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Managing Opioid Side Effects

The developments of side effects such as nausea, vomiting, somnolence, constipation and occasionally hiccups and allergic reactions are reversible with medication withdrawal and supportive therapy. To minimize potential side effects it is generally recommended to prescribe opioids at the lowest dose possible as well as an addition of an opioid sparing regimen (addition of a non-steroidal anti-inflammatory or adjuvant analgesic). Even with the use of these methods, patients may still experience side effects¹.

Nausea and Vomiting

Postoperative nausea and vomiting is particularly unpleasant for the patient, leaving a negative overall impression regarding the surgical experience and increases the recovery period. Retching can also contribute to post-operative facial swelling due to the increased venous pressure in the head and neck region. There are many antiemetics on the market however, Ondansetron (Zofran) is the best choice for managing nausea from analgesics, particularly narcotic analgesics. Ondansetron, an antiemetic agent, is a 5-HT₃ receptor antagonist that has been found to be well tolerated and effective in controlling post-operative nausea and vomiting (PONV), yet it does not cause the sedative effects that other common antiemetics do². It has been shown to be effective in the control of PONV after various ambulatory surgical procedures requiring outpatient anesthesia^{3,4}. The typical healthy adult dosing methods are as follows:

- 1) Patient with a history of nausea with the use of narcotic analgesics
 - a) Intravenous route: 4mg IV push pre-operative and is effective for up to 8 hours after administration.
 - b) Oral route: 8mg tablet every 8 hours while taking the narcotic analgesic.
- 2) Patient who reports nausea/vomiting following the consumption of an analgesic.
 - a) Oral dissolving tablet Zofran 8mg: have the patient dissolve the tablet under their tongue to allow it to absorb through the mucosa for the floor of mouth and tongue. Generally relieves PONV within 30 minutes.

An alternative to Ondansetron (Zofran) is a transdermal patch: Scopolamine 1.5mg patch, remove backing from the patch and apply to the hairless post-auricular mastoid area. The patch is designed to have its maximum effect in the first 24 hours after placement. Its effectiveness will dissipate over the next 48 hours. It is most effective when placed at least one hour prior to taking medication that may elicit nausea/vomiting. The major side effects include sedation, pupil dilation (photo sensitivity) and dry mouth. Swallowing an anti-emetic while the patient is experiencing nausea/vomiting is likely to elicit vomiting and eject the pill before it has a chance to dissolve and absorb through the GI tract into the blood stream. Therefore it is best to use an oral dissolving tablet, transdermal patch or IV administration. If oral administration is the only option, Phenergan (promethazine) 12.5-25mg PO every 4-6 hours as needed for PONV, may be considered. The major side effects are sedation, confusion and disorientation. There is a Black Box FDA Warning for IV administration of Phenergan (promethazine) and therefore should be avoided. Prochlorperazine (Compazine) has been associated with risk of extrapyramidal symptoms and there is also a Black Box FDA Warning and should be avoided.

Allergy and Anaphylaxis

Allergy and anaphylaxis are immunologic hypersensitivity from initial exposure or repeated exposure to an antigen such as an opioid. Reactions may be immediate or delayed and mild allergy to severe life threatening anaphylaxis. As a general rule the faster onset of the reaction after exposure, the more severe the allergy.

1. Mild allergy is characterized by but not limited to, itching, rash and redness and is treated with diphenhydramine 50mg IM followed by 50mg PO every 4 hours for two days⁵.
2. Severe allergy/anaphylaxis is characterized by, but not limited to, dyspnea, wheezing, substernal tightness, tachycardia, hypotension, intense pruritus, conjunctivitis and rhinitis. Treatment consists of ACLS, .3mg epinephrine and repeat every 3-5 minutes as necessary. 100% oxygen with respiratory support as necessary. When the clinical condition improves diphenhydramine 25-50mg IV/IM and 100mg hydrocortisone IV/IM to help prevent recurrence⁵.

It is advisable to have an emergency allergy kit in your office that is readily available. The kit should include commercially packaged drugs that are ready to administer IM or IV without having to mix or draw drugs from a multi dose vial. For example; epinephrine 1:1000 syringe, diphenhydramine 50mg syringe, Hydrocortisone, however has to be reconstituted prior to administration. Allergy symptoms and the proper dosing instructions should be written on an index card for quick reference.

Constipation

Constipation is a common problem, occurring in 40-95% of patients treated with opioids⁶. Opioids activate mu receptors in the gastrointestinal tract responsible for gut motility from a vascular distribution as well as a local application to the gut⁷. This decreases gut motility, secretions, and blood flow and may lead to dry, hard stool. A constellation of symptoms may manifest including incomplete evacuation, bloating, abdominal distention and increased gastric reflux⁸. Constipation, similar to nausea is unlikely to improve over time and must be anticipated,

monitored and if symptomatic, addressed⁹. Numerous medications exist for treatment of constipation and are available to the practitioner to prescribe at their discretion.

Currently available treatments available to the practitioner include bulk laxatives, stool softeners, osmotic laxatives and stimulant laxatives. Typically, monotherapy with stool softeners is considered ineffective, and use of scheduled stimulant laxative is often required¹⁰. Bulk laxatives (ex. Citrucel [methylcellulose], Metamucil [psyllium]) add bulk and water to stool so that they can pass more easily through the intestine. Stool softeners (ex. Colace [docusate]) act as a surfactant, enabling additional water and fats to be incorporated into stool. Osmotic laxatives (ex. MiraLAX [polyethylene glycol], magnesium citrate) retain water within the colon therefore, softening the stool. Stimulant laxatives (ex. Dulcolax [biscodyl], Senokot [senna]) stimulate mucosa altering water, electrolyte and peristaltic action of the intestines, to stimulate motility¹¹.

Constipation may lead to multiple side effects and it is this practitioner's philosophy to obtain a detailed history of current as well as past medications and side effects. If a history of constipation with opioid medications is obtained a typically bowel regimen of a bulk laxative (ex. Metamucil 2.5-7.5g in 8 oz of water per day) is employed. A patient may furthermore be instructed to maintain fluid intake as well as activity as tolerated. If the patient develops constipation, dual therapy including a stool softener (ex. Colace 50-100mg/day) and a stimulant laxative (ex. Senokot 15-25mg/day) are utilized. Finally, if constipation continues, an osmotic laxative (ex. MiraLAX 17g in 8 oz of water, not to exceed treatment for 1 week) may be added to the regimen.

Sedation and Psychomotor Performance

The reported incidence of sedation following opioid administration is 20-60% and is commonly associated with the initiation of opioid therapy or dose increases¹². In the acute post-operative setting sedation may be a desirable side effect however, when opioids are initially administered, the ability to operate heavy equipment including automobiles is diminished and should not be allowed. The sedative effect of opioids ultimately stabilizes with chronic use as tolerance develops¹³ however; the patient should be advised not to operate heavy equipment in the acute post-operative setting or if the opioid dosage is increased.

Regarding the elderly population (Greater than 70 years of age) is at an increased risk for sedation and psychomotor deficits due to decreased renal function⁶. This may lead to an increase in accumulation of opioids and their metabolites¹⁴. To reduce the risk of sedation and psychomotor deficits, downward dose adjustments or prolonging the opioid interval should be utilized. Perhaps employing an opioid sparing regimen if applicable or prescribing a medication such as Ultram (tramadol) (50mg q4-6h), which is a weak mu agonist, metabolized in the liver and excreted in the kidneys¹⁵. As always, a detailed medication history and interactions should be obtained prior to prescribing any medication.

Hiccups

Hiccups are a fairly common phenomenon associated with general anesthesia as well as administration of various medications such as opioids, benzodiazepines and dexamethasone¹⁶. They commence most often during inspiration and are inhibited by elevations in PaCO₂; which serves as the basis for breath holding or breathing into a paper bag as a common therapeutic intervention¹⁷. Hiccups are generally only a nuisance but may become troubling when prolonged. It is this author's opinion, initial treatment should consist of breath holding and/or breathing into a paper bag in an attempt to elevate the PaCO₂. If prolonged, pharmacological intervention may be considered. Currently, Thorazine (chlorpromazine) (25-50mg t.i.d.) is the only drug that has been approved by the U.S. Food and Drug Administration and is effective for the management of hiccups.

Conclusion

Opioid induced side effects; especially nausea, vomiting and constipation are common in the acute post-surgical phase of a patient's treatment. Most of these side effects may be potentially managed by behavior modification and through pharmacologic intervention. A philosophy including opioid sparing, dose and duration dependent analgesia as well as symptomatic treatment of side effects should be utilized to maintain adequate pain control for the post-operative patient.

Use of the PDR in clinic practice because older generic medications are often omitted from newer versions and the use of the PDR is cumbersome. Quick concise information is readily available with smart phone applications. There are many to choose from, however there are two free applications that we recommend. The first is Medscape form WebMD®. It the most comprehensive drug reference, with concise information on dosing, interactions, adverse side effects, pharmacology, indications and administration. The second is Epocrates®, which provides a quick reference for dosing, formulation and administration.

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