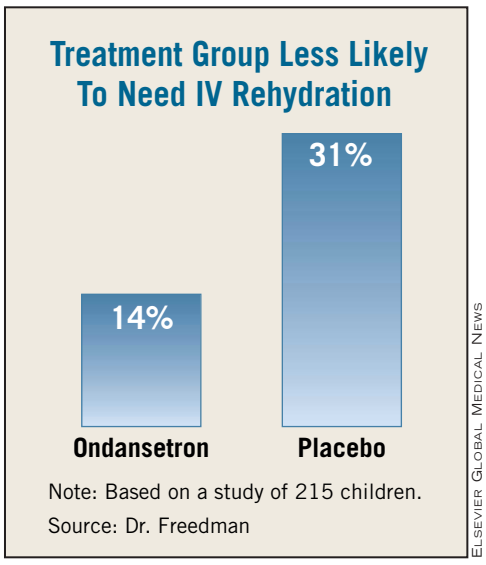
Ondansetron Cuts Vomiting, Need for IV in Gastroenteritis

BY SHERRY BOSCHERT
San Francisco Bureau

A single oral dose of the antiemetic ondansetron significantly reduced vomiting and mild to moderate dehydration in children treated in a pediatric emergency department for gastroenteritis, allowing more children to be rehydrated orally rather than intravenously, Dr. Stephen B. Freedman reported.

A prospective, double-blind study randomized 215 children aged 6 months through 10 years to receive a disintegrating tablet of oral ondansetron (Zofran) or placebo administered by a nurse while the physicians and research assistants were out of the room. Five seconds after placing the tablet on the patient's tongue, the nurse asked or helped the child to swallow. Children who vomited within 15 minutes received a second dose. Fifteen minutes later, clinicians started a 1-hour period of intense oral rehydration, and oral rehydration could be continued until the patient was sent home or admitted. After the first hour of oral rehydration, the treating physician could choose to give intravenous fluids.



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The investigators primarily assessed how many children vomited during oral rehydration therapy by conducting phone interviews with the families 3-7 days later and reviewing patients' records.

Among 107 children in the ondansetron group, 14% vomited while receiving oral rehydration therapy, compared with 35% of 107 children in the placebo group. One child in the ondansetron group was not included in the analysis because parental consent had not been obtained before randomization, said Dr. Freedman, of the University of Toronto, and his associates (N. Engl. J. Med. 2006;354:1698-705). Ondansetron also significantly reduced the mean number of episodes of vomiting, compared with placebo (0.18 vs. 0.65 episodes, respectively). Significantly fewer children in the ondansetron group received intravenous rehydration—14%, versus 31% in the placebo group.

Among the children who did not vomit during oral rehydration in either group, intravenous fluids were started in 5% given ondansetron and 17% given placebo, a significant difference.

Contrary to a study that looked at multiple doses, the single dose of ondansetron did not cause any significant adverse events, and the groups did not differ in the rate of return visits to the emergency department (19% with ondansetron and 22% with placebo). The ondansetron group did have more episodes of diarrhea during the oral rehydration than the placebo group—1.4 vs. 0.5 episodes—but this difference was not significant.

GlaxoSmithKline, which makes ondansetron, provided the tablets but had no other role in the study, and the investigators did not report any other potential conflicts of interest.

The ondansetron dosing was 2 mg for children weighing 8-15 kg, 4 mg for those weighing 16-30 kg, and 8 mg for heavier children.

At a cost of $35.75 per 4-mg tablet, the ondansetron in the study cost a total of $3,825 but saved the hospital $4,145 by avoiding insertion of intravenous catheters (at a cost of $124.74/child) and hospitalizations ($1,900/admission). ■

Blood Test Predicts Steatohepatitis in Patients Who Have Nonalcoholic Fatty Liver Disease

ATLANTA — A blood test can predict nonalcoholic steatohepatitis in patients with nonalcoholic fatty liver disease, according to results of a study presented at a meeting sponsored by the American Association for the Study of Liver Diseases.

Hepatocyte apoptosis is known to mediate liver injury in nonalcoholic fatty liver disease (NAFLD). The activation of caspases that mediate apoptosis can be measured in the plasma, thus allowing an indirect evaluation of liver damage.

Caspase activation was detected in the plasma using an enzyme-linked immunosorbent assay for cytokeratin-18 fragments, which are a byproduct of caspase activation. In the study, caspase activation was strongly associated with disease severity; a cutoff value of 395 U/L was 99.9% sensitive and 85.7% specific in predicting nonalcoholic steatohepatitis (NASH).

"A liver biopsy is the only reliable method to differentiate simple steatosis from NASH and stage disease severity," noted study author Dr. Anna Wieckowska of the Cleveland Clinic. However, biopsy has inherent risks and is not practical to perform multiple times. Her group thus evaluated a caspase activity blood test in 44 consecutive patients with suspected NAFLD. They measured caspase activity in plasma samples obtained at liver biopsy and then correlated the blood test results with histopathologic features. Five patients were excluded due to a hemolyzed blood sample, two were excluded because they had borderline NASH, and two had alternative diagnoses, which left 39 evaluable patients.

Caspase activation was significantly elevated in patients with definitive NASH, with median cytokeratin-18 levels of 767 U/L, compared with 202 U/L in patients with simple steatosis. After adjustment for confounding variables, including AST/ALT ratio and body mass index, cytokeratin-18 levels were independently predictive of NASH, with a positive predictive value of 99.9% and a negative predictive value of 85.7%.

Dr. Keith D. Lindor of the Mayo Clinic in Rochester, Minn., noted that "a noninvasive way to accurately predict mild degrees of fibrosis would allow us to select patients for treatment trials."

—Melinda Tanzola

Surgery Still Top Tx for Enterocutaneous Fistulas

BY JEFF EVANS
Senior Writer

LOUISVILLE, KY. — Treatment of enterocutaneous fistulas continues to rely primarily on surgery, augmented in some cases by octreotide or vacuum-assisted closure, according to a review of 106 patients.

The management of enterocutaneous fistulas continues to be a problem because of 5%-15% mortality, a spontaneous healing rate of less than 30%, and an overall healing rate hovering around 80%-90%, Dr. John M. Draus said at the annual meeting of the Central Surgical Association.

He and his colleagues in the surgery department at the University of Louisville, Ky., reviewed cases of gastrointestinal-cutaneous fistulas that occurred from 1997 to 2005 at two large teaching hospitals. The investigators excluded patients with inflammatory bowel disease and those with esophageal, pancreatic, or anorectal fistulas.

Among the 106 patients, fistulas most often resulted from a previous operation (81) and originated from the small bowel (67), colon (26), stomach (8), or duodenum (5). These operations were performed to treat cancer, adhesions, small bowel obstruction, gynecologic problems, or ventral hernias. Other fistula etiologies included trauma (15), hernia mesh erosion (6), diverticulitis (2), and radiation (2).

The group of patients comprised 31 with high-output fistulas (leaking more than 200 mL/day), 44 with low-output fistulas (less than 200 mL/day), and 31 whose fistula output was managed with a single gauze dressing. The analysis showed that the rate of healing or need for operation did not differ among patients with low- or high-output fistulas.

In general, the initial treatment plan for each of the patients consisted of the correction of fluid and electrolyte imbalances, nutritional support through total parenteral or enteral feeding, wound care, diagnostic imaging, early recognition of sepsis, drainage of abscesses, and an operation when necessary.

Among 13 patients who received treatment with vacuum-assisted closure (VAC), all had improved wound care and overall healing, but only 1 patient had complete healing that was attributed to VAC. The other 12 required an operation. No septic complications occurred with the use of VAC and fistula output did not increase, Dr. Draus noted.

VAC should be used in the subset of patients whose wounds are free of active infection, have no exposed bowel, and have a healthy layer of surrounding soft tissue, he advised.

The application of fibrin glue resulted in only one completely healed fistula among eight patients, all of whom had small bowel fistulas with high output. The glue transiently healed one patient's fistula for 11 days.

Of 24 patients who received treatment with octreotide, 8 responded with at least a 50% decrease in fistula output within 3 days; 4 of these 8 patients healed without an operation.

"Octreotide responders appear more likely to heal their fistula without operation" than those who receive other nonoperative modalities, Dr. Draus said. He recommended that most patients with an enterocutaneous fistula be given at least a 3-day trial of octreotide. If there isn't a dramatic decrease in fistula output by the end of 3 days, there is probably not much benefit in continuing octreotide, he suggested. Most patients in the study began receiving 100 mcg of octreotide three times per day, but the dose was increased to 500 mcg three times per day in one patient.

Audience member Dr. Bruce A. Harms of the University of Wisconsin, Madison, found this recommendation to be "a little bit of a stretch" in light of the fact that there is no hard efficacy data to back up Dr. Draus' advice. Octreotide should fall into the category of an ancillary treatment, said Dr. Harms.

Of 77 patients who had a planned operation, 69 (90%) healed. The average time from fistula formation to operation was 12 weeks. Some audience members said that 12 weeks was too short of an interval to wait to repair the fistulas, but Dr. Draus noted that the operation occurred after 3-6 months in about half of the patients.

"It is frustrating that in 2006 we still have made so little progress in treating fistulas with nothing but an operation," said audience member Dr. Merril Dayton of the State University of New York at Buffalo.

Fistulas healed in 82% of patients regardless of which treatment was used. Seven of the patients in the study died as a result of continued sepsis or persistent cancer. ■