Expression of Peroxisome Proliferator-Activator Receptor Gamma in Human Gallbladder Epithelium and Gallstones

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Backgrounds: ATP-binding cassette (ABC) transporter in bile canaliculi plays an important role in controlling the proportion of cholesterol content in bile. In vitro study with gallbladder (GB) epithelial cell, expression of PPARγ and expression of ABCA1 protein and mRNA were increased when treated with PPAR ligand. Induction of ABCA1 by PPARγ ligand was so prominent that excessive accumulation of cholesterol in GB epithelial cells may be prevented and stone formation may be reduced. This study aimed 1) to document the expression of PPARγ in human gallbladder by immunohistochemistry, 2) to compare the intensity of PPARγ staining and clinical factors according to gallstone composition. Methods: 60 patients with symptomatic gallstone who underwent cholecystectomy were prospectively enrolled. Paraffin-embedded GB samples were immunostained with PPARγ. The intensity of staining with PPARγ antibody in GB epithelium was graded on a scale of 0-3 by single observer. Patients with acute cholecystitis documented by clinically and radiographically were excluded. Physical analysis of gallstones was performed by Fourier transform infrared spectroscopy (FT-IR). Gallstones were classified as cholesterol and pigment stones based on the IR spectrum patterns. Between cholesterol and pigment stone groups, intensity of PPAR staining and clinical factors (age, sex, obesity, diabetes) were compared by chi-square test. Results: Male to female ratio was 25 to 35 and mean age was 54 years (23-85). 9 patients had diabetes. According to the 2 different criteria for obesity, abdominal circumference (>85 cm for female and >90 cm for male) and body mass index (>25), 25 and 29 patients were classified as having obesity, respectively. PPARγ immunostaining was positive in 45 patients; 16 in 25, 2 in 25. 34/45 patients (75%) and pigment (n=27) groups, there was no significant difference in PPAR immunostaining (27.33 vs. 18/27, p=0.178). In addition, there was no difference in diabetes, obesity and hypercholesterolemia according to the positivity for PPARγ immunostaining. Patients with age <50 and body mass index >25 were more frequent in cholesterol than pigment stone group (p<0.03), whereas diabetes, sex, abdominal circumference and hypercholesterolemia showed no significant difference. Conclusions: PPARγ was expressed in human GB epithelium. There was no significant difference in PPARγ expression in gallbladder epithelium according to the gallstone composition or obesity. Quantitative analysis of PPAR expression in gallbladder tissue may disclose its relationship with gallstone composition and obesity.

Frequency of the Genetic Polymorphism Xbal of ApolipoproteinA 1-100 (apo B-100) in Patients With Gallbladder Lithiasis of a Population Sinaloa, Mexico: Comparative Study

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In Mexico, the prevalance of gallbladder lithiasis is 14%. Are recorded an average of 100,000 cholecystectomies annually in Mexico. The objective of the study was to compare the frequency of genetic polymorphism Xbal Apo B-100 in patients with cholesterol gallstones and subjects without gallstones. The methodological design was observational, cross-sectional, comparative, and prospective. Studied patients hospitalized of the May 2008 to April 2009 in Culiacan, Sinaloa state located to the north of Mexico. The population studied were two groups. Group 1(n=101) patients with cholesterol gallstones by 18 to 80 years of age, cholesterol and presence of gallstones. In the biochemical study of gallstones should contain cholesterol>50%. Group 2(n=101) control subjects without gallstones demonstrated by the completion of two upper abdominal ultrasound, by two different radiologists. They were matched by age and gender. We measured the genotypic and allelic frequencies of Xbal genetic polymorphism of Apo B-100 using chain reaction (PCR) and restriction enzyme digestion (RFLP). Were measured and plasma cholesterol, HDL, LDL, triglycerides, total lipids and glucose, measured the body mass index. The statistical analysis used for comparison of means and frequencies was the Student's t-test and Chi-square tests. Results: Group 1(patients) with an average age of 51.69±11.29 years and group 2 (controls) with age of 51.7D±10.9 years, (p=0.904). The ratio woman/men was 6:1. The X-allele frequency in group 1 and group 2 was 40.6% and 33.7% respectively (p=0.070). The genotype frequency Xx-Xx between group 1 and group 2 was 50.5% and 49.5% for each group respectively. The genotype frequency Xx-Xx in group 1 and group 2 was 16.8% respectively. The X- allele frequency was in group 1 of 65.8% and group 2 of 58.8%.The X- allele frequency in group 1 was in 31.4% and group 2 of 41.6%. The hazard ratio was for the presence of the X-allele genotype (OR 1.6295%CI 0.9-2.9 8.3) in patients with cholesterol gallstones. For genotype Xx-Xx was (OR 0.49%95%CI 0.2-1.1) and for genotype xx was not significant (p>0.05). In BMI there were no differences between groups significance. We found in average levels of cholesterol, LDL, triglycerides, total lipids, and glucose were identical in group 1 and group 2 (p>0.05). The average blood glucose was significantly higher (p<0.05) in patients with gallstones than in controls. The frequency of obesity (BMI>30) and hypercholesterolemia according to the positivity for PPAR-γ was (27/33 vs. 18/27, p=0.178). In addition, there was no difference in diabetes, obesity and hypercholesterolemia according to the positivity for PPAR-γ immunostaining. Patients with age <50 and body mass index >25 were more frequent in cholesterol than pigment stone group (p<0.03), whereas diabetes, sex, abdominal circumference and hypercholesterolemia showed no significant difference. Conclusions: PPARγ was expressed in human GB epithelium. There was no significant difference in PPARγ expression in gallbladder epithelium according to the gallstone composition or obesity. Quantitative analysis of PPAR expression in gallbladder tissue may disclose its relationship with gallstone composition and obesity.

Profiling of Causative Organisms and Multiresistant Strains for Acute Cholangitis: An Analysis of Cultured Microorganisms in Recent 9 Years in Korea

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Background: The multidrug-resistant (MDR) strains such as extended spectrum beta-lactamase (ESBL) or carbapenemase producers, vancomycin resistant Enterococcus (VRE) and methicillin-resistant Staphylococcus aureus (MRSA) are increasing all over the world. Acute cholangitis may have a potential risk of the emergence of these MDR strains because of recurrent cholecystitis or maluring biliary devices. This study analyzed the microbiology of bile and blood, and the MDR strains identified in cases with acute cholangitis for recent 9 years in Korea. Methods: By retrospective review of the medical record, 282 cases with acute cholangitis that had isolated organisms in bile or blood from July 2000 to June 2009 (M: 147, L: 33 patients) were enrolled. The etiologies of the acute cholangitis were choledocholithiasis in 157 cases (57.8%), malignant strictures in 114/41 (31.3%) cases, and benign strictures in 93 (2.2%) cases. The profiles of the causative agents for acute cholangitis and the MDR strains were compared in 3 groups arranged by time. Results: The culture rates of bile and blood were 98.1% and 85.4%, respectively. Three most common bacterial species were E. coli (50%), Klebsiella (20%), Enterococcus (11%) in blood and E. coli (34%). Enterococcus (25%), Pseudomonas (24%) in bile. The bacteria isolated from bile and from blood were identical in 210/745 times. Enterococcus and Enterobacter species in bile increased in recent years. Multiple organisms were isolated in 37 cases (21%) and bile and blood, respectively. Multiple organisms of bile increased during recent years in cases with biliary stent and PTBD. MDR strains were 14 ESBL and 3 carbapenemase in bile and 22 ESBL, 7 Carbapenemase, one VRE, and one MRSA in bile. The rates of MDR strains were 9.7% in blood, and 16.7% in bile. In bile, if bile was frequent in cases with multiple organisms isolated. The MDR organisms did not associated with recurrence of cholangitis and with the lapse of time. Conclusions: While the profiles of causative agents for acute cholangitis in blood were similar in time-grouped, Enterobacter and Enterococcus from bile increased in recent years. The rates of MDR strains were higher in bile than from blood, which was not changed during these study periods. Multiple organisms of bile increased over time in biliary stent and PTBD cases, which was associated with ESBL emergence.

Short-Term Antibiotic Therapy for Acute Cholangitis After Successful Endoscopic Biliary Drainage

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Background: Biliary drainage and antibiotics are the most important elements of treatment for acute cholangitis. Although antibiotic therapy is usually given for 7 to 10 days, no studies addressing the optimal duration of antibiotic therapy are lacking. Therefore, we evaluated the efficacy and safety of short-term antibiotic therapy for acute cholangitis when antibiotic administration was discontinued immediately after biliary drainage was established and fever had subsided. (No UMIN0000017016). Methods: This prospective study includes patients with "moderate" or "severe" acute cholangitis, which is defined by "Tokyo Guidelines for the management of acute cholangitis and cholecystitis," and who received biliary drainage within 24 hrs after diagnosis. The planned number of subjects was 20. Initial antibiotic therapy employed Cefmetazole Sodium for moderate cases and Meropenem Hydrate for severe cases. When <37 degrees body temperature was maintained for 24 hrs, administration of antibiotics was stopped. The primary endpoint of the study was the recurrence rate of cholangitis 3 days after the withdrawal of antibiotic therapy. The secondary endpoints were: 1) presence of inflammation (C-reactive protein, CRP), 2) incidence of complications (liver abscess and sepsis, etc.) related to cholangitis, 3) readmission rate of antibiotics, and 4) medical costs. Results: Eighteen patients fulfilled the study criteria (MF: 12/6, age: 38-89 years). The causes of cholangitis were bile duct stones in 17, and bile duct cancer in 1. ASA scores were 1.3, II: 10, and III: 5. The severity grades were severe in 4 and moderate in 14 (including 6 sepse cases). Seven patients received ENBD and 11 patients received a plastic stent. The median duration of antibiotic therapy was 3 days (range: 2-7). No recurrence of cholangitis occurred, and there were no complications related to cholangitis. Conclusions: Short-term antibiotic therapy appears to be sufficient when adequate drainage is achieved and fever has abated.