

MIDDLE EAST COUNTRIES

Peginterferon Alfa-2b Plus Ribavirin for the Treatment of Chronic Hepatitis C Genotype 4

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BACKGROUND: The hepatitis C virus (HCV) genotype is an important predictive parameter for the success of pegylated interferon plus ribavirin therapy. To date, most published therapeutic trials have enrolled patients infected mainly with HCV genotypes 1, 2, and 3. Data regarding the responsiveness of genotype 4, the predominant type of HCV in the Middle East, are very limited.

OBJECTIVE: To assess the efficacy of peginterferon alfa-2b in combination with ribavirin for the treatment of chronic hepatitis caused by HCV genotype 4.

METHODS: Sixty-six treatment-naive patients infected with HCV genotype 4 were enrolled in this open label, prospective study. Cohort characteristics included the following: 48 M/18 F, mean age 45 ± 9 years, and mean weight 74 ± 8 kg. All patients had raised alanine aminotransferase (ALT) and were compensated. The mean pretreatment HCV-RNA level was 4.2×10^6 copies/ml (8.4×10^5 iu/ml) and median was 2.15×10^6 copies/ml. Twenty patients (29%) exhibited cirrhosis or severe fibrosis on pretreatment liver biopsy specimens. Participants were to receive peginterferon alfa-2b, 1.5 mcg/kg/wk plus ribavirin

1,000-1,200 mg/day for 48 wk. Patients were followed up for 24 wk after completing therapy. End of treatment viral response and sustained viral response (SVR) were defined as the absence of HCV-RNA from serum (<100 copies/ml) at 48 wk of treatment and at the end of follow-up, respectively. Data were analyzed on an intention-to-treat basis.

RESULTS: End of treatment and sustained virologic response were 77% and 68%, respectively. Among patients with pretreatment HCV-RNA 2×10^6 SVR was 55% compared with SVR of 86% among patients with HCV-RNA $< 2 \times 10^6$ ($p = 0.05$). Patients with cirrhosis or severe fibrosis had significantly lower SVR rate compared to those with mild or no fibrosis (29 vs 84%; $p < 0.0002$). Three patients (4%) discontinued therapy because of severe flu-like symptoms. Four patients developed hypothyroidism. Dose reduction of ribavirin and peginterferon alfa-2b was necessary in 15% and 6% of the patients, respectively.

CONCLUSION: Peginterferon alfa-2b in combination with ribavirin is effective in the treatment of HCV genotype 4. The treatment was well tolerated by most of the patients.

Effect of preventive applications on prevalence of hepatitis B virus and hepatitis C virus infections in West Turkey.

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OBJECTIVE: Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are community health problems in developing countries and the most common causative agents of chronic hepatitis, cirrhosis and hepatocellular carcinoma.

This study investigates the prevalence and the effect of preventive applications on prevalence of HBV and HCV infections in blood donors.

METHODS: Blood donors enrolled to the University and State Hospital Blood Banks in Aydin region of Turkey through the years 1993 to 2002 were retrospectively analyzed. Blood donors were investigated in 2 groups, Group I (1993-1997) and Group II (1998-2002) to compare the prevalence difference in 10-years period. Serum hepatitis B antigen (HbsAg) and anti-HCV were tested by commercially available enzyme-linked immunosorbent assay kits and anti-HCV positive results were confirmed by recombinant immune blot assays HCV test.

RESULTS: The prevalence of HBV and HCV infections was determined as 1.5% and 0.19% over the period 1993-2002. Although, the prevalence of HBV infection declined significantly in Group II (1.17%) in comparison with Group I (2.27%) ($p < 0.0001$), there was no significant difference in both groups regarding HCV infection ($p = 0.238$).

CONCLUSION: Preventive applications against blood transfusion related diseases succeed to decrease HBV infection significantly in West Turkey. Vaccination seems to be the most effective method to prevent hepatitis infection.

Chronic hepatitis C associated with Coombs-positive hemolytic anemia.

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Hepatitis C virus (HCV) is a recognized cause of significant extrahepatic disease. Induction of autoimmune hemolytic anemia (AIHA) has been reported, either during or after interferon (IFN) treatment of HCV infection. We herein report a 56-year-old patient with HCV infection who developed severe Coombs-positive AIHA in the absence of treatment with IFN. Prednisone therapy was initiated, but intravenous

immunoglobulins were added because of persistent hemolysis. Clinical course was complicated by rapid deterioration and the development of Creutzfeldt-Jakob disease. Having discarded other possible causes of AIHA, we suggest a possible association between AIHA and infection by HCV.

The current status of hepatitis B in Lebanon.

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The current status of hepatitis B infection in Lebanon is unknown due to the scarcity of published studies on the subject. This study was conducted to summarize the available information on hepatitis B in Lebanon since 1966, as well as to determine the current status of the problem, by analyzing the prevalence of positive hepatitis B surface antigen (HBsAg) reported from different laboratories of major hospitals covering the six districts of Lebanon in the year 2000. The overall HBsAg carrier rate among 61,271 tested individuals was 2.2%, being 13% among 30,809 blood donors, and 3.6% among 13,669 tested individuals in serology laboratories. There were marked geographical variations in the HBsAg

carrier rate being 0.8% in Mount Lebanon, 1.9% in each of Bekaa and Greater Beirut, 2.2% in North Lebanon, 2.4% in Nabatiyeh, reaching up to 4.7% in South Lebanon. These findings are comparable to the previously reported studies on pregnant women and children, thus confirming that Lebanon is moderately endemic for hepatitis B. Such information stresses the urgent need for efficient national public health surveillance campaigns, and mass vaccination programs. In addition, the universal screening of pregnant women for HBsAg, and the implementation of universal newborn vaccination against hepatitis B virus (HBV) should be the standard of medical care for the control and eradication of HBV in Lebanon.

TREATMENT RESPONSE IN HCV RELATED CHRONIC HEPATITIS

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OBJECTIVE: To evaluate the virological response to treatment with interferon and ribavirin in patients with hepatitis C related liver disease.

DESIGN: A descriptive study. Place and Duration of Study: January to September 2002 at Virology Department, Armed Forces Institute of Pathology Rawalpindi.

MATERIAL AND METHODS: Two hundred seventy-nine patients were included in the study. These patients had taken interferon and ribavirin treatment for HCV related chronic hepatitis, and were referred to AFIP for HCV RNA testing by polymerase chain reaction (PCR) between January 2002 and September 2002. Out of 279 cases, 229 had taken the treatment for 06 or 12 months and were tested for end-of-treatment response (ETR). Fifty patients had completed their treatment regimens of 6 or 12 months

treatment, at least 24 weeks before their PCR test and were having follow-up testing for sustained viral response (SVR). The sera of these patients were tested for HCV RNA by PCR, using a commercial kit of Amplicor (Roche) for qualitative detection of HCV RNA.

RESULTS: Out of 229 cases tested for end-of-treatment response, 198 (86.5%) had no detectable HCV RNA (responders) and 31 (13.5%) were PCR positive (non-responders). Thirty-eight out of 50 cases, tested for a sustained viral response, had a negative result for HCV PCR thus showing sustained response rate of 76%.

CONCLUSION: The viral remission/response to interferon and ribavirin combination therapy in our patients was better than that quoted in other regions.

Intra-household clustering of hepatitis C virus infection in Karachi, Pakistan

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Transmission rates of hepatitis C virus (HCV) infection through non-sexual household contacts have been considered to be very low. This study evaluated intra-household clustering of cases of HCV infection in a low socio-economic community in Karachi, Pakistan. Serum samples from 341 household contacts of 86 thalassaemic HCV-seropositive children were evaluated for antibodies to HCV using an ELISA. Spatial analysis of data was carried out to test for intra-household clustering. Seventy of 341 (20.5%) household contacts were HCV-seropositive. Of the households studied, 44.2% (38/86) had one or more contacts

who tested HCV-seropositive. Ecological analysis of variables at household level showed that in households where HCV-seropositive index thalassaemic children were male HCV tended to be transmitted to one or more familial contacts. Spatial analysis with an asymptotic score test of the null hypothesis of no extra within-family infectivity revealed that there was a significant tendency of HCV infection to cluster within a household (score statistic = 19.44). The results showed that non-sexual household exposure may play a role in efficient HCV spread to household contacts of HCV-infected persons and needs further evaluation.

Plasma copper and zinc levels in chronic viral hepatitis

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OBJECTIVE: The relationship between chronic hepatitis and trace metals has not been understood clearly. Copper (Cu) and zinc (Zn) are essential trace elements for several metabolic processes. Overload or deficiency of these elements can lead to metabolic disorders and some other diseases. In this study, we aimed to examine the relationship between chronic hepatitis and plasma Cu and Zn levels.

METHODS: Forty-three patients with chronic viral hepatitis (CVH) and 30 healthy controls were included in this study. The patients were consecutively admitted to the Department of Infectious Disease and Clinical Microbiology, Faculty of Medicine, Gaziantep University, Turkey, between January 2000 and November 2000. Plasma Cu and Zn levels and hepatic function test results of the patients and controls were compared.

Serologic and virologic markers and histopathologic assessments were performed for confirmation of CVH. Plasma Cu and Zn concentrations were determined with Bathocuproin, using deproteinization method and 5-Br-PAPS methods.

RESULTS: Patients plasma Cu level was 16.0 +/- 2.8 and plasma Zn level was 26.0 +/- 7.3. The corresponding

values were 12.2 +/- 5.4 and 26.6 +/- 5.6 in the healthy controls. The patients with CVH had a higher plasma Cu level than the controls ($p < 0.05$) while the Zn levels were similar in both groups ($p > 0.08$).

CONCLUSION: Although there is an increased plasma Cu level in CVH, its mechanism is unclear. However, this condition may have clinical importance as Cu is a hepatotoxic element.

Molecular epidemiology of hepatitis B, C and D viruses in Turkish patients

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Bozdayi AM, Aslan N, Bozdayi G, Turkyilmaz AR, Sengezer T, Wend U, Erkan O, Aydemir F, Zakirhodjaev S, Orucov S, Bozkaya H, Gerlich W, Karayalcin S, Yurdaydin C, Uzunalimoglu O

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Different genotypes of the hepatitis viruses may influence the clinical outcome of the disease. The distribution of genotypes may vary according to geographical regions. The aim of this study was to evaluate hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis D virus (HDV) genotypes in Turkish patients with chronic hepatitis in a large cohort of patients. Genotyping was performed in 41, 59 and 365 patients with chronic hepatitis B, D and C, respectively, and 36 hemodialysis patients with chronic hepatitis C. Genotypes were determined by direct sequencing in hepatitis B and by polymerase chain reaction-restriction fragment length polymorphism in hepatitis C and D patients. In addition, HBV subtyping by multiplex PCR and subtype specific ELISA were performed in 83 and 71 HBsAg (+) blood donors, respectively. All hepatitis B (100%) and hepatitis D (100%) patients had genotype D and type I,

respectively. HBsAg subtyping by two methods yielded that 99% of the patients were subtype ayw. S gene amino acid sequence in the 41 patients included for HBV genotyping revealed the ayw2 subtype. Genotype distribution of 365 patients with chronic C hepatitis were as follows: 306 (84%) patients genotype 1b, 43 (11%) patients genotype 1a, 10 (3%) patients genotype 2, 3 (1%) patients genotype 3, 3 (1%) patients genotype 4. Among 36 patients receiving hemodialysis, 28 (78%) patients had genotype 1b and 8 (22%) patients had genotype 1a. The study indicates that Turkish patients with chronic viral hepatitis show very little genotypic heterogeneity. Subtype ayw and the genotype D of HBV DNA, and the type I of HDV RNA represent almost 100% of related infections. The genotype 1b of HCV RNA was found to be significantly dominant in Turkish patients.