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Analysis of Sustained Virological Response to Pegylated Interferon & Ribavirin Treatment in Compensated Cirrhosis Due to Hepatitis C Virus, Genotype 3 Infection

Amna Subhan Butt
_Aga Khan University, amna.subhan@aku.edu_

Wasim Jafri
_Aga Khan University, wasim.jafri@aku.edu_

Khalid Mumtaz
_Aga Khan University, khalid.mumtaz@aku.edu_

Saeed Hamid
_Aga Khan University, saeed.hamid@aku.edu_

Shahab Abid
_Aga Khan University, shahab.abid@aku.edu_

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Authors
Amna Subhan Butt, Wasim Jafri, Khalid Mumtaz, Saeed Hamid, Shahab Abid, Syed H Shah, Nida Jafri, Javed Yakoob, and Zubair Ahmad

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Treatement of Hepatitis C Associated Severe Mixed Cryoglobulinemic Syndrome with Plasma Exchange Improves Tolerability and Response to Interferon-Based Therapy

Todd Frederick, Jamie Zagorski, Robert G. Goh, Jan C. Hoffmann

Introduction: Treatment of severe mixed cryoglobulinemic syndrome (MCS) associated with hepatitis C virus (HCV) is often difficult due to renal dysfunction, vasculitis, and neutropenia. We reviewed the medical records of 20 patients (pts) who were diagnosed with severe hepatitis C associated MCS and received interferon-based therapy and/or plasma exchange (PE). The mean age of pts was 54 years (46-63 years old) and 8 pts (40%) were male. 16 pts (80%) had HCV genotype 1a or 1b. 13 pts (65%) had elevated HCV RNA (>400,000 IU/ml) and 11 pts (55%) had cirrhosis or advanced fibrosis. Clinical Presentation: 17 pts (85%) presented with renal disease. 12 pts (60%) had chronic renal insufficiency, and 5 pts (25%) presented with acute renal failure requiring hemodialysis (HD): 10 pts (50%) had elevated 24-hour urine protein. 13 pts had neutrophilic reactive proteinemia. 13 pts (65%) presented with active vasculitic skin lesions. 7 pts (35%) had peripheral neuropathy. 1 pt had severe CNS and pulmonary vasculitis. Treatment: Of 20 pts who received PE treatment, 16 pts (80%) were candidates to start (or re-start) IFN/RBV therapy (intent to treat-ITT group). 11 of these pts successfully started Peg 2a-b IFN therapy, and 10 pts started RBV. 4 pts (20%) were not IFN/RBV candidates because of prior SVR or IFN/RBV failure. The mean number of inpatient PE treatments (ixx) was 8.6 (3-12 ixv). 8 pts (40%) received cyclophosphamide; 5 pts (25%) received rituximab (4-6 doses): 6 pts (30%) required chronic PE treatment (1-8x/month). Results: 18 pts (90%) experienced clinical improvement after initial course of intensive PE therapy. Of 13 pts with neutrophilic reactive proteinemia, 9 pts (69%) had significant decline in urinary protein. 3 of 5 pts (60%) on HD were able to stop dialysis. 12 pts (92%) demonstrated significant improvement in vasculitic skin lesions. 5 pts (71%) had slight improvement in peripheral neuropathy. 11 pts who received IFN/RBV post-PE (ITT success), 3 pts had SVR, 3 pts were NR, 4 pts have ongoing treatment (2 pts are HCV RNA neg, 2 are HCV RNA pos.), and 1 pt died but had EVR. The pts with SVR had marked improvement in MCS symptoms, whereas the NR pts all required chronic PE for refractory disease. Of 9 pts who did not receive IFN/RBV post-PE (ITT failure), 3 pts died (2 of complications of MCS) before starting IFN/RBV, 1 pt underwent transplantation, and 1 pt was not clinically stable for antiviral therapy. Conclusion: Treatment of hepatitis C associated severe mixed cryoglobulinemic syndrome with plasma exchange appears to improve tolerability and response to interferon-based therapy.

Feasibility of Interferon-Beta Induction By Twice-Daily Administration Prior to the Standard Combination Therapy Using Pegylated Interferon-Alfa-2b Plus Ribavirin

Toshiya Nakatani, Eri Satani, Shinya Takeyama, Sanar Murata, Shinshu Nagamatsu, Koji Hashimoto, Hideki Matsus, Eiryo Kokuichi

Aims: It has been reported that longer treatment with combination therapy using pegylated interferon (IFN)-alpha-2b plus ribavirin (RBV) for patients infected with hepatitis C virus (HCV) leads to more effective viral eradication. However, in Japan where treatment period is limited, the achievement of early viral clearance should be necessary. We already reported the effectiveness of IFN-beta induction prior to the standard 48-week combination therapy in achieving early viral response (EVR). In this study, we evaluated whether IFN-beta induction is also effective in achieving sustained viral response (SVR). Methods: Sixty-two patients chronically infected with genotype 1b HCV were divided into 2 groups. Forty-two patients underwent standard 48-week combination therapy using 1.5mcg/kg pegylated IFN-alpha-2b plus RBV (600-1000 mg/day depending on body weight) (group1). Twenty patients received 3MU IFN-beta twice-daily for 2 weeks, followed by the standard combination therapy (group2). Results: There were 46 (67.7%) patients with genotype 1b infection and 14 patients with genotype 1a infection. Factors predictive of SVR were age <35 years (p=0.01), treatment naïve status (p=0.04), EVR (p=<0.01). Five patients were unable to complete the treatment due to side effects or cytopenias not responding to erythropoietin and or G-CSF therapy. Conclusions: Long-term combination therapy using pegylated IFN-alpha-2b plus RBV is limited to 48 weeks. IFN-beta induction may be feasible in achieving SVR throughout successful achievement of EVR.

Treatment After Liver Biopsy in Patients with Hepatitis C Virus (HCV) and HIV Co-Infection

Karolita Gopal, Pauline Sawandhi, Arkady Broder, Henry C. Bodenheimer, Albert D. Min

Highly active antiretroviral therapy for HIV infection has decreased HIV-related mortality. However, due to an accelerated progression of liver fibrosis and decompensation in HCV/HIV co-infected patients, the incidence of liver-related mortality has risen significantly. The aim of our study was to evaluate the number of liver biopsies in HCV/HIV co-infected patients and the influence on treatment decision. Method: We reviewed charts of patients with HCV/HIV co-infection who had a liver biopsy from 1/1998 to 10/2007, who have been followed at our medical center. Results: Among the 238 patients with HCV/HIV co-infection seen during this study period, 152 (64%) had HCV infection. Patients were predominantly male (116/112, 77%), and mean age at biopsy was 47.8 years (range 31-66). Majority of the patients were infected with genotype 1 (123, 81%). History of intravenous drug use and heavy alcohol consumption were documented in 104 (68%) and 32 (21%) patients, respectively. Fifty-three (33%), 82 (54%) and 13 (9%) patients had stage 0, 1-2, and 3 fibrosis, respectively. Stage 4 was indeterminate in 3 (2%) patients. The number of liver biopsies and the rate of subsequent HCV treatment are shown in the figures 1 and 2. Fifty-seven of 152 (38%) patients were started on HCV treatment. Common reasons for not starting treatment after liver biopsy were patients lost to follow up in 26 (27%), minimal liver disease on biopsy in 21 (21%) and patients refused in 17 (18%). Conclusions: The number of co-infected patients evaluated for treatment with a liver biopsy has decreased over past few years possibly due to a low threshold to start treatment in the co-infected patient. Low post-biopsy treatment rates with 21% of patients showing favorable histology, suggests that liver biopsy remains a useful tool in directing management in selected HIV/HCV co-infected patients.

Analysis of Sustained Virological Response to Pegylated Interferon & Ribavirin Treatment in Compensated Cirrhosis Due to Hepatitis C Virus, Genotype 3 Infection


BACK GROUND: Chronic hepatitis C virus (HCV) infection in patients with cirrhosis is difficult to treat and data on the outcome of treatment for this patient group is limited. AIM: To study sustained virologic response (SVR) in predictive factors in patients with compensated cirrhosis due to hepatitis C, treated with pegylated interferon and ribavirin METHODS: Data of patients with compensated cirrhosis due to HCV genotype 3 with positive HCV RNA PCR was collected from our Gastroenterology clinic database during 2004 to 2010. Cirrhosis was diagnosed either by liver biopsy or on biochemical testing with ultrasound of abdomen. Primary end point of treatment was SVR. Treatment was terminated or modified in case of hepatic decompensation or if hemoglobin dropped to <7 g/100 ml, absolute neutrophil count (ANC) <1000 x10E 9, platelets <50,000x10E 9. We also evaluated the predictors of outcomes of SVR RESULTS: Out of 66 patients, 32 (48.5%) were male. Mean age was 46±10. 34/66 (51.5%) patients were non-naive. There were 61/92 (65%) patients who were diagnosed with severe hepatitis C associated MCS and received interferon-based therapy. Of these, 21% of patients showed favorable histology, suggests that liver biopsy remains a useful tool in directing management in selected HIV/HCV co-infected patients.