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EVALUATION OF TREATMENT RESPONSE IN PATIENTS OF CHRONIC HEPATITIS 'C' VIRUS WITH RIBAVARIN THERAPY AND CONVENTIONAL INTERFERON AND TO KNOW THEIR THERAPEUTIC EFFECTS ON SUSTAINED VIRAL RESPONSE

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Abstract:

Objective: *An economic perspective for patients who cannot pay and to obtain a permanent viral response (SVR) with conventional interferon therapy and ribavirin over a period of twenty-four weeks.*

Design: *An open label study.*

Venue and duration: *In the Gastroenterology Department, Jinnah Hospital, Lahore for one year duration from July 2016 to July 2017.*

Methods: *Certified cases of chronic hepatitis C were selected by HCV RNA (Roche amplifier Switzerland). Double ALT than (UNL) received conventional Interferon and Ribavirin from 800 to 1200 mg / kg body weight for 24 weeks.*

Results: *A total of 100 patients with confirmed and chronic hepatitis C were included in the study, 90 (56.25%) were male and 70 (43.75%) were female. After 12 weeks of response to treatment, early virologic response (EVR), ie HCV RNA was not detected in 135 patients (84.37%), and response to treatment (ETR) was observed at the end of the week. 24 patients (81.25%) were detected with HCV among 130 patients and detectable HCV-RNA 30 (18.75%). Five patients (2.64%) with early virologic response developed; PCR was positive at 24 weeks. Twenty-two patients developed relapse after discontinuing 6 months of treatment. Therefore, the continuous virological response (SVR) was 67.5%. The biochemical response between the responders in the normalization of ALT / AST was 145.63% in 145 patients. At the 24th week of treatment, the side effects of treatment were fever, myalgia, fatigue (100%), epigastric discomfort in 60 patients (37.5%), and diarrhea in 15 patients (9.37%). Severe anxiety and depression and insomnia and irritable behavior were observed in 50 patients (31.25%). The observed hematological abnormalities were Hb <10gm 37% (23.13%), white blood cell count <4000 105 (62.6%) and platelet count <100,000 28 (17.5%).*

Conclusion: *This study suggests that interferon alfa is highly effective in the combination of ribavirin and that SVR can be achieved in patients suffering from chronic hepatitis C virus.*

Key words: *Hepatitis C, interferon, ribavirin, SVR.*

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INTRODUCTION:

Hepatitis C is a chronic viral disease that can lead to a progressive inflammation of the liver and ultimately death in the presentation of a silent disorder. It has become a major problem in Pakistan, its prevalence is very high despite efforts to control viral infections. 130 million people worldwide are infected with hepatitis C virus, and in Pakistan, genotype 3 is common and the response to conventional INF is between 68% and 70%. First-line therapies are based on the combined therapies of interferon alfa and ribavirin, which suppress RNA virus (hepatitis C). With conventional interferon treatment, a permanent virological response can be achieved with 53%. Conventional interferon and ribavirin respond well and this combination is not expensive. Due to its profitability, some research institutions recommend conventional Interferon. In some areas of Pakistan, prevalence is up to 16%. Approximately 3-4 million new cases have been reported each year9. Liver cirrhosis may develop if 20% of chronic hepatitis C cases are not treated. Therefore, it is suggested that early treatment of hepatitis C may prevent complications such as cirrhosis and hepatic failure, and a small number of cirrhosis cases between 20 and 25 years may develop liver cancer. Therefore, eradication of the virus may result in clinical improvement and regression of fibrosis. Late relapses may be due to the presence of viruses in liver tissues and peripheral blood mononuclear cells (after reaching SVR). Only 20-55% of patients can eliminate HCV without interferon treatment.

MATERIALS AND METHODS:

This is an Open Label Study held in the Gastroenterology Department, Jinnah Hospital, Lahore for one year duration from July 2016 to July 2017.One hundred and thirty patients were included in the study and 90 men and 70 women aged 40-60 years were included in the study. All patients were informed about treatment events, side effects, and outcomes of treatment; written informed consent was obtained from all patients. We excluded patients with cardiac patients and patients with pregnant women, kidney failure, low Hb and low platelet count. HCV RNA was performed by Roche reverse transcriptase method. LFT was performed and double ALT (UNL) was accepted to begin treatment. Before initiating treatment, all investigations were performed on CBC LFT, serum albumin, urea, creatinine, FBS, lipid profile, prothrombin time (PT) base, aPTT, TSH, qualitative HCV RNA and genotyping. All abdominal ultrasonography was performed. Interferon alpha subcutaneous interferon alpha with Ribavirin, based on the body weight of the whole patient, began 3 million units three times a week. Initially for follow-up, patients were examined monthly with CBC and ALT in the first month followed by two weeks. The treatment was continued for 24 weeks. HCV-RNA treatment was performed at the end of the qualitative response to the qualitative end of HCV-RNA to evaluate the end of treatment response performed at the 12th week. Qualitative repetition of HCV-RNA was performed to see a continuous virological response.

RESULTS:

Chronic hepatitis C confirmed cases were included in this study. The male age group was 90 (56.25%) and 70 females (43.75%) between the ages of 40 and 60 years. The most common mode of administration of HCV was intravenous / drug use injections, intravenous 65 (40.63%), different surgical / dental procedures 29 (18.13%), blood transfusion, 30 (15.62%), transmission was used in 12.5% of patients with acute tinnitus. and 6.88% of the patients had family infection.

Table 1: Mode of transmission

Risk Factors	=n	%age
I/V Injections/ I/V drug abuse	65	40.63
H/o surgery / dental procedure	29	18.14
Blood Transfusion	25	15.62
Transmission through sharp	20	12.5
Unknown case	10	6..25
unknown cause	11	6.88

As shown in Table 1, however, in many of these patients, patients with multiple risk factors had received interferon

3million unit s / c three times a week and Ribavirin 800-1200 mg according to body weight for 24 weeks. Throughout the 24-week treatment, the treatment effects were fever, muscle pain, fatigue, headache, 100 (62.5%) and gastrointestinal effects, which were mainly observed in almost all patients.

Table 2: Adverse effects of treatment

Symptoms	=n	%age
Fever, fatigue and myalgia	160	100
Headache	100	100
Epigastric discomfort	60	37.5
Anorexia	46	28.75
Nausea	25	15
Diahhroea	15	9.37
Hb< 10gm%	37	23.13
Leucocyte Count < 4000	105	62.6
Platelet Count < 100,000	28	17.5
Hypothyroidism	3	1.87

As epigastric discomfort was observed in 60 (37.5%), anorexia 46 (28.75%), 15 patients (9.37%) nausea 24 (15%) and diarrhea. Severe anxiety and depression and insomnia and irritable behavior were observed in 50 patients (31.25%). The observed hematological abnormalities were Hb <10gm 37% (23.13%), white blood cell count <4000 105 (62.6%) and platelet count <100,000 28 (17.5%). Three patients developed hypothyroidism. All these anomalies are shown in Table 2. Response to treatment observed after 12 weeks, early virologic response (EVR) HCV-RNA 135 was not detected (84.37%), at the end of treatment (ETR) response was recorded at 24th week among 130 patients (81.25). %) and those not responding with detectable HCV-RNA 30 (18.75%). Five patients (2.64%) with early virologic response showed a great improvement, ie PCR was positive at 24 weeks. The biochemical response between the responder and ALT / AST normalization was 145 patients. 63%. Twenty-four patients developed relapse after stopping treatment. Therefore, the overall continuous virological response (SVR) was 67.5% (Table 3).

Table 3: Response to therapy

Investigation	=n	%age
HCV-RNA Undetectable at week 12	135	84.37
HCV-RNA Undetectable at week 24	130	81.25
Breakthrough	5	2.64
Sustained virological response	108	67.5
ALT normalization	145	90.63

DISCUSSION:

Hepatitis C Viral infection is one of the leading causes of chronic liver disease in Pakistan and around the world. It is also the most common cause of liver transplantation worldwide. Due to the chronic nature of this disease, these figures are expected to grow many times over the next decade. Due to multiple risk factors, the natural history of HCV infection is difficult to study. The majority of hepatitis C virus patients is asymptomatic and has a slowly progressive disease. This study shows that the adverse effect profile of antiviral therapy is comparable with previous studies. These were fever, myalgia, fatigue, epigastric discomfort, anorexia, nausea and diarrhea. Mild anxiety and depression and irritable behaviors along with insomnia have also been observed in a significant number of patients. The observed hematological abnormalities were Hb <10gm 37% (23.13%), white blood cell count <4000 105 (62.6%) and platelet count <100,000 28 (17.5%). Three patients had hypothyroidism. As is well known, hepatitis C virus in lymphocytes, hepatocytes and macrophages cannot be detected and in some cases relapses may occur after a while. Some studies suggest that destruction of the hepatocyte virus may result in an HCV RNA that cannot be detected up to 12 years15. In another cohort, patients were followed for 18 years after the end of treatment. HCV RNA could not be detected in serum, but can be detected in liver biopsies16. In these cases, patients treated with pagular INF were obtained as 78% in some studies and as reported in only 53% with traditional INF. In our study, it was shown that SVR could be preserved in most cases (67.5%). In our country, genotype 3 is more common and has been found to be highly sensitive and sensitive to conventional INF, therefore the standard duration of treatment is 24 weeks for 2 and 3 genotypes. However, the treatment beyond 24 weeks, with> 600,000 IU / ml or steatosis, previously treated in RNA patients, may increase the response. Many researchers, however, think that optimal treatment of hepatitis C is not available. Time is needed to introduce some other economic modalities that should be economical for non-pay patients.

CONCLUSION:

This study supports that patients treated with interferon alfa with ribavirin combination are extremely effective who cannot respond to pagylated INF treatment and can reach SVR after 6 months of treatment.

REFERENCES:

1. Damiani, Giovanni, Chiara Franchi, Paolo Pigatto, Andrea Altomare, Alessia Pacifico, Stephen Petrou, Sebastiano Leone, Maria Caterina Pace, and Marco Fiore. "Outcomes assessment of hepatitis C virus-positive psoriatic patients treated using pegylated interferon in combination with ribavirin compared to new Direct-Acting Antiviral agents." *World journal of hepatology* 10, no. 2 (2018): 329.
2. Kleefeld, Felix, Sophie Heller, Patrick Ingiliz, Heiko Jessen, Anders Petersen, Ute Kopp, Antje Kraft, and Katrin Hahn. "Interferon-free therapy in hepatitis C virus (HCV) monoinfected and HCV/HIV coinfected patients: effect on cognitive function, fatigue, and mental health." *Journal of neurovirology* (2018): 1-13.
3. Indolfi, Giuseppe, Loreto Hierro, Antal Dezsofi, Jörg Jahnel, Dominique Debray, Nedim Hadzic, Piotr Czubowski et al. "Treatment of Chronic Hepatitis C Virus Infection in Children: A Position Paper by the Hepatology Committee of European Society of Paediatric Gastroenterology, Hepatology and Nutrition." *Journal of pediatric gastroenterology and nutrition*66, no. 3 (2018): 505-515.
4. Indolfi, Giuseppe, Loreto Hierro, Antal Dezsofi, Jörg Jahnel, Dominique Debray, Nedim Hadzic, Piotr Czubowski et al. "Treatment of Chronic Hepatitis C Virus Infection in Children: A Position Paper by the Hepatology Committee of European Society of Paediatric Gastroenterology, Hepatology and Nutrition." *Journal of pediatric gastroenterology and nutrition*66, no. 3 (2018): 505-515.
5. Gragnani, L., Cerretelli, G., Lorini, S., Steidl, C., Giovannelli, A., Monti, M., Petraccia, L., Sadalla, S., Urraro, T., Caini, P. and Xheka, A., 2018. Interferon-free therapy in hepatitis C virus mixed cryoglobulinaemia: a prospective, controlled, clinical and quality of life analysis. *Alimentary pharmacology & therapeutics*, *48*(4), pp.440-450.
6. Weiss, Jeffrey J., Sarah Prieto, Norbert Bräu, Douglas T. Dieterich, Sue M. Marcus, Alicia Stivala, and Jack M. Gorman. "Multimethod assessment of baseline depression and relationship to hepatitis C treatment discontinuation." *The International Journal of Psychiatry in Medicine* (2018): 0091217417749796.
7. Méndez-Lagares, G., Lu, D., Chen, C., Terrault, N., Segal, M.R., Khalili, M., Monto, A., Shen, H., Manos, M.M., Lanier, L.L. and Ryan, J.C., 2018. Memory T Cell Proliferation before Hepatitis C Virus Therapy Predicts Antiviral Immune Responses and Treatment Success. *The Journal of Immunology*, *200*(3), pp.1124-1132.
8. Yurdaydin, Cihan, Onur Keskin, Çağdaş Kalkan, Fatih Karakaya, Aysun Çalişkan, Gökhan

Kabaçam, F. Oğuz Önder et al. "Interferon treatment duration in patients with chronic delta hepatitis and its effect on the natural course of the disease." *The Journal of Infectious Diseases* 217, no. 8 (2018): 1184-1192.

9. Kozbial, Karin, Stephan Moser, Ramona Al-Zoairy, Remy Schwarzer, Christian Datz, Rudolf Stauber, Hermann Laferl et al. "Follow-up of sustained virological responders with hepatitis C and advanced liver disease after interferon/ribavirin-free treatment." *Liver International* 38, no. 6 (2018): 1028-1035.
10. Hayashi, Kazuhiko, Masatoshi Ishigami, Satoshi Yasuda, Yoji Ishizu, Teiji Kuzuya, Takashi Honda, Tetsuya Ishikawa, Yoshiki Hirooka, and Hidemi Goto. "Occurrence of late relapse of hepatitis C virus confirmed by molecular analysis after sustained virologic response to interferon–ribavirin-based therapy." *Hepatology Research* 48, no. 3 (2018): E78-E86.
11. Hayashi, Kazuhiko, Masatoshi Ishigami, Satoshi Yasuda, Yoji Ishizu, Teiji Kuzuya, Takashi Honda, Tetsuya Ishikawa, Yoshiki Hirooka, and Hidemi Goto. "Occurrence of late relapse of hepatitis C virus confirmed by molecular analysis after sustained virologic response to interferon–ribavirin-based therapy." *Hepatology Research* 48, no. 3 (2018): E78-E86.
12. Höner zu Siederdissen, Christoph, Bernhard Schlevogt, Philipp Solbach, Kerstin Port, Markus Cornberg, Michael P. Manns, Heiner Wedemeyer, and Katja Deterding. "Real-world effect of ribavirin on quality of life in HCV-infected patients receiving interferon-free treatment." *Liver International* 38, no. 5 (2018): 834-841.
13. Biswas, Aritra, Nabyendu Gupta, Debanjali Gupta, Abira Datta, Rushna Firdaus, Prosanto Chowdhury, Maitreyee Bhattacharyya, and Provash C. Sadhukhan. "Association of TNF-alpha (− 308 A/G) and IFN-gamma (+ 874 A/T) gene polymorphisms in response to spontaneous and treatment induced viral clearance in HCV infected multitransfused thalassemic patients." *Cytokine* 106 (2018): 148-153.
14. Akhil, Mohammed Shujauddin, Balaji Kirushnan, Melvin Martin, Kanakaraj Arumugam, N. K. Ganesh Prasad, and Rajan Ravichandran. "Sofosbuvir-based treatment is safe and effective in Indian hepatitis C patients on maintenance haemodialysis: A retrospective study." *Nephrology* 23, no. 5 (2018): 446-452.
15. Pires de Mello, Camilly, George Drusano, Jaime Rodriquez, Ajeet Kaushik, and Ashley Brown. "Antiviral Effects of Clinically-Relevant Interferon-α and Ribavirin Regimens against Dengue Virus in the Hollow Fiber Infection Model (HFIM)." *Viruses* 10, no. 6 (2018): 317.