CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
http://doi.org/10.5281/zenodo.4271613

Avalable online at: http://www.iajps.com *Research Article*

CONCENTRATION AND DOSE OF RIBAVIRIN IN TREATMENT OF CHRONIC HEPATITIS-C INFECTED PATIENTS

Dr Shahr Bano[1], Dr Fatima Khosa[2], Dr Jawaria Qureshi[1]
[1]Rawalpindi Medical University, [2]Shalamar Hospital Lahore.

Article Received: September 2020 **Accepted:** October 2020 **Published:** November 2020

Abstract:

Introduction: *Approximately 170 million people worldwide are chronically infected by hepatitis C virus (HCV), which can result in progressive hepatic injury and fibrosis, culminating in cirrhosis and end-stage liver disease.* ***Objectives:*** *The main objective of the study is to find the concentration and dose of Ribavirin in treatment of chronic hepatitis-C infected patients.*

Material and methods: *This cross sectional study was conducted in Rawalpindi Medical University and Shalamar Hospital Lahore during 2019. The data was collected from 100 patients of chronic Hepatitis-C. The primary outcome was to evaluate the efficacy of the regimen used.*

Results: *The data was collected from 100 hepatitis patients. The mean age was 36.5 + 10.1 years and BMI of the patients was 21.7 ± 2.7 (kg/m^2). The mean duration of HIV was 38 ± 43.8 months. There were non-significant relationship present in diseased group treated with different therapies like interferon and glutathione as as $p<0.05$. The level of micronutrients become decreases in diseased group.*

Conclusion: *It is concluded that there are no alternatives to RBV for the treatment of HCV infection, and therefore, maintaining patients on their indicated dose and length of therapy is crucial if the goal of a high rate of SVR is to be achieved.*

Corresponding author:
Dr. Shahr Bano,
Rawalpindi Medical University.

QR code

Please cite this article in press Shahr Bano et al, ***Concentration And Dose Of Ribavirin In Treatment Of Chronic Hepatitis-C Infected Patients.,*** *Indo Am. J. P. Sci, 2020; 07(11).*

INTRODUCTION:

Approximately 170 million people worldwide are chronically infected by hepatitis C virus (HCV), which can result in progressive hepatic injury and fibrosis, culminating in cirrhosis and end-stage liver disease. Among adults in the Western world, chronic hepatitis C (CHC) is the major cause of cirrhosis and the principal indication for liver transplantation. CHC also contributes to the increasing incidence of hepatocellular carcinoma (HCC), for which few satisfactory therapies exist [1].

The primary treatment goal in patients with chronic HCV infection is viral eradication. The benchmark therapy for untreated HCV-patients is a combination of pegylated interferon-alpha (PEG-IFN) and ribavirin (RBV). HCV genotype should be systematically determined before treatment, because it dictates the indication, treatment duration, RBV dose, and virological monitoring procedure. HCV genotype 2- and 3-infected patients require 24 weeks of treatment and a low dose of RBV-i.e., 800 mfg daily [2].

Hepatitis C virus (HCV) incurs a major disease burden in the United States and worldwide. Nearly 4 million Americans have been exposed to HCV, and approximately 2.7 million harbor chronic HCV. AAlthough the incidence of newly acquired infection has been declining, the number of identified cases continues to rise as public awareness and screening for HCV increase; this trend is not expected to reach its peak until 2015. In addition, the number of HCV complications such as end-stage liver disease, hepatocellular carcinoma, and death has also increased with the age of the infected population. Consequently, hepatitis C-related cirrhosis and hepatocellular carcinoma have become the leading indications for liver transplantation in the United States [3].

Significant advances have been achieved in the treatment for chronic HCV over the past three decades. In the early 1990s, a 6-month course of interferon alfa (IFN-alfa) monotherapy, the first approved therapy for chronic HCV, resulted in sustained virologic response rates (SVR) of 6–12% [4]. The extension of therapy duration to 12 months improved SVR to 16–20%. The addition of ribavirin to IFN-alfa significantly enhanced SVR to 35–40%. More recently, the pegylation of IFN-alfa, when used concomitantly with ribavirin, has further enhanced SVR to 54–56%. This combination regimen is currently the standard of care for chronic HCV and will likely remain the foundation of HCV therapy in the near future [5].

Objectives:

The main objective of the study is to find the concentration and dose of Ribavirin in treatment of chronic hepatitis-C infected patients.

MATERIAL AND METHODS:

This cross sectional study was conducted in Rawalpindi Medical University and Shalamar Hospital Lahore during 2019. The data was collected from 100 patients of chronic Hepatitis-C. The primary outcome was to evaluate the efficacy of the regimen used. Efficacy was shown by complete elimination of the virus from the serum as indicated by a negative/undetectable viral load via PCR qualitative analysis at four weeks since starting medication, i.e., rapid virological response (RVR), 24 weeks since starting medication i.e. end of treatment response (ETR) and six months post-treatment, i.e., sustained virological response (SVR). All patients were followed up with a complete blood count (CBC), liver function tests (LFTs), prothrombin time (PT), international normalized ratio (INR), urea with creatinine levels, and serum electrolyte levels at induction, four, 12 and 24 weeks after starting medications. Ultrasound abdomen was also performed at initial evaluation.

The data was collected and analysed using SPSS version 19. All the values were expressed in mean and standard deviation.

RESULTS:

The data was collected from 100 hepatitis patients. The mean age was 36.5 + 10.1 years and BMI of the patients was 21.7 ± 2.7 (kg/m^2). The mean duration of HIV was 38 ± 43.8 months. There were non-significant relationship present in diseased group treated with different therapies like interferon and glutathione as as $p<0.05$. The level of micronutrients become decreases in diseased group.

Table 01: Associations of Clinical Parameters with Abnormal Liver Function Tests

Parameter	LFTs	*P* value
Age (years)	36.5 + 10.1	0.54
BMI (kg/m^2)	21.7 ± 2.7	0.88
Duration of HIV infection (months)	38 ± 43.8	0.95
Significant alcohol consumption	24 (50%)	0.15
HBV & HCV Co-infection	19 (39.6%)	0.002
HBsAg positive	11 (22.9%)	0.01
Anti HCV positive	06 (12.5%)	0.27
Combined HBV& HCV	02 (4.1%)	–

Ribavirin is used in combination with other antiviral medications (such as interferon, sofosbuvir) to treat chronic (long-lasting) hepatitis C, a viral infection of the liver. Chronic hepatitis C infection can cause serious liver problems such as scarring (cirrhosis), or liver cancer. Ribavirin works by reducing the amount of hepatitis C virus in your body, which may help your liver recover [6].

Dosage of Ribavirin:

The main serious adverse event that is associated with the use of RBV is dose-dependent hemolytic anemia. Anemia is frequently observed in patients receiving combination treatment with standard interferon or PEG-IFN plus RBV [7]. RBV-induced anemia has been shown to be primarily affected by plasma RBV concentration, not by dose per kilogram body weight. A recent publication supports the individualization of RBV dosing according to HCV genotype and body weight and highlights several clinical variables that have an effect on the likelihood of SVR versus the occurrence of anemia [8]. A higher apparent clearance of RBV, older age, and cirrhosis have a negative impact on achieving an SVR. Gender and RBV dose/kg are the most important prognostic factors for the occurrence of anemia. However, because anemia is not a universal risk in all treated patients, the initial high-dose strategy of 1,000 or 1,200 mg per day based on body weight, appears to be appropriate. For heavier patients, RBV doses greater than 1,200 mg/day may be initiated, because they are likely to be associated with additional efficacy and a manageable risk of anemia [9].

The specific dose and duration of ribavirin therapy depends on the hepatitis C genotype, the patient's prior treatment experience, degree of liver fibrosis, and the concomitant medications used for hepatitis C therapy. When used in combination with direct-activing antiviral agents (or combinations), the dose and duration of therapy with ribavirin is variable [10].

A relationship between RBV dose and response to therapy with both IFN alpha-2a and alpha-2b has been established in genotype 1 patients, who benefit from doses that exceed 800 mg/day. When RBV is combined with PEG-IFN alpha-2a, relatively small reductions to 800 mg/day lead to significantly lower rates of SVR [11]. Similarly, a large comparative trial of fixed-dose RBV compared with weight-based dosing in combination with PEG-IFN alpha-2b demonstrated that stratifying patients of all genotypes to receive starting doses ranging from 800-1400 mg/day depending on weight effects higher SVR rates than using a fixed dose of 800 mg/day for all patients [12].

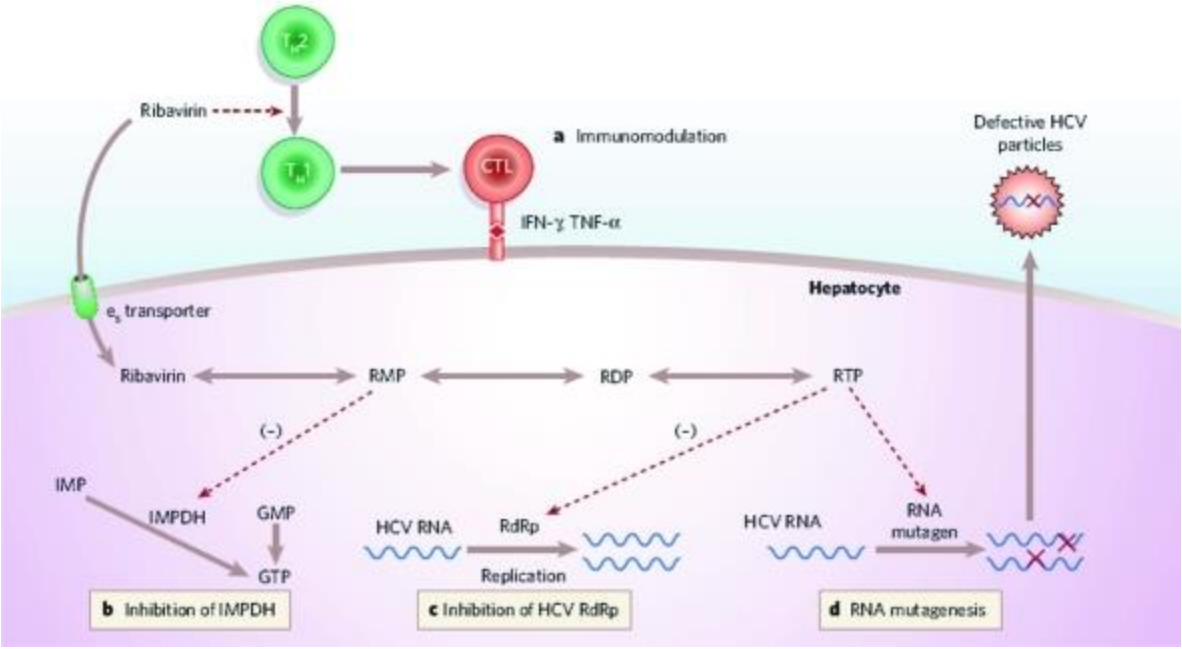

Figure 01: Mechanism of Ribavirin

CONCLUSION:

It is concluded that there are no alternatives to RBV for the treatment of HCV infection, and therefore, maintaining patients on their indicated dose and length of therapy is crucial if the goal of a high rate of SVR is to be achieved. However, due to the limited data available, further studies on RBV dose and treatment duration are warranted before any recommendations can be made.

REFERENCES:

1. Pradhan SC and C Girish (2006). Hepato protective herbal drug, silymarin from experimental pharmacology to clinical medicine Indian J Med Res 124, pp 491-504.
2. Patel, V.K. and Bhatt H.V., 1985.Toxicity antiseptic effect of chicory root extract in Pyorrhea. The antiseptic 904-906.
3. Crapnell K., Zanjani E. D., Chaudhuri A., Ascensao J. L., Jeor S. S., Maciejewski J. P. In vitro infection of megakaryocytes and their precursors by human cytomegalovirus. *Blood*. 2000;95(2):487–493.
4. Gavrilovskaya I. N., Shepley M., Shaw R., Ginsberg M. H., Mackow E. R. β_3 integrins mediate the cellular entry of hantaviruses that cause respiratory failure. *Proceedings of the National Academy of Sciences of the United States of America*. 1998;95(12):7074–7079. doi: 10.1073/pnas.95.12.7074.
5. Martell M., Gomez J., Esteban J. I., et al. High-throughput real-time reverse transcription-PCR quantitation of hepatitis C virus RNA. *Journal of Clinical Microbiology*. 1999;37(2):327–332.
6. Chen C.-H., Yang P.-M., Huang G.-T., Lee H.-S., Sung J.-L., Sheu J.-C. Estimation of seroprevalence of hepatitis B virus and hepatitis C virus in Taiwan from a large-scale survey of free hepatitis screening participants. *Journal of the Formosan Medical Association*. 2007;106(2):148–155.
7. Stephan C, Berger A, Carlebach A, et al. Impact of tenofovir-containing antiretroviral therapy on chronic hepatitis B in a cohort co-infected with human immunodeficiency virus. J Antimicrob Chemother. 2005;56:1087–93
8. S. Shigeta, S. Mori, M. Baba et al., "Antiviral activities of ribavirin, 5-ethynyl-1-*β*-D-ribofuranosylimidazole-4-carboxamide, and 6'-(R)-6'-C-methylneplanocin A against several ortho- and paramyxoviruses," *Antimicrobial Agents and Chemotherapy*, vol. 36, no. 2, pp. 435–439, 1992.
9. R. W. Sidwell, J. H. Huffman, G. P. Khare, L. B. Allen, J. T. Witkowski, and R. K. Robins, "Broad-spectrum antiviral activity of virazole: 1-β-D-ribofuranosyl-1, 2,4-triazole-3-carboxamide," *Science*, vol. 177, no. 4050, pp. 705–706, 1972.

10. C. Bonaventure, V. Calay, M. Chevallier, P. Merle, P. Pradat, and C. Trepo, "Long-term ribavirin monotherapy in patients with chronic hepatitis C not responding or intolerant to interferon alpha," *Journal of Hepatology*, vol. 40, pp. 152–153, 2004.
11. J. Dumortier, O. Guillaud, M.-C. Gagnieu et al., "Anti-viral triple therapy with telaprevir in haemodialysed HCV patients: is it feasible?" *Journal of Clinical Virology*, vol. 56, no. 2, pp. 146–149, 2013.
12. G. Hatu, F. Bailly, E. Pourcelot et al., "Lower ribavirin biodisponibility in patients with HIV-HCV coinfection in comparison with HCV monoinfected patients," *BMC Infectious Diseases*, vol. 14, no. 1, article 150, 2014.