

Assessment and Early Management of Pain in Hip Fractures: The Impact of Paracetamol

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Abstract

Introduction: As the number of patients sustaining hip fractures increases, interventions aimed at improving patient comfort and reducing complication burden acquire increased importance. Frailty, cognitive impairment, and difficulty in assessing pain control characterize this population. In order to inform future care, a review of pain assessment and the use of preoperative intravenous paracetamol (IVP) is presented. **Materials and Methods:** Systematic review of preoperative IVP administration in patients presenting with a hip fracture. **Results:** Intravenous paracetamol is effective in the early management of pain control in the hip fracture population. There is a considerable decrease in use of breakthrough pain medications when compared with other pain relief modalities. Additionally, IVP reduces the incidence of opioid-induced complications, reduces length of stay, and lowers mean pain scores. Another significant finding of this study is the poor administration of all analgesics to patients with hip fracture with up to 72% receiving no prehospital analgesia. **Discussion:** The potential benefits of IVP as routine in the early management of hip fracture-related pain are clear. Studies of direct comparison between analgesia regimes to inform optimum bundles of analgesic care are sparse. This study highlights the need for properly constructed pathway-driven comparator studies of contemporary analgesia regimes, with IVP as a central feature to optimize pain control and minimize analgesia-related morbidity in this vulnerable population.

Keywords

hip fracture, pain management, pain assessment, paracetamol

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Introduction

Globally over 1 million hip fractures occur annually, with the highest numbers occurring in Europe and North America.^{1,2} An aging population with an increased prevalence of bone fragility, who are better able to maintain activity level into old age, will drive the global cost of this injury up to \$446 billion by 2050.³

In the United Kingdom, an average of 65 000 patients attend hospital with hip fractures each year, representing the most common cause of admission to orthopedic wards.^{4,5} Burdened with significant comorbidities, at least one short-term complication is seen in half of this patient group.⁶ Characterizing the population, 20% to 25% of patients have moderate cognitive impairment consistent with delirium as assessed by the 4AT screening tool or a score less than 7 on the Abbreviated Mental Test Score.^{7,8} The tail of the comorbid burden does not end at the admitting unit as half of the patients are left with long-term disability and

one-quarter require long-term nursing care.⁹ Despite significant progress in the structured delivery of care to this vulnerable patient group, 1-year mortality remains high at up to 30%.¹⁻⁶

In an era of austerity, societal cost features highly in health-care interventions. The average UK treatment cost of a proximal femur fracture is £25 424.00 with an annual combined health and social care economic burden to the United Kingdom for this specific patient group in the region of £1 billion.^{8,10,11}

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Both the incidence and cost of hip fracture are expected to increase in the future, with an estimated incidence of 101 000 hip fractures annually in the United Kingdom by 2020.^{1,8}

At rest, one-third of patients with a proximal femur fracture will have mild or no pain, one-third will have moderate pain, and one-third will have severe pain. Extracapsular fractures are more painful than intracapsular fractures due to the greater degree of periosteal damage.⁸

Effective pain management is associated with significantly improved outcomes, while poor pain control predisposes patients with hip fracture to delirium, which itself greatly increases 1-year mortality and morbidity.^{6,7} Postoperatively, optimizing analgesia aids early mobilization and reduces length of hospital stay, thus reducing costs and preventing patients being exposed to the threats of the health-care environment.^{7,10}

The existing evidence base regarding the impact of paracetamol on this vulnerable group with unique analgesia requirements has been described as “low-to-moderate quality.”^{12,13} This poor evidence underpins the management of patients with complex medical needs, difficulty in pain assessment, and substantial potentially modifiable societal costs. We aim to review the current evidence regarding the efficacy and extent of use of paracetamol, particularly intravenously (IV) and prehospital, as this is highlighted as an area lacking in evidence by the National Institute of Clinical Excellence (NICE) guidelines.¹³ We will describe methods used to assess pain and detail how they can be used to optimize care and assessment of pain interventions. The literature identified by NICE suggests that intravenous paracetamol (IVP) may be advantageous when compared to morphine and nerve block analgesia regimens.¹²

Materials and Methods

An evidence synthesis was undertaken using the “Ovid” search engine. Databases searched included the Cochrane Library, Embase, MEDLINE, CINAHL, AMED, and NICE evidence search. Additional advice was sought from specialist academic library staff to ensure comprehensive searching, and thus reliability. Search terms “hip fracture” OR “Neck of femur” AND “fracture” were searched. These were combined with (“AND”); “assessment” AND “pain” OR “management” OR “analgesia” AND “pain.” The results from these searches were then combined (“AND”) with the results from a separate “paracetamol” search.

The “Literature Search Process: Guidance for NHS Researchers” version 6.0 by Thames Valley and Wessex Healthcare Librarians was utilized to structure and record the search methodology employed.

Results

The Assessment of Pain

A comprehensive multidimensional assessment of patients presenting with hip fracture should be undertaken preoperatively. This assessment should routinely include nutritional, cognitive, frailty, and pain assessments.^{6,7,10}

A number of barriers have been identified that can make the assessment of pain in the hip fracture demographic challenging. These include, but are not limited to:

- Absence of a standardized, “gold-standard,” pain intensity tool suitable for elderly patients.^{10,14}
- Assumption that pain is a “normal part of aging” or that the “elderly patients feel less pain.”^{14,15}
- Sensory and/or cognitive impairment of patients.^{10,15-17}
- Age-related stoicism and reticence to report and quantify pain.^{15,18}

Additionally, Zanker et al identified the inability to offer analgesics until diagnosis as the primary barrier to pain control in the emergency setting, followed by the lack of understanding of the pharmacology of analgesia by health-care professionals.⁶

The Impact of Cognitive Impairment on the Assessment and Management of Pain

There is significant evidence to suggest that patients with cognitive impairment treated for hip fracture receive inadequate analgesia, reflecting the difficulty associated with reliable assessment and communication with this particular patient group.^{6,14-16} In trying to address these specific challenges, it has become apparent that health-care professionals need greater awareness of the vulnerability of this patient group to unrecognized and undertreated pain, and need to be more adept at observing and assessing for nonverbal manifestations of pain. This can include autonomic features of pallor, tachycardia, tachypnea, sweating, and hypertension; nuances of facial expression; altered gait pattern as a consequence of bracing and guarding; repetitive vocalizations; as well as changes in interpersonal interactions, activity patterns, and mental status. Many of these elements are difficult to assess without input from carers and close family who have insight into a patient’s baseline function.¹⁸ In recognition of these challenges, there have been standardized pain intensity measures developed that score patients’ nonverbal indicators of pain, such as the Mobilization-Observation-Behaviour-Intensity-Dementia scale, useful for assessing pain during daily care in a ward setting. Pain scores in the cognitively impaired have been shown to have excellent reliability in assessing inferred pain in those with severe cognitive impairment.^{18,19} The Pain Assessment in Advanced dementia scale and the Abbey pain scale are also designed for use on the cognitively impaired, both reliably measuring changes in pain intensity in response to analgesic interventions, and are suitable for use in the prehospital and emergency department setting.²⁰ The commonly used numerical rating scores and visual analog scores (VAS) are both limited in their application to patients with cognitive impairment.²¹

Inadequate assessment and management of significant perioperative pain has a well-documented association with increased risk of delirium as well as prolonged immobilization.²² This disrupts physiotherapy and delays postoperative

mobilization, leading to an increase in risk of thromboembolism and functional impairment in these patients.²³ The effects on cognition of delirium in addition to underlying cognitive impairment worsen prognosis considerably and will tend to increase length of stay.

Early management of pain. Only a minority of elderly patients with hip fracture receive adequate analgesia prior to arrival at hospital. Oberkirche et al found that 72% of patients received no prehospital analgesia, despite all of the patients in the study reporting significant pain at first assessment.²⁴

In this study, by contrast, the administration of prehospital analgesia was found to significantly relieve pain at the time of arrival to hospital, without meaningful side effects. High levels of early pain correlate with increased complications, possibly due to immobilization as a result of pain.²⁴

Opioid analgesia dominates current pain management regimens in hip fracture and is recommended for the treatment of moderate-to-severe pain as part of the World Health Organization (WHO) analgesic ladder, as an adjunct to oral paracetamol.^{7,22,25} Given that an estimated two-thirds of patients with hip fracture experience moderate-to-severe pain, opioid analgesics are widely used perioperatively to manage both baseline and breakthrough pain.^{8,25}

Due to the elderly nature of patients presenting with hip fracture, physicians are often reluctant to prescribe opioids for fear of side effects.^{23,26} Closs et al and Feldt et al have found that 61.3% of older orthopedic patients were given less than 25% of their prescribed opioid analgesics during the first 48 hours after surgery, no patients received >50% of their prescribed opioids, and patients aged ≥ 65 years hospitalized for a hip fracture received <25% of the mean amount of opioid analgesics prescribed.^{27,28}

Additionally, Feldt et al reported 66.1% of patients received $\leq 50\%$ of their prescribed nonopioid analgesics.²⁷

Although the deleterious effects and the poor delivery of opioids are transparent, the literature regarding the use of paracetamol for perioperative pain in hip fracture is comparatively scarce.^{7,29} There are no placebo-controlled trials investigating the efficacy of preoperative administration of paracetamol in this patient group, as it is considered “unethical” by the NICE in view of the perceived severity of pain experienced by patients with hip fracture, particularly on movement.^{7,30} However, given the reluctance of some health-care professionals to administer IV morphine prior to diagnosis, this may be an argument for the prehospital period being the ideal opportunity for such a trial.

Oral paracetamol (acetaminophen in the United States) is routinely given as the first step of the WHO analgesic ladder²⁵ and NICE recommends oral paracetamol should be offered every 6 hours, unless contraindicated, before and after surgery with appropriate adjustment for those adults of particularly low body weight.^{7,13,31}

Issues with prescribing and delivery are not confined to opiates. Ardery et al reported that although oral paracetamol was prescribed (in doses of 350-1000 mg) in 7 of 8 patients at

the time of admission, 4 of these 7 patients fail to receive any of the prescribed paracetamol within the first 24 hours. At 48 hours from admission, these 4 patients were still to receive any paracetamol. Furthermore, none of the patients received the full daily dose of 4000 mg.¹⁴ Although only a small study, it highlights the poor consistency in administration of prescribed medications as a significant consideration when considering drug efficacy, and the lack of importance assigned to the prescription of paracetamol, suggesting that paracetamol is grossly underused as an analgesic. There may also be some underlying concern regarding risks of hepatotoxicity in this patient group.^{14,29,32}

Oral paracetamol is generally a very safe analgesic, but its bioavailability when given orally can be reduced by first pass hepatic metabolism up to 40%. Furthermore, gastrointestinal absorption can be slowed by concomitant opioid administration.³³ Propacetamol, an earlier prototype of IVP, has been proven to be an effective and safe analgesic with an opioid-sparing effect in orthopedic postoperative care.^{34,35} Propacetamol is a prodrug that is rapidly and completely hydrolyzed by nonspecific plasma esterase's into paracetamol.³² Intravenous paracetamol reaches a higher peak plasma concentration than its oral equivalent.^{22,36} One thousand milligram oral paracetamol given to patients with osteoarticular injury significantly reduces pain within 60 minutes,³⁷ but by contrast when administered IV has been found to take effect within 5 minutes and reaching peak analgesic effect after 1 hour (IVP has a half-life of 4-6 hours).^{38,39}

Intravenous paracetamol has been proven to be safe given at a dose of up to 4000 mg daily in 4 divided doses,⁴⁰ and unlike its nonsteroidal and cyclooxygenase 2 inhibitor counterparts, has no significant impact on kidney function or gastric side effects.²² Care should, however, be taken when prescribing IVP in patients known to be at risk of hepatotoxicity, and dosing adjusted for those of low body weight (under 50 kg).²⁹

In a randomized controlled trial, Cuvillon et al reported that 2 g of IVP given over 6 hours (equivalent to 1 g IVP) can be as effective at management of baseline pain as nerve blocks or subcutaneous morphine in the postoperative phase.¹² Cuvillon et al found that when comparing 0.2% ropivacaine continuous femoral nerve block (FNB) with 2 g IVP every 6 hours, there was significant reductions in the amount of morphine required to treat breakthrough pain. Patients on the propacetamol regime required on average 8 mg of morphine, whereas patients given FNB required significantly more; 26 mg on average. Over one-quarter (28%) of patients given IVP required no additional opioid analgesia, a proportion that is mirrored in the patient group with continuous femoral block.¹² No difference in pain intensity as measured by VAS was identified between the groups.¹²

Tsang et al conducted a prospective cohort study investigating the opioid-sparing effect of regular IVP against regular oral paracetamol in patients with preoperative hip fracture, both groups receiving 1000 mg doses at 6 hourly intervals. They found that the regime of IVP was associated with a 70% reduction in mean dose of morphine required, compared to the

control group taking the same regime orally. This translated to a 58% reduction in daily morphine use preoperatively when adjusted for any preoperative delay, with a reduction of 16 mg of morphine for every 6 g IVP, when compared to the standard oral regime.⁴¹ Equivalent pain levels were identified between both groups, with the same degree of pain control achieved from both regimes. Similar studies in cardiac surgery patients reported morphine reductions of 50 mg when patients were given 12 g of IV paracetamol over 72 hours.⁴²

Bollinger et al conducted a retrospective review of the effect of IVP on a range of patient outcomes following geriatric hip fractures. Outcomes were compared between a group managed with IVP (1000 mg every 8 hours) with IV morphine for breakthrough pain, and second group given oral paracetamol (same dose) + oral tramadol or oxycodone + IV morphine for breakthrough pain.²² Pain intensity was measured using VAS with word descriptors. The study found that patients who received IVP had a statistically significant shorter mean length of stay, lower mean pain score, lower usage of opioids, missed fewer physiotherapy sessions, and a higher likelihood of discharge home.²² No statistically significant difference was detected, however, in the length of time from admission to theater between the 2 groups. This is an independent predictor of functional outcome and return to independent living, upon which IVP analgesia had no impact, compared to standard opioid analgesia regimens in the Bollinger study.^{22,43}

Finally, we have also reviewed the option for rectal administration of paracetamol. It is known that there is greater variation in bioavailability when given rectally, compared to the IV route. There are currently no studies comparing paracetamol administered via the oral or rectal routes in the hip fracture population.⁷ In US practice adult laparoscopic surgery, rectal paracetamol is favored as an adjunct to nonsteroidal anti-inflammatory drugs for adults postoperatively, but the literature search did not produce any evidence regarding its use perioperatively for orthopedic surgery.³²

Discussion

This study set out to provide a narrative review of the available literature evaluating the current assessment and management of acute pain in patients with hip fracture, focusing on the impact of paracetamol for the early management of pain. Several key themes were identified in review of the literature.

Hip fracture is a significant cause of mortality and morbidity in older people in the United Kingdom and is expected to increase in scale as a burden on health care in the future.¹⁻¹⁰ Patients with hip fracture regularly experience severe pain on admission.⁸ The approach to management of this pain is often inconsistent and inadequate to achieve sufficient pain control, with significant side effects as a result of analgesic choice. Furthermore, many patients do not receive any analgesia prehospital.²⁴

Pain is often underappreciated in patients with hip fracture, with cognitive impairment cited as a barrier to effective assessment of pain. Cognitively intact patients often receive better

pain management than those with some decline, the challenging nature of ongoing assessment being a contributing factor. Visual scales with verbal descriptors are felt to be preferential to the commonly used numerical scales in this patient group. Clinicians should also assess nonverbal communicators of pain if the patient struggles to self-report. A standardized pain intensity rating scale has been proposed, and the importance of repeated assessment following analgesic intervention has been stressed.

Intravenous paracetamol (and its prototype, propacetamol) has been demonstrated to be a safe and effective analgesic when managing preoperative pain for patients with hip fracture. When used with opiates such as morphine for breakthrough pain, IVP has been found to significantly reduce morphine requirements, with no adverse effects or compromise in pain management when compared to standard oral paracetamol regimes.^{12,22,41} No adverse effects associated with the use of IVP for hip fracture were reported in the literature reviewed. Intravenous paracetamol may be considered as a more cost-effective alternative to peripheral nerve block, the literature having reported comparable pain control and a superior opioid-sparing effect when compared to FNB.^{7,12,37,41} Indirectly, IVP would also seem to have the potential to reduce delirium and constipation, through reduction of pain and opioid analgesia.^{12,22}

While it is compelling to declare benefits in efficacy, a decreased side effect profile, and possible economic advantage of IVP, this is not a robust premise. The evidence base cannot fully support any of these claims fully, but there is sufficient literature suggestive of benefit across multiple domains for further investigation to be prioritized. Differences between funding models influence any health-care economic analysis. For example, when a nerve block is billed separately and/or is covered by a separate funding stream, this prevents meaningful comparison. In addition, the cost of differing formulations of paracetamol varies widely, strengthening the requirement for a controlled study. Equally, factors impacting on length of stay are influenced by patient, department, and health-care-specific factors. The current literature that we have analyzed is heterogenic in that it represents several low-level evidence studies from differing health-care systems. The limitations of this work are, therefore, construed by the literature on which it is based. We have provided a narrative summary pertinent to specific features of pain management and the role of paracetamol that should serve as a primer for any unit considering its analgesic management in this population. We have highlighted the need for a properly controlled stratified trial of preadmission IVP, given the independently demonstrated benefits of both IVP and preadmission paracetamol.^{12,22,24,41} The importance of a properly controlled trial (in which all of the previously mentioned variables can be more tightly matched and controlled) is thrown into greater context by the established size of the problem as we have discussed, both to the patient group and the health systems looking after them. Many significant advantages have been identified for the use of IVP compared to oral paracetamol.^{37,38} Additionally, administration of oral

paracetamol prehospital improves pain management and reduces pain at point of admission.²⁴ A potential for the improvement of pain management by the administration of IVP prehospital has therefore been identified as an emergent theme from review of the current literature.

Conclusion

We demonstrate that there is literature to suggest the efficacy and advantages of managing pain in hip fracture with IVP compared to its oral equivalent.^{37,38}

However, the studies to date lack scale and a number of key outcomes—notably the incidence of complications associated with conventional oral regimes—such as delirium and constipation—have not been studied. Furthermore, the current literature is based on relatively small-scale studies, with only one randomized study identified. The importance of a properly controlled trial is thrown into greater context by the established size of the problem as we have discussed, both to the patient group and the wider health systems tasked looking after them.

Any intervention in pain control must be introduced alongside validated measures of delirium and pain scoring. We have demonstrated the issues with pain recognition, scoring, and cognitive assessment when discussing pain control in this group. Cognitive assessment and stratification using screening tools such as 4AT are imperative; equally, once patients are correctly stratified, assessment of pain must use a system dedicated to the appropriate level of cognition. These factors are currently poorly addressed in clinical practice but would be vital in underpinning any clinical comparator study. This review suggests that there is a need for a large-scale randomized controlled trial to investigate the efficacy of regular IVP in prehospital and preoperative patients with hip fracture.

Author's Note

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Declaration of Conflicting Interests

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