'New' Post-Op Vomiting Drug Doesn't Spew Out Much Benefit

By Josh Bloom — February 28, 2020

Surgery is bad enough, but postoperative nausea and vomiting make it far worse. There's a "new" drug that has been shown to help prevent PONV. But how well does it work? Plus TWO quizzes for all you masochists out there.

It's bad enough having surgery, especially these days since there's a decent chance that you won't get enough pain meds afterward, as we continue to attribute the root of today's opioid problem to the wrong drugs [2]. (Some idiots [1] are pushing for alternatives to post-op opioids [2], such as high-dose Tylenol as a replacement for opioids even though it works no better than placebo. Or moose urine. See IV Tylenol As Good As Moose Urine For Post-Op Pain Control [3]).

But many patients are more afraid of postoperative nausea and vomiting (PONV) from the general anesthesia. And if you happen to have both undertreated pain and can't stop hurling that's gonna make for one miserable day. Fortunately, the wonder drug Zofran, which was originally invented as an antiemetic for chemo patients, is routinely used prophylactically before surgery. It works pretty well, but it is not perfect. Depending on the type of surgery and (especially) the method of general anesthesia used, 5-40% of post-surgical patients will still vomit.

Since surgery could be pretty much listed on my CV under "Hobbies," [3] I was especially interested in the press release [4] first-ever approved rescue drug for post-op patients who have
failed standard treatment. The drug is called Barhemsys (generic name amisulpride, Acacia Pharma [5]). How well did it work? Keep reading.

The chemical structure of amisulpride.

Double quiz time!!!!!

1) Does anyone see a potentially problematic portion of the molecule? 2) And if you find it, explain why it's probably not going to be a problem in this case. Good luck with this. You'll need it.

Barhemsys is the first member of a new class of antiemetic drugs that work by a novel mechanism – selective dopamine D2 and D3 antagonists. Barhemsys is not a new drug – it was launched by Sanofi in the 1990s for depression and schizophrenia. It has been generic since 2008.

Quiz #2!!!

(Am I getting seriously annoying with the quizzes? It would hardly be the first time I've been called annoying)

How could Acadia patent a 25-year old drug which had its own patent coverage until about 10 years ago?

There are plenty of other dopamine antagonists out there (e.g., Haldol, which is also an anti-emetic drug) but the list of side effects, sometimes severe, is long and scary. The good news is that Barhemsys has few (and minor) side effects. The bad news is that it won't help many people. Here's why.

Phase III summary:

- Barhemsys at a dose of 10 mg (IV) was given to patients who had failed the first treatment (presumably Zofran). Although it worked for 42% of this group placebo worked for 29%, so the drug only helped about one in 10 patients.
- When Barhemsys (5 mg) was given to patients at a high risk of PONV in combination with another anti-emetic drug, the combination was effective in 58% of the patients but the other anti-emetic alone helped 47% of them. Once again, the drug made a difference in only one in 10 people.

Although these results are far from spectacular there are a number of positives here

- Barhemsys had very few side effects.
• Coming up with a new use for an old drug is easier than discovering a novel drug, but there had to be some clever scientists behind this. It is not intuitively obvious that an old schizophrenia drug would work prophylactically to prevent PONV.
• Most importantly, the **first drug in a new class is rarely the best.** Although the drug is old it is still first-in-class for a novel use. Second-generation drugs are usually more potent, have fewer side effects, or both. This should spur additional research, either by Acacia or other companies. The chances of finding a more effective analog are good.

So, Acacia should get credit for its discovery, even though it is far from perfect. I wish them well. You should too.

NOTES:

(1) What idiots might I be referring to? Buy a vowel.

(2) The idea of using some crap like Tylenol for post-op pain is doubly ridiculous since 1) it doesn't work, 2) the number of people who become addicted from a day's worth of morphine after surgery is vanishingly close to zero.

(3) ALL of the surgeries were self-inflicted from seriously stupid accidents, not gall bladder removal, appendicitis, etc. If I wrote the s### I've done to myself no one would believe it. Except for my friends and family. Which is why my brother gave me this awesome tee shirt. I wear it proudly.

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