfalls when treating such patients.

Table 6: Common pitfalls in cancer pain management in the emergency department

Pain assessment
Inadequate pain assessment (failing to systematically assess pain using validated scales)
Underestimation of pain
Poor communication with patients (failure to understand patient expectations and develop a shared plan)
Poor communication with patients (failure to understand patient expectations and develop a shared plan)
Treatment approach issues
Delayed initiation of analgesics
Oligoanalgesia
Failure to use a multimodal approach (no use of adjuvant medications or nonpharmacological interventions)
Addressing breakthrough pain without providing a viable plan for home
Opioid-related pitfalls
Opiophobia
Overemphasis on addiction risk
Not anticipating and managing side effects
Abrupt discontinuation
System and knowledge gaps
Insufficient provider education
Regulatory barriers
Poor continuity of care
Limited access to pain specialists
Psychosocial factors
Ignoring psychological components (not addressing anxiety, depression, and catastrophizing that amplify pain)
Cultural insensitivity (not considering cultural differences in pain expression and treatment preferences)
Social support neglect (failing to involve caregivers in pain management plans)
Patient-related factors
Self-medicating
Unrealistic expectations

Take-home pearls

- Consider acute cancer/treatment complications and comorbidities as potential causes of pain and avoid "cancer pain bias"
- Communicate goals and expectations with patients and their families and utilize a multimodal approach of nonpharmacologic and pharmacologic treatment modalities
- Calculate opioid requirements based on home regimens and use careful titration in renal/hepatic dysfunction. Use short-acting opioids for breakthrough pain. If the patient is discharged, provide a discharge analgesic rescue plan
- Use NSAIDs (with caution), ketamine (for opioid-tolerant patients), and adjuncts (anticonvulsants for neuropathic pain, antiemetics) for pain control
- Consider ultrasound-guided nerve blocks

- Acknowledge anxiety, depression, stress, and distress. Exercise empathy and consider anxiolytics if appropriate
- When in doubt, consult: Do not hesitate to seek guidance from palliative care specialists and/or pain management experts.

Emergency Department Pain Management of Older Adults

Managing acute pain in elderly patients (>64 years) in the ED requires a nuanced approach. Older patients are often more sensitive to medication effects and side effects. They tend to have more comorbid conditions, higher rates of polypharmacy, and reduced physiological reserves. The primary focus of pain management in geriatric patients is to minimize potential harm while providing effective, multi-modal analgesia.

Challenges in geriatric pain management in the emergency department

Older adults often present to the ED with acute pain, yet they consistently receive less adequate pain management compared to younger patients.[136-138] These challenges in safely assessing and managing pain in this population [Table 7] necessitate a carefully crafted approach to pain management that considers the unique characteristics and needs of each patient.

Approach to assessing pain in the emergency department

In patients able to communicate, pain can be assessed via different tools and pain scales, such as a numeric scale or Visual Analog Scale.[139-140] However, these scales are highly subjective, fail to capture personal and cultural differences, and do not convey the patient's wishes or needs regarding medication administration. A simple, useful approach can be to ask the patient if they need medication for pain. If they answer affirmatively, a follow-up question can be to inquire what has worked well for their pain in the past. For patients with moderate to severe dementia, unable to give a verbal account of their pain, the Pain Assessment in Advanced Dementia Scale (PAINAD) and Abbey Pain Scale, relying on nonverbal cues to pain, such as body positioning, moaning, or facial expressions, are found to be valuable.[141,142]

Table 7: Challenges to safely managing pain in older adult patients

Challenge	Causes and factors
Assessing pain can be more challenging	Dementia, acute delirium, changes in pain sensation, and presentation of painful conditions. Overall complexity in presentations and more co-morbidities
Risks of side effects or adverse drug events	Greater risk for respiratory depression or over-sedation. Lower physiologic reserve. Higher rates of polypharmacy and risk of drug–drug interactions. Higher rates of renal and hepatic dysfunction lead to changes in rates of drug excretion or metabolism
Risks of under-treating pain	Worsens or prolongs suffering. Contributes to delirium and other adverse outcomes[3]

Approach to pain management in older adults

A useful framework for managing pain in older adults is to use a patient-centered, holistic, and diverse therapeutic approach that considers potential drug-patient, drug-disease, and drug-drug factors and interactions.

Patient-centered

Putting patients' desires and interests at the center of conversation by asking what matters the most to them will align clinicians' care with the patient's goals. Incorporating what matters to the patient is a cornerstone of the Age-Friendly Health Systems' "5 Ms" framework that includes: mentation, mobility, medications, multi-complexity, and what matters most.[143]

Holistic

Pain and the experience of suffering are multifactorial and personal, and can be exacerbated by emotional distress and other unmet needs. Identifying whether pain is acute or chronic, neuropathic or nociceptive, visceral or somatic can help guide treatment selection. In addition, it is important to address the patient's other needs, such as food, hydration, and physical comfort.[136,143]

Drug-patient effects

When selecting a medication and dose, consider potential interactions between the drug and the patient, such as the patient's baseline level of frailty or physiologic reserves, their underlying fall risk, and whether they have physiologic tolerance or are naïve to a given class of medications.[136,137]

Drug-disease effects

Renal, hepatic, or cardiac dysfunction; peptic ulcer disease; orthostatic hypotension; and delirium may necessitate medication adjustments. For example, NSAIDs can cause acute renal failure, particularly in the setting of chronic kidney disease (CKD). NSAIDs can also worsen gastritis and peptic ulcer disease. They can also interact with ACE inhibitors, diuretics, steroids, and warfarin, potentially increasing INR for patients on warfarin.

Renally-cleared opioids such as oxycodone, hydrocodone, and morphine should be used cautiously in patients with chronic kidney disease or end-stage kidney disease, as the medication or its metabolites can have prolonged or more severe adverse effects or sedation.[144]

Drug–drug effects

When prescribing medications for use over time, as well as a single dose in the ED, it is important to

review the patient's home medication list to look for potential medication interactions. For pain management, high-risk combinations to avoid to prevent oversedation, respiratory depression, or other side effects include opioids with gabapentinoids, muscle relaxants, or benzodiazepines.[136,143]

A tiered treatment approach

After assessing the patient's source, severity, and chronicity of pain, aligning with patient goals, and reviewing the underlying drug-patient, drug-drug, and drug-disease factors, emergency clinicians should employ a tiered approach to safely managing their pain. Commonly used analgesics with their starting doses and routes of administration are summarized in Table 8.

Nonpharmacologic approaches

Addressing unmet physical or emotional needs can help reduce the experience of suffering. Simple interventions such as adjusting the bed or chair for physical comfort, providing warm blankets, and addressing hunger, thirst, or toileting needs. Heating pads, distraction, or reassurance can be useful as well.[143]

Pharmacologic approaches

Targeted approaches

Certain types of pain are particularly amenable to targeted approaches. For example, femoral or fascia iliaca nerve blocks offer effective analgesia for hip fractures, reducing opioidconsumption.[145] Nerve blocks

Table 8: Common analgesics with routes of administration and starting doses

Medication class, examples, and initial dosing	Considerations
Topical approaches	
NSAIDs	It can be highly effective for sprain, strain as well as joint and osteoarthritis pain and has fewer complications compared with oral NSAIDs
Diclofenac 1%–1.6% gel	
2–4 g applied Q8 h	
Local anesthetics	Can be used topically for postherpetic neuralgia and for localized pain. Patches are frequently used for musculoskeletal back pain and chest wall injuries or rib fractures
Lidocaine 5% ointment	
Apply 3–4 times per day	
Lidocaine 4%–5% patch	
Apply up to 3 patches for 12 h/day	
Systemic nonopioids	
Acetaminophen	Max daily dose of 4 g, or 2 g for those with hepatic dysfunction or alcohol abuse. A safe, first-line option
500–1000 mg PO or IV Q6 h	
NSAIDs	Avoid or use with caution in patients with renal disease and gastritis or peptic ulcers. Chronic use can lead to acute kidney injuries and hyperkalemia, as well as GI bleeding
Ibuprofen	
200–400 mg PO Q6 h	
Naproxen 220 mg PO BID	
Ketorolac 10 mg IV once	
Ketamine, sub-dissociative dosing	It may be effective in patients who have refractory pain despite opioids but has higher rates of psycho-behavioral side effects and early discontinuation
0.15–0.3 mg/kg over 30 min IV	
Gabapentin	It is effective for neuropathic pain such as postherpetic neuralgia but can cause sedation or dizziness. May require renal dose adjustment
100–300 mg PO QHS with up-titration over 1 week	
Pregabalin	It can be used for neuropathic pain and diabetic neuropathy. May cause dizziness and sedation. May require renal dose adjustment
50 mg PO BID-TID	
Systemic opioids	
Hydrocodone: Acetaminophen	Caution to avoid exceeding 4g of acetaminophen daily
2.5–5 mg hydrocodone PO Q4 h	
Morphine IR	Can be an option for discharge medication, with lower abuse potential than oxycodone
7.5–10 mg PO Q6–8 h	
Oxycodone	Can cause constipation, nausea, headaches, dizziness, sedation, and respiratory depression. Higher abuse potential
2.5–5 mg PO Q4–6 h	
Fentanyl	Very effective for acute pain, but short-acting, requiring frequent re-assessment and re-dosing
0.25–0.5 µg/kg IV Q10–15 min	
Morphine	Can cause constipation, nausea, vomiting, sedation, and respiratory depression. Renally cleared, so can have prolonged or more severe side effects for patients with renal impairment
2–4 mg IV Q 15–20 min	
2.5–10 mg PO Q4–6 h	
Hydromorphone	Maybe safer than morphine for patients with renal insufficiency
0.2–0.4 mg IV Q15–20 min	
1–2 mg PO Q3–4 h	

IV: Intravenous, PO: Oral, BID: Twice a day, TID: Three times per day, QHS: Once at night, Q-every, NSAIDs: Nonsteroidal anti-inflammatory drugs, GI: Gastrointestinal, IR: Immediate release

may also be appropriate for other fractures (upper extremities, ribs) or prior to procedures, repairs, or reductions.

Topical approaches

Topical agents, such as diclofenac, can be used alone or as adjuvants for many painful MSK disorders, such as sprains and strains. Topical diclofenac is effective, well-absorbed locally, has little systemic absorption, and reduced side effects.[146] Topical lidocaine patches are effective for postherpetic neuralgia and other neuropathic pain disorders. Lidocaine patches are also useful in chest wall trauma and rib fractures and lead to a decrease in opioid use.[147,148]

Systemic nonopioid medications

Acetaminophen is a common first-line medication for mild or moderate pain in older adults, as there are few side effects and medication interactions, and it can be used in patients with renal disease. It can be given orally or intravenously and can be used in conjunction with other pain medications for a multi-modal approach.[149]

NSAIDs administered orally or parenterally are effective for pain control in the elderly in the ED, with caution in patients with gastric ulcers or renal impairment. NSAIDs are particularly effective for renal colic and other nociceptive (rather than neuropathic) pain.[150] Drug-disease and drug-patient factors should be closely considered before longer-term prescribing, as NSAIDs are involved in close to 25% of adverse drug reactions leading to hospitalization.[151]

Ketamine, when used for acute pain in the ED, provides analgesia comparable to morphine but caries a higher risk of psycho-perceptual side effects such as dizziness, light sedation, or feelings of unreality,[152] with one-third of older patients requiring discontinuation of the ketamine due to the effects.[153]

Gabapentin or pregabalin can be effective for neuropathic pain, but their dosing requires titration. Combinations with benzodiazepines or opioids should be avoided or used with extreme caution.[154]

Systemic opioid medications

Opioids can be used alone or in conjunction with other treatment modalities for acute moderate or severe pain. Opioid medications carry the risk of sedation, urinary retention, and respiratory depression acutely, as well as tolerance and addiction with chronic use. It is generally wise to begin with a lower initial dose, monitoring, and frequent titration as needed to avoid respiratory depression or sedation.[155]

Opioids should also be used for the shortest duration necessary to avoid the risk of addiction or dependence. Tramadol is a weak mu-opioid agonist that is commonly prescribed in the outpatient setting. However, it has significant potential side effects for older adults, including hypoglycemia, hyponatremia, lower seizure threshold, and higher mortality, so it should generally be avoided in favor of safer alternatives.[156,157] Certain opioids, such as oxycodone and hydromorphone, tend to create more euphoria compared with hydrocodone and morphine, which could lead to higher abuse potential.[158]

When prescribing opioids on discharge, it is important to also prescribe a bowel regimen. A combination of stimulant laxatives, such as senna, and/or an osmotic laxative such as polyethylene glycol, is effective.[159] For patients who require longer-term opioid use or who fail stimulant laxatives, peripherally acting mu-opioid receptor antagonists like methylnaltrexone, naldemedine, or naloxegol may be indicated.[160]

Conclusion

Effective pain management for older adult patients in the ED requires a comprehensive approach that balances efficacy with safety. By understanding and addressing the unique challenges faced by this population, clinicians can improve patient safety and enhance the quality of care for elderly patients experiencing acute pain. Clinicians should take a patient-centered, holistic approach and consider drug-patient, drug-disease, and drug-drug interactions to help ensure they are selecting the best medication, dose, and duration for each patient.

Take-home pearls

1. Thorough assessment: Use a holistic approach to assessing a patient's pain, their desires, and what matters most to them. Both verbal and non-verbal indicators are important, especially in patients with cognitive impairment
2. Individualized treatment plans: Develop treatment plans that consider the patient's overall health, current medications, and personal preferences. Incorporate both pharmacologic and nonpharmacologic approaches
3. Dosing strategy: Start with the lowest effective dose, particularly with opioids and sedatives. Reassess or monitor patients frequently and avoid long-term prescriptions when possible
4. Education and communication: Ensure that patients and caregivers understand the treatment plan, potential adverse effects, and the importance of follow-up. On discharge, communicate potential adverse effects and dosing adjustments with the patient and caregiver, such as the risk of dizziness or falls
5. Discharge management: For patients who are prescribed an opioid, it is important to also prescribe a stimulant bowel regimen.

Therapeutic strategies at discharge

While each of the unique and challenging populations requires an individualized treatment plan at discharge from the ED, several important concepts are uniformly applicable to all of them. At discharge, ED clinicians should engage patients in shared decision-making about the nature of their painful syndromes and their expectations with respect to pain relief and functional improvement; commonly used analgesic modalities and their alternatives, as well as short- and long-term adverse effects; and the importance of outpatient follow-up with the specialists (obstetricians and gynecologists, hematologists and sickle-cell specialists, oncologists and palliative care specialists, geriatricians, and pain management specialists with expertise in pain management of these vulnerable groups). In addition, ED clinicians should emphasize the need to return to the ED for re-evaluation in the absence of acceptable pain relief and/or development of severe adverse effects related to prescribed analgesics.

Summary

Effective pain management in special populations requires emergency physicians to adopt tailored approaches that acknowledge the unique physiological, pharmacological, and psychosocial factors affecting these vulnerable groups. For pregnant patients, SCD patients, geriatric individuals, and those requiring cancer or palliative care, standard pain management protocols often prove insufficient or potentially harmful. Implementation of population-specific pain management strategies, early multimodal analgesia, appropriate utilization of non-pharmacological interventions, and interdisciplinary collaboration are essential components of optimal care.

As emergency medicine continues to evolve, further research focusing on these special populations will be critical to developing more refined, evidence-based pain management strategies that would improve patient outcomes, minimize adverse effects, and address the persistent disparities in pain management that these populations frequently encounter.

Author contribution statement

KV: Writing original subchapter (lead); review and editing of the entire paper (equal). AH: Writing original subchapter (lead); review and editing of the entire paper (equal). AR: Writing original subchapter (lead); review and editing of the entire paper (equal). GN: Writing original subchapter (lead); review and editing of the entire paper (equal). CS: Writing original subchapter (lead); review and editing of the entire paper (equal). SM: Conceptualizing the entire paper (lead), review and editing of the entire paper (equal); preparing and editing the final draft (lead).

All authors made substantial contributions to the concept of the work, to manuscript preparation and revisions. All authors have approved the submitted version. All authors have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Conflicts of interest

None Declared.

Funding

None.

References

1. Chang HY, Daubresse M, Kruszewski SP, Alexander GC. Prevalence and treatment of pain in EDs in the United States, 2000 to 2010. Am J Emerg Med 2014;32:421-31.
2. Cordell WH, Keene KK, Giles BK, Jones JB, Jones JH, Brizendine EJ. The high prevalence of pain in emergency medical care. Am J Emerg Med 2002;20:165-9.
3. Matthews L, Lim G. Analgesia in pregnancy. Obstet Gynecol Clin North Am 2023;50:151-61.
4. Tanabe P, Silva S, Bosworth HB, Crawford R, Paice JA, Richardson LD, *et al*. A randomized controlled trial comparing two vaso-occlusive episode (VOE) protocols in sickle cell disease (SCD). Am J Hematol 2018;93:159-68.
5. By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS beers criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2023;71:2052-81.
6. Scarborough BM, Smith CB. Optimal pain management for patients with cancer in the modern era. CA Cancer J Clin 2018;68:182-96.
7. Eiland LS, Harris JB, Holmes AP. Considerations for treating nonobstetric diseases in pregnant patients in the emergency department setting. Ann Pharmacother 2023;57:1415-24.
8. Zerfas I, McGinn R, Smith MA. Pharmacologic management of cancer-related pain in pregnant patients. Drugs 2023;83:1067-76.
9. U.S. Food and Drug Administration- Pregnancy and Lactation Labeling Resources. Available from: https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-resources. [Last accessed on 2025 May 05].
10. American College of Obstetricians and Gynecologists. Response to Consensus Statement on Paracetamol Use during Pregnancy. Available from: https://www.acog.org/news/news-articles/2021/09/response-to-consensus-statement-on-paracetamol-use-during-pregnancy. [Last accessed on 2025 May 05].
11. Society for Maternal-Fetal Medicine (SMFM) Publications Committee. Electronic address: pubs@smfm.org. Prenatal acetaminophen use and outcomes in children. Am J Obstet Gynecol 2017;216:B14-5. [doi: 10.1016/j.ajog.2017.01.021].
12. Ahlqvist VH, Sjöqvist H, Dalman C, Karlsson H, Stephansson O, Johansson S, *et al.* Acetaminophen use during pregnancy and children's risk of autism, ADHD, and intellectual disability. JAMA 2024;331:1205-14.
13. Patel R, Sushko K, van den Anker J, Samiee-Zafarghandy S. Long-term safety of prenatal and neonatal exposure to paracetamol: A systematic review. Int J Environ Res Public Health 2022;19:2128.
14. Castro CT, Gama RS, Pereira M, Oliveira MG, Dal-Pizzol TS, Barreto ML, *et al.* Effect of acetaminophen use during pregnancy on adverse pregnancy outcomes: A systematic review and meta-analysis. Expert Opin Drug Saf 2022;21:241-51.
15. Kim J, Hébert MF. Pharmacological treatment of musculoskeletal conditions during pregnancy and lactation. In: Fitzgerald C, Segal N, editors. Musculoskeletal Health in Pregnancy and Postpartum- An Evidence-Based Guide for Clinicians. Switzerland: Springer International Publishing; 2015. p. 227-43.

16. Shah S, Banh ET, Koury K, Bhatia G, Nandi R, Gulur P. Pain management in pregnancy: Multimodal approaches. Pain Res Treat 2015;2015:987483.
17. U.S. Food and Drug Administration-Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Drug Safety Communication: Avoid use of NSAIDs in Pregnancy at 20 Weeks or Later. Available from: https://www.fda.gov/safety/medical-product-safety-information/nonsteroidal-anti-inflammatory-drugs-nsaids-drug-safety-communication-avoid-use-nsaids-pregnancy-20. [Last accessed on 2025 May 05].
18. Choi EY, Jeong HE, Noh Y, Choi A, Yon DK, Han JY, *et al.* Neonatal and maternal adverse outcomes and exposure to nonsteroidal anti-inflammatory drugs during early pregnancy in South Korea: A nationwide cohort study. PLoS Med 2023;20:e1004183.
19. Fiat F, Merghes PE, Scurtu AD, Almajan Guta B, Dehelean CA, Varan N, *et al*. The main changes in pregnancy-therapeutic approach to musculoskeletal pain. Medicina (Kaunas) 2022;58:1115.
20. Brown HL. Opioid management in pregnancy and postpartum. Obstet Gynecol Clin North Am 2020;47:421-7.
21. Esposito DB, Huybrechts KF, Werler MM, Straub L, Hernández-Díaz S, Mogun H, *et al.* Characteristics of prescription opioid analgesics in pregnancy and risk of neonatal opioid withdrawal syndrome in newborns. JAMA Netw Open 2022;5:e2228588.
22. Ito S. Opioids in breast milk: Pharmacokinetic principles and clinical implications. J Clin Pharmacol 2018;58 Suppl 10:S151-63.
23. Dean L, Kane M. Tramadol therapy and CYP2D6 genotype. In: Pratt VM, Scott SA, Pirmohamed M, Esquivel B, Kattman BL, Malheiro AJ, editors. Medical Genetics Summaries. Bethesda (MD): National Center for Biotechnology Information (US); 2015.
24. National Guideline Alliance (UK). Evidence Review for Long-Term Systemic Steroids: Intrapartum Care for Women with Existing Medical Conditions or Obstetric Complications and Their Babies: Evidence Review E. (NICE Guideline, No. 121.) London: National Institute for Health and Care Excellence (NICE); 2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK576742/. [Last accessed on 2025 May 05].
25. Filippini C, Saran S, Chari B. Musculoskeletal steroid injections in pregnancy: A review. Skeletal Radiol 2023;52:1465-73.
26. Chi CC, Wang SH, Wojnarowska F, Kirtschig G, Davies E, Bennett C. Safety of topical corticosteroids in pregnancy. Cochrane Database Syst Rev 2015;2015:CD007346.
27. Hamilton KT, Robbins MS. Migraine treatment in pregnant women presenting to acute care: A retrospective observational study. Headache 2019;59:173-9.
28. Urits I, Jung JW, Amgalan A, Fortier L, Anya A, Wesp B, *et al*. Utilization of Magnesium for the Treatment of Chronic Pain. Anesth Pain Med 2021;11:e112348.
29. Liu J, Song G, Zhao G, Meng T. Effect of oral magnesium supplementation for relieving leg cramps during pregnancy: A meta-analysis of randomized controlled trials. Taiwan J Obstet Gynecol 2021;60:609-14.
30. Corbo J, Esses D, Bijur PE, Iannaccone R, Gallagher EJ. Randomized clinical trial of intravenous magnesium sulfate as an adjunctive medication for emergency department treatment of migraine headache. Ann Emerg Med 2001;38:621-7.
31. Patorno E, Hernandez-Diaz S, Huybrechts KF, Desai RJ, Cohen JM, Mogun H, *et al.* Gabapentin in pregnancy and the risk of adverse neonatal and maternal outcomes: A population-based cohort study nested in the US Medicaid Analytic eXtract dataset. PLoS Med 2020;17:e1003322.
32. Bockbrader HN, Wesche D, Miller R, Chapel S, Janiczek N, Burger P. A comparison of the pharmacokinetics and pharmacodynamics of pregabalin and gabapentin. Clin Pharmacokinet 2010;49:661-9.
33. Turner MD, Singh F, Glickman RS. Dental management of the gravid patient. N Y State Dent J 2006;72:22-7.
34. Hagai A, Diav-Citrin O, Shechtman S, Ornoy A. Pregnancy outcome after *in utero* exposure to local anesthetics as part of dental treatment: A prospective comparative cohort study. J Am Dent Assoc 2015;146:572-80.
35. Michalowicz BS, DiAngelis AJ, Novak MJ, Buchanan W, Papapanou PN, Mitchell DA, *et al.* Examining the safety of dental treatment in pregnant women. J Am Dent Assoc 2008;139:685-95.
36. Ebrahimi N, Maltepe C, Einarson A. Optimal management of nausea and vomiting of pregnancy. Int J Womens Health 2010;2:241-8.
37. Moini J, Logalbo A, Schellmann JG. Skeletal muscle relaxants. In: Moini J, Logalbo A, Schellmann JG. Neuropsychopharmacology, London, United Kingdom. Academic Press. Elsevier 2023. p. 215-26.
38. Sibrack J, Patel P, Hammer R. Methocarbamol. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK565868/. [Last accessed on 2025 May 05, Last updated on 2024 Sep 10].
39. Menon JM, van Luijk JA, Swinkels J, Lukas E, Ritskes-Hoitinga M, Roeleveld N, *et al*. A health-based recommended occupational exposure limit for nitrous oxide using experimental animal data based on a systematic review and dose-response analysis. Environ Res 2021;201:111575.
40. Aldridge LM, Tunstall ME. Nitrous oxide and the fetus. A review and the results of a retrospective study of 175 cases of anaesthesia for insertion of Shirodkar suture. Br J Anaesth 1986;58:1348-56.
41. Crawford JS, Lewis M. Nitrous oxide in early human pregnancy. Anaesthesia 1986;41:900-5.
42. European Society of Anaesthesiology Task Force on Use of Nitrous Oxide in Clinical Anaesthetic Practice. The current place of nitrous oxide in clinical practice: An expert opinion-based task force consensus statement of the European Society of Anaesthesiology. Eur J Anaesthesiol 2015;32:517-20.
43. Vallejo MC, Zakowski MI. Pro-con debate: Nitrous oxide for labor analgesia. Biomed Res Int 2019;2019:4618798.
44. Pacilio RM, Lopez JF, Parikh SV, Patel PD, Geller JA. Safe ketamine use and pregnancy: A nationwide survey and retrospective review of informed consent, counseling, and testing practices. J Clin Psychiatry 2024;85:24m15293.
45. Cheung HM, Yew DT. Effects of perinatal exposure to ketamine on the developing brain. Front Neurosci 2019;13:138.
46. Paule MG, Li M, Allen RR, Liu F, Zou X, Hotchkiss C, *et al.* Ketamine anesthesia during the first week of life can cause long-lasting cognitive deficits in rhesus monkeys. Neurotoxicol Teratol 2011;33:220-30.
47. Coronel-Oliveros CM, Pacheco-Calderón R. Prenatal exposure to ketamine in rats: Implications on animal models of schizophrenia. Dev Psychobiol 2018;60:30-42.
48. Lodge D, Mercier MS. Ketamine and phencyclidine: The good, the bad and the unexpected. Br J Pharmacol 2015;172:4254-76.
49. Neuman G, Koren G. Safety of procedural sedation in pregnancy. J Obstet Gynaecol Can 2013;35:168-73.
50. Koukoulithras I Sr., Stamouli A, Kolokotsios S, Plexousakis M Sr., Mavrogiannopoulou C. The effectiveness of non-pharmaceutical interventions upon pregnancy-related low back pain: A systematic review and meta-analysis. Cureus 2021;13:e13011.
51. Liddle SD, Pennick V. Interventions for preventing and treating low-back and pelvic pain during pregnancy. Cochrane Database Syst Rev 2015;2015:CD001139.
52. Nanji JA, Carvalho B. Pain management during labor and vaginal birth. Best Pract Res Clin Obstet Gynaecol 2020;67:100-12.
53. Thuvarakan K, Zimmermann H, Mikkelsen MK, Gazerani P. Transcutaneous electrical nerve stimulation as a pain-relieving approach in labor pain: A systematic review and meta-analysis of randomized controlled trials. Neuromodulation 2020;23:732-46.
54. Ternov NK, Grennert L, Aberg A, Algotsson L, Akeson J.

Acupuncture for lower back and pelvic pain in late pregnancy: A retrospective report on 167 consecutive cases. Pain Med 2001;2:204-7.
55. Smith CA, Collins CT, Levett KM, Armour M, Dahlen HG, Tan AL, *et al.* Acupuncture or acupressure for pain management during labour. Cochrane Database Syst Rev 2020;2:CD009232.
56. Drugs and Lactation Database (LactMed®). Bethesda (MD): National Institute of Child Health and Human Development; 2006. Drugs and Lactation Database (LactMed) – Record Format. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547442/. [Last accessed on 2025 May 05].
57. GBD 2021 Sickle Cell Disease Collaborators. Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000-2021: A systematic analysis from the Global Burden of Disease Study 2021. Lancet Haematol 2023;10:e585-99.
58. Takaoka K, Cyril AC, Jinesh S, Radhakrishnan R. Mechanisms of pain in sickle cell disease. Br J Pain 2021;15:213-20.
59. Attell BK, Barrett PM, Pace BS, McLemore ML, McGee BT, Oshe R, *et al.* Characteristics of emergency department visits made by individuals with sickle cell disease in the U.S., 1999-2020. AJPM Focus 2024;3:100158.
60. Ballas SK, Dampier C. Risk factors associated with increased emergency department utilization in patients with sickle cell disease: A systematic literature review. Ann Hematol 2020;99:2483-95.
61. Brandow AM, Carroll CP, Creary S, Edwards-Elliott R, Glassberg J, Hurley RW, *et al.* American Society of Hematology 2020 guidelines for sickle cell disease: Management of acute and chronic pain. Blood Adv 2020;4:2656-701.
62. Ulrich M, Chamberland M, Bertoldi C, Garcia-Bournissen F, Kleiber N. Newly approved IV acetaminophen in Canada: Switching from oral to IV acetaminophen. Is IV worth the price difference? A systematic review. Paediatr Child Health 2021;26:337-43.
63. Baichoo P, Asuncion A, El-Chaar G. Intravenous acetaminophen for the management of pain during vaso-occlusive crises in pediatric patients. P T 2019;44:5-8.
64. Dhebaria T, Sivitz A, Tejani C. Does intravenous acetaminophen reduce opioid requirement in pediatric emergency department patients with acute sickle cell crises? Acad Emerg Med 2021;28:639-46.
65. Panda PC, Mishra NR, Patra CS, Nayak BK, Panda SK. Intravenous acetaminophen versus intravenous diclofenac sodium in management of skeletal vaso-occlusive crisis among children with homozygous sickle cell disease: A randomized controlled trial. Indian Pediatr 2021;58:229-32.
66. Kenney MO, Smith WR. Moving toward a multimodal analgesic regimen for acute sickle cell pain with non-opioid analgesic adjuncts: A narrative review. J Pain Res 2022;15:879-94.
67. Reddy SP, Jondhale SN, Rathia SK, Yusuf S, Shah S, Goel AK. Ketorolac versus morphine for severe vaso-occlusive crisis in sickle cell disease: An open-label randomized controlled trial (KISS study). Indian Pediatr 2025;62:15-9.
68. Doluee MT, Kakhki BR, Mir HH, Fateminayyeri M, Madanitorbati F, Hosseini S. Pain relief in the sickle-cell crisis: Intravenous morphine versus ketorolac; a double-blind, randomized clinical trial. Iran Red Crescent Med J 2019;21:e83614.
69. Cooper TE, Hambleton IR, Ballas SK, Johnston BA, Wiffen PJ. Pharmacological interventions for painful sickle cell vaso-occlusive crises in adults. Cochrane Database Syst Rev 2019;2019:CD012187.
70. Han J, Saraf SL, Lash JP, Gordeuk VR. Use of anti-inflammatory analgesics in sickle-cell disease. J Clin Pharm Ther 2017;42:656-60.
71. Brandow AM, DeBaun MR. Key components of pain management for children and adults with sickle cell disease. Hematol Oncol Clin North Am 2018;32:535-50.
72. Arzoun H, Srinivasan M, Sahib I, Fondeur J, Escudero Mendez L, Hamouda RK, *et al.* Opioid use in patients with sickle cell disease during a vaso-occlusive crisis: A systematic review. Cureus 2022;14:e21473.
73. Ojo AS, Odipe OG, Owoseni O. Improving the emergency department management of sickle cell vaso-occlusive pain crisis: The role and options of sublingual and intranasally administered analgesia. J Clin Med Res 2023;15:10-22.
74. De Franceschi L, Mura P, Schweiger V, Vencato E, Quaglia FM, Delmonte L, *et al.* Fentanyl buccal tablet: A new breakthrough pain medication in early management of severe vaso-occlusive crisis in sickle cell disease. Pain Pract 2016;16:680-7.
75. Oon MB, Nik Ab Rahman NH, Mohd Noor N, Yazid MB. Patient-controlled analgesia morphine for the management of acute pain in the emergency department: a systematic review and meta-analysis. Int J Emerg Med 2024;17:54.
76. Sampaio-Cunha TJ, Martins I. Knowing the enemy is halfway towards victory: A scoping review on opioid-induced hyperalgesia. J Clin Med 2022;11:6161.
77. Bakshi N, Gillespie S, McClish D, McCracken C, Smith WR, Krishnamurti L. Intraindividual pain variability and phenotypes of pain in sickle cell disease: A secondary analysis from the pain in sickle cell epidemiology study. Pain 2022;163:1102-13.
78. Alshahrani MS, AlSulaibikh AH, ElTahan MR, AlFaraj SZ, Asonto LP, AlMulhim AA, *et al.* Ketamine administration for acute painful sickle cell crisis: A randomized controlled trial. Acad Emerg Med 2022;29:150-8.
79. Alshahrani MS, Alghamdi MA. Ketamine for sickle cell vaso-occlusive crises: A systematic review. Saudi J Med Med Sci 2021;9:3-9.
80. Bawany MH, Motov SM. Subdissociative-dose ketamine for sickle cell vaso-occlusive crisis: A narrative review for the emergency physician. Clin Exp Emerg Med 2022;9:169-75.
81. Puri L, Morgan KJ, Anghelescu DL. Ketamine and lidocaine infusions decrease opioid consumption during vaso-occlusive crisis in adolescents with sickle cell disease. Curr Opin Support Palliat Care 2019;13:402-7.
82. Nguyen NL, Kome AM, Lowe DK, Coyne P, Hawks KG. Intravenous lidocaine as an adjuvant for pain associated with sickle cell disease. J Pain Palliat Care Pharmacother 2015;29:359-64.
83. Zavala NA, Knoebel RW, Anitescu M. Lidocaine and ketamine infusions as adjunctive pain management therapy: A retrospective analysis of clinical outcomes in hospitalized patients admitted for pain related to sickle cell disease. Front Pain Res (Lausanne) 2022;3:878985.
84. Howie BA, Rajput K, Chow R. Regional anesthesia and analgesia in sickle cell pain episodes: A scoping review. Interv Pain Med 2022;1:100108.
85. Williams H, Tanabe P. Sickle cell disease: A review of nonpharmacological approaches for pain. J Pain Symptom Manage 2016;51:163-77.
86. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action, Martinez RM, Osei-Anto HA, McCormick M, editors. Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action. Washington (DC): National Academies Press (US); 2020.
87. Martin OY, Thompson SM, Carroll AE, Jacob SA. Emergency department provider survey regarding acute sickle cell pain management. J Pediatr Hematol Oncol 2020;42:375-80.
88. Zempsky WT. Evaluation and treatment of sickle cell pain in the emergency department: Paths to a better future. Clin Pediatr Emerg Med 2010;11:265-73.
89. Glassberg JA. Improving emergency department-based care of sickle cell pain. Hematology Am Soc Hematol Educ Program 2017;2017:412-7.
90. Hutcherson TC, Rowlee PB, Abeles J, Cieri-Hutcherson NE.

Systematic review of emergency department management of vaso-occlusive episodes in adults with sickle cell disease. J Sickle Cell Dis 2025;2. Available from: https://academic.oup.com/jscd/article/2/1/yoaf001/7943499?login=true. [Last accessed on 2025 Jun 12].

91. Caterino JM, Adler D, Durham DD, Yeung SJ, Hudson MF, Bastani A, *et al.* Analysis of diagnoses, symptoms, medications, and admissions among patients with cancer presenting to emergency departments. JAMA Netw Open 2019;2:e190979.
92. Mayer DK, Travers D, Wyss A, Leak A, Waller A. Why do patients with cancer visit emergency departments? Results of a 2008 population study in North Carolina. J Clin Oncol 2011;29:2683-8.
93. Patel PM, Goodman LF, Knepel SA, Miller CC, Azimi A, Phillips G, *et al.* Evaluation of emergency department management of opioid-tolerant cancer patients with acute pain. J Pain Symptom Manage 2017;54:501-7.
94. Turgeman I, Campisi-Pinto S, Habiballah M, Bar-Sela G. Approach to cancer pain management in emergency departments: Comparison of general and oncology based settings. Pharmaceuticals (Basel) 2022;15:805.
95. Rupp T, Delaney KA. Inadequate analgesia in emergency medicine. Ann Emerg Med 2004;43:494-503.
96. Shah M, Rajha E, DiNardo C, Muckey E, Wierda WG, Yeung SJ. Adverse events of novel therapies for hematologic malignancies: What emergency physicians should know. Ann Emerg Med 2020;75:264-86.
97. Gould Rothberg BE, Quest TE, Yeung SJ, Pelosof LC, Gerber DE, Seltzer JA, *et al*. Oncologic emergencies and urgencies: A comprehensive review. CA Cancer J Clin 2022;72:570-93.
98. Azizoddin DR, Beck M, Flowers KM, Wilson JM, Chai P, Johnsky L, *et al.* Psychological evaluation of patients with cancer presenting to the emergency department with pain: Independent predictors of worse pain severity, interference, and higher hourly opioid administration. JCO Oncol Pract 2022;18:e1648-60.
99. Azizoddin DR, Schreiber K, Beck MR, Enzinger AC, Hruschak V, Darnall BD, *et al.* Chronic pain severity, impact, and opioid use among patients with cancer: An analysis of biopsychosocial factors using the CHOIR learning health care system. Cancer 2021;127:3254-63.
100. Paice JA, Bohlke K, Barton D, Craig DS, El-Jawahri A, Hershman DL, *et al.* Use of opioids for adults with pain from cancer or cancer treatment: ASCO guideline. J Clin Oncol 2023;41:914-30.
101. Paice JA, Portenoy R, Lacchetti C, Campbell T, Cheville A, Citron M, *et al.* Management of chronic pain in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2016;34:3325-45.
102. Gilligan T, Coyle N, Frankel RM, Berry DL, Bohlke K, Epstein RM, *et al.* Patient-clinician communication: American Society of Clinical Oncology consensus guideline. J Clin Oncol 2017;35:3618-32.
103. Swarm RA, Paice JA, Anghelescu DL, Are M, Bruce JY, Buga S, *et al.* Adult cancer pain, version 3.2019, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2019;17:977-1007.
104. Denlinger CS, Ligibel JA, Are M, Baker KS, Demark-Wahnefried W, Friedman DL, *et al.* Survivorship: Pain version 1.2014. J Natl Compr Canc Netw 2014;12:488-500.
105. Bechakra M, Moerdijk F, van Rosmalen J, Koch BC, van der Rijt CC, Sillevis Smitt PA, *et al.* Opioid responsiveness of nociceptive versus mixed pain in clinical cancer patients. Eur J Cancer 2018;105:79-87.
106. Leppert W, Łuczak J. The role of tramadol in cancer pain treatment – A review. Support Care Cancer 2005;13:5-17.
107. Wiffen PJ, Derry S, Moore RA. Tramadol with or without paracetamol (acetaminophen) for cancer pain. Cochrane Database Syst Rev 2017;5:CD012508.
108. Aman MM, Mahmoud A, Deer T, Sayed D, Hagedorn JM, Brogan SE, *et al.* The American Society of Pain and Neuroscience (ASPN) best practices and guidelines for the interventional management of cancer-associated pain. J Pain Res 2021;14:2139-64.
109. Sulistio M, Wojnar R, Key S, Kwok J, Al-Rubaie Z, Michael N. The role of methadone in cancer-induced bone pain: A retrospective cohort study. Support Care Cancer 2021;29:1327-35.
110. Schmidt-Hansen M, Bromham N, Taubert M, Arnold S, Hilgart JS. Buprenorphine for treating cancer pain. Cochrane Database Syst Rev 2015;2015:CD009596.
111. Poulain P, Denier W, Douma J, Hoerauf K, Samija M, Sopata M, *et al.* Efficacy and safety of transdermal buprenorphine: A randomized, placebo-controlled trial in 289 patients with severe cancer pain. J Pain Symptom Manage 2008;36:117-25.
112. Wiffen PJ, Knaggs R, Derry S, Cole P, Phillips T, Moore RA. Paracetamol (acetaminophen) with or without codeine or dihydrocodeine for neuropathic pain in adults. Cochrane Database Syst Rev 2016;12:CD012227.
113. Leiva-Vásquez O, Letelier LM, Rojas L, Viviani P, Gonzalez A, Castellano J, *et al.* Is Acetaminophen Beneficial in Patients With Cancer Pain Who are on Strong Opioids? A Randomized Controlled Trial. J Pain Symptom Manage 2023;66:183-192.e1.
114. Israel FJ, Parker G, Charles M, Reymond L. Lack of benefit from paracetamol (acetaminophen) for palliative cancer patients requiring high-dose strong opioids: A randomized, double-blind, placebo-controlled, crossover trial. J Pain Symptom Manage 2010;39:548-54.
115. Vardy J, Agar M. Nonopioid drugs in the treatment of cancer pain. J Clin Oncol 2014;32:1677-90.
116. Magee DJ, Jhanji S, Poulogiannis G, Farquhar-Smith P, Brown MR. Nonsteroidal anti-inflammatory drugs and pain in cancer patients: A systematic review and reappraisal of the evidence. Br J Anaesth 2019;123:e412-23.
117. Simoff MJ, Lally B, Slade MG, Goldberg WG, Lee P, Michaud GC, *et al.* Symptom management in patients with lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:S455-97.
118. Salas S, Frasca M, Planchet-Barraud B, Burucoa B, Pascal M, Lapiana JM, *et al*. Ketamine analgesic effect by continuous intravenous infusion in refractory cancer pain: Considerations about the clinical research in palliative care. J Palliat Med 2012;15:287-93.
119. Singh V, Gillespie TW, Lane O, Spektor B, Zarrabi AJ, Egan K, *et al*. A dose-escalation clinical trial of intranasal ketamine for uncontrolled cancer-related pain. Pharmacotherapy 2022;42:298-310.
120. Jiao J, Fan J, Zhang Y, Chen L. Efficacy and safety of ketamine to treat cancer pain in adult patients: A systematic review. J Pain Symptom Manage 2024;67:e185-210.
121. Peixoto RD, Hawley P. Intravenous lidocaine for cancer pain without electrocardiographic monitoring: A retrospective review. J Palliat Med 2015;18:373-7.
122. Hui D, Bohlke K, Bao T, Campbell TC, Coyne PJ, Currow DC, *et al.* Management of dyspnea in advanced cancer: ASCO guideline. J Clin Oncol 2021;39:1389-411.
123. Leppert W, Buss T. The role of corticosteroids in the treatment of pain in cancer patients. Curr Pain Headache Rep 2012;16:307-13.
124. Haywood A, Good P, Khan S, Leupp A, Jenkins-Marsh S, Rickett K, *et al.* Corticosteroids for the management of cancer-related pain in adults. Cochrane Database Syst Rev 2015;2015:CD010756.
125. Loprinzi CL, Lacchetti C, Bleeker J, Cavaletti G, Chauhan C, Hertz DL, *et al.* Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. J Clin Oncol 2020;38:3325-48.
126. Jiang J, Li Y, Shen Q, Rong X, Huang X, Li H, *et al.* Effect of pregabalin on radiotherapy-related neuropathic pain in patients with head and neck cancer: A randomized controlled trial. J Clin Oncol 2019;37:135-43.
127. Bennett MI, Laird B, van Litsenburg C, Nimour M. Pregabalin for the management of neuropathic pain in adults with cancer:

A systematic review of the literature. Pain Med 2013;14:1681-8.
128. Tambon M, Montarnal B, Lepetit M, Lapeyre-Mestre M. Non-opioid antinociceptive drugs: Risk of respiratory depression and death related to concomitant use of gabapentinoids in addition to opioids. Expert Opin Drug Saf 2023;22:183-94.
129. Chung F, Lane R, Spraggs C, McQuade B, Jacka M, Luttropp HH, *et al.* Ondansetron is more effective than metoclopramide for the treatment of opioid-induced emesis in post-surgical adult patients. Ondansetron OIE post-surgical study group. Eur J Anaesthesiol 1999;16:669-77.
130. Hardy J, Daly S, McQuade B, Albertsson M, Chimontsi-Kypriou V, Stathopoulos P, *et al*. A double-blind, randomised, parallel group, multinational, multicentre study comparing a single dose of ondansetron 24 mg p.o. With placebo and metoclopramide 10 mg t.d.s. p.o. In the treatment of opioid-induced nausea and emesis in cancer patients. Support Care Cancer 2002;10:231-6.
131. Merz-Herrala J, Leu N, Anderson E, Lambeck A, Jefferson J, Sobrero M, *et al*. Safety and pain reduction in emergency practitioner ultrasound-guided nerve blocks: A one-year retrospective study. Ann Emerg Med 2024;83:14-21.
132. Goldsmith A, Driver L, Duggan NM, Riscinti M, Martin D, Heffler M, *et al.* Complication rates after ultrasonography-guided nerve blocks performed in the emergency department. JAMA Netw Open 2024;7:e2444742.
133. Hashemi M, Mahmood SM, Fernandez J, Oswald J. Cryoneurolysis of intercostal nerve for rib trauma and intercostal neuralgia in the emergency department: A multidisciplinary approach. J Emerg Med 2022;63:376-81.
134. Gabriel RA, Seng EC, Curran BP, Winston P, Trescot AM, Filipovski I. A narrative review of ultrasound-guided and landmark-based percutaneous cryoneurolysis for the management of acute and chronic pain. Curr Pain Headache Rep 2024;28:1097-104.
135. Finneran Iv JJ, Ilfeld BM. Percutaneous cryoneurolysis for acute pain management: Current status and future prospects. Expert Rev Med Devices 2021;18:533-43.
136. Hwang U, Richardson LD, Harris B, Morrison RS. The quality of emergency department pain care for older adult patients. J Am Geriatr Soc 2010;58:2122-8.
137. Platts-Mills TF, Esserman DA, Brown DL, Bortsov AV, Sloane PD, McLean SA. Older US emergency department patients are less likely to receive pain medication than younger patients: Results from a national survey. Ann Emerg Med 2012;60:199-206.
138. Patel KV, Guralnik JM, Dansie EJ, Turk DC. Prevalence and impact of pain among older adults in the United States: Findings from the 2011 national health and aging trends study. Pain 2013;154:2649-57.
139. Schofield P. The assessment of pain in older people: UK national guidelines. Age Ageing 2018;47:i1-22.
140. Hadjistavropoulos T, Herr K, Turk DC, Fine PG, Dworkin RH, Helme R, *et al.* An interdisciplinary expert consensus statement on assessment of pain in older persons. Clin J Pain 2007;23:S1-43.
141. Malara A, De Biase GA, Bettarini F, Ceravolo F, Di Cello S, Garo M, *et al.* Pain assessment in elderly with behavioral and psychological symptoms of dementia. J Alzheimers Dis 2016;50:1217-25.
142. Warden V, Hurley AC, Volicer L. Development and psychometric evaluation of the pain assessment in advanced dementia (PAINAD) scale. J Am Med Dir Assoc 2003;4:9-15.
143. Molnar F, Frank CC. Optimizing geriatric care with the GERIATRIC 5Ms. Can Fam Physician 2019;65:39.
144. Owsiany MT, Hawley CE, Triantafylidis LK, Paik JM. Opioid management in older adults with chronic kidney disease: A review. Am J Med 2019;132:1386-93.
145. Wan HY, Li SY, Ji W, Yu B, Jiang N. Fascia Iliaca Compartment Block for Perioperative Pain Management of Geriatric Patients with Hip Fractures: A Systematic Review of Randomized Controlled Trials. Pain Res Manag 2020;2020:8503963.
146. Zacher J, Altman R, Bellamy N, Brühlmann P, Da Silva J, Huskisson E, *et al.* Topical diclofenac and its role in pain and inflammation: An evidence-based review. Curr Med Res Opin 2008;24:925-50.
147. Argoff CE. Topical analgesics in the management of acute and chronic pain. Mayo Clin Proc 2013;88:195-205.
148. Johnson M, Strait L, Ata A, Bartscherer A, Miller C, Chang A, *et al.* Do lidocaine patches reduce opioid use in acute rib fractures? Am Surg 2020;86:1153-8.
149. Borsheski R, Johnson QL. Pain management in the geriatric population. Mo Med 2014;111:508-11.
150. Merrick M, Grange R, Rudd S, Shipway D. Evaluation and treatment of acute trauma pain in older adults. Drugs Aging 2023;40:869-80.
151. Franceschi M, Scarcelli C, Niro V, Seripa D, Pazienza AM, Pepe G, *et al.* Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: A prospective study of 1756 patients. Drug Saf 2008;31:545-56.
152. Motov S, Mann S, Drapkin J, Butt M, Likourezos A, Yetter E, *et al.* Intravenous subdissociative-dose ketamine versus morphine for acute geriatric pain in the emergency department: A randomized controlled trial. Am J Emerg Med 2019;37:220-7.
153. Ginsburg AD, Heaton HA, Beaudrie-Nunn A, E Silva LO, Canterbury E, Brown CS, *et al.* High- versus low-dose ketamine for analgesia in older adults in the emergency department. Am J Emerg Med 2024;86:120-4.
154. Haslam C, Nurmikko T. Pharmacological treatment of neuropathic pain in older persons. Clin Interv Aging 2008;3:111-20.
155. Cepeda MS, Farrar JT, Baumgarten M, Boston R, Carr DB, Strom BL. Side effects of opioids during short-term administration: Effect of age, gender, and race. Clin Pharmacol Ther 2003;74:102-12.
156. Zeng C, Dubreuil M, LaRochelle MR, Lu N, Wei J, Choi HK, *et al.* Association of tramadol with all-cause mortality among patients with osteoarthritis. JAMA 2019;321:969-82.
157. Bush DM. Emergency department visits for adverse reactions involving the pain medication tramadol. In: The CBHSQ Report. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2015. p. 1-7.
158. Wightman R, Perrone J, Portelli I, Nelson L. Likeability and abuse liability of commonly prescribed opioids. J Med Toxicol 2012;8:335-40.
159. Saha S, Nathani P, Gupta A. Preventing opioid-induced constipation: A teachable moment. JAMA Intern Med 2020;180:1371-2.
160. Pergolizzi JV Jr., Christo PJ, LeQuang JA, Magnusson P. The use of peripheral μ-opioid receptor antagonists (PAMORA) in the management of opioid-induced constipation: An update on their efficacy and safety. Drug Des Devel Ther 2020;14:1009-25.