PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #25
OPIOIDS AND NAUSEA

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Background Why do patients get nauseated and vomit after receiving an opioid? Commonly described as an "allergy", opioid-induced nausea/vomiting is not an allergic reaction. In fact, rather than indicating a pathologic reaction, nausea indicates normal functioning of the brain. Opioid-induced nausea occurs through the following mechanisms:

- At the base of the 4th ventricle lies the chemoreceptor trigger zone (CTZ), a "sampling port", to detect substances that do not belong in the blood. Adjacent to the CTZ lies the medullary vomiting center which controls the complex muscular sequence of vomiting. When the CTZ detects a noxious chemical in the blood, a signal is sent to the VC and the vomiting reflex is initiated. Of note, this is the same mechanism when patients vomit after receiving chemotherapy.
- Opioids can directly stimulate the vestibular apparatus—patients note a spinning sensation with their nausea.
- Opioids cause constipation which can lead to nausea via stimulation of afferent cholinergic pathways.

Do all opioids produce the same degree of nausea? There is little research data on this topic. In clinical practice, morphine and codeine are often mentioned as the worst offenders. Some clinical studies along with preclinical data in rats suggest that the transdermal fentanyl patch may have less nausea and constipation than morphine.

Why are some patients more sensitive to the emetic effects of opioids than others?
Unknown

What is the natural history of opioid-induced nausea? Most patients develop tolerance to the emetic effects, so that within 3-7 days, at a constant opioid dose, the emetic effect will abate.

What are management approaches?

- Dose adjustment—if good pain relief is achieved but associated with nausea, it may be possible to lower the opioid dose, still retain good analgesia, but eliminate the nausea.
- Switching opioids—there is variability in emetic reaction to different opioids. Note: since tolerance to nausea develops, one never knows if a reduction in nausea is from the change of drug or tolerance.
- Anti-emetics— Whenever possible, choose a drug directed at the most likely cause of nausea (see *Fast Fact* # 5). There are little published data to guide physicians in specific choice of anti-emetic for opioid-induced nausea.
  - Start with low-cost dopamine antagonists (e.g. prochlorperazine, haloperidol, or metoclopromide) or anti-cholinergics (e.g. scopolamine);
  - Anti-histamines may be helpful for patients who note a spinning sensation.
  - $5HT_3$ antagonists (e.g. ondansetron) can be used for more refractory cases. Two multi-center randomized trials have examined control of emesis associated with opioids not used for anesthesia. In one, 16 mg of ondansetron was more effective than 8 mg or placebo. In the other trial, stopped early due to lack of patient accrual, 24 mg ondansetron was no better than placebo or metoclopramide.
- Non-pharmacological approaches: there is little evidence to support non-pharmacological treatments for nausea outside of chemotherapy associated nausea; suggested approaches include acupressure and behavioral treatments.

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