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# Hepatitis C Treatment in Patients with Drug Addiction Is Effective or Not Effective?

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## ABSTRACT

**Introduction:** Patients with drug addiction have high risk for hepatitis C virus (HCV). Effective treatment response is essential to optimize treatment for drug abusers infected by hepatitis C virus. **Aim:** The aim of this present study was to show that hepatitis C treatment in patients with drug addiction is effective like patients without drug addiction. **Material and Methods**: Total amount of 57 patients with hepatitis C (25 drug abuser and 32 non–drug abuser) that referred to Shahid Motahari clinic of Shiraz were selected. All patients infected with HCV treated by combination regimens of ribavirin, sofosbuvir and interferon. Patients received sofosbuvir (400mg once a day) in combination with peg-IFN-alpha (92a180m/w›92b1/5m/kg/w) and RBV (under 75 kg 1000mg, over 75 kg 12000kg) for 12 weeks. The Kolmogorov–Smirnov test was used for testing normality. Associations between variables were analyzed using a Chi-square, Fisher exact, T student and Mann–Whitney U test. **Results:** Out of 25 HCV patients (43.9%) were drug addicts and 32 patients (56.1%) were non-drug addicts. Insomnia (61.4%), fatigue (63.1%) and debility (49.1%) were more common adverse effects of therapy in drug abusers and non-drug abusers. Alanine transaminase (ALT) and HCV RNA was normal in the end of therapy (EOT). White blood cell (WBC) count decreased in during two-week after starting of the treatment and then increased to normal levels at the end of treatment. Reduction of WBC count was considerable in during two-week. Hematologic result was not considerable. Reduction of hemoglobin was <10 g/dL in 9.37% of non-injecting drug addicts and <8.5 g/dL in 6.25% of injecting drug addicts. The results of this study did not demonstrated a significant relationship about sustained virologic response (SVR) between the drug abusers and non-drug abusers (P = 0.99). **Conclusions:** In conclusion, patients with drug addiction can receive hepatitis C treatment on the history of their past or current drug use status. Combination therapy with sofosbuvir plus peginterferon and ribavirin can lead to high treatment response in HCV patients were drug abuser. In addition, this treatment combination was with low discontinuation rates and low adverse effects. Effective intervention in HCV patients with drug addiction to reduce injection- related risk.

**Keywords: Hepatitis C virus, Drug Addiction, Treatment.**

## 1. INTRODUCTION

Hepatitis C virus infection remains a significant cause of mortality and morbidity in the worldwide population (1, 2). Complications cause of 350,000 global deaths is related to HCV (3, 4). Cirrhosis, end-stage liver disease, and hepatocellular carcinoma (HCC) are high level HCV-related complications in up to 20% of patients (5, 6). Also injection drug users are at risk of HCV infection and 50%–90% are infected with hepatitis C virus (7-14).

Treatment success of HCV is estimated based on sustained virological response (15). SVR is the one of significant elements for estimating prognosis after antiviral treatments against chronic HCV infection (16). SVR after antiviral treatment can be reduced HCV-related complications (5, 17, 18). SVR in HCV patients treated with peginterferon plus ribavirinat 24 weeks after completion of treatment (19).

Sofosbuvir (SOF) as a new direct-acting antiviral agent (DAA) was confirmed for effective treatment of chronic HCV -infected patients. Some investigation have shown that adding Sofosbuvir as a HCV polymerase inhibitor to the conventional therapy of pegylated-interferon (PegIFN) plus Ribavirin (RBV) can be increased the rate of SVR. However combination therapy of ribavirin, sofosbuvir and interferon is a highly effective therapy for treatment of HCV infection (20). European association

| Basic characteristic | | Addict (N=25 ) | Non Addict (N=32) | p- value |
|---|---|---|---|---|
| Age | | *43.52 ± 9.66 | 46.97 ± 9.94 | 0.194 |
| Sex | male | **24 (96) | 22 (68.8) | 0.016 |
| | female | 1 (4) | 10 (31.3) | |
| Marital status | Single | 6 (24 ) | 3 (9.4 ) | 0.294 |
| | Married | 17 (68) | 27 (84.4) | |
| | Divorce | 2 (8 ) | 2 (6.3 ) | |
| Education | Illiterate | 0 (0) | 6 (18.8 ) | 0.117 |
| | High school | 15 (60) | 19 (59.4) | |
| | Diploma | 8 (32) | 4 (12.5 ) | |
| | University degree (BA ) | 1 ( 4 ) | 1 (3.1) | |
| | University degree ( BSc ) | 1 (4) | 2(6.3) | |
| Occupation | Self – employed | 11 ( 44 ) | 0 (0) | 0.33 |
| | Office worker | 2 (8 ) | 14 (43.75) | |
| | Housewife | 1 (4 ) | 7 ( 21.87 ) | |
| | Unemployed | 5 (20 ) | 3 (9.38) | |
| | other | 6 (24 ) | 8 (25.8) | |
| Drug usage | Opium | 8 (32 ) | 1(100) | -- |
| | Crystal | 3 (12 ) | 0 (0) | |
| | Ecstasy | 1 ( 4 ) | 0 (0) | |
| | Heroin | 13(52 ) | 0 (0) | |
| BMI | | 25.26 ± 5.63 | 24.95± 4.44 | 0.83 |
| History of previous HCV treatment | yes | 7 (28) | 12 (37.5) | 0.45 |
| | no | 18 (72) | 20 (62.5) | |
| ALT pre – treatment | | 76.96± 38.02 | 83.90 ± 56.44 | 0.88 |
| AST pre – treatment | | 60.52 ± 34.49 | 60.87 ± 34.38 | 0.67 |
| ALB pre – treatment | | 3.99 ±0.996 | 4.23± 0.39 | 0.91 |
| DM | yes | 2 (8 ) | 5 (15.6 ) | 0.45 |
| | no | 23 (92) | 27 (84.4) | |
| HBV | yes | 1 (4) | 1 (3.1% ) | 0.99 |
| | no | 24 (96) | 31 (96.9) | |
| HIV | yes | 1 (4 ) | 0 (0 ) | 0.44 |
| | no | 24 (96) | 32 (100) | |
| Cirrhosis | yes | 5 (20) | 1 (3.1) | 0.07 |
| | no | 20 (80) | 31 (96.9) | |
| Genotype | 1 | 17 (68 ) | 24 (75 ) | 0.56 |
| | 3 | 8 (32) | 8 (25) | |

**Table 1. Demographic and baseline characteristics of Hepatitis C patients treated with Ribavirin, Sofosbuvir and Interferon. *Mean± SD **N (%)**

for the study of the liver (EASL) has recommended treatment guidelines of hepatitis C for patients with drug addiction. EASL suggest the anti-HCV regimens that can be used in patients with drug addiction are the same as in non-drug abusers (21). Evidence for treatment outcomes among people who addict to drugs is restricted (22).

## 2. AIM

The aim of this study is to show that hepatitis C treatment in patients with drug addiction is effective like patients without drug addiction. Drug abusers are the largest subpopulation infected with hepatitis C virus. Therefore, comprehensive efforts should be made to guarantee that treatment of drug users is possible, accessible and optimal like non-drug users.

## 3. MATERIAL AND METHODS

Between September 2015 and December 2015, all 25 addicts and 32 non-addicted patients with hepatitis C were enrolled at Motahari clinic affiliated of Shiraz University of Medical Sciences. In this study, 25 patients addicted to heroin or opium and juice, as injectable and intravenous. Patients were eligible for inclusion criteria if they met the following indicators: age over 18 years, presence of HCV RNA in peripheral blood in a quantitative manner, approved chronic hepatitis (Over 6 months of diagnosis of hepatitis C). HCV RNA was measured by real-time PCR assay. Written informed consent was obtained from all patients. Globally, this study was according to ethical guidelines. Exclusion criteria included pregnancy, hypothyroidism, GFR<50, PLT<50000/MM3, severe mental disorders and depression that did not receive interferon with the approval of the psychiatrist, clinical or biochemical signs of decompensated cirrhosis. Patients surveyed by Child-Pugh score for estimating of decompensated cirrhosis.

Hematological and biochemical tests were performed before starting of the treatment and after stoppage of

| Adverse effects | | Addict N (%) N=25 | Non addict, N (%) N=32 | P value |
|---|---|---|---|---|
| Discontinue of treatment | | 0 (0) | 1 (3.1) | 0.99 |
| Thrombocytopenia | | 0 (0) | 0 (0) | - |
| Nausea | | 2 (8 ) | 3(9.4 ) | 0.99 |
| Nasopharyngitis | | 3 (12 ) | 9(28.1 ) | 0.14 |
| Skin dryness | | 8 (32 ) | 15 (46.9 ) | 0.26 |
| Cough | | 1 (4 ) | 7 (21.9 ) | 0.07 |
| Diarrhea | | 1 (4 ) | 3 (9.4 ) | 0.62 |
| Headache | | 7 (28 ) | 18 (56.3 ) | 0.03 |
| Debility | | 12 (48 ) | 19 (59.4 ) | 0.39 |
| Insomnia | | 5 (20 ) | 10 (31.3 ) | 0.34 |
| Shortness of Breath | | 4 (16 ) | 11 (34.4 ) | 0.12 |
| Fatigue | | 13 (52 ) | 23 (71.9 ) | 0.12 |
| Anemia | < 8.5 gr/dl | 8 (32 ) | 16 (50 ) | 0.12 |
| | < 10 gr/dl | 0 (0) | 2 (6.5) | |
| Itching | | 8 (32 ) | 16 (50 ) | 0.172 |

**Table 2. Adverse effects of Hepatitis C patients treated with Ribavirin, Sofosbuvir and Interferon**

| EOT | | Addict | Non-Addict | P value |
|---|---|---|---|---|
| EOT and genotype | 1 | **17(68) | 24(75) | 0.001 |
| | 2 | 0 (0) | 0 (0) | |
| | 3 | 8(32) | 8(25) | |
| | 4 | 0 (0) | 0 (0) | |
| EOT | Male | 24(96) | 22(68.8) | 0.39 |
| | female | 1(4) | 10(31.2) | |
| Treatment of Hepatitis C with interferon and ribavirin regimen | | 7 (28) | 12(37.5) | 0.001 |
| ALT post – treatment | | *45.6± 18.0 | 50.9 ± 56.44 | 0.96 |
| AST post- treatment | | 25.30 ± 20.48 | 28.87 ± 19.38 | 0.07 |
| SVR | | 25(100 ) | 31 (96.87) | 0.001 |

**Table 3. End of Therapy of Hepatitis C patients treated with Ribavirin, Sofosbuvir and Interferon. *Mean± SD **N (%)**

the therapy. Tests were performed before starting of the treatment including: βhCG levels in woman of child-bearing age, creatinine and urease test, complete blood count (CBC), standard liver function tests, alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP), qualitative assays for HBsAg, anti-HBc, anti-HIV.

All patients infected with HCV treated by combination regimens of ribavirin, sofosbuvir and interferon. Patients received sofosbuvir (400mg once a day) in combination with peg-IFN-alpha (92a180m/w،92b1/5m/kg/w) and RBV (under 75 kg 1000mg, over 75 kg 12000kg) for 12 weeks. One to two weeks after starting of the treatment, the patients were visited and hematological and biochemical tests were requested again. During treatment, patients with an ANC <500/microL and platelet count is less than 50,000/mm3 were analyzed and necessary procedures were performed. Patient visiting was performed every 4 weeks (28 days) and HCV RNA was measured by qualitative assays after the end of treatment. SVR was analyzed after 3 month of therapy.

The Kolmogorov–Smirnov test was used for testing normality. Associations between variables were analyzed using a Chi-square, Fisher exact, T student and Mann–Whitney U test and p-values < 0.05 were considered statistically significant.

## 4. RESULTS

Total amount of 57 patients chronically infected with HCV were enrolled in the present study. 25 HCV patients (43.9%) were drug addicts and 32 patients (56.1%) were non-drug addicts. Among 57 patients, 46 (80.7%) were male and 11 (19.2%) were female. The mean age (±SD) of injecting drug addicts were 43.25 ± 9.65 and non-injecting drug addicts were 45.69 ± 12.92. Demographic and baseline characteristics are shown in Table 1.

Adverse effects of therapy were analyzed in studied two groups (Table 2). Insomnia (64%), fatigue (52%), debility (50%) and shortness of breath (34.4%) were more common adverse effects of therapy in drug addicts respectively. Fatigue (71.9%), insomnia (59%), headache (56.2%) and debility (50%) were more common adverse effects of therapy in non- drug addicts. Only one case had severe adverse effect of therapy. This patient was non-drug addict and adverse effect of therapy was cerebrovascular accident (CVA). ALT and HCV RNA was normal in the end of therapy (EOT). White blood cell (WBC) count decreased in during two-week after starting of the treatment and then increased to normal levels at the end of treatment. Reduction of WBC count was considerable in during two-week. Hematologic result was not considerable. Reduction of hemoglobin was<10 g/dL in 9.37% of non-drug addicts and <8.5 g/dL in 6.25% of drug addicts. The results of this study did not demonstrated a significant relationship about sustained virologic response (SVR) between the drug users (100%) and non- drug users (%96.87) (P = 0.99). Table 3 showed end of therapy details of hepatitis C patients treated with ribavirin, sofosbuvir and interferon.

## 5. DISCUSSION

The prevalence of HCV in drug injection users is predicted 67% with the highest prevalence rate (23, 24). In this study, 43.8% of patients were drug injection users. Also the higher HCV percent of infection prevalence was males compared with females. Therefore, an optimal treatment strategy with broad access for this high risk population has key role in the reduction of HCV in drug injection users (25). In our study, HCV genotype 1 was the most prevalent and was detected in 71.9% of patients. HCV genotype 3 was the most prevalent and was detected in findings of Gigi E and co-authors are according to this study (26).

Before 2011 year, selected HCV therapy was combination regimen of pegIFN and RBV with high side effects (27-29). Combination regimen of PegIFN, RBV plus SOF was shorter duration of therapy and effective regimen in compared with PegIFN and RBV combination therapy (29).Combination of PegIFN, RBV and SOF lead to reduction in HCV RNA in about 95% of HCV-infected patients at treatment week 4 (30, 31). Our study was demonstrated HCV RNA was normal in the end of therapy (EOT). The results of this study did not demonstrated a significant relationship about sustained virologic

response (SVR) between the drug users and non- drug users. Also result of investigations indicate none found a statistically significant difference in rates of SVR between drug users and non- drug users (32).

More common adverse effects of interferon regimen were fatigue, nausea, decreased appetite, myalgia, flu-like illness, and rash (33). Ribavirin as a HCV therapy options increased severe adverse events rates (34). In despite of this finding, one patient had severe adverse effect of therapy and our findings were shown one patient discontinued treatment due to CVA. Their results of Kowdley and co-authors shows a small proportion of patients discontinued combination treatment of sofosbuvir 400 mg plus peginterferon and ribavirin for 12 weeks due to adverse events. The most common adverse events during therapy was fatigue (32). In the Lancet, Lawitz and co-authors refer to 6.5% of patients who discontinued treatment due to adverse events in their study (35). Laboratory abnormalities among patients, including white blood cell and hemoglobin count was not considerable (33). Because of the limitations, we were not able to investigate other factors that effect on treatment process.

Sofosbuvir plus peginterferon and ribavirin for 12 weeks provides high rates of SVR (33). Our study demonstrated SVR rates after treatment was high in the both of groups. Investigations were demonstrated that appropriate treatment outcomes can be achieved in patients who report actively addicted drugs (22).

Further, EASL guidelines approved that HCV successful therapy for drug abusers with high SVR rates require personalized treatment within a multidisciplinary team setting (13). Although guidelines recommend that drug abusers should not be excluded from HCV treatment, some of the hepatitis C therapy procedures demonstrate that patients with drug addiction excluded from the treatment process (36). Some concerns are risk of reinfection and increased susceptibility in the patients with drug addiction (37). The result of a meta-analysis demonstrated that appropriate treatment outcomes can be achieved in patients with active drug addiction who selected for HCV therapy plan (22). The benefits of HCV treatments recommend more opportunity to increase access of therapy among drug addiction users than ever before action plan on HCV of the Scottish government and European and global guidelines offer expansion of therapy in this population group (37). Investigations demonstrate that treatment for chronic hepatitis C was safety and effectively in drug addiction group (26). Further studies can detect suitable approaches of expanding the numbers of drug addiction users who access to safe and cost-effective services.

Also the results of this survey approved that there isn't a significant relationship about sustained virologic response (SVR) between the drug users and non- drug users. Also both of groups in our survey were with the same treatment method and the anti-HCV regimens that can be used in drug abusers were the same as in non-drug abusers. However, treatment of HCV related infection in the patients with drug addiction can be suitable and essential procedure. Survey limitations include the small sample size, which may have limited our qualification to detect associations between variables.

## 6. CONCLUSION

As a consequence, patients with drug addiction can receive hepatitis C treatment on the history of their past or current drug use status. Combination therapy with sofosbuvir plus peginterferon and ribavirin can lead to high treatment response in HCV patients were drug abuser. In addition, this treatment combination was with low discontinuation rates and low adverse effects. Effective intervention in HCV patients with drug addiction to reduce injection- related risk. Further investigations are needed to survey the long time effectiveness of HCV treatment in patients with drug addiction.


- Authors' contributions: Each authos gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data for the work. Each authos had a part in article preparing for drafting or revising it critically for important intellectual content, and all authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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