Selected Summary

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1. A Randomized Trial Comparing Omeprazole, Ranitidine, Cisapride, or Placebo in *Helicobacter pylori* Negative, Primary Care Patients with Dyspepsia: The CADET-HN Study (Am J Gastroenterol July 2005; 100: 1477)

Background: The management of *Helicobacter pylori* negative patients with dyspepsia in primary care has not been studied in placebo-controlled studies.

Methods: *H. pylori* negative patients with dyspepsia symptoms of at least moderate severity (□ 4 on a seven-point Likert scale) were recruited from 35 centers. Patients were randomized to a 4-wk treatment of omeprazole 20 mg od, ranitidine 150 mg bid, cisapride 20 mg bid, or placebo, followed by on-demand therapy for an additional 5 months. Treatment success was defined as no or minimal symptoms (score □ 2 out of 7), and was assessed after 4 wk and at 6 months.

Results: Five hundred and twelve patients were randomized and included in the intention-to-treat (ITT) analysis. At 4 wk, success rates (95% CI) were: omeprazole 51% (69/135; 43-60%), ranitidine 36% (50/139, 28-44%), cisapride 31% (32/105, 22-39%), and placebo 23% (31/133, 16-31%). Omeprazole was significantly better than all other treatments ($p < 0.05$). The proportion of patients who were responders at 4 wk and at 6 months was significantly greater for those receiving omeprazole 31% (42/135, 23-39%) compared with cisapride 13% (14/105, 7-20%), and placebo 14% (18/133, 8-20%) ($p = 0.001$), but not ranitidine 21% (29/139, 14-27%) ($p = 0.053$). The mean number of on-demand study tablets consumed and rescue antacid used was comparable across groups. Economic analysis showed a trade-off between superior efficacy and increased cost between omeprazole and ranitidine.

Conclusion: Treatment with omeprazole provides superior symptom relief compared to ranitidine, cisapride, and placebo in the treatment of *H. pylori* negative primary care dyspepsia patients.

Comment :

This study was done by Sander J.O. and colleaques from Division of Gastroenterology, Dalhousie University, Halifax, Nova Scotia, Canada. They focused on *H. pylori* negative primary care dyspepsia patients whom were randomized to a 4-wk treatment of omeprazole 20 mg od, ranitidine 150 mg bid, cisapride 20 mg bid, or placebo, followed by on-demand therapy for an additional 5 months. It was a multicenter, double-blind, placebo-controlled, parallel design study with equal numbers of allocation to treatment (1:1:1:1). From the 705 enrolled patients, there were 512 were randomized to one of the four treatment groups. In 90 patients (13.8%), serology was false negative as the UBT was positive and these patients were excluded. Due to the increased concerns of serious, cardiac side effects related to the use of cisapride, so the committee decided to stop enrollment in the cisapride arm in January 2000. All patients who were taking cisapride were informed about these potential side effects and were withdrawn from the study. Demographic baseline characteristics were well balanced in the ITT . Epigastric pain/discomfort was most frequently ranked (40%) as the most bothersome symptom followed by heartburn (25%) and bloating (13%) with the average duration of symptom was 8 years. The results was interesting and need to be discussed to improved for further study in some aspects as follows:

1. The use of a proton-pump inhibitor provides superior symptom relief compared to ranitidine, cisapride, and placebo as the initial treatment for dyspepsia patients, but its efficacy achieved with 51% which was meant that the rest of 49% remained nonresponders. While the success rate of placebo group was 23%

2. The data showed the responder to omeprazole was those patients who rated epigastric pain/discomfort and heartburn/regurgitation as their major symptom. However, in the dysmotility subgroup, the number of patients was too small to analyze among the treat-

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ment- groups.

3. The definition of dyspepsia which used in multicenter study is essential and need to clarify for the definite criteria. In patients presenting with a complex symptom of upper GI, there were the higher tendency of misunderstanding of the definition of dyspepsia.

2. The Natural History of Nonalcoholic Fatty Liver Disease: A Population-Based Cohort Study (Gastroenterology July 2005; Volume 129: Number 1)

Background & Aims: The natural history of nonalcoholic fatty liver disease (NAFLD) in the community remains unknown. We sought to determine survival and liver-related morbidity among community-based NAFLD patients. Methods: Four hundred twenty patients diagnosed with NAFLD in Olmsted County, Minnesota, between 1980 and 2000 were identified using the resources of the Rochester Epidemiology Project. Medical records were reviewed to confirm diagnosis and determine outcomes up to 2003. Overall survival was compared with the general Minnesota population of the same age and sex.

Results: Mean (SD) age at diagnosis was 49 (15) years; 231 (49%) were male. Mean follow-up was 7.6 (4.0) years (range, 0.1-23.5) culminating in 3192 person-years follow-up. Overall, 53 of 420 (12.6%) patients died. Survival was lower than the expected survival for the general population (standardized mortality ratio, 1.34; 95% CI, 1.003-1.76; p = .03). Higher mortality was associated with age (hazard ratio per decade, 2.2; 95% CI, 1.7-2.7), impaired fasting glucose (hazard ratio, 2.6; 95% CI, 1.3-5.2), and cirrhosis (hazard ratio, 3.1, 95% CI, 1.2-7.8). Liver disease was the third leading cause of death (as compared with the thirteenth leading cause of death in the general Minnesota population), occurring in 7 (1.7%) subjects. Twenty-one (5%) patients were diagnosed with cirrhosis, and 13 (3.1%) developed liver-related complications, including 1 requiring transplantation and 2 developing hepatocellular carcinoma. Conclusions: Mortality among community-diagnosed NAFLD patients is higher than the general population and is associated with older age, impaired fasting glucose, and cirrhosis. Liver-related death is a leading cause of mortality, although the absolute risk is low.

Comment :

This study was done by Leon A. Adams. and colleaques which enrolled the patients residing in Olmsted County who had been diagnosed with NAFLD, fatty liver, hepatic steatosis, steatohepatitis, or cryptogenic cirrhosis over a 20-year period between January 1, 1980, and January 1, 2000. All medical records were reviewed in detail, and patients were included only if fatty infiltration of the liver was confirmed on imaging studies (ultrasound, computed tomography, or magnetic resonance imaging) or liver biopsy. The metabolic syndrome was defined using the criteria proposed by the National Cholesterol Education Program (ATP III), ie, at least 3 of the 5 following features: fasting glucose >110 mg/dL; blood pressure >130/>85 mm Hg; fasting triglyceride >150 mg/dL; high-density lipoprotein (HDL) cholesterol (<40 mg/dL for males, <50 mg/dL for females); and obesity (body mass index [BMI] >30 [kg/m2]). The remaining 435 patients of the initial 620 cases or 70 % was the number need to be considered for the power of statistical analysis .

The interesting results were noted and discussed as follows:

1. This study confirmed the increasing problem of fatty liver in the community. The adjusted incidence rate of NAFLD diagnosis increased significantly over the study period, from an average of 4.2/100,000/year during 1980-1985 to 38.0/100,000/year during 1995-1999 (p <.001).

2. This was the first study to describe the natural history of NAFLD in a large cohort of community-based patients and showed the survival among NAFLD patients which was significantly less than the expected survival of the general Minnesota population of similar age and sex, with a standardized mortality ratio (SMR) of 1.34 (95% CI: 1.003-1.76, p = 0.03). In a multivariable Cox regression model, only IFG/diabetes, cirrhosis, and age remained significantly associated with death

3. Cirrhosis was diagnosed in 21 (5%) patients, with 8 (2%) diagnosed at initial presentation and 13 diagnosed (3%) during follow-up and it also significantly associated with death so any treatment of NAFLD which can prevent progression to cirrhosis may also decrease the mortality rate in these group of patients.