

## Opioid-induced constipation

Opioid-induced constipation is the most common side effect of opioid therapy. Up to 95% of people prescribed an opioid report constipation as a side effect. It can occur as soon as after the first dose of an opioid. Older people in residential aged care facilities are at higher risk due to immobility, poor diet, poor fluid intake and concurrent use of other constipating medications. Prevention is the key strategy for opioid-induced constipation.

### Opioid-induced bowel dysfunction

Adverse effects of opioids include somnolence and mental clouding, delirium, neuroendocrine effects, sleep-disordered breathing, respiratory depression, pruritus, urinary retention, allergic reactions, weight gain, abnormal glycaemic control, hyperalgesia, and opioid-induced bowel dysfunction (OIBD).

Symptoms of OIBD include nausea, vomiting, epigastric pain, heartburn, dysphagia, dyspepsia, retrosternal pain, bloating, flatulence, abdominal pain, distention, tenesmus, narcotic bowel syndrome, and constipation.

For OIBD to be clinically diagnosed, these symptoms should start or worsen during opioid therapy and continue for at least two weeks. Many of the symptoms of OIBD improve over time, except for opioid-induced constipation.

### Opioid-induced constipation

Opioid-induced constipation has been described as a change when initiating opioid therapy from baseline bowel habits that is characterised by any of the following: reduced bowel movement frequency, development or worsening of straining to pass bowel movements, a sense of incomplete rectal evacuation, or harder stool frequency.

Opioids cause constipation by reducing bowel motility, increasing gastric tone, and decreasing gastric emptying and mucosal secretions. Overall, this causes slowed colonic transit time. This reduced motility also causes excessive water and electrolyte re-absorption from faeces which further dehydrates the stool. The result is a harder stool and less frequent and less effective defaecation.

The 2016 Rome IV criteria for a diagnosis of opioid-induced constipation includes new or worsening symptoms of constipation when initiating, changing, or increasing opioid therapy that must include 2 or more of the following:

- straining during more than 25% of defaecations
- lumpy or hard stools during more than 25% of defecations
- sensation of incomplete evacuation during more than 25% of defecations
- sensation of anorectal obstruction or blockage during more than 25% of defecations
- use of manual manoeuvres (e.g. digital evacuation, support of the pelvic floor) to facilitate more than 25% of defecations
- fewer than 3 spontaneous bowel movements per week

The degree of opioid-induced constipation depends on a range of factors, including the resident's comorbidities, the choice of opioid (including the route of administration and dosage), and the patient's diet and lifestyle. Prolonged constipation can lead to faecal impaction, causing urinary and faecal overflow incontinence.

Constipation in people with dementia may be associated with aggression.

### Management of opioid-induced constipation

Diet and lifestyle factors should always be considered. Adequate dietary fibre and fluid intake, and activity within limits are usually considered the first steps. Kiwifruit has been shown to relieve constipation. Eating two kiwifruit per day has been shown to be more effective than the bulk-forming laxative psyllium. Toileting should occur as soon as possible in response to the urge to defaecate.

Concurrent medications can increase the risk of developing opioid-induced constipation. These may include medications with anticholinergic effects, aluminium- and calcium-containing antacids, oral calcium supplements, oral iron supplements, verapamil, gabapentinoids (pregabalin, gabapentin), and GLP-1 receptors agonists. Medications with anticholinergic effects include tricyclic antidepressants (TCAs), oxybutynin, antihistamines and antipsychotics. A medication review can identify medications that commonly cause constipation and provide options for alternatives or deprescribing.

Routine preventive therapy is recommended with opioids. Combination oxycodone/naloxone (*Targin*) for management of chronic pain is associated with a lower risk of constipation.

## Laxatives

Stimulant laxatives are recommended for prevention and treatment of opioid-induced constipation. Stimulant laxatives directly stimulate intestinal motility and reduce colonic water absorption. They are best administered at night to help produce a bowel motion the following morning. There is no evidence that routine use of stimulant laxatives is harmful.

Stimulant laxatives include:

- bisacodyl (*Bisalax, Dulcolax, Lax-Tab*)
- senna (*Senna-Ge, Senokot, Laxettes with Senna, Laxettes with Sennosides*)

Senna stimulant laxatives are also available in combination with docusate, a stool softener (e.g. *Coloxyl with Senna, Sennesoft, Colaxsen, ColoxEase, Co-Senna*). Stool softeners allow water and lipids to penetrate the stool but have limited benefit when used alone.

Stimulant laxatives can also be used alone or combined with an osmotic laxative such as macrogol (*OsmoLax, Movicol*), sorbitol (*Sorbilax, Sorbisol*) or lactulose (*Actilax, Dulose*). Osmotic laxatives work by drawing water into the gut thereby hydrating the stool. They may take several days for effect. Macrogol products may contain significant amounts of sodium, which may be unsuitable for residents with heart failure. Lactulose and sorbitol may cause flatulence, and may be mixed with fruit juice, water or milk to reduce the sweet taste.

Bulk-forming laxatives (*Metamucil, Fybogel, Normacol Plus, Normafibe*) should be avoided in the prevention or treatment of opioid-induced constipation as the increased bulk may worsen constipation, particularly when the resident is dehydrated or immobile.

If stimulant or osmotic laxatives are not effective, glycerol suppositories or small volume enemas may be required. They should be not be used regularly.

Prucalopride (*Resotrans, Rospride*) is approved for treatment of chronic functional constipation in adults without adequate relief from at least two laxatives from different classes at highest tolerated recommended doses for 6 months or more. In older persons, the initial recommended dose is 1mg per day, increasing to 2mg daily if required.

In palliative care, methylnaltrexone (*Relistor*) may be considered. Methylnaltrexone is an opioid antagonist administered by subcutaneous injection as a single dose on alternate days. It reduces constipation associated with opioid therapy without affecting the central analgesic effects of the opioid. Relistor is not recommended in patients with severe hepatic impairment or with end-stage renal impairment requiring dialysis. It must be used in combination with oral laxatives. Abdominal pain, flatulence or diarrhoea are common adverse effects.

## Summary

Constipation is common with use of opioid analgesics. It is important to ensure that the indication for opioid therapy is appropriate, and the lowest effective dose is prescribed. Preventing opioid-related constipation is the best treatment. Regular stimulant and/or osmotic laxatives are recommended for prevention of constipation when opioids are prescribed. Bulk forming laxatives are not recommended. Medication reviews can identify other medications that might also be contributing to constipation.

## References

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