Hepatitis in The World

Hepatitis B virus: prevalence of precore/core promoter mutants in different clinical categories of Indian patients

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To determine the association of precore (Pre-C)/basal core promoter (BCP) mutants with clinical outcome of hepatitis B in Western India, 192 hepatitis B virus (HBV) infected individuals were investigated. HBV-DNA PCR positivity among asymptomatic hepatitis B surface antigen (HBsAg) positive carriers (61/100) was lower ($P < 0.0001$) than chronic hepatitis B (CHB), acute ($P = 0.0001$), and fulminant hepatitis B patients ($P = 0.047$). Pre-C status was based on restriction fragment length polymorphism (RFLP, n = 153) and sequencing (n = 118.(

Prevalence of Pre-C mutants was higher among carriers (23/61) than CHB (10/62, $P = 0.0071$) or acute (3/22; $P = 0.037$) patients. Children from carrier and CHB categories showed significantly higher circulation of Pre-C-wild than mutant HBV. Clinical manifestations were independent of BCP mutations (1762/64-T/A). Hepatitis B e antigen (HBeAg) negative CHB patients [62.5% (15/24)] were circulating wild HBV. Higher HBV-DNA levels were associated with chronic hepatitis and HBeAg positivity, whilst Pre-C mutant positives had lower levels. BCP mutations did not affect HBV-DNA levels. Multivariate regression analysis identified HBeAg (OR = 4.3) and Pre-C mutants (OR = 3.1) to be associated with chronic hepatitis and carriers respectively. In a separate sub-set analysis (n = 59), HBV-DNA level was identified as the only variable. In conclusion, chronic or fulminant hepatitis B was not associated with Pre-C or BCP mutants and switching over to Pre-C mutant was beneficial for the infected individual in maintaining disease free status for extended periods.

Change of acute hepatitis B transmission routes in Japan

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Background: Many years have passed since various prophylactic policies for preventing hepatitis B virus (HBV) transmission were begun. We studied the chronological alterations in HBV infectious routes in patients with acute hepatitis B in the past 27 years. Methods: Seventy two patients with acute HBV infection who were admitted to our hospital during the period 1976 to 2002 were enrolled in this study. This study was divided into two periods (first period, 1976–1990; and second period, 1991–2002), and the HBV infectious routes were studied. Results: Infectious routes have been changing. Posttransfusion hepatitis was seen only in the first period. In the second period, sexual transmission was the major infectious route (68%), followed by infection at a medical facility or occupational exposure such as needle stick injury (8%). Conclusions: Transmission from sexual contact has become the main infectious route of HBV in Japan.

A randomized trial to assess the efficacy of interferon-alpha daily in combination with ribavirin in the treatment of naïve patients with chronic hepatitis C

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A randomized trial was conducted to assess the efficacy of interferon-alpha (IFN) daily in combination with ribavirin in 301 naïve patients with chronic hepatitis C (CHC). Patients were randomized to receive ribavirin 1.2 g daily (QD) for 48 weeks with either IFN 5 MU (thrice weekly) TIW for 8 weeks followed by IFN 3 MU TIW for 40 weeks (IFN TIW, n = 154) or IFN 5 MU QD for 8 weeks followed by IFN 3 MU QD for 16 weeks followed by IFN 3 MU TIW for 24 weeks (IFN QD, n = 147). Treatment discontinuation rates, because of adverse events, were similar in the two arms (14.9% in IFN TIW and 14.3% in IFN QD, P = 0.87). The proportion of patients with sustained virological response (SVR) was 27.9% for patients treated TIW and 38.8% for those treated QD (P = 0.046). According to logistic regression analysis, patients in the IFN QD arm had 1.7 times higher probability of achieving SVR, than those receiving IFN TIW (P = 0.038). Low baseline viral load (P = 0.017) and genotype non-1 (P = 0.036) were associated with higher SVR rates. Combination of IFN/ribavirin for 48 weeks is more effective when IFN is administered daily for the first 24 weeks in naïve patients with CHC.

Systematic Review: Peginterferon vs. standard interferon in the treatment of chronic hepatitis C

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Background: Randomized controlled trials over the last decade have demonstrated incremental improvement in the treatment efficacy of chronic hepatitis C with combination interferon and ribavirin therapy when compared with interferon monotherapy.

Aim: To perform a systematic review of clinical trials directly comparing interferon formulations to test the hypothesis that a true difference in terms of efficacy exists between standard interferon (with and without ribavirin) and peginterferon (with and without ribavirin.(

Methods: A search of the on-line bibliographic databases MEDLINE and PUBMED was performed independently by two authors to identify all relevant articles. In addition, the reference sections of all relevant articles were manually searched to identify any missed articles. Quality was assessed using the Jadad scale, which is an accepted scale specific for randomized controlled trials. A priori, it was decided to include only articles with a Jadad score of three or higher in the final analysis. Data were abstracted on to pre-determined abstraction sheets. The inclusion of articles, the data abstracted and the methodological score differences were adjudicated by consensus with agreement of the authors performing the search.

Results: Seven citations of randomized controlled trials, comparing at least two different interferon formulations and evaluating the sustained virological response as a primary end-point, were identified. These relevant articles were abstracted, and five of the seven were found to have a Jadad score of three or higher and comprised the final set of citations reviewed. The studies consistently demonstrated that peginterferon monotherapy was superior to standard interferon, even in patients with advanced fibrosis. With regard to combination interferon therapy, only two high-quality articles compared peginterferon plus ribavirin with standard interferon plus ribavirin. Both studies demonstrated that the overall sustained virological response was statistically better with peginterferon plus ribavirin.

Conclusions: On the basis of this systematic review, peginterferon-based regimens are superior to standard interferon-based regimens for the treatment of chronic hepatitis C.

Hepatitis C Virus Structural Proteins Impair Dendritic Cell Maturation and Inhibit In Vivo Induction of Cellular Immune Responses

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Hepatitis C virus (HCV) chronic infection is characterized by low or undetectable cellular immune responses against HCV antigens. Some studies have suggested that HCV proteins manipulate the immune system by suppressing the specific antiviral T-cell immunity. We have previously reported that the expression of HCV core and E1 proteins (CE1) in dendritic cells (DC) impairs their ability to prime T cells in vitro. We show here that immunization of mice with immature DC transduced with an adenovirus encoding HCV core and E1 antigens (AdCE1) induced lower CD4+- and CD8+-T-cell responses than immunization with DC transduced with an adenovirus encoding NS3 (AdNS3). However, no differences in the strength of the immune response were detected when animals were immunized with mature DC subsequently transduced with AdCE1 or AdNS3. According to these findings, we observed that the expression of CE1 in DC inhibited the maturation caused by tumor necrosis factor alpha or CD40L but not that induced by lipopolysaccharide. Blockade of DC maturation by CE1 was manifested by a lower expression of maturation surface markers and was associated with a reduced ability of AdCE1-transduced DC to activate CD4+- and CD8+-T-cell responses in vivo. Our results suggest that HCV CE1 proteins modulate T-cell responses by decreasing the stimulatory ability of DC in vivo via inhibition of their physiological maturation pathways. These findings are relevant for the design of therapeutic vaccination strategies in HCV-infected patients.

Hepatocellular carcinoma

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The number of papers published in the topic of hepatocellular carcinoma (HCC) increased remarkably from last year. The prevalence of chronic hepatitis C infection has increased the incidence of HCC. However, studies confirm that obesity and nonalcoholic fatty liver disease are important factors for the development of HCC in the United States. Alpha-fetoprotein is the most widely used tumor marker, but has poor diagnostic accuracy and ethnic variability. Using proteonomic genome analysis, new candidate tumor markers have been identified but await validation. Dynamic gadolinium magnetic resonance imaging seems to be more sensitive than spiral computed tomography scan for the identification of HCC, and seems to be modality of choice in most centers. Transplantation offers the best long-term option for patients with HCC, but in a certain group of patients without portal hypertension and well-preserved liver function, surgical resection is an acceptable option. A large study from Europe confirms the utility of resection in some patients with early HCC. However, most patients are not candidates for curative intervention. A meta-analysis and a randomized, controlled trial showed that chemoembolization offers a survival advantage in selected patients (Child class A and B) with nonresectable HCC. Finally, chemoprevention in patients with chronic hepatitis C infection with interferon is a promising strategy to prevent HCC.