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Clinical, biochemical and imaging-verified regression of hepatitis B-induced cirrhosis

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In a 65-year-old patient with ascites, jaundice and positive hepatitis B surface antigen (HBsAg), the histological diagnosis of cirrhosis with knodell total score 13 was made in 1995. The patient was followed up for 8 years. Spontaneous seroconversion of HBsAg appeared. Except for slight hyperbilirubinemia, all pathologic, clinical laboratory data remained normal from the second year of diagnosis till 8 years of follow-up. In the last follow up, the markers of liver fibrosis were all normal. The portal vein diameter was decreased and the esophageal varices disappeared. The imaging of liver by sonography and CT-scan did not reveal any abnormality.

Reliability of hepatitis C virus core antigen assay for detection of viremia in HCV genotypes 1, 2, 3, and 4 infected blood donors: a collaborative study between Japan, Egypt, and Uzbekistan.

J Med Virol. 2004 Jun;73(2):216-22.

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Nucleic acid amplification-based methods are used for confirmation of viremia in antibody to hepatitis C virus (anti-HCV)-positive patients. However, this technology is labor intensive, time consuming, requires complex laboratory conditions, and expensive. The aim of this study was to evaluate the sensitivity and specificity of the HCV core antigen (HCVcAg) assay as an alternative approach for confirmation of viremia in HCV-infected subjects with HCV genotype 1-4. Two hundred forty-six asymptomatic HCV RNA- positive donors were enrolled in this study, consisting of 122 blood donors from Egypt (116 with genotype 4, 4 with genotype 1, and 2 with 1 + 4 genotypes), 109 from Japan (85 with genotype 1, and 24 with genotype 2), and 15 from Uzbekistan (all with genotype 3). A total of 234 (95.1%) of 246 RNA-positive specimens were detected by the HCVcAg assay; the sensitivity of HCVcAg assay consisted 93.4, 100, 100, and 94.8% for genotypes 1, 2, 3, and 4, respectively in comparison with RT-PCR assay. The specificity of the assay was confirmed in the absence of the false-positive results among 53 anti-HCV-negative, but anti-Schistosoma mansoni (anti-Sm) positive donors from Egypt. A positive correlation between HCVcAg and HCV RNA concentration levels ($r = 0.671$, $P < 0.05$) was observed among specimens with HCV genotype 4. The mean HCVcAg level was significantly lower in specimens with genotype 4 (2,935 fmol/L)

comparing to genotypes 1, 2, and 3 (5,034, 4,962, and 4,740 fmol/L, respectively). No specific mutation was found in the core-encoding region of the studied specimens. In conclusion, HCVcAg is shown to be specific, sensitive, and informative qualitative index for HCV viremia in asymptomatic carriers.

Detection and genotyping of TT virus in healthy and subjects with HBV or HCV in different populations in the United Arab Emirates.

J Med Virol. 2004 Mar;72(3):502-8.

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TT virus (TTV) and TTV-like viruses (TTVLs) have been reported to be associated with non-A-E hepatitis. To determine the rate of infection and genotypic characteristics of TTV in the United Arab Emirates (UAE), a total of 449 serum samples representing different populations in the UAE and comprising healthy as well as patients positive for HBsAg and HCV were screened. National subjects (n = 200) and non-nationals residing in the UAE (n = 249) were tested by PCR. The results obtained showed that the rate of TTV infection in healthy nationals, and those with HBsAg or antibody to HCV were 34.9, 97.9, and 95.7, respectively, compared to 89.1% (115/129), 89.2% (66/74), and 84.8% (39/46), respectively, in non-nationals. Sequence analysis of the untranslated region (UTR) using 71 clones generated from the PCRproducts of eight serum samples from healthy individuals (four nationals and four non-nationals) showed that 83.1% of the TTV clones were classified into groups 1-4, whereas 16.9% into possibly new genotype(s). The analysis also revealed that healthy national subjects carried multiple viruses. Phylogenetic analysis of representative sequences revealed clustering of clones into at least five major groups. Also, when compared to reference genotypes (from GenBank), two of our clones belonged to two previously identified genotypes. Non-significant gender differences were seen in all ethnic groups studied ($P > 0.05$). In conclusion, the rate of TTV infection in the UAE nationals is significantly lower ($P < 0.05$) than that of the non-nationals and several genotypes were isolated with common multi-infections.

Cost-effectiveness of screening for hepatocellular carcinoma in patients with cirrhosis due to chronic hepatitis C

Alimentary Pharmacology & TherapeuticsVolume 19 Issue 11 Page 1159 - June 2004

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Background: Screening for hepatocellular carcinoma in cirrhotic patients using abdominal ultrasonography and alpha-foetoprotein levels is widely practiced.

Aim: To evaluate its cost-effectiveness using a Markov decision model.

Methods: Several screening strategies with abdominal ultrasonography or computerized tomography and serum alpha-foetoprotein at 6-12-month intervals in 40-year-old patients with chronic hepatitis C and compensated cirrhosis were simulated from a societal perspective, resulting in discounted costs per quality-adjusted life-year saved. Extensive sensitivity analysis was performed.

Results: For the least efficacious strategy, annual alpha-foetoprotein/ultrasonography, the incremental cost-effectiveness ratio (vs. no screening) was $23 043/quality-adjusted life-year. Biannual alpha-foetoprotein/annual ultrasonography, the most commonly used strategy in the United States, was more efficacious, with a cost-effectiveness ratio of $33 083/quality-adjusted life-year vs. annual alpha-foetoprotein/ultrasonography. The most efficacious strategy, biannual alpha-foetoprotein/ultrasonography, resulted in a cost-effectiveness ratio of $73 789/quality-adjusted life-year vs. biannual alpha-foetoprotein/annual ultrasonography. Biannual alpha-foetoprotein/annual computerized tomography screening resulted in a cost-effectiveness ratio of $51 750/quality-adjusted life-year vs. biannual alpha-foetoprotein/annual ultrasonography screening.

Conclusions: Screening for hepatocellular carcinoma is as cost-effective as other accepted screening protocols. Of the strategies evaluated, biannual alpha-foetoprotein/annual ultrasonography gives the most quality-adjusted life-year gain while still maintaining a cost-effectiveness ratio <$50 000/quality-adjusted life-year. Biannual alpha-foetoprotein/annual computerized tomography screening may be cost-effective.

Lack of Evidence of Sexual Transmission of Hepatitis C among Monogamous Couples: Results of a 10-Year Prospective Follow-Up Study

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The risk of sexual transmission of hepatitis C virus (HCV) infection was evaluated among 895 monogamous heterosexual partners of HCV chronically infected individuals in a long-term prospective study, which provided a follow-up period of 8,060 person-years. Seven hundred and seventy-six (86.7%) spouses were followed for 10 yr, corresponding to 7,760 person-years of observation. One hundred and nineteen (13.3%) spouses (69 whose infected partners cleared the virus following treatment and 50 who ended their relationship or were lost at follow-up) contributed an additional 300 person-years. All couples denied practicing anal intercourse or sex during menstruation, as well as condom use. The average weekly rate of sexual intercourse was 1.8. Three HCV infections were observed during follow-up corresponding to an incidence rate of 0.37 per 1,000 person-years. However, the infecting HCV genotype in one spouse (2a) was different from that of the partner (1b), clearly excluding sexual transmission. The remaining two couples had concordant genotypes, but sequence analysis of the NS5b region of the HCV genome, coupled with phylogenetic analysis showed that the corresponding partners carried different viral isolates, again excluding the possibility of intraspousal transmission of HCV. Our data indicate that the risk of sexual transmission of HCV within heterosexual monogamous couples is extremely low or even null. No general recommendations for condom use seem required for individuals in monogamous partnerships with HCV-infected partners.

Sudden Hearing Loss in Patients with Chronic Hepatitis C Treated with Pegylated Interferon/Ribavirin

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BACKGROUND: Sudden hearing loss has been reported on standard interferon (IFN)-a2 therapy. This is the first report on the occurrence of sudden hearing loss in six cases of chronic hepatitis C in temporal relation to treatment with pegylated (PEG)-IFN alfa2a or b/ribavirin combination therapy. Three patients were treated in an ongoing randomized placebo–controlled trial comparing the addition of 200 mg amantadine or placebo to the combination of 180 mg PEG-IFN a2a (PEGASYS®, Roche, Basel, CH)/wk and 1–1.2 g ribavirin/d (COPEGUS®, Roche, Nutley, USA) in de novo patients infected with HCV genotype 1. Sudden hearing loss and tinnitus developed on day 1 and after 4, 23, 25, 36, and 40 wk of treatment, respectively.

CONCLUSIONS: Sudden hearing loss may occur in about 1% of patients on PEG-IFN/ribavirin combination therapy. This rate was not different to that observed in an untreated population. Possible mechanisms involved include direct ototoxicity of IFN, autoimmunity, and hematological changes. In contrast to published cases on auditory disability due to standard IFN, hearing loss did not fully resolve after discontinuation of therapy with PEG-IFN. On the other hand, symptoms did not worsen on continued treatment. Therefore, the decision whether to continue or to stop the treatment when signs of ototoxicity appear is based on the clinical judgment of the treating physician.

Mycophenolate mofetil for the treatment of autoimmune hepatitis in patients refractory to standard therapy

The Canadian Journal of Gastroenterology May 2004, Volume 18, Number 5 : 321-326

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There are limited therapeutic options available for patients with autoimmune hepatitis in whom conventional treatment fails. A case series of five patients unresponsive to or unable to take azathioprine, 6-mercaptopurine or corticosteroids who were treated with mycophenolate mofetil (MMF) is reported. While on MMF, alanine aminotransferase normalized or remained normal in all patients. MMF had a steroid-sparing effect and histological remission was demonstrated in one patient after seven months of MMF. One patient experienced an uncomplicated episode of pyelonephritis. In conclusion, MMF can effectively induce and maintain remission in refractory autoimmune hepatitis patients.

Serum beta2-microglobulin levels in hepatitis B e antigen-negative chronic hepatitis B patients under long term lamivudine monotherapy: Relationship with virological breakthrough

The Canadian Journal of Gastroenterology May 2004, Volume 18, Number 5 : 307-313

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OBJECTIVES: To evaluate the predictive value of serum beta2-microglobulin (b2m) levels for virological breakthrough in hepatitis B e antigen-negative chronic hepatitis B patients under long term lamivudine monotherapy.

METHODS: Serum b2m levels were calculated at baseline and every three months during lamivudine monotherapy in 25 patients with chronic hepatitis B, using microparticle enzyme immunoassay technology to investigate their association with biochemical, virological and histological outcome data. Cox proportional hazard models were used to investigate the association between serum b2m levels and virological breakthrough.

RESULTS: Seven of 25 (28%), nine of 25 (36%) and 14 of 25 (56%) chronic hepatitis B patients exhibited virological breakthrough at months 12, 24 and 36 of treatment, respectively. All chronic hepatitis B patients who did not show virological breakthrough in the follow-up period exhibited b2m elevation in month 3 of treatment. The duration (in months) of serum b2m elevation was significantly higher in the responders group than the nonresponders group (7.3±2.6 versus 3.8±3.4, P=0.02). In contrast to patients whose serum b2m levels were increased at three months, patients whose b2m levels were decreased had a 4.6 times higher risk of experiencing virological breakthrough (hazards ratio 4.6, 95% CI 1.22 to 17.36). When age, pretreatment serum alanine aminotransferase and hepatitis B virus DNA levels, and grade of liver disease were simultaneously included in the same Cox model, decreased b2m status was still associated with increased risk of virological breakthrough (hazards ratio 12.2, 95% CI 1.28 to 116.8).

CONCLUSIONS: In hepatitis B e antigen-negative chronic hepatitis B patients under long term lamivudine monotherapy, serum b2m levels at three months of treatment, compared with baseline levels, are good predictors of risk for virological breakthrough.

Non-alcoholic fatty liver disease: a multicentre clinical study by the Italian Association for the Study of the Liver

Digestive and Liver Disease 36 (2004) 398–405

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Aim: To define the characteristics of the Italian patient presenting non-alcoholic fatty liver disease. Patients and methods. A total of 305 patients with abnormally high plasma aminotransferase and/or gamma-glutamyl-transpeptidase levels for at least 12 months, with no known cause of chronic liver damage, were consecutively enrolled in the study. Clinical, routine biochemical and liver histology investigations were carried out in all patients. Also evaluated were: (a) oral glucose load; (b) insulinaemia and insulin-resistance using theHOMAtest model; and (c) plasma endotoxaemia, total antioxidant plasma capability, tumour necrosis factor-alpha, plasma interleukin-6 and -10 levels. Malondialdehyde and 4-hydroxynonenal content were determined on liver samples from 120 patients.

Results: The majority of patients were young overweight or obese males, with dyslipidaemia (20–60%), diabetes (10.5%), hyperinsulinaemia (40%), hyperferritinaemia (35%). Endotoxaemia was negative in all patients and cytokines were only sporadically altered. Total antioxidant plasma capability was decreased in 38.4% of the patients. Eighty percent of the cases had histological steatosis with a mild degree of inflammation and fibrosis. Seven patients had cirrhosis. Lipid peroxidation markers were increased in 90% of the cases, inversely correlated with fibrosis. Even if at univariate analysis, age, ferritin and tissue 4-hydroxynonenal were independent factors of steatosis ($P < 0.01$), and insulin, HOMA and ferritin of inflammation and fibrosis ($P < 0.01$), at multivariate analysis no single factor was found to be an independent predictor of hepatic lesions.

Conclusions: The typical Italian patient with non-alcoholic fatty liver disease is a young male, obese, not diabetic, with a variable incidence of dyslipidaemia and hyperinsulinaemia. Only liver biopsy may define the type of liver damage.

Tamoxifen induced hepatotoxicity in breast cancer patients with pre-existing liver steatosis: the role of glucose intolerance.

European Journal of Gastroenterology & Hepatology. 16(6):593-598, June 2004.

Elefsiniotis, Ioannis S a; Pantazis, Konstantinos D a; Ilias, Anastasios b; Pallis, Loukas c; Mariolis, Anargiros a; Glynou, Irene d; Kada, Helen d; Moulakakis, Antonios a

Objective: Tamoxifen induced hepatotoxicity has not been investigated in breast cancer patients with pre-existing liver steatosis. The aim of our study was to investigate the most common predisposing factors for non-alcoholic fatty liver disease in breast cancer patients with liver steatosis, treated with adjuvant tamoxifen therapy, in order to evaluate their role in the appearance of tamoxifen induced hepatotoxicity.

Methods: Clinical and laboratory evaluation, including an oral glucose tolerance test, was done in 60 women with breast cancer and liver steatosis before the beginning of adjuvant tamoxifen treatment and every 6 months during treatment. Tamoxifen induced hepatotoxicity was defined as abnormal liver function tests during tamoxifen treatment whereas these test results were below the normal range at baseline control. Statistical evaluation of data was performed using parametric methodology (the chi-squared test, and Student's t-test, $P < 0.05$).

Results: Twenty-six patients (43.3%) exhibited tamoxifen induced hepatotoxicity (group A) whereas 34 (56.7%) did not (group B). The mean overall follow-up period for the whole group was 37.5 months (SD 27.8, range 6-120 months) and did not differ between the two groups ($P = 0.055$). There was significant statistical difference in body mass index (BMI) and baseline fasting glucose, cholesterol and triglyceride levels between the two groups. Eighteen of 26 patients (69.2%) from group A had impaired glucose tolerance compared with only 8/34 patients (23.5%) from group B ($P < 0.001$), a finding observed even in BMI matched patients from the two groups (62.5% vs 12.5%, $P = 0.002$).

Conclusions: Tamoxifen induced hepatotoxicity is observed in a great proportion of breast cancer patients with pre-existing liver steatosis, especially those with higher BMI and higher glucose and lipid levels at baseline control. Glucose intolerance before the beginning of tamoxifen treatment seems to be a predictor of the hepatotoxicity, unrelated to baseline BMI.

Frequency and predictive factors for overlap syndrome between autoimmune hepatitis and primary cholestatic liver disease.

European Journal of Gastroenterology & Hepatology. 16(6):585-592, June 2004.

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Objectives: To evaluate the frequency of cholestatic pattern in patients with autoimmune hepatitis (AIH) and to identify predictive factors associated with the development of the overlap syndrome.

Methods: Eighty-two consecutive patients diagnosed with AIH at the referral centre between January 1998 and June 2002 were included in the study. The new scoring system modified by the International Autoimmune Hepatitis Group was used to classify patients as definite/probable. Overlap syndrome was considered when the patient had clinical, serological and histological characteristics of two conditions: AIH and primary biliary cirrhosis (PBC) or AIH and primary sclerosing cholangitis (PSC).

Results: From the 82 AIH patients (76 female and six male), 84.1% presented definite AIH (> 15 points) and 15.9% probable AIH (10-15 points). The frequency of the overlap syndrome was 20%: 13% with PBC and 7% with PSC. In the univariate analysis the overlap syndrome was associated with male gender ($P = 0.01$), age < 35 years ($P < 0.0001$), histopathological aspect of cholestasis ($P < 0.0001$), suboptimal response to treatment ($P < 0.0001$) and probable AIH ($P < 0.0001$). Age < 35 years, probable AIH and the absence of anti-nuclear antibody (ANA) have been identified as independent indicators of the overlap diagnosis by the logistic regression analysis.

Conclusion: Patients with overlap syndrome between AIH and primary cholestatic liver disease are frequently diagnosed in clinical practice, representing 20% of AIH cases in our study. The independent predictive factors associated with the diagnosis of overlap syndrome are young age, ANA(-) profile, and probable diagnosis according with the scoring system for AIH.

Diagnosis of spontaneous bacterial peritonitis in cirrhotic patients by use of two reagent strips.

European Journal of Gastroenterology & Hepatology. 16(6):579-583, June 2004.

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Objective: Spontaneous bacterial peritonitis (SBP) is one of the potentially life-threatening complications in ascitic cirrhotic patients with a mortality rate ranging between 30 and 50%. The improved survival might be explained by a more rapid diagnosis and treatment. The aim of our study was to assess the utility of two reagent strips, the Multistix test and the Combur2 test LN, for the rapid diagnosis of SBP.

Methods: Thirty-one unselected consecutive cirrhotic patients with ascites were included and a total of 100 paracenteses were performed. All ascitic fluid was analysed with the two reagent strips, leucocyte and polymorphonuclear (PMN) leucocyte cell count and blood-bottle culture if the strips were positive. The strips were considered positive if the colour turned to purple: i.e. grade 3 or 4 for the Multistix test and 2 or 3 for the Combur2 test LN on a colorimetric scale.

Results: We diagnosed nine infections of which four were SBP defined by PMN >= 250 cells/mm3 and a positive culture in ascitic fluid and five were culture negative neutrocytic ascites (PMN >= 250 cells/mm3 and a negative culture). The results of the two strips were concordant and were negative in only one SBP. The sensitivity, specificity, positive and negative predictive values of these two strips were 89%, 100%, 100% and 99%, respectively.

Conclusions: These reagent strips are very sensitive and specific for the diagnosis of SBP, allowing immediate commencement of empirical antibiotic therapy. These strips should be used for the diagnosis of SBP, especially on an emergency basis.

PROSPECTS FOR EXTRACORPOREAL LIVER SUPPORT

Gut 2004; 53:890–898

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This present review is timely with the increasing use of the molecular adsorbents recirculating system (MARS) for the management of liver failure, with over 3000 patients having been treated with this device worldwide. In the UK, MARS is being used for the treatment of individual patients both in the National Health Service and also in the private sector. In order to investigate the latest position with respect to bioartificial liver devices, a meeting was held at University College London Hospital in September 2003 and this article is based on the most up to date data presented there. Liver failure, whether of the acute variety with no pre-existing liver disease (acute liver failure (ALF)) or an acute episode of decompensation superimposed on a chronic liver disorder (acute on chronic liver failure (ACLF)), carries a high mortality. In patients with ALF, lack of detoxification, metabolic, and regulatory functions of the liver leads to life threatening complications, including kidney failure, encephalopathy, cerebral oedema, severe hypotension, and susceptibility to infections culminating in multiorgan failure.1 The only established therapy for such patients is liver transplantation (LTx) but currently one third of these patients die while waiting for a transplant and the organ shortage is increasing (fig 1).2 However, liver failure, whether of the acute or acute on chronic variety, is potentially reversible, and considerable work has been carried out over many years to develop effective liver support devices. The development of these devices has been approached in two very different ways. The biological devices, which aim to provide all of the functions of the normal liver,3 4 are based on the use of living liver cells with either human hepatic cells as in the extracorporeal liver assist device (ELAD) device5 or porcine hepatocytes as in the BAL device6 and in various other European devices being developed in the Netherlands7 and in Germany.8 The other approach is based on detoxification functions only using membranes and adsorbents which can remove the putative toxins associated with liver failure. Such entirely artificial devices are substantially less costly, by a factor of at least a tenth, than those based on living liver cell lines. The earliest of the artificial systems developed was based on perfusion of the patient's blood through the adsorbent charcoal.9 10 Although some of the toxins present in liver failure were shown to be adsorbed to the charcoal, other compounds tightly bound to proteins in the plasma were not removed.9 10 Another system known as a Biologic-DT is a combination of flat membrane dialysis against adsorbent solution11 but several studies have shown only limited efficacy in terms of removal of protein bound substances.3 12 MARS is the only available device able to remove free and albumin bound low and middle weight toxins with high selectivity due to use of a polysulfone membrane, and human serum albumin as a selective adsorbent in removal and transport of the toxins.13–15 In addition to the facility for removing protein bound substances, there is an additional dialysis component for removal of water soluble toxins. In this review, we will define the goals of artificial liver support, discuss the design of the existing liver support systems, and critically analyse the available data from clinical studies to establish their current status in the management of patients with liver failure.

A randomized controlled trial of consensus interferon with or without lactoferrin for chronic hepatitis C patients with genotype 1b and high viral load

Hepatology Research 29 (2004) 9–12

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Recently, lactoferrin has been reported to have anti-HCV effects. The aim of this study was to investigate the effect of combination therapy using consensus interferon (CIFN) and lactoferrin in patients with chronic hepatitis C. Twenty-one patients with chronic HCV infection, who were positive for HCV-RNA genotype 1b with serum viral loads from 100 to 700 KIU/ml, were randomly assigned to two groups; the CIFN+ Lac group received CIFN with lactoferrin and the CIFN group received CIFN alone. Nine patients in each group completed this trial; the other patients dropped

out because of side effects. Three, two and four patients were categorized as complete responders, relapsers and non-responders, respectively, in the CIFN + Lac group, and four, one and four in the CIFN group, respectively. There was no statistically significant difference in virologic response between the two groups. During the follow up after CIFN therapy with continued lactoferrin, there were two relapsers in the CIFN + Lac group and their HCV-RNA titers before treatment were over 400 KIU/ml. In conclusion, the combination therapy of CIFN and lactoferrin did not increase the response rate or prevent relapse after discontinuation of IFN.

The Prevalence of Hepatic Granulomas in Chronic Hepatitis C.

Journal of Clinical Gastroenterology. 38(5):449-452, May/June 2004.

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Objectives: Hepatic granulomas are not usual findings in chronic hepatitis C. A few studies addressing the frequency of hepatic granulomas in chronic hepatitis C reported it as less than 10%. The presence of it has been suggested to predict a favorable response to interferon treatment. Also, case reports described the development of hepatic granulomas after interferon treatment. In this study, we aimed to detect the prevalence of hepatic granulomas in chronic hepatitis C and to identify the causes other than chronic hepatitis C, if present, to search whether there is an association between the presence of granuloma and response to interferon treatment and also to see whether interferon leads to the formation of hepatic granulomas.

Methods: Patients from 3 university clinics were included. All patients with chronic hepatitis C were determined. All patients with hepatic granulomas were screened for the other causes of hepatic granuloma with tuberculin skin test, chest X-ray and computed tomography, Venereal Disease Research Laboratory, and Brucella agglutination tests. The histologic assessment of liver biopsies was done by the same pathologist in each center.

Results: A total of 725 liver biopsies of 605 patients with chronic hepatitis C were screened. In 8 patients, hepatic granulomas were detected in the initial liver biopsies. Four patients had repeat biopsies, and all had hepatic granulomas again. The prevalence of hepatic granulomas in patients with chronic hepatitis C was calculated as 1.3% (8 of 605) in reference to patient population. Presence or absence of hepatic granulomas was seemingly stable. All patients with hepatic granulomas had negative results of tuberculin skin test, Venereal Disease Research Laboratory, chest X-ray and computed tomography, and Brucella agglutination tests. All repeat biopsies were obtained after interferon (+/- ribavirin) in varying doses and duration. Four of 8 patients with hepatic granulomas were found to respond interferon therapy. No patient was found to develop hepatic granulomas after interferon therapy.

Conclusion: Hepatic granulomas are a rare finding in HCV infection. The presence of it does not seem to predict the response to interferon therapy. The development of hepatic granulomas during interferon therapy is not usual.

Occupational Risk for Hepatitis A: A Literature-based Analysis.

Journal of Clinical Gastroenterology. 38(5):440-448, May/June 2004.

Keeffe, Emmet B MD

Hepatitis A virus is the most frequently occurring vaccine-preventable disease. Although generally self-limiting, acute hepatitis A is associated with substantial morbidity and related economic burden. Hepatitis A virus is transmitted by the fecal-oral route, and children are a main source of infection. Some occupational workers are at risk for hepatitis A virus infection based on the potential for contact with infected fecal matter and, in many regions in the United States and other developed countries, low overall rates of natural immunity. These at-risk occupations include daycare providers, hospital workers who have direct patient contact (nurses, nurses' aides, laundry workers), and sewage workers. Additionally, food handlers, particularly in the hospital setting, should be vaccinated if seronegative for hepatitis A virus because of their ability to rapidly spread disease among vulnerable populations if infected.

Quantitation of hepatitis B lamivudine resistant mutants by real-time amplification refractory mutation system PCR

Journal of Hepatology, Vol. 40 (6) (2004) pp. 986-992

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Background/Aims: Lamivudine is an antiviral drug that is used to treat hepatitis B virus (HBV) infection. Long-term therapy does not completely suppress viral replication, and resistant mutants emerge. Resistance is mediated by changes in the tyrosine-methionine-apartate-aspartate (YMDD) motif in the catalytic site of the HBV polymerase gene. We describe a method to detect and quantify mutant viral populations using amplification refractory mutation system (ARMS) PCR.

Methods: We developed a real-time ARMS-PCR to detect point mutations in the polymerase gene. Using real-time PCR (LightCycler) with a ResonSense probe, PCRs were performed using clones of the HBV polymerase gene containing the different YMDD mutations. Dilution series of the templates were made and tested against each of the primer pairs. This method was applied to quantify mutant virus in patient serum samples.

Results: As little as 0.01% mutant DNA in 105-109 copies wild-type DNA were detected. The method is more sensitive than amplicon sequencing, which is the current method of mutant determination in the YMDD motif.

Conclusions: This study demonstrates a rapid, highly sensitive and reproducible method of quantifying mutant HBV virus in lamivudine treated patients. It can be used to monitor patients before and during lamivudine therapy.