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ORIGINAL ARTICLE

Comparison of Frequency of Rapid Virological Response in Patients of Hepatitis C being Treated with 25-OH Vitamin D along with Sofosbuvir/Ribavirin with Those Treated with Sofosbuvir/Ribavirin only

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ABSTRACT

Background: Hepatitis C is the leading cause of liver damage that lead to death if left untreated. Sofosbuvir has recently attained enormous success due to high rate of virological response. Recent studies have shown that addition of vitamin D to antiviral therapy improves the efficacy of treatment in patients with Hepatitis C.

Objective: To compare the frequency of virological response in hepatitis C patients treated with vitamin D along with sofosbuvir plus ribavirin to those treated with sofosbuvir plus ribavirin only

Study Design: Randomized-controlled-trial

Place and Duration of Study: Department of Medicine, Pak Emirates Military Hospital, Rawalpindi from 1st November 2017 to 30th April 2018.

Methodology: One hundred patients of chronic hepatitis C were included. Patients were randomly divided into two groups; group A receiving vitamin D along with sofosbuvir plus ribavirin and group B receiving sofosbuvir plus ribavirin therapy only. Patients were treated for 6 months and their RVR was monitored.

Results: The mean age of patients in combination group was 39.0±12.92 years and in control group were 36.66±13.80years. After 4 weeks, RVR (no HCV RNA detected on PCR) was achieved in 31 (62%) cases in combination group while in 19 (38%) cases there was still HCV RNA present. In control group, RVR could be achieved in 18 (36%) cases while in 32 (64%) cases, RVR could not be achieved. The difference was significant between both groups ($p<0.05$).

Conclusion: The addition of vitamin D can help in achieving RVR in >50% cases within 4 weeks. So addition of vitamin D in standard therapy may help to improve the quality of treatment.

Keywords: Rapid virological response, Hepatitis C, 25-OH vitamin D, Sofosbuvir, Ribavirin

INTRODUCTION

Hepatitis C is among the leading causes of relentless liver disease, including hepatocellular carcinoma and cirrhosis-related end-stage liver disease.[1] The overall worldwide population affected by hepatitis C is around 170 million, averaging at 3% of the global community.[2] In Pakistan, the percentage is comparable to the international populace of around 3%.[3]

Combination of drugs are used for treating hepatitis C virus and proved extremely beneficial. These drugs can be given orally and acted as direct anti-viral agents that consequently enhanced the efficacy of interferon free therapy. Sofosbuvir, an anti-viral drug worked as chain terminator of RNA synthesis and showed high virological response with minimal side-effects.[4]

Moreover, it can be administered safely to those groups who are deemed intolerant or have any contraindication to interferon therapy such as those with autoimmune thyroid disorders, myaesthenia gravis, psychiatric disorders, autoimmune hepatitis and decompensated cirrhosis.[5]

Recent studies have shown that addition of vitamin D to antiviral therapy improves the efficacy of treatment in patients with hepatitis C. It helped in the suppression of pro-inflammatory cytokines, increases the production of anti-inflammatory cytokines and helps in the improvement of T-cell hyperresponsiveness.[6] With vitamin D addition to antiviral and ribavirin SVR of 44% as compared to 17% in control.[7]

Vitamin D deficiency is very common (92%) among patients with chronic liver disease, and at least one-third of them suffer from severe vitamin D deficiency (<12ng/mL).[8] Low serum vitamin D is not only related to severe fibrosis but also reduces effectiveness of treatment in hepatitis C chronic patients.[9] Addition of vitamin D also enhances the patient's outcome had mild to moderate fibrosis.[10] Vitamin D not only improves bone mineralization but also reverses hepatic fibrosis and suppresses hepatitis C viral replication and thus improves virological response in patients with chronic hepatitis C with and without cirrhosis.[11]

The purpose of this study is to establish role of 25-OH Vitamin D in patients with hepatitis C infection by comparing the frequency of RVR after 4 weeks in patients being treated with sofosbuvir, ribavirin plus vitamin D and sofosbuvir plus ribavirin only. Role of vitamin D has been postulated to improve the treatment outcomes in combination with interferons and not with the direct-acting antiviral agents like sofosbuvir which are the standard of care according to new guidelines.[12]

Once the role of vitamin D is established, it would be a cost effective addition to the standard modality of treatment of hepatitis C. Addition of vitamin D to the standard regimen would not only improve the efficacy of treatment without adding significant cost.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Medicine, Military Hospital Rawalpindi from 1st November 2017 to 30th April 2018. A total of 100 patients of chronic hepatitis C with positive qualitative and/or quantitative assay of more than or equal to 15 IU/ml was enrolled. They were divided in two groups, each group comprised 50 patients. Group A included patients receiving vitamin D along with sofosbuvir plus ribavirin and group B included patients receiving ribavirin therapy and sofosbuvir. All hepatitis C patients, 18-60 years old, positive qualitative and/or quantitative assay of HCV RNA of more than 1.2 log IU/ml (15 IU/ml) and genotypes 1, 2, 3 and 4 were included. Severe renal impairment/end stage renal disease, hemoglobinopathies, prior treatment failure/relapse, co-infection with hepatitis B/HIV and pregnancy and lactation were excluded. Renal function test, liver function tests and ultrasound for structure of the liver was also conducted. Patients were treated for 6 months and their RVR was monitored. The data was entered and analyzed through SPSS-23. Chi square test was applied to compare RVR between the groups. P value ≤0.05 was considered significant.

RESULTS

The mean age of patients in combination group was 39.0±12.92 years and in control group were 36.66±13.80 years. There were 30 (60%) males and 20 (40%) females in combination group and in control group, 34 (68%) males and 16 (32%) females. There were 10 (20%) patients had genotype 1, 5 (10%) had genotype 2, 17 (34%) had genotype 3 and 18 (36%) had genotype 4 in combination group while in control group, 6 (12%) patients had genotype 1, 13 (26%) had genotype 2, 15 (30%) had genotype 3 and 16 (32%) had genotype 4 (Table 1).

After 4 weeks, RVR (no HCV RNA detected on PCR) was achieved in 31 (62%) cases in combination group while in 19 (38%) cases there was still HCV RNA present. In control group, RVR could be achieved in 18 (36%) cases while in 32 (64%) cases, RVR could not be achieved. The difference was significant between both groups ($p<0.05$) [Table 2].

Table 1: Demographic information of the patients in both groups (n=100)

Variable	Vitamin D + sofosbuvir + ribavirin	Sofosbuvir + ribavirin
Age (years)	39.0±12.92	36.66±13.80
Gender		
Male	30 (60%)	34 (68%)
Female	20 (40%)	16 (32%)
Genotype		
1	10 (20%)	6 (12%)
2	5 (10%)	13 (26%)
3	17 (34%)	15 (30%)
4	18 (36%)	16 (32%)

Table 2: Comparison of RVR in both groups

RVR achieved (PCR at 4 weeks)	Vitamin D + sofosbuvir + ribavirin	Sofosbuvir + ribavirin
Yes	31 (62%)	18 (36%)
No	19 (38%)	32 (64%)

χ^2= 6.763 P = 0.009 (Significant)

DISCUSSION

Direct anti-viral drugs have revolutionized the field of medical sciences with high rate of cure in less duration and also proved as successful treatment strategy for hepatitis C virus.[13] In the present study, after 4 weeks, RVR (no HCV RNA detected on PCR) was achieved in 31 (62%) cases in combination group while in 19 (38%) cases there was still HCV RNA present. In control group, RVR could be achieved in 18 (36%) cases while in 32 (64%) cases, RVR could not be achieved. The difference was significant between both groups ($p<0.05$) [Table 2]. Abu-Mouch et al[7] found that with addition of vitamin D to antiviral and ribavirin, virological response was achieved in 44% as compared to 17% in patients received antiviral and ribavirin only. Significant difference was observed in HCV-RNA concentration when vitamin D was added. Thus, it proved that, vitamin D prove beneficial in reducing viral load in HCV patients.[14]

Another study by Terrier et al[15] highlighted that HCV patients with genotype 1 and 4 did not show any EVR improvement if when vitamin D was given to the patient with the ongoing treatment plan. Another meta-analysis showed that, no improvement was observed in HCV patients when vitamin D was administered despite of the genotype.[16]

Exact biochemical pathway in EVR, RVR and SVR due to vitamin D is still not well-understood. This phenomenon can be explained by multiple connection is present between immune system and vitamin.[17,18]

CONCLUSION

The addition of vitamin D can help in achieving RVR in >50% cases within 4 weeks. So addition of vitamin D in standard therapy may help to improve the quality of treatment. Thus in future we will implement the addition of vitamin D along with antiviral therapy to achieve RVR in maximum number of patients and more success can be achieved.

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