Su1835

Serologically Determined Gastric Mucosal Condition Is a Predictive Factor for Bone Deterioration in Japanese Men

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Introduction: The ABC method involves assessment of gastric mucosal condition by using the combination of serum anti-*Helicobacter pylori* antibody (HP-Ab) positivity and the levels of serum pepsinogens (PGs), and has recently been used as screening for the group at high risk of gastric cancer in Japan. Gastric mucosal condition estimated by the ABC method may influence not only carcinogenesis of the stomach but also conditions of the whole body. In the present study, we thus attempted to assess whether the result of the ABC method is available as a biomarker for bone deterioration. **Methods:** We studied men in their 50s and 60s who were subjected to both the ABC method and ultrasonic bone densitometry. We excluded any participants who had diabetes mellitus, chronic kidney disease, a history of HP eradication or a history of gastrointestinal surgery. Participants who used steroid drugs, acid-suppressive drugs or drugs for the treatment of osteoporosis were also excluded. Blood samples were obtained and serum was separated to examine HP-Ab and PGs. AG was diagnosed on the basis of the serum pepsinogen I (PGI) and II (PGII) criteria: cases with a PGI level $\leq$ 70 ng/ml and PGI/PGII ratio $\leq$ 3.0 were defined as AG (+). The subjects were divided into the following 4 groups: Group A consists of HP-Ab (-) and AG (-) subjects; Group B consists of HP-Ab (+) and AG (-) subjects; Group C consists of HP-Ab (+) and AG (+) subjects; and Group D consists of HP-Ab (-) and AG (+) subjects. The characteristics of bone were measured using an ultrasonic bone densitometry system which can calculate such bone parameters as trabecular bone density (TBD), elastic modulus of trabecular bone (EMTb) and cortical thickness (CoTh). Logistic regression analysis was used to calculate age- and BMI-adjusted odds ratios (ORs) and their 95% confidence intervals (CIs). **Results:** The subjects were 230 males: 92 in their 50s and 138 in their 60s. HP infection significantly increased the risk of low TBD (OR = 1.83, 95% CI 1.04-3.21, P = 0.03). The presence of AG significantly increased the risk of low TBD (OR = 2.22, 95% CI 1.17-4.22, P = 0.01) and low EMTb (OR = 1.86, 95% CI 1.01-3.42, P = 0.04). Compared with Group A, Group C was a significant high-risk group for low TBD (OR = 2.65, 95% CI 1.27-5.55, P = 0.01). As the ABC classification advanced from A to D, the rates of subjects having low TBD (P = 0.003) and low EMTb (P = 0.006) significantly increased. When we regarded Group C and Group D as one group (Group C+D), Group C+D was a significant high-risk group for low TBD (OR = 2.37, 95% CI 1.19-4.69, P = 0.01) and low EMTb (OR = 1.93, 95% CI 1.01-3.69, P = 0.04) compared with Group A. **Conclusions:** Serological diagnosis of HP infection and consequent AG, which is utilized for assessment of the risk of gastric cancer, was suggested to be useful for the risk assessment of osteoporosis.

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Gastric Granulomas and *Helicobacter pylori*

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Aims: Clinical studies investigating the relationship between granulomatous gastritis and *Helicobacter pylori* (*H. pylori*) infection have yielded inconclusive results. The aim of this study was to evaluate the association between *H. pylori* infection and the presence of gastric granulomas. **Methods**: From a national pathology database, we extracted 877,924 patients who underwent esophagogastroduodenoscopy with gastric biopsy. In a case-control study, we evaluated the occurrence of *H. pylori* infection in patients with and without gastric granulomas. **Results:** *Helicobacter* infection was present in 83 of 659 (12.6%) patients with gastric granulomas, compared to 94,632 of 877,265 (10.8%) in the control group (OR = 1.19, 95% CI = 0.95-1.50, p = 0.1354). Of the patients with gastric granulomas, 144 had a readily identifiable cause, including 91 (13.8%) with Crohn's disease, 41 (6.2%) with multifocal gastrointestinal granulomas consistent with Crohn's or other systemic granulomatous disease, 9 (1.4%) with sarcoidosis, 2 (0.3%) with mycobacterial infection, and 1 (0.2%) with histoplasmosis. *Helicobacter* infection was present in 14 of the 144 (9.7%) patients with an explainable cause of granulomas (OR = 0.891, 95% CI = 0.51-1.55, p = 0.681). In contrast, in patients without an apparent etiology for granulomas, *Helicobacter* was present in 71 of 515 (13.8%) (OR = 1.32, 95% CI = 1.03-1.70, P = 0.0288) patients. **Conclusion**: Our data suggest that, in patients without a clear cause for granulomatous disease, there is a weak, but significant, association between *H. pylori* infection and gastric granulomas. Hence, in *H. pylori*-positive cases of so-called idiopathic granulomatous gastritis, repeat biopsy after appropriate antimicrobial therapy should be considered.

Su1837

The Promising Risk Marker for Gastric Cancer Developing After *Helicobacter pylori* Eradication

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Background: Aberrant DNA methylation of gastric mucosa is induced by *Helicobacter pylori* (*H. pylori*) infection, and plays a pivotal role for development of pre-malignant lesions. Although aberrant DNA methylation generally decreases after *H. pylori* eradication, the methylation level in the stomach with severe inflammation do not normalize to that in non-infected stomach, even after *H. pylori* eradication. Thus, aberrantly methylated genes might be useful markers, so-called "Point of No Return" markers, to identify high-risk individuals for gastric cancer developing after *H. pylori* eradication. From this point of view, we have previously identified and reported candidate markers (Nanjo et al. Gastric Cancer. 15:382-8, 2012). In the present study, we aimed to evaluate the proper marker in clinical follow-up after *H. pylori* eradication. **Method:** Fifty-eight gastric mucosae at lesser curvature of the middle body were obtained from 22 subjects with *H. pylori* infection before and 16 months after *H. pylori* eradication, and fourteen patients with gastric cancer developing after *H. pylori* eradication. *H. pylori* infection was analyzed by serum IgG test, urea breath test, and Giemsa staining for the diagnosis. Successful *H. pylori* eradication was confirmed by urea breath test. Methylation levels of *EMX1*, *NEFM*, and *NKX6-1*, which are risk markers previously reported among subjects after *H. pylori* eradication (Nanjo et al. Gastric Cancer), were measured in the biopsy specimens by quantified methylation-specific PCR. **Result:** Methylation levels of *EMX1* and *NEFM* after *H. pylori* eradication were significantly associated with the extend of endoscopic atrophy before *H. pylori* eradication (*P*=0.008 and 0.03, respectively, by Jonckheere-Terpstra trend test), which is known to be a risk marker for gastric cancer developing after *H. pylori* eradication (Take et al. J Gastroenterology, 2011). The methylation level of *EMX1* after *H. pylori* eradication was significantly associated with pathological atrophic score of updated Sydney system before *H. pylori* eradication ($P=7.2\times10^{-4}$ by Jonckheere-Terpstra trend test). And, the methylation level of *EMX1* of patients with gastric cancer developing after *H. pylori* eradication was significantly higher than that of subjects without (52.5% vs 27.0%, *P*=0.003 by t-test). The odds ratio between the two groups was 23.0 using 68.4% as a cut-off value, which is mean plus two standard deviations of the methylation level in *H. pylori*-eradicated mucosae without gastric cancer. **Conclusion:** Our small case-control study suggested that the methylation level of *EMX1* had strong power as a risk marker for gastric cancer developing after *H. pylori* eradication and is a promising risk marker for gastric cancer developing after *H. pylori* eradication. To confirm it, a large-scale prospective study is required.

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Differential Effect of Fiber Type and Fermentability on the Intestinal Immune Response of Pigs Fed High-Fiber Diets

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High-fiber diets are prescribed as therapies for patients because they reduce the incidence or severity of GI inflammatory diseases. Similarly, inclusion of corn dried distiller's grains with solubles (DDGS) in a commercial diet reduced ileitis in pigs. Diets rich in fiber and low in fermentable oligo-, di-, mono-saccharides and polyols (FODMAP) alter the gut microbiota, local immune response, and intestinal endocrine function. Most studies on the effect of fiber on intestinal immune response have used purified fiber sources that may not model the effect of complex diets. We analyzed the changes in the inflammatory response induced by complex fiber sources with different fermentability. Experimental procedures were approved by the University of Minnesota Institutional Animal Care and Use Committee. Wheat straw (WS), DDGS, and soybean hulls (SBH) were used as sources of dietary fiber. Fiber sources were added (23%, 55% and 30% respectively) to a basal diet consisting of corn and soybean meal to obtain 16.7 ± 0.1% neutral detergent fiber. *In vitro* dry matter fermentabilities of the fiber sources were 22.4%, 71.8% and 84.6% respectively. Barrows (83.4 ± 6.7 kg, n = 12 per dietary treatment) were fed an amount equivalent to 2.5% their body weight in two equal meals for 13 days. Pigs were fasted overnight and tissue samples were collected after euthanasia. Ileum RNA was extracted and analyzed for gene expression of inflammatory cytokines and receptors using a RT^2 Profiler PCR array (Qiagen, PASS-011ZA). Two genes were induced (IL23A and TNF10) and 39 genes were repressed when comparing pigs fed WS with those fed the DDGS diet. Feeding DDGS induced 53 genes and repressed IL5RA compared with SBH. Feeding WS induced 48 genes and repressed 5 genes (IL5RA, IL1RN, IL12B, CXCL9 and CSF2) when compared with the SBH diet. The greatest change observed was the induced expression of IL23A by feeding the WS diet, which was 413-fold higher than that of the SBH diet, and 12-fold higher than for the DDGS diet. Overall, feeding the DDGS diet accounted for higher expression levels of cytokines and receptors, particularly of IL17A, IL17F, IL-4, IL-9, CCL1, CCL17, CCR3, IL27 and IL5, most of which are associated to Th2 and T regulatory cells. In contrast, feeding the SBH diet resulted in induction of the Th1 response mediators IL2RB, LTB, TNFSF4, IL1A and INFG. The inflammatory profile of pigs fed the WS diet was closer to those fed DDGS than those fed SBH. Our observations suggest that highly fermentable fiber sources (SBH) induce Th1 related cytokines, while low fermentability fiber sources (WS) induce Th17 responses. When feeding a high-fiber diet, the biochemical characteristics of the fiber source may significantly affect the host intestinal immune response.

Su1839

Probiotic Administration Among Free-Living Older Adults: A Randomized Controlled Trial

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Background: Gastrointestinal problems are deliberating conditions, commonly affecting older adults. Despite this fact the distribution of gut problems among free-living older adults has not been investigated. Furthermore, therapeutic strategies directed towards age-associated gut problems do not yet exist. Here, we aim to 1) elucidate the distribution of gastrointestinal problems among a Swedish population of free-living older adults and 2) conduct a double blinded, randomized, placebo-controlled trial (RCT) to investigate if the probiotic strain *Lactobacillus (L) reuteri* has the potential to decrease symptoms of gastrointestinal problems. **Method:** 249 older adults (≥ 65 years, mean age: 72.5 yrs, IQR: 68-75) representing the general Swedish population were recruited through advertisements in the local newspaper. Exclusion criteria was set to any known gastrointestinal disease and inclusion criteria to 65 years or older. The questionnaire Gastrointestinal Symptoms Rating Scale (GSRS) was used to assess the distribution of gut problems. All subjects were enrolled in the phase III RCT. The subjects were randomized to a 12-week daily supplementation with *L reuteri*, or placebo. The primary outcome measure was set to changes of symptoms as judged by GSRS. Secondary outcome measures were set to any changes reported on the questionnaires Hospital Anxiety and Depression Scale, Perceived Stress Scale (PSS) and EQ-5D-5L. All questionnaires were completed before study start and at week 8 and 12. The study was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants, ethical approval dnr: 2012/309. **Results:** In total 74% of the subjects were found to suffer from gastrointestinal problems as judged by a score ≥ 2 on any of the domains measured by GSRS. Indigestion, constipation and diarrhoea were found to be the most common gut problems affecting older adults. No differences in mean values between the probiotic and placebo supplemented group was found. However, in a subpopulation of subjects (n=53) experiencing high stress levels at baseline (PSS score over >15) a trend of decreased perceived stress in the probiotic-supplemented subjects was revealed, as compared to the placebo group (p= 0.095). **Conclusion:** Gastrointestinal discomfort is a substantial problem among older adults and should thus not be neglected. The probiotic compound investigated here