Less costly drugs work for nausea, vomiting

With an estimated 1 in 3 patients having postoperative nausea and vomiting (PONV) at an annual cost of several hundred million dollars, preventing this common complication is a priority.

A new study by Christian Apfel, MD, and his colleagues provides the first comprehensive head-to-head comparison of common treatments for preventing PONV.

Their findings, published in the June 10 New England Journal of Medicine, show that drugs costing a dollar or two per dose, such as dexamethasone (Decadron) and droperidol (Inapsine), work just as well as ondansetron (Zofran) that costs $10 to $15 per dose.

Not only is the study 20 times larger than most previous ones, but also it is the first with an adequate design and size to compare all of the approaches to PONV and their combinations, Dr Apfel told OR Manager.

“We have shown for the first time that all of the strategies work independently—that is, any double combination or any triple combination is similarly effective. Therefore, all things being equal, the safest or least expensive drugs should be used first.”

More than 5,000 patients in 28 medical centers in 7 European countries were enrolled in the trial and randomly assigned to 1 of 64 possible combinations of 6 prophylactic interventions:

• 4 mg of ondansetron or no ondansetron
• 4 mg of dexamethasone or no dexamethasone
• 1.25 mg of droperidol or no droperidol
• propofol or a volatile anesthetic
• air or nitrous oxide (both with 30% oxygen) for ventilation
• remifentanil or fentanyl.

In the study, ondansetron, dexamethasone, and droperidol each reduced the risk of nausea and vomiting by about 25%. Combinations of 2 approaches were more effective than any single approach but not twice as much, notes Dr Apfel, who is professor of anesthesiology at the University of Louisville in Kentucky.

Propofol reduced the risk by 19%, and nitrogen/oxygen reduced it by 12%. The reduced risk of both (defined in the study as total intravenous anesthesia) was similar to that observed with each of the antiemetics.

“We found that not only are the drugs similarly effective despite the fact that one is cheaper than the other but that the relative risk reduction is constant for every drug,” notes Dr Apfel. “If a patient has a very high risk, he benefits a lot because we can reduce his absolute risk. If his risk is very low, it doesn’t make sense to give antiemetics because it can’t be very effective—patient-wise or cost-wise.”

Risk factors are key

For the first time, the study provides strong evidence on how to select optimal approaches depending on patients’ risks. Dr Apfel’s team developed a simplified risk score with 4 major risk factors validated in previous studies:

• female gender
• nonsmoking status
• history of nausea or vomiting after anesthesia
• use of opioids after surgery.

One risk factor translates to a 20% risk, and each additional factor increases the risk by 20%, Dr Apfel explained.

For low-risk patients, such as 10% or 20%, an antiemetic should not be given
because this would incur unnecessary costs and side effects. Patients with a moderate risk, such as 40%, would benefit from a single antiemetic, such as dexamethasone, which is low cost, effective, and has no known side effects. Patients at high risk, such as 60%, benefit from a double combination. For the few patients at very high risk, such as 80%, a triple combination should be considered. This could be a total IV anesthesia with propofol and oxygen plus dexamethasone plus a second antiemetic such as droperidol or ondansetron.

**Will the study impact droperidol use?**

Dr Apfel says he would use ondansetron first as a postoperative rescue treatment for PONV, because it has almost no sedating side effects. Ondansetron is expensive, however, and if it has already been given or the first dose doesn't work, repeating it won't help.

Droperidol is especially effective against opioid-induced nausea and vomiting and is low in cost. But many clinicians avoid it because of a Food and Drug Administration (FDA) warning. Originally, droperidol was used at high doses in psychiatric patients, but isolated reports of cardiac problems in perioperative patients led the FDA to put a “black box” warning on the drug’s packaging. With the much lower dose used by anesthesiologists, risks in otherwise healthy patients are negligible, Dr Apfel says. Also, in his study, droperidol was not associated with an increased risk of cardiac complications. He believes the new study may have an impact on use of droperidol, which many anesthesiologists believe has been unfairly labeled as unsafe.

—Judith M. Mathias, RN, MA

**References**
