Alosetron and Complications

Outcomes of colonic ischemia, hospitalized complications of constipation and bowel surgery in 3,631 Lotronix users (Alosetron), and 2,480 comparison irritable bowel subjects were evaluated using diagnoses, procedures and drugs recorded in the United Health Care insurance Claims database and were validated by chart review. The initial assessment was to last for 3 years, beginning with the start of Alosetron treatment, and was to include 10,000 Lotronix users. However, the observation period ended by 12/31/00, after suspension of marketing.

A total of 3,631 Alosetron users were reviewed and 2,480 comparison irritable bowel syndrome-only patients were evaluated with follow-up time of about 5 months in both groups. There were no instances of colonic ischemia in either cohort. Thirty incidences of bowel surgery occurred, giving a rate of 10.2 per 1,000 person/years in the Alosetron cohort and 11.8 per 1,000 person/years in the irritable bowel syndrome (no Alosetron) cohort. There were three cases of hospitalized complications of constipation. The incidence rates were essentially the same in Alosetron users and irritable bowel syndrome patients, with no Alosetron.

It was concluded that Alosetron users did not differ from irritable bowel patients not using Alosetron in the incidence of bowel surgery or hospitalized complications of constipation. There were no cases of colonic ischemia. The statistical upper limit of colonic ischemia rates in Alosetron users was 2.28 per 1,000 person/years. The statements about the safety of Alosetron were limited by the size of the cohort and the duration of follow-up. (Miller DF, Alfredson T, Cook SS, et al. “Incidence of Colonic Ischemia, Hospitalized Complications of Constipation and Bowel Surgery in Relation to the Use of Alosetron Hydrochloride.” *American Journal of Gastroenterology*, 2003; Vol. 58, pp. 1177-1122.)

MELD, Child-Pugh and Emory Model For Survival In TIPS

Baseline risk scores for 162 unselective, consecutive TIPS patients followed until death were calculated and respective concordance statistics for the predictive accuracy of 3, 12 and 36 month survival were compared statistically. All three models predicted short term survival with similar accuracy. The MELD model generated the best statistics for both 12 months and 36 months survival. The predicted survival of the Emory score was significantly lower, and in comparison with the Child-Pugh model, only a trend favoring MELD for the prediction of a one year survival in patients with intestinal bleeding could be observed.

It was concluded that the MELD model is superior to the Emory score, but only slightly superior to the Child-Pugh classification for prediction of long term survival in TIPS patients. (Schepke M, Roth F, Fimmers R, et al. “Comparison of MELD, Child-Pugh and Emory Model for the Prediction of Survival in Patients Undergoing Transjugular Intrahepatic Portosystemic Shunting.” *American Journal of Gastroenterology*, 2003; Vol. 98, pp. 1167-1174.)

Fatigue in Quiescent IBD

Eighty subjects with proven IBD were evaluated using the clinical activity index for ulcerative colitis and the Crohn’s disease activity index. Quality of life was measured by the inflammatory bowel disease questionnaire and fatigue was assessed using the multidimensional fatigue inventory (MFI).

Routine biochemical and hematologic tests were performed and basal cortisol was determined. A low dose adrenal corticotropin hormone test was utilized to evaluate adrenal cortical reserve. Healthy age and sex-matched subject served as controls.

More than 40 percent of the IBD patients in remission suffered from fatigue. Multidimensional fatigue inventory scores of the IBD patients were comparable to those reported in cancer patients. The inflammatory bowel disease questionnaire showed a negative correlation with that MFI. No correlation was found between fatigue and basal cortisol levels or other laboratory parameters.

It was concluded that fatigue is an important feature in IBD in remission, adversely affecting the quality of life. It does not, however, affect all patients, but it doesn’t seem to be the result of hypocortisolism. (Minderhoud IM, Oldenburg B, Van Dam PS, Henegouwen GPV. “High Prevalence of Fatigue in Quiescent Inflam-
matory Bowel Disease is Not Related to Adrenal Insufficiency.” *American Journal of Gastroenterology*, 2003; Vol.98, pp.1088–1090.)

**Esophageal Motility in Iron Deficiency Anemia**

The oropharyngeal esophageal transit and esophageal motility of 12 patients, 11 of whom were women age 31 to 50 years of age with iron deficiency anemia and 17 normal volunteers, 16 of whom were women age 26 to 52 years, were studied. The esophageal motility was evaluated manometrically with continuous perfusion and ten swallows of 2 mm bolus of water, alternating with 10 swallows of 7 mm bolus. Oropharyngeal and esophageal transits were studied by scintography. Motility and transit were studied in the supine position. The amplitude, duration and area under the curve of contractions were lower in patients than in volunteers. There was no difference in peristaltic contraction velocity, lower esophageal sphincter pressure and lower esophageal sphincter relaxation duration. There was no difference in oropharyngeal transit.

In the esophagus, the transit was slower in patients than in volunteers. The time needed by the scintigraphic activity to reach a peak in the proximal esophagus was longer in patients than in volunteers.

It was concluded that iron deficiency may decrease esophageal contractions and impair esophageal transit. (Miranda ALM, Dantas RO. “Esophageal Contractions in Oropharyngeal and Esophageal Transits in Patients with Iron Deficiency Anemia.” *American Journal of Gastroenterology*, 2003; Vol. 98, pp. 1000–1004.)

**GERD in Asthmatics**

A total of 62 patients post gastroesophageal reflux disease and asthma entered a randomized study of reflux treatment for at least 2 years. Twenty-four controls utilizing antacids as needed and 22 medical patients treated with Ranitidine 150 mg t.i.d. and 16 surgical patients treated with Nissen fundoplication were studied. Overall clinical status, asthma symptom scores and pulmonary medication requirements were recorded monthly. Peak expiratory flow rates were reported up to 7 times per day for one week of each month through the years. Pulmonary function, esophageal manometry and endoscopy with biopsy were repeated yearly. Sixty-two patients were followed for 19.1 years. In the surgical group, but not in the medical or control groups, there was an immediate and sustained reduction in acute nocturnal exacerbation with wheezing, coughing and dyspnea. By the end of two years, improvement, marked improvement or cure in overall asthma status occurred in 74.9 percent of the surgical group, 9.1 percent of the medical group and 4.2 percent of the control group, whereas the overall status worsened in 47.8 percent of the control group, 36.4 percent of the medical group and 12.5 percent of the surgical group.

The mean asthma symptom scores of the surgical group improved 43 percent, compared to less than 10 percent in the medical and control groups. As determined by changes in peak expiratory flow rate, there was no statistical significance in pulmonary function during the two year period and regular scheduled follow-ups. There was no difference in medication requirements among the groups. Therefore, there was no difference between the groups in overall survival.

It was concluded in patients with both gastroesophageal reflux disease and asthma, anti-reflux surgery, but not medical therapy with Ranitidine, has minimal effect on pulmonary function, pulmonary medication requirements or survival, but significantly improved asthma symptoms and overall clinical status. (Sontag SJ, O’Connell S, Khandwal S, et al. “Asthmatics with Gastroesophageal Reflux: Long-Term Result of a Randomized Trial with Medical and Surgical Anti-reflux Therapies.” *American Journal of Gastroenterology*, 2003; Vol. 98, pp. 987–999.)

Murray H. Cohen, D.O., editor of “From the Literature” is a member of the Editorial Board of *Practical Gastroenterology.*
Nobody Does It Better—Lansoprazole and Esomeprazole Equal for Treating GERD Symptoms

Results from a large-scale, prospective, double-blind clinical trial in which 3,034 patients with symptomatic GERD were treated with either of two leading proton pump inhibitors show that lansoprazole and esomeprazole are equally effective for relieving heartburn and related symptoms. The study examined heartburn relief over a period of two weeks at 360 study sites nationwide. Patients were at least 18 years of age, and had a history of at least two episodes of heartburn per week before being randomized to receive one of the two therapies.

On the first day of treatment, approximately 45% of patients receiving either lansoprazole 30 mg or esomeprazole 40 mg were free of heartburn. Heartburn severity progressively decreased during the course of the study in both treatment groups, as did the average number of days and nights on which heartburn was reported in patient symptom diaries.

No statistically significant differences in the incidence or severity of heartburn were seen when the two PPIs were compared, whether on the first day, on days 1–3, during the first week, or over a period of two weeks, after adjusting for differences in baseline heartburn severity. Through day 14 of the study, patients were free from heartburn an average 64% of recorded days with lansoprazole and 62% with esomeprazole (p = NS.) The severity of heartburn decreased over the first three days in both treatment groups, from a range of 0.81–0.86 on day 1 to 0.69–0.78 on days 1–3.

According to William Chey, MD, of the University of Michigan Health System and lead author of the study, heartburn relief on the first few days of treatment is a significant clinical parameter. "For patients, it’s very important that they experience some degree of relief as soon as possible. I myself experience heartburn on a regular basis. It’s an absolutely miserable experience. When I’m experiencing symptoms, I don’t want to have to wait four or five days for relief. I want to experience relief as quickly as possible. There’s also the issue of patient compliance—if patients don’t experience any relief, they may be less inclined to continue taking their medication."

Most recent studies of PPIs have examined the ability of these medications to heal erosive esophagitis. “From a purely practical viewpoint, fewer than half of all patients with heartburn-related symptoms have erosive esophagitis. Studies that focus solely on erosive disease are important, but they don’t accurately reflect the patient population that primary care physicians see on a daily basis,” says Dr. Chey. Previous studies have suggested that roughly 40% of GERD patients may have erosive esophagitis. However, the majority of patients with regular heartburn symptoms who consult their physicians do not receive endoscopies.

“It’s interesting that the response rates for symptomatic GERD for both drugs in this study are lower than the healing rates reported in erosive esophagitis studies,” notes Dr. Chey. “This has to do with the difference between treating erosive and nonerosive GERD.” Paradoxically, treating purely symptomatic GERD appears to be more difficult than healing erosive esophagitis, generally considered to be the more severe condition.

The investigators specifically evaluated the incidence and severity of heartburn at night, as well as during the day. "Nocturnal heartburn is actually very common," says Dr. Chey, "and it really does have a significant impact on quality of life. In addition to GERD symptoms, individuals with nocturnal heartburn suffer all the consequences of disturbed sleep, including daytime drowsiness, fatigue, difficulty concentrating, and impaired work performance." According to a Gallup Survey commissioned by the American Gastroenterological Association in 2000, approximately 79% of U.S. adults who report having heartburn at least once a week experience heartburn during sleeping hours. Recent studies have reported that people with nighttime heartburn experience significantly greater impairment in quality of life compared with those who have heartburn only during waking hours, and may be at greater risk for developing GERD-related complications.

In the current study, both lansoprazole and esomeprazole groups experienced comparable decreases in the incidence and severity of nighttime heartburn over the two-week study period.

“Most important result,” says Dr. Chey, “is that in patients with symptomatic GERD, both lansoprazole and esomeprazole provide clinically significant relief of heartburn and related symptoms, including regurgitation, dysphagia, and epigastric pain.”
Both medications were well tolerated, with fewer than 10% of patients in each treatment group experiencing any adverse event. The only notable difference was that significantly more patients treated with esomeprazole reported treatment-emergent dry mouth (0.5% vs 0.1%, p = 0.021) and vomiting (0.5% vs 0.1%, p = 0.038) compared with the lansoprazole group.

“When we asked whether they would recommend their study medication to other heartburn sufferers, 86% of patients receiving either lansoprazole or esomeprazole said they would,” noted Dr. Chey. “Overall, patient treatment compliance was high, with approximately 92% of patients taking more than 90% of their study medication. That speaks well of both these medications as treatments for symptomatic GERD.”

Reference

TAP Pharmaceutical Products Inc. Makes Landmark Gift to AGA’s Foundation for Digestive Health and Nutrition

$1.5 Endowment Provides for Young GIs to Pursue Academic Career In Gastroenterology

TAP Pharmaceutical Products Inc. (TAP) has contributed $1.5 million to the AGA’s Foundation for Digestive Health and Nutrition (FDHN) to establish an endowed Acid-Related Gastrointestinal Diseases Research Scholar Award.

TAP is also providing an additional $150,000 to initiate funding in 2003 of the Acid-Related Gastrointestinal Diseases Research Scholar Award. This additional money will sustain the award while the remainder of the TAP Endowed Fund is invested to generate future income.

“An endowed Research Scholar Award is a distinguished gift to AGA’s Foundation for Digestive Health and Nutrition and an ongoing contribution to research and society,” says James W. Freston, MD, FDHN president. “We appreciate TAP’s ongoing commitment to research and advances in acid-related research. The award will address a critical problem in gastroenterology—the lack of money for research and the resulting shortage of young investigators entering the field. The problem is one that impacts industry, academia and ultimately the patients we serve. Income from the TAP Endowment Fund will be indispensable in sustaining vibrant, imaginative and productive scientific work by encouraging young investigators to pursue academic careers in gastroenterology. TAP is to be applauded for its willingness to share in the responsibility of ensuring the perpetuation of strong science through the encouragement of young physician investigators.”

Research Scholar Awards were established to enable young physicians to develop independent and productive research careers in digestive diseases by ensuring that a major portion of their time is protected for research. The AGA Gastroenterology Research Committee, in accordance with FDHN policies and practices governing Research Scholar Awards, selects recipients of the TAP Research Scholar Award. Members of the AGA Gastroenterology Research Committee review grant applications and select awardees based on novelty, feasibility and significance of the applicant’s proposal; attributes of the candidate, including potential for independent research careers; evidence of institutional commitment; and the nature of the laboratory environment.