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Opioid-induced constipation – a preventable problem

One of the most common adverse effects of chronic opioid therapy is constipation.[1-4] Up to 95% of patients prescribed an opioid report constipation as a side effect,[4-6] which can occur soon after taking the first dose.[6]

Older adults tend to be at higher risk of constipation because of immobility, poor diet, poor fluid intake and concurrent use of constipating medicines.[7] Older adults suffering from chronic pain are likely to be less active, treated with opioid analgesics and therefore, are at considerable risk of developing constipation.

To prevent opioid-induced constipation, Australian guidelines recommend prescribing suitable laxatives concurrently with opioid analgesics.[1,7,8] An analysis of the DVA dataset found that of the 42,000 members in the veteran community dispensed an opioid analgesic, over 70% were not concurrently dispensed a laxative.[9]

Other medicines, particularly those that are highly anticholinergic, can also cause constipation, which may further compound the problem.[10]

This therapeutic brief outlines how to prevent and treat opioid-induced constipation, including the most appropriate laxatives to use, and highlights commonly used medicines that may also contribute to constipation.

Inside

Key points

- Constipation is a debilitating adverse effect of opioid analgesics.
- When initiating an opioid analgesic, consider a combined stimulant laxative with a stool softener.
- Osmotic laxatives may be appropriate for patients in palliative care or for those with non-responsive constipation.
- Review use of bulking agents.
- Review other medicines that may further contribute to constipation.

How opioids cause constipation

Opioids cause constipation by binding to specific receptors in the gastrointestinal tract and central nervous system, resulting in reduced bowel motility through direct and indirect (anticholinergic) mechanisms. The delayed colonic transit time discourages defecation, and causes excessive water and electrolyte re-absorption from faeces, which further dehydrates stool.[4,5]

Most patients develop some degree of constipation after opioid initiation. Even though tolerance develops to some opioid adverse effects, constipation often persists unless remedial measures are taken.[2,4,5,11]

Impact of opioid-induced constipation

Opioid-induced constipation can be so intolerable that it causes significant social and psychological trauma for patients. It has been reported to be the most bothersome side effect of opioid analgesics.[5] Unmanaged chronic constipation may cause rectal pain and bleeding, abdominal pain and distension, urinary incontinence, faecal impaction, rectal tearing, and, in very severe cases, bowel obstruction and colonic perforation.[6,7,12] In a study of patients who had dementia and were living in a nursing home, physical aggression was shown to be associated with constipation.[13]

Opioid-induced constipation has an impact on quality of life that is comparable to other common chronic conditions.[6,12,14] Some patients would rather endure chronic pain than suffer from the severe constipation that can arise with long-term opioid therapy.[3] One study found that approximately one-third of patients missed, decreased or stopped using opioids in order to make it easier to have a bowel motion; the majority (86%) of these patients experienced increased pain as a result, which reduced their quality of life.[5,6] Reducing the opioid dose is not considered useful, as analgesia may be compromised and constipation may not resolve.[3,4]

Managing opioid-induced constipation

*The aim is to **prevent** opioid-induced constipation.* If a patient develops this adverse effect, the goal is to return bowel function to an acceptable level for that patient.

Assessment

There is no objective definition of constipation because of the great individual variation in normal bowel habits, and because patients and healthcare professionals can vary significantly in their definition of constipation.[4, 7,10] In broad terms, constipation is described as infrequent defecation (generally fewer than 3 times per week), often with straining and passage of hard, uncomfortable stools.[1]

In established cases of constipation, a rectal examination is usually necessary as it can reveal the presence of soft or dry faeces, or faecal impaction, which may influence the laxative choice. Sometimes, a plain abdominal x-ray is also performed, although there is a poor correlation between symptoms and the extent of faecal loading shown on x-ray.[7,15]

Pharmacological management

Before starting opioid therapy, discuss the associated risk of constipation and the possible need for taking laxatives with the patient.[3,4]

In conjunction with lifestyle measures (page 4), consider a combined stimulant laxative with a stool softener when initiating opioids.[1,7,8] The use and choice of laxative may also be influenced by patients' preferences, routes of administration, side effects and the required onset of action. Osmotic laxatives may be appropriate for patients in palliative care, those with malignant neoplasia or for those with non-responsive constipation (see table 1).

Generally, bulking agents are not recommended for patients with opioid-induced constipation as they increase the risk of bowel obstruction, especially if the patient has poor fluid intake or is immobile.[7]

These recommendations also apply to palliative care patients taking opioid analgesics.

Table 1 includes a list of laxatives by class that are appropriate for managing opioid-induced constipation.

Table 1: Laxatives used for opioid-induced constipation[1,7,8,15,16]

Class	Generic name (Brand name)	Administration & Safety considerations
Oral laxatives		
Combined stimulant laxative with stool softener	Docusate sodium + senna (e.g. Coloxyl with Senna®) **RPBS**	Can be used long-term in patients taking opioids. There is no convincing evidence to suggest that chronic use of stimulant laxatives causes cathartic colon or colonic injury.
Stimulant laxatives	Senna standardised (e.g. Senokot®) **RPBS**	
	Bisacodyl (e.g. Bisalax®, Dulcolax®) **PBS Restricted** [a,b,c]	
Stool softeners	Docusate sodium (e.g. Coloxyl®) **RPBS**	Often combined with a stimulant laxative for opioid-induced constipation. There is limited evidence to show effectiveness of stool softeners when used alone.
Osmotic laxatives	Macrogol (polyethylene glycol) laxative (e.g. Movicol®, Osmolax®) **PBS Restricted** [b,c,d]	Fluid and electrolyte disturbances may occur – use with caution in cardiovascular disease (e.g. heart failure) and renal impairment (less of a risk with macrogol laxatives). Laxatives containing sodium phosphate are not recommended for the elderly (e.g. Fleet®).
	Saline laxatives containing magnesium (e.g. Epsom Salts) **Not PBS listed**	
	Lactulose syrup (e.g. Actilax®, Duphalac®) **PBS Restricted** [b,c]	Contraindicated in intestinal obstruction. Flatulence is a common adverse effect. Avoid lactulose if fluid intake is poor. Lactulose contains galactose and lactose.
	Sorbitol liquid (e.g. Sorbilax®) **Not PBS listed**	
Rectal laxatives		
Osmotic laxatives	Sodium citrate + sodium lauryl sulfoacetate + sorbitol enemas – also known as saline laxatives (e.g. Microlax®) **RPBS**	Rectal laxatives may be used for faecal impaction or if there is insufficient response to oral laxatives. Avoid embedding suppositories in faecal matter, as it delays the laxative effect. Avoid sodium phosphate enemas (e.g. Fleet®).
	Glycerol suppositories **RPBS**	
Stimulant laxatives	Bisacodyl enemas (e.g. Bisalax®) and suppositories (e.g. Bisalax®, Dulcolax®) **PBS Restricted** [a,b,c]	

[a] Patient in residential aged care facility. [b] Palliative care. [c] Malignant neoplasia. [d] Non-responsive constipation or faecal impaction.
See PBS Schedule for complete list of restricted benefits.

Prevention and treatment of opioid-induced constipation*[1,7,8,15]

Scenario	Recommendation	Considerations
Prevention		
Opioid initiation	Consider the use of a combined stimulant laxative with a stool softener, such as docusate sodium + senna (e.g. Coloxyl with Senna®). An osmotic laxative may also be appropriate, such as macrogol (e.g. Movicol®, Osmolax®) or lactulose (e.g. Actilax®).	Since opioids reduce peristalsis, causing hard faeces to form, the most useful laxatives are those that increase peristalsis and soften the stool. **Bulking agents are not recommended.**
Treatment		
Established constipation	If not initiated with opioid therapy, consider use of a combined stimulant laxative with a stool softener – such as docusate sodium + senna (e.g. Coloxyl with Senna®). If initial management is ineffective: • for hard faeces consider adding an oral osmotic laxative, such as macrogol (e.g. Movicol®, Osmolax®) or lactulose (e.g. Actilax®). • for soft faeces consider adding another oral stimulating agent, such as bisacodyl (e.g. Bisalax®).	
Non-responsive (refractory) constipation	If the regular laxative regimen is unsuccessful, consider the following management options: • glycerol suppository • small volume enema (e.g. Bisalax®, Microlax®) • macrogol (polyethylene glycol) laxative (e.g. Movicol®, Osmolax®) • saline** laxative.	For palliative care patients, methylnaltrexone may be added when conventional laxatives are unsuccessful.
Impaction – confirmed by symptoms (faecal soiling or overflow diarrhoea***) and rectal examination	Enemas and suppositories are generally recommended to clear the rectum before starting a bowel management program. Management options include: • glycerol suppository • daily saline** enema (e.g. Microlax®) if softening is effective but peristalsis is ineffective. If rectal treatment is contraindicated, macrogol can be used (e.g. Movicol®, Osmolax®)	Manual removal of impacted faeces may be required before laxatives can be effective. Start regular laxative regime once impaction has been alleviated to prevent further opioid-induced constipation.

*RPBS availability and PBS restricted benefits are outlined in table 1.

**Laxatives containing sodium phosphate are not recommended (e.g. Fleet®).

***Antidiarrhoeal agents are not recommended to stop overflow diarrhoea.

New developments

Tapentadol (Palexia IR®), a centrally acting opioid analgesic that also inhibits noradrenaline re-uptake, and the combined preparation oxycodone/naloxone (Targin®) have been recently approved by the Therapeutic Goods Administration (TGA). In clinical studies, constipation has been reported as a common side effect for both preparations;[17,18] therefore the advice provided on page 3 is also applicable.

Lifestyle measures[4,7,8]

In addition to pharmacological management, and where appropriate, patients should be advised to:

- go to the toilet regularly, preferably at the same time each day, and take advantage of the gastrocolic reflex that occurs after eating or drinking hot drinks.
- ensure comfort and privacy to facilitate unhurried, complete defecation.
- not suppress the urge to defecate; for example, when out, they should use public toilets instead of waiting to get home.
- where possible, drink adequate amounts of fluids, and eat optimal levels of fibre-rich foods (e.g. prune or pear juice) if current intake is deficient.
- increase general activity and exercise within their capabilities, as movement can be difficult when chronic pain is involved.

Other factors affecting constipation

Multiple factors can contribute to constipation in older adults suffering from chronic pain, including adverse effects of other medicines, neurological disorders and mechanical obstructions.[10] Questioning the patient and conducting a thorough assessment can help to identify the cause(s).

Other medicines

Besides opioid analgesics, there are some other medicines that can commonly cause constipation:[7,8,19,20]

- Aluminium- and/or calcium-containing antacids
- Agents with anticholinergic effects – e.g. tricyclic antidepressants, oxybutynin, antihistamines, antipsychotics
- Antipsychotics – e.g. chlorpromazine, pericyazine, prochlorperazine, clozapine, olanzapine, risperidone, quetiapine
- Gabapentin and pregabalin
- Iron supplements
- Calcium supplements
- Verapamil (the most likely of all calcium channel blockers to cause constipation)

For patients taking medicines that are likely to cause constipation, if appropriate, consider reducing the dose or using a different medicine where possible.

Pre-existing constipation

A discussion with your patient can reveal any pre-existing constipation and laxatives the patient is taking to treat it, particularly over-the-counter medicines. This will help to develop a treatment plan to ensure that the constipation is managed and does not worsen with opioid treatment. For example, if the patient is taking a bulking agent, consider changing to a combined stimulant laxative with a stool softener if suitable.[4]

To establish effective management options, a **Home Medicines Review (HMR)** may help to identify other causative medicines. Ensure this concern is mentioned when you make the referral.

Ongoing patient management

When reviewing patients taking opioids, ask about their bowel function. Any improvements or decline in their condition may require stopping the laxative, adjusting the dose or adding another agent.

When monitoring patients, also consider recent lifestyle and environmental factors that can affect their bowel function, such as any newly added medicine(s) and/or diagnosed medical condition(s), changes to diet or mobility levels, and weather conditions; for example, a heat wave can cause significant dehydration and electrolyte loss.

Further information

- Palliative Care Therapeutic Guidelines 2010 (Gastrointestinal symptoms)
- Continence Foundation of Australia www.continence.org.au

Full reference list available at:
www.veteransmates.net.au

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