

Recommendations for Nonanesthesiologist Administration of Propofol for Endoscopy

The American Association for the Study of Liver Diseases, the American College of Gastroenterology, the American Gastroenterological Association Institute, and the American Society for Gastrointestinal Endoscopy recently issued a joint statement providing an evidence-based assessment of propofol-mediated sedation by properly trained gastroenterologists and other nonanesthesiologists. The guidelines, which were published in the December issues of *Hepatology*, the *American Journal of Gastroenterology*, *Gastroenterology*, and *Gastrointestinal Endoscopy*, included the following findings, among others:

- The safety profile of nonanesthesiologist-administered propofol (NAAP) is equivalent to that of standard sedation in terms of the risks of hypoxemia, hypotension, and bradycardia for upper endoscopy and colonoscopy. When administered during endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS), the safety profile of NAAP appears to be equivalent to that of standard sedation, even though the worldwide experience with NAAP during these two procedures is insufficient for forming definitive conclusions.
- The time for sedation induction and recovery time are both shorter with NAAP than with standard sedation for upper endoscopy, colonoscopy, ERCP, and EUS. Patient satisfaction with NAAP is the same as or slightly superior to that of standard sedation.
- NAAP is more cost-effective than standard sedation for ERCP and EUS. Sedation with NAAP, as compared to sedation with commonly used agents, improves practice efficiency. For healthy, low-risk patients undergoing routine endoscopy, anesthesiologist-administered sedation is more expensive and has no proven benefits in terms of patient safety or procedural efficacy.

Liver Transplantation Outcomes for Nonalcoholic Steatohepatitis Cirrhosis Versus Alcoholic Cirrhosis

Researchers at the University of Miami School of Medicine in Miami, Florida conducted a retrospective chart review to compare liver transplantation (LT) outcomes for nonalcoholic steatohepatitis (NASH) cirrhosis and

alcoholic cirrhosis (ETOH) in patients who underwent LT for cryptogenic cirrhosis with the NASH phenotype or for ETOH at a single medical center from January 1997 to January 2007. Cryptogenic cirrhosis was defined as the absence of significant alcohol usage (>20 g/day), negative tests for viral hepatitis, negative autoimmune markers such as antinuclear antibody and antimitochondrial antibody, and negative markers for hemochromatosis, Wilson disease and alpha-1 antitrypsin deficiency. The ETOH arm included patients who had a history of significant alcohol usage, had no biochemical, serologic, or histologic evidence of other known causes of cirrhosis, and underwent liver transplantation during the stated time period. (Patients with hepatocellular carcinoma and alcoholic cirrhosis with the NASH phenotype were excluded from this arm.)

According to the results of this study, which were published in the December issue of *Liver Transplantation*, despite a trend toward decreased survival in the NASH arm ($P=.1699$), there was no significant difference in survival between the arms. The leading cause of post-transplant death was sepsis in both arms, followed by cardiovascular causes in the NASH arm (26% vs 7% in the ETOH arm; $P=.21$) and malignancies in the ETOH arm (29% vs 0% in the NASH arm; $P=.024$). Recurrent steatohepatitis (33% vs 0%; $P<.0001$) and acute rejection (41% vs 23%; $P<.023$) were significantly more frequent in the NASH arm than in the ETOH arm. No difference was found in graft failure between the arms (24% in the NASH arm vs 18% in the ETOH arm; $P=.3973$).

Endoscopic Ultrasound–Fine Needle Aspiration and Pancreatic Endocrine Tumors

According to the November issue of *Gastrointestinal Endoscopy*, researchers at the Institut Paoli-Calmettes in Marseilles, France conducted a single-center, retrospective, cohort study in a tertiary referral hospital to determine the value of EUS–fine needle aspiration (FNA) in the diagnosis of pancreatic endocrine tumors (PETs) and the classification of their malignant potential based upon World Health Organization (WHO) classification. The study population consisted of 86 consecutive patients (44 men, mean age 58 ± 14 years) who had been diagnosed with PETs and underwent EUS-FNA from January 1999 to August 2008.

Overall, PET was diagnosed via EUS-FNA in 90% (77 of 86) of the study patients. The sensitivity did not

differ with tumor size, type, location, or the presence of hormonal secretion. Out of the total population (86 patients), 30 (35%) underwent surgical resection. The kappa correlation index between the WHO classification from EUS-FNA and surgery was 0.38 ($P=.003$). In the group of patients diagnosed with endocrine tumor of uncertain behavior by EUS-FNA, there were discrepancies because 72% were found to have well-differentiated endocrine carcinoma. During the mean follow-up period of 34 ± 27 months, 16 patients (27%) died. Five-year survival rates were 100% for endocrine tumors, 68% for well-differentiated endocrine carcinomas, and 30% for poorly differentiated endocrine carcinomas ($P=.008$, log-rank test). Although the researchers noted that the study was limited by its retrospective design, selection bias, and small sample size, they pointed out that it was the largest single-center experience thus far showing the accuracy of EUS-FNA in diagnosing and determining the malignant behavior of PETs.

New Warnings for Coadministration of Clopidogrel and Omeprazole/Esomeprazole

Due to the emergence of new data, the US Food and Drug Administration recently recommended that patients avoid the coadministration of omeprazole and clopidogrel. Updated from a January 2009 Early Communication, these new recommendations are based on study results confirming that coadministration of omeprazole with clopidogrel decreases the levels of clopidogrel's active metabolite, which reduces clopidogrel's anticlotting effect. Omeprazole inhibits the drug-metabolizing enzyme CYP2C19, which is responsible for converting clopidogrel into its active metabolite. The new studies assessed the amount of clopidogrel's active metabolite in the blood and its effect on platelets in patients who took clopidogrel plus omeprazole versus patients who took only clopidogrel. A decrease of approximately 45% was found in the active metabolite levels of patients who took clopidogrel with omeprazole compared to patients who took only clopidogrel. Clopidogrel's effect on platelets was reduced by as much as 47% in patients taking clopidogrel and omeprazole in combination. The study noted that these reductions were seen whether the drugs were administered simultaneously or 12 hours apart.

As the level of inhibition among other proton pump inhibitors varies, it is unknown to what degree other proton pump inhibitors may interfere with clopidogrel. Esomeprazole, cimetidine, and other potent inhibitors of the CYP2C19 enzyme should be avoided in combination with clopidogrel. In contrast, drugs that do not inhibit CYP2C19 activity and are not thus expected to interfere

with the anticlotting activity of clopidogrel (such as ranitidine, famotidine, nizatidine, or antacids) do not have to be avoided in combination with clopidogrel at this time. The Food and Drug Administration will continue to investigate other drug interactions with clopidogrel.

Sequential Therapy Versus Triple Therapy for *Helicobacter pylori* Infection

In the December issue of the *American Journal of Gastroenterology*, researchers at several institutions in the United States and Italy published the results of a systematic review and meta-analysis evaluating the efficacy of sequential therapy (ST) in adults and children for *Helicobacter pylori* infection compared to triple therapy (TT). The researchers conducted an electronic search of the Cochrane Trial Register (until Issue 4, 2008), MEDLINE (1966 to 21 October 2008), and EMBASE (1980 to 21 October 2008), as well as abstracts from the major US, European, and Asian gastroenterology conferences.

The meta-analysis included 10 randomized controlled trials (RCTs), consisting of 3,006 adults and an odds ratio (OR) of 2.99 for eradicating *H. pylori* infection with ST (as compared to TT; 95% confidence interval [CI], 2.47–3.62). The number needed to treat (NNT) was 6 (95% CI, 5–7) and favored ST. The OR for eradicating ST compared to 10-day TT was 2.92 (95% CI, 1.95–4.38), and the NNT here was 8 (95% CI, 6–12) and favored ST. As for patients with clarithromycin resistance, the OR for ST was 10.21 (95% CI, 3.01–34.58) compared to TT, though the researchers noted that the sample size here was small. In terms of children and adolescents, there were 3 RCTs found, with a total of 260 subjects and an eradication OR of 1.98 (95% CI, 0.96–4.07). No difference was noted in the rate of side effects between ST and TT (OR, 1.01; 95% CI, 0.78–1.30). The researchers concluded that ST appeared to be more effective than TT for eradicating *H. pylori* infection and that ST was a promising therapy, though additional trials were needed before it could be recommended as a first-line treatment.

Cyclooxygenase Inhibitors and Gastrointestinal Recovery Following Surgery

As abdominal surgery can cause ileus that may be severe and inhibition of prostaglandin release has been found to decrease postoperative ileus in a rat model, researchers at Flinders Medical Centre in Bedford Park, Australia examined whether prostaglandin inhibition via cyclooxygenase inhibitors (celecoxib or diclofenac) could improve gastrointestinal recovery and decrease postoperative ileus in humans. According

to the November issue of *Alimentary Pharmacology & Therapeutics*, 210 patients undergoing elective major abdominal surgery were randomized to twice-daily placebo (n=67), celecoxib (100 mg; n=74), or diclofenac (50 mg; n=69) prior to the operation and then for up to 7 days. The primary outcomes of the study consisted of hallmarks of gut recovery, whereas the secondary outcomes included paralytic ileus, pain, and complications.

The researchers found no clinically significant difference between the arms in terms of bowel function restoration. However, there was a significant decrease in paralytic ileus in the celecoxib arm (n=1; 1%) compared to diclofenac (n=7; 10%) and placebo (n=9; 13%). The arms reported similar pain scores, analgesia, transfusion requirements, and adverse event rates. The researchers concluded that perioperative low-dose celecoxib (but not diclofenac) decreased the development of paralytic ileus after major abdominal surgery, though it did not speed early bowel function recovery. This finding was independent of narcotic usage and was not associated with an increase in postoperative complications.

In Brief

According to a randomized multicenter trial of patients with chronic hepatitis C genotype 1/4, extending therapy with peginterferon alfa-2a/ribavirin to 72 weeks decreases the probability of relapse in patients with an early virologic response. If they can be maintained on extended duration therapy, sustained virologic response rates may also improve. *Gastroenterology*. 2009 Nov 9. [Epub ahead of print]

In a retrospective study of two tertiary referral university hospitals, EUS and EUS-FNA were found to be feasible and safe and to have a significant impact on the management of pediatric gastrointestinal, pancreatobiliary, and mediastinal diseases. *Gastrointest Endosc*. 2009;70:892-898.

Using a nationwide database of 541 adults with nonalcoholic fatty liver disease, researchers found that the FIB4 index was superior to 7 other noninvasive markers of fibrosis. However, they noted that the index's performance characteristics highlighted the need for even better noninvasive markers. *Clin Gastroenterol Hepatol*. 2009;7:1104-1112.