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News You Can Use

Insights Into Clinical Practice

A Rose by Any Other Name...

For patients about to undergo surgery, nausea and vomiting which in the airline industry is known as a “round trip-meal ticket” (a.k.a..jettisoning the chunky cargo) is fraught with trepidation and definitely rates high on their concern scale. Many healthcare professionals, particularly anesthesia providers, often feel that the best way to prevent the “gastro geysers” is to prophylactically treat every patient scheduled for surgery with an antiemetic. I say this is overkill. Not every patient will experience the “technicolor yawns”; in fact only about 30% of all patients who have surgery will “share his or her inner feelings” . And if you really think about it, most drug prophylaxis against “reworking the stew” is ineffective and thus a waste of money. And why is? Well, consider that for most antiemetics, the number needed to treat is 5. What this means is that five patients need to be treated to prevent one additional case of “calling the buffalos”. So if the incidence of nausea and vomiting following surgery is 30%, then out of a group of 100 people only 30 people will actually experience the “Call of the Walrus” and only 6 of these people will effectively be treated prophylactically. If we decided that all our patients should be treated prophylactically with ondansetron (Zofran®), for example, then at \$26.71 per 4 mg vial, the cost of effectively treating these 6 patients actually equates to \$2671.00. Oh, by the way, this cost does NOT include the cost of needles or syringes or any other supplies associated with drug administration . Of course as an administrator of a health care organization, you may decide that using zofran is prohibitive and choose to use something less expensive to prophylactically treat these 100 patients. After all, you may be one of those die hards who believe it is best to treat everyone prophylactically, despite evidence that it is probably not the best approach to warding off the “upchucks”. So you decide to use droperidol. At a cost of \$11.32 per amp and with a number needed to treat of about 3, you spend \$1132.00 to treat only 10 patients.

Hopefully by now you get my drift. Treating patients prophylactically is just not cost effective. So what is the best approach? Is there any time you treat patients prophylactically? And what conditions or situations do you consider in deciding when to pretreat the patient .

Much research on the control of PONV has been conducted during the last four decades. The majority of clinical trials focuses on prophylaxis of PONV (i.e. patients receive an antiemetic at induction of anaesthesia, during surgery or shortly before they wake up). There are, however, several problems with the prevention of PONV. First, the efficacy of prophylactic antiemetic interventions in the daily surgical setting (i.e. when the baseline risk for PONV is not particularly high) is often disappointing . Second, there is no evidence that prophylaxis decreases the likelihood of unanticipated admission Third, prophylaxis of PONV is likely to be less cost-effective than treatment of established symptoms. And finally, with prevention strategies, patients who actually do not need any prophylaxis are unnecessarily exposed to a drug, and are thus put at risk of suffering from unnecessary adverse drug reactions.

Many factors can influence the risk and severity of postoperative nausea and vomiting. The risk is higher in adults than children, in women (especially premenopausal women) than in men, in obese patients, in patients who have a high level of preoperative anxiety, and in patients with a previous history of motion sickness or postoperative nausea and vomiting. Gastric emptying disorder or gastric hypomotility, certain types and length of operative procedure, or preanesthetic medications can all influence the risk of postoperative nausea and vomiting.(4) Thus the decision to provide prophylactic therapy should be based on the presence of risk factors for nausea and vomiting and the potential for serious sequelae from vomiting.(4)

While many factors can affect a patient's risk for nausea and vomiting after surgery, the primary predictors of a patient's likelihood of experiencing postoperative nausea and vomiting (PONV) are as follows:

- A history of nausea and vomiting following surgery .
- History of motion sickness
- Female gender - women are more likely than men to suffer nausea and vomiting after surgery, especially if they are within one week of their menstrual cycle(women, not men)
- Nonsmokers more likely to experience nausea and vomiting after surgery.
- Use opioids to control pain after surgery

- Type and Length of Surgery

The part of the body being operated upon correlates very highly to the incidence of PONV. Surgeries involving the alimentary canal or gall bladder have an incidence of almost 70%; the incidence of PONV following gynecological procedures ranges between 58% to 75% while surgeries of the ear nose and throat and mouth have been implicated in causing the “wretched spews” 38% to 48% of the time. Although laparoscopic procedures have been touted to reduce the incidence of postoperative pain and hence the use of opioids, they have been implicated in increasing the incidence PONV by 36% to 60%.

Oh, yes and lets not leave out the patients undergoing plastic surgery. Breast augmentation has been associated with an 8- to 10-times higher incidence of nausea and vomiting than other types of plastic or reconstructive surgery.

Often, the type surgery goes hand in hand with the length of time it takes to accomplish the surgical task and the longer the surgery lasts, the higher the risk of nausea and vomiting, especially if the surgery exceeds 3 hours

Anesthesia also plays a role in increasing risk of nausea and vomiting:

General anesthesia increases the risk of nausea and vomiting more than 10 times over all other types of anesthesia. Ideally it would be best to do all surgeries without general anesthesia but, alas, this is not an ideal world and as we have often heard, “You can’t have your cake and eat it too” which makes no sense to me, but there you have it!

But there are certain things anesthesia clinicians can do to make their anesthesia less emetogenic. In some cases **nitrous oxide** can be omitted. Fifteen percent of patients receiving nitrous oxide will experience nausea and vomiting and omitting it from a general anesthetic has been proven in three systematic reviews to reduce the incidence of PONV. This was also most pronounced in high-risk patients, with a number needed to treat of 5.

Omitting reversal of neuromuscular blockade. Neostigmine increases salivation, lower esophageal and gastric tone, gastric acid output and lower gastrointestinal tract motility, thus nausea and vomiting may occur. Omitting anticholinesterase drugs at the end of surgery may decrease the incidence of PONV, but only in doses greater than 2.5 mg of neostigmine.

Propofol appears to possess intrinsic antiemetic properties, possibly by the antagonism of dopamine D2 receptors. It has been used in the treatment of refractory nausea and vomiting in chemotherapy patients. When used for induction and maintenance there is a reduction in the incidence of PONV, with a number needed to treat of 5. Induction alone has no influence. Total intravenous anaesthesia with propofol is an expensive option, both in terms of the cost of the propofol itself, and the equipment required.

Ether is one of the most emetogenic of all the inhalational anesthetic agents. And if you haven’t noticed all currently used inhalation agents except for halothane are ethers. Ethers are associated with an over-all incidence of PONV in excess of 80% of patients. It seems to be worse when high inspired concentrations are used, or when administered over prolonged periods.

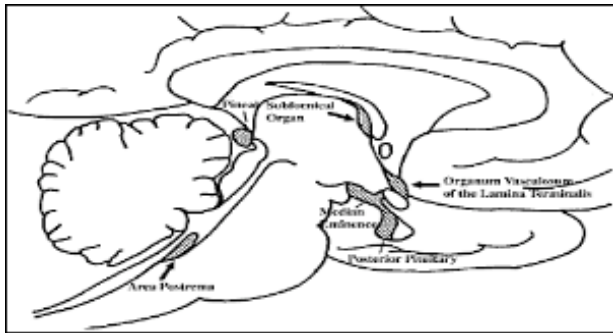
Finally, pain after surgery is a major cause of nausea and vomiting, especially when the pain is in the pelvic area or the gut.

Treating the Buffalos

If you’re going to invest the time and financial resources to forestall” throwing the patient into reverse”, then it is probably best to employ a combination of drugs. And this makes sense since the neurochemistry of the vomiting center is complicated, with some 40 neurotransmitters being implicated. Two that are believed to be particularly important are acetylcholine and histamine hence drugs that antagonize these substances have a central effect on PONV.

Chemoreceptor Trigger Zone (CTZ) Revisited.

The CTZ is a group of cells situated close to the area postrema on the floor of the fourth ventricle.



This area is extremely vascular and is situated outside the blood-brain-barrier making it vulnerable to circulating drugs and toxins. It is thought to have a major impact on the activity of the vomiting centre. The CTZ is also sensitive to systemic stimuli and is linked with the control of blood pressure, food intake and sleep. Two important neurotransmitters located here are dopamine and 5-hydroxytryptamine (5-HT, serotonin) and antagonists of these will have an indirect effect on the vomiting center to reduce nausea and vomiting.

Thus antagonists of four neurotransmitters, acetylcholine, histamine, dopamine and 5-HT, have acquired much interest in the development of the pharmacological treatment of nausea and vomiting, and most of the currently used anti-emetic drugs are antagonists at one of these receptors.

Anticholinergic (antimuscarinic) drugs

Anticholinergic drugs that can cross the blood-brain barrier, will act directly on the vomiting center and have anti-emetic properties. This is the oldest group of drugs used to treat nausea and vomiting, although this was not their original intention. Atropine was used to block the vagal effects of chloroform and later used for its drying effect on salivary secretions during ether anaesthesia. It was subsequently replaced by Scopolamine. Both are still used to treat nausea and vomiting, with Scopolamine being the more potent and effective. They are most effective against motion sickness, labyrinthine disease, vestibular disorders, after surgery in the posterior fossa and to counter the emetic effects of opioids. However, as a result of antimuscarinic actions, side effects include sedation, dry mouth, blurred vision and urinary retention, all more common after Scopolamine.

Antihistamines

This group of drugs is similar to the above in that they act on the vomiting center antagonizing the histamine (H₁) receptors. They are effective in the treatment of motion sickness, the management of labyrinthine disorders and to counter the emetic effects of opioids.

Dopamine antagonists

There is a wide range of drugs that antagonize dopamine (D₂ receptors) at the CTZ and therefore have antiemetic properties. These include the phenothiazines, butyrophenones, metoclopramide and domperidone.

Phenothiazines. This class of drugs, which includes prochlorperazine (Compazine®), chlorpromazine (Thorazine®), and promethazine (Phenergan®) have been associated with a whole array of extrapyramidal side effects and have been known to produce acute oculogyric crises with high doses and prolonged treatment. The neuroleptic malignant syndrome (catatonia, cardiovascular instability, hyperthermia and myoglobinemia) has been reported in association with prochlorperazine.

Butyrophenones. This group of drugs was originally developed to treat major psychoses (eg schizophrenia) and includes haloperidol and droperidol. The latter was widely used as a component of "neurolept anaesthesia", but associated with unpleasant side effects including extrapyramidal symptoms, hypotension, hypothermia and unpleasant hallucinations. However, in much smaller doses it has been shown to be a very effective anti-emetic when administered orally or intravenously.

Metoclopramide. In addition to having an effect on the CTZ, metoclopramide (Reglan®) has prokinetic actions on the gut, promoting gastric emptying and increases the barrier pressure of the lower esophageal sphincter by about 17 mm Hg. Although widely used as an antiemetic evidence for its efficacy in treating PONV is limited. It is perhaps best reserved for use preoperatively in those cases where there is evidence for delayed gastric emptying or patients at risk of gastro-esophageal reflux. Not recommended following gastrointestinal surgery involving anastomoses. Like the phenothiazines and butyrophenones, metoclopramide can produce a myriad of extrapyramidal side effects; the neuroleptic malignant syndrome has been reported in association with its use.

Domperidone. Domperidone (Motilium®) is widely available in every country in the world EXCEPT the United States, which doesn't surprise me. The FDA is always a "day late and a dollar short". In Canada, domperidone was approved more than 20 years ago by Health Canada. Domperidone is similar to metoclopramide, but does not

cross the blood-brain-barrier and therefore not associated with sedation or extrapyramidal side effects.

5-HT3 receptor antagonists

This is the most recently introduced (and therefore the most expensive) group of antiemetics available. Although it is thought that their main action is to antagonize 5-HT3 receptors that are found in a high concentration in the CTZ, they may also have a peripheral effect. Ondansetron is the most commonly used and appears effective when used orally preoperatively and intravenously for PONV. It is well tolerated with few side effects, headache being the most commonly reported. This class of drugs appear to produce greater anti-vomiting effects than anti-nausea effects.

Other drugs used for anti-emesis

Dexamethasone has been shown to be anti-emetic in a dose of 10 mg in adults. It appears to be of most use in combination with a 5-HT3 receptor antagonist, working via an additive or even synergistic effect. And before you ask, no, I don't know how it prevents PONV

Which drug shall I use?

When using drugs to prevent or treat PONV, find out what is available, then consider what to use, when to use it and how to use it.

It has been shown that ondansetron is as effective as droperidol, and that both are more effective than metoclopramide. However the administration of one receptor antagonist will reduce the incidence of PONV by only 30%, but a combination anti-emetic therapy (typically a 5-HT3 receptor antagonist with droperidol or dexamethasone) can achieve a response rate of up to 90%.

What to use will also depend upon what are you treating. Ondansetron has more anti-vomiting than anti-nausea properties, dopamine receptor antagonists have more anti-nausea properties than they do anti-vomiting properties.

If you are thinking about making a preemptive approach to attacking the "dreaded spews" just remember "number needed to treat" with anti-emetics ranges from 5 for ondansetron to more than 10 with metoclopramide. What this means in practical terms is that if everyone received anti-emetic prophylaxis, 80% of patients would still be at risk of PONV. The benefit of this has to be weighed up against the exposure to potential side-effects.

It is my opinion that the prevention and treatment of PONV using drugs alone is not especially effective. It makes more sense to identify those patients at high risk and first try to use an anesthetic technique or anesthetic agents associated with less nausea and vomiting and then supplement this with anti-emetic agents as required .

[Read more on nitrous oxide-click here](#)

[Read more on how to awaken patients from general anesthesia-click here](#)

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