



## Opioid induced constipation management in orthopaedic and trauma patients: treatment and the potential of nurse-initiated management

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### ABSTRACT

**Background:** Opioid analgesics treat moderate to severe pain with proven analgesic efficacy, although their use is associated with dose-limiting side effects, such as constipation. Orthopaedic and trauma patients are at high risk of developing opioid-induced constipation (OIC) due to reduced mobility and increased opioid requirements to manage prolonged pain after injury.

**Objectives:** To examine the evidence base to guide clinicians on the most effective or tolerated laxative regimen for the management of OIC and nurse-initiated management of OIC.

**Method:** A review of the literature was undertaken. Databases were searched to identify studies on OIC, laxatives and nurse-initiated management.

**Results:** Laxatives do not address the underlying cause of OIC and there is currently insufficient evidence to guide clinicians on the most effective or tolerated laxative regimen for the management of OIC. The use of peripheral acting mu-opioid receptor antagonists (PAMORAs) could be considered in those for whom regular use of a combination of laxatives has not been successful, and nurses should take a broader role in the assessment of symptoms and response to treatment.

**Conclusion:** The important balance between adequate analgesia and minimising OIC symptoms is an ongoing challenge for clinicians, and an area of patient care where nurses could be leading management.

### Introduction

Opioid analgesics are used to treat moderate to severe pain with proven analgesic efficacy. Their use is associated with dose-limiting side effects, most commonly constipation (Reimer et al., 2009; Hjalte et al., 2010). Constipation is an often-overlooked aspect of patient care and increases the risk of postoperative complications, can prolong hospital stay, increase financial costs and add to demand for nursing care (Trads and Pedersen, 2015). Orthopaedic and trauma patients are a high risk patient group for developing opioid-induced constipation (OIC) due to increased requirements for opioid analgesics to manage prolonged pain relating to their injury and surgery (ANZCA, 2015; Sinatra et al., 2002; Park et al., 2016). Although there are treatment options for OIC, the literature demonstrates that effective management is problematic and is an area where nurses may be best placed to provide high-quality holistic care (Reimer et al., 2009; Andrews and Morgen, 2012).

Orthopaedic and trauma patients have a high prevalence of chronic post-surgical pain (CPSP), which is described as pain that develops and persists beyond the time expected for the normal healing process, resulting in an increased demand on opioid analgesics for this demographic (ANZCA, 2015; Sinatra et al., 2002). Although a multi-modal approach to analgesia is desirable, opioids are often heavily relied upon

in managing moderate to severe acute pain (Lamplot et al., 2014). Short and long term pain after orthopaedic trauma are predictive factors for physical disability, delayed return to work, psychological distress, low satisfaction with healthcare and failure to participate in physical therapy (Sinatra et al., 2002). According to a systematic review, reduced mobility, low fluid and fibre intake, hospital stay, opioid medications and gender (women develop constipation 2 to 3 times more often) are all risk factors for developing constipation post-operatively, and are all potential risk factors that impact orthopaedic and trauma patients (Madsen et al., 2010; Tradts and Pedersen, 2015).

Constipation is the most common side effect resulting from opioid consumption, and a symptom that remains with chronic opioid use. The gastrointestinal (GI) effects of opioids cause up to one third of patients to cease or decrease their analgesic medications, leading to untreated chronic pain and a reduction in quality of life (QoL) (Hjalte et al., 2016; Crockett et al., 2019; Hanson et al., 2019). This review examines OIC, management with laxatives and the potential role for nurses in improving the management of OIC.

### Method

A review of the literature was undertaken to “use objective and transparent methods to identify, evaluate and summarise all relevant

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**Table 1**  
Laxatives used for the management of OIC (Argoff et al., 2015; Nelson et al., 2016; Adis Medical Writers, 2017; Australian Medicines Handbook, 2017; Therapeutic Guidelines Limited, 2017).

Laxative	Mechanism of action	Generic Name	Onset of full effect	Considerations
Oral laxatives				
Bulk-forming	Absorb water into the colon to increase faecal bulk, which stimulates peristaltic activity	Ispaghula husk Psyllium Sterculia	2–3 days	<ul style="list-style-type: none"> <li>Not routinely recommended for OIC</li> <li>For mild constipation when dietary fibre intake is poor</li> <li>Less effective in immobility and chronic constipation</li> <li>Ensure adequate fluid intake</li> <li>Flatulence and bloating (especially with rapid increase in dose)</li> <li>Useful for immobility and chronic constipation</li> <li>More frequent doses are better than large</li> <li>Flatulence and tastes very sweet (can mix with juice, water or milk)</li> <li>Contains electrolytes to minimise electrolyte and water loss</li> <li>The addition of sodium sulfate (saline laxative) for faster onset (bowel preps)</li> <li>Reduced absorption of oral medications taken during or 1 h before administration of bowel prep</li> <li>Likely more effective and tolerable than lactulose in chronic constipation</li> </ul>
Osmotic	Not absorbed; draws or keeps water in the colon, expanding and softening the stool resulting in increased intraluminal pressure to stimulate peristalsis	Lactulose Sorbitol	Constipation: 1–3 days Bowel prep: 0.5–3 h	
	Macrogols or polyethylene glycols (PEGs) are large polymers with osmotic action	Macrogol 3350 with sodium sulfate and electrolytes Macrogol 3350 with electrolytes Macrogol 3350 without electrolytes		<ul style="list-style-type: none"> <li>Risk of electrolyte disturbance in the elderly, children and renal impairment or cardiovascular disease</li> <li>Avoid phosphate laxatives in the elderly</li> <li>Ensure adequate hydration</li> <li>Reduced absorption of oral medications taken during or 1 h before administration of bowel prep</li> <li>Evidence is lacking for use alone</li> <li>Mostly combined with stimulant or osmotic laxative</li> <li>Paraffin may reduce absorption of fat-soluble vitamins (ADEK)</li> <li>Risk of aspiration with viscous solutions</li> <li>Poloxamer only in children &lt; 3 years</li> <li>For OIC or severe constipation</li> <li>Short-term is preferable but no convincing evidence that chronic use is harmful to the colon</li> <li>Commonly causes abdominal cramps</li> </ul>
Stool softeners	Assist with mixing water (lubricating) into faeces and increase intestinal fluid secretion	Docusate Liquid paraffin Poloxamer	1–3 days	
Stimulant	Direct stimulation of nerve endings in colonic mucosae to increase intestinal motility; accumulation of water and electrolytes in the colonic lumen	Bisacodyl Senna Sodium picosulfate	6–12 h	
Rectal laxatives				
Osmotic	Draws water into the colon, has lubricating and stimulant properties (through local irritant effects)	Glycerol Saline	2–30 min	<ul style="list-style-type: none"> <li>Correct admin to minimise damage to rectal mucosa</li> <li>If oral laxatives fail</li> </ul>
Stimulant	As above for oral stimulant laxative	Bisacodyl	5–60 min	<ul style="list-style-type: none"> <li>Adverse effects per relevant laxative class outlined above</li> </ul>

research findings” relating to the symptoms, presentation and management of OIC, use and efficacy of laxatives and nurse-initiated management of bowel function (Centre for Reviews and Dissemination, 2009). Electronic databases were broadly scanned prior to a more refined search: the MEDLINE, EMBASE, CINAHL, PubMed and OVID databases were searched to identify studies and seminal works published relating to the topic. The keywords used to search the literature included: opioid-induced constipation, opioid, opioid bowel dysfunction, nurse bowel management, constipation management, chronic constipation, nurse initiated treatment, laxatives, orthopaedic, trauma and opioid side effects. Almost 55 articles were reviewed, of which 39 are cited in this paper. The inclusion criteria were restricted primarily to the following studies: (1) published between 2000 and 2019; (2) written in English; and (3) examining the presentation and management of OIC, use and efficacy of laxatives for OIC and nurse management of bowel function. The primary intent of the review was to examine the evidence base to guide clinicians on the most effective or tolerated laxative regimen for the management of OIC for opioid use, and to identify the broader role that nurses can undertake in managing OIC.

## Results

### OIC

The American Gastroenterological Association (AGA) Institute released guidelines in January 2019 on the Medical Management of Opioid-Induced Constipation, with recommendations for management strategies (Crockett et al., 2019). These strategies are supported by and formulated from the literature and clinical evidence relating to OIC management published prior to the guideline release (Argoff et al., 2015; Müller-Lissner et al., 2017; Hanson et al., 2019). Constipation is the primary symptom, recognised by both patients and clinicians, of opioid-induced bowel dysfunction (OIBD), and a common reason for reduced opioid dosing or cessation. The constipation effects from opioids vary depending on the type and dose of opioid used, as well as length of treatment and underlying patient risk factors (Pappagallo, 2001; Hjalte, Berggren, Bergendahl & Hjortsberg, 2011). OIC is a complex condition for healthcare providers to manage whilst patients continue their opioid use and an area of patient care in which nurses could undertake a greater role.

The distinction between severe constipation and post-operative ileus are vague in terms of pathogenesis, clinical features and treatment options. OIC is one aspect of OIBD (Opioid-Induced Bowel Dysfunction) and is characterised clinically by: (1) hard, dry stools; (2) straining; (3) incomplete evacuation; (4) bloating; (5) abdominal distention; and (6) increased gastric reflux (Twycross et al., 2012). Post-operative ileus is defined as temporarily impaired gastrointestinal motility following surgery without obstruction (Lee et al., 2015). Opioids segment intestinal activity, reduce motility (propulsive peristalsis), secretion (water and electrolytes) and increased fluid absorption due to a prolonged bowel transit time (Meissner et al., 2009; Twycross et al., 2012). OIC results in harder stools and less frequent and less effective defecation and, due to the specific cause of constipation, warrants dedicated attention (Crockett et al., 2019). Unlike many of the other opioid-induced side effects, such as respiratory depression, nausea and vomiting, patients rarely develop tolerance to the constipation effects of opioids, which can significantly impact a their QoL (Pappagallo, 2001; Reimer et al., 2009).

### Selection of laxative

Prevention and management of OIC primarily involves lifestyle measures followed by the addition of laxatives. Lifestyle measures include: adequate dietary fibre and fluid intake, activity or exercise and immediately responding to urges to defecate (Crockett et al., 2019). If

these fail, or are not possible, because of issues such as reduced mobility during a hospital admission, oral laxatives are recommended upon initiation of opioids.

Constipation symptoms associated with opioids can be treated by the use of laxatives, which aim to restore the amount of water in the faeces or stimulate peristalsis. Laxative choice is often based on symptoms, required onset of action, patient preference, stool consistency, previous response, cost and adverse effects. Table 1 outlines the laxatives used for the management of OIC and highlights the considerations, benefits and limitations to their clinical use. Numerous laxatives are available which stimulate or facilitate bowel motion. The AGA guidelines recommend the use of laxatives as first-line agents in patients with OIC (Crockett et al., 2019). Management of OIC may require one or a combination of laxatives with different mechanisms of action. As laxatives do not specifically target the underlying pathophysiology of OIC, symptoms often continue despite their concurrent use and alternative therapy needs to be considered (Leppert, 2010; Reimer et al., 2009).

There have been recent advancements in the use of peripheral acting mu-opioid receptor antagonists (PAMORAs) for targeted treatment of OIC, including methylnaltrexone and prolonged release (PR) naloxone-oxycodone (Targin<sup>®</sup>) preparations, but each have various reasons for limited clinical use (Leppert, 2010). Opioids act on both central and peripheral opioid receptors in the body, with OIC believed to result from interactions between opioids and mu opioid receptors in the gastrointestinal (GI) tract, including the stomach, small intestine and colon (Reimer et al., 2009; Crockett et al., 2019). PAMORAs could be considered in those whose regular use of a combination of laxatives has failed, as outlined in Table 2. Cost, availability, route of administration and limited evidence, currently restrict the routine use of methylnaltrexone and naloxegol (Nelson and Camilleri, 2016). Methylnaltrexone is a peripheral mu opioid receptor antagonist for subcutaneous administration, and is indicated for patients with OIC not amenable or responsive to oral treatments (Leppert, 2010). The use of PR oral naloxone in PR naloxone-oxycodone formulation is aimed at reducing or preventing the GI tract actions of opioids, whilst maintaining analgesia from the PR oxycodone (Reimer et al., 2009; Meissner et al., 2000, 2009).

Naloxone, a competitive antagonist at mu-receptors, is available in parenteral form for the treatment of opioid toxicity and, more recently, formulated with PR oral oxycodone to reduce OIC and misuse of oxycodone. When administered orally, naloxone exerts local activity in the GI tract. Due to high first pass intestinal and liver metabolism to inactive metabolites, in the absence of liver impairment, naloxone has negligible oral bioavailability, which limits its effect on reversing the analgesic effects of systemic opioids. PR oral oxycodone-naloxone, in a ratio of 2 to 1, is considered more superior to oxycodone without laxative prophylaxis in improving bowel function in chronic opioid treatment (DePriest and Miller, 2014). However, unequivocal improvement in bowel function has not been demonstrated in several postoperative studies (DePriest and Miller, 2014), leading some clinicians to query its clinical role. A more recent study (Kokki et al., 2017) of opioid naïve patients demonstrated PR oral oxycodone-naloxone was beneficial in reducing OIC, but not significantly in the chronic opioid users; PR oral oxycodone-naloxone reduced but did not eliminate the need for laxative use to manage OIC (Kokki et al., 2017; DePriest and Miller, 2014).

The use of PR oral oxycodone-naloxone plus laxative is currently more costly than PR oral oxycodone plus laxative. In Canda, Goeree et al. conducted a cost-effectiveness analysis of PR oral oxycodone-naloxone versus oxycodone alone, which showed superior clinical effectiveness of PR oral oxycodone-naloxone in managing OIC at a small additional cost (Goeree and Goeree, 2016). Further studies are required to determine the cost-effectiveness of oral opioid-naloxone to usual opioid with laxative regimens. Although cost should not be a determining factor of best practice, it is important to consider the

**Table 2**

Peripheral acting mu opioid receptor antagonists (PAMORAs) available for OIC (Argoff et al., 2015; Nelson et al., 2016; Adis Med Writers, 2017; Australian Medicines Handbook, 2017; Therapeutic Guidelines Limited, 2017).

PAMORAs	Mechanism of action	Registered indication	Dose and considerations
Naloxone (combined with PR oral oxycodone)	Mu opioid receptor antagonist (peripherally acting when given orally and normal liver function)	TGA <sup>a</sup> : Mod-severe chronic pain unresponsive to non-narcotic analgesia including therapy, prophylaxis of OIC FDA: management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate EMA <sup>a</sup> : severe pain only managed with opioids	<ul style="list-style-type: none"> <li>• Twice a day</li> <li>• Oxycodone-naloxone 2:1 (e.g. 10mg/5 mg)</li> </ul>
Methylnaltrexone	Peripherally acting mu opioid receptor antagonist; limited ability to cross the blood-brain barrier Limited data; placebo controlled studies < 300 pts for up to 2 weeks with smaller open label extension studies for < 4months	TGA: treatment of OIC in advanced illness with insufficient response to laxative therapy  FDA: treatment of OIC in adults with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care  EMA: treatment of OIC when response to laxative therapy has not been sufficient in adult patients, aged 18 years and older	<ul style="list-style-type: none"> <li>• Single dose; can repeat after 24 h or alternate day</li> <li>• 62–114 kg, subcut 12 mg (0.6 mL)</li> <li>• 38–61 kg, subcut 8 mg (0.4 mL)</li> <li>• &lt; 38 or &gt; 114 kg, subcut 0.15 mg/kg</li> <li>• OIC chronic non-cancer pain: 450 mg oral daily or 12mcg subcut daily</li> <li>• OIC advanced illness: weight based subcut dosing as above</li> <li>• OIC chronic pain: 12 mg subcut daily as needed</li> <li>• OIC palliative care: weight based subcut dosing as above</li> </ul>
Naloxegol	PEGylated derivative of naloxone, peripherally acting mu opioid receptor antagonist, with limited ability to cross the blood-brain barrier	TGA and EMA: Treatment of OIC in adult patients who have had an inadequate response to laxative(s) FDA: Treatment of OIC in adult patients with CNCP	<ul style="list-style-type: none"> <li>• 25 mg mane on an empty stomach</li> <li>• If not tolerated reduce to 12.5 mg mane</li> </ul>

CNCP = chronic non-cancer pain.

TGA = Therapeutic Goods Administration (Australia).

EMA = European Medicines Agency.

FDA = US Food and Drug Administration.

<sup>a</sup> Second line symptomatic treatment of patients with severe to very severe idiopathic restless legs syndrome after failure of dopaminergic therapy.

financial impacts associated with OIC, as these have a serious negative impact on patient's QoL and daily activities. Until further studies are available, laxatives should be co-prescribed with opioids for the management of OIC. Patients with OIC have been shown to have higher health care utilisation, are absent from work more often and report impairment in performing their daily activities compared with non-constipated patients (Hjalte, Berggren, Bergendahl & Hjortsberg, 2011). The risk of discontinuation of short-term opioids due to OIC, and associated poor acute pain management, leads to the potential for increased risk of persistent or chronic pain, particularly following surgery associated with trauma (ANZCA, 2015). With 1 in 5 Europeans and Australians experiencing chronic pain, OIC is likely to be an ongoing issue for all clinicians to consider (Reimer et al., 2009; Chronic Pain Association of Australia, 2017).

#### Nurses' role in OIC management

The importance of maintaining a balance between adequate analgesia and minimising OIC symptoms is an ongoing challenge for clinicians and an area of patient care where nurses should be leading management. Andrews and Morgen (2002) highlight that “nurses are the health professionals who are best placed to conduct ongoing patient assessments and work in partnerships with patients and their families/carers” to manage constipation and the associated symptoms, as well as advocate independent nurse prescribing of laxatives. Within the orthopaedic setting, Do Souza (2002) states that nursing care considers the “patient as a whole person” focussing on the “biophysical, psychological and spiritual problems” that face orthopaedic patients, including reduced self-care abilities and mobility, altered nutrition, pain and constipation. DeSouza (2002) also highlights that as nurses are the initial step in identifying many orthopaedic patient issues, so they are subsequently more likely to provide effective nursing interventions to alleviate their patient's problems because of their established and

ongoing relationship. Madsen et al. (2010) compared two bowel treatment protocols with orthopaedic surgical patients for early prevention and treatment of constipation. Both bowel treatment protocols were implemented in a hospital, where nurses could then initiate laxatives according to the protocol, improving post-operative constipation (Madsen et al., 2010).

LoCasale et al. (2015) found that only half of chronic pain patients may have sufficient laxative use and, over time, this reduced to a third of patients able to maintain sufficient laxative use. Regular assessment of symptoms and response is important to guide appropriate adjustment of laxative dose and choice, an aspect of OIC where nurses can undertake a broader role. Although nurses can initiate aperients, this is often restricted to a once only dose. Nurses are often responsible for undertaking regular assessment and documentation of bowel function, placing them in an optimal position to undertake initiatives and an enhanced scope of practice for bowel management.

Andrews and Morgen (2012) stated that nurse-initiated laxatives in the palliative care community setting are “paramount in achieving a successful outcome in relation to constipation symptom management”. This is also supported by the findings of Quinn and Lawrie (2010). Nurses are commonly the key reporters and documenters of constipation, associated symptoms and effects of treatments to other clinicians, placing them in a pivotal position to initiate OIC treatments (McKenna et al., 2001). Nurse-initiated protocols in Emergency Departments have been implemented for faster administration of medications for management of conditions such as pain, asthma and sepsis (Cabilan and Boyde, 2017; Varndell et al., 2018) and bowel management protocols (BMP) are used in intensive care units to reduce the incidence of constipation and implement early management of associated symptoms. The effect of BMPs on clinical outcomes remains uncertain, with randomised-controlled trials required to determine their impact on patient outcomes (Oczkowski et al., 2017). Knowles et al. (2015) highlighted that the presence of an implemented BMP does not necessarily equate

to clinicians implementing evidence based constipation treatments and that awareness and education is not sufficient in changing attitudes to clinical practice. Knowles et al. (2013) also highlight that attitudes and cultural change towards the management of constipation is crucial for effective implementation of BMP and constipation management strategies. Current evidence emphasises the important role that nurses can have in BMP by initiating or advocating for constipation treatments for their patients, and nurses could undertake a greater clinical role in mitigating and managing constipation.

## Conclusion

OIC can reduce the QoL for patients and generate a greater demand on healthcare utilisation, but continues to be an aspect of patient care overlooked or not prioritised. The use of laxatives may mitigate symptoms and nurses can undertake an active role in the management towards reducing the likelihood of onset of OIC by extending their scope of practice beyond assessment to collaborative initiation of bowel management and treatment of OIC. Further research is required to determine the most cost-effective strategies and medication regimens to prevent and manage OIC.

## Conflicts of interest

The authors do not have any financial nor personal relationships with other people or organizations that could have inappropriately influenced (biased) the content of this paper.

## Submission declaration

The work described has not been published previously, is not under consideration for publication elsewhere, the publication is approved by all authors and if accepted, the work will not be published elsewhere in the same form, in English or in any other language, without the written consent of the copyright-holder.

## Ethical statement

This paper adheres to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, issued by the International Committee for Medical Journal Editors code of conduct.

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