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 (SVR) (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 (PEG-IFN) 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...
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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

| Basic characteristic | Addict (N=25) | Non Addict (N=32) | p-value |
|----------------------|--------------|-------------------|---------|
| Age                  | **43.52 ± 9.66** | 46.97 ± 9.94 | 0.194   |
| Sex                  | **24 (96)** | 22 (68.8) | 0.016   |
| Marital status       | **6 (24)** | 3 (9.4) | 0.294   |
| Education            | **15 (60)** | 19 (59.4) | 0.117   |
| Occupation           | **2 (8)** | 14 (43.75) | 0.33    |
| Drug usage           | **8 (32)** | 1 (100) | --      |
| BMI                  | 25.26 ± 5.63 | 24.95 ± 4.44 | 0.83    |
| History of previous HCV treatment | yes | 7 (28) | 12 (37.5) | 0.45 |
| 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 |
| HBV                  | yes | 1 (4) | 1 (3.1) | 0.99 |
| HIV                  | yes | 1 (4) | 0 (0) | 0.44 |
| Cirrhosis            | yes | 5 (20) | 1 (3.1) | 0.07 |
| Genotype             | 1 | 17 (68) | 24 (75) | 0.56 |

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

Table 2. Adverse effects of Hepatitis C patients treated with Ribavirin, Sofosbuvir and Interferon. *Mean± SD **N (%)

Table 3. End of Therapy of Hepatitis C patients treated with Ribavirin, sofosbuvir and interferon.

The therapy. Tests were performed before starting of the treatment including: βhCG levels in woman of childbearing age, creatinine and urease test, 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 1200mg/kg/w) 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 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

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 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 71.9% of patients.
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.

REFERENCES

1. Alavian S-M, Tabatabaei S-V, Mahboobi N. Epidemiology and risk factors of HCV infection among hemodialysis patients in countries of the Eastern Mediterranean Regional Office of WHO (EMRO): a quantitative review of literature. J Public Health. 2011; 19(2): 191-203.
2. Hesamizadeh K, Alavian SM, Najafi Tireh Shabankareh A, Sharafi H. Molecular Tracing of Hepatitis C Virus Genotype 1 Isolates in Iran: A NS5B Phylogenetic Analysis with Systematic Review. Hepat Mon. 2016; 16(12): e2938.
3. Lavanchy D. Evolving epidemiology of hepatitis C virus. Clin Microbiol Infect. 2011; 17(2): 107-115.
4. Organization WH. Guidelines for the screening, care and treatment of persons with hepatitis C infection: World Health Organization, 2014.
5. Kanda T, Nakamoto S, Sasaki R, Nakamura M, Yasui S, Haga Y, et al. Sustained Virologic Response at 24 Weeks after the End of Treatment Is a Better Predictor for Treatment Outcome in Real-World HCV-Infected Patients Treated by HCV NS3/4A Protease Inhibitors with Peginterferon plus Ribavirin. J Med Sci. 2016; 13(4): 310-315.
6. Naggie S, Patel K, McHutchison J. Hepatitis C virus directly acting antivirals: current developments with NS3/4A HCV serine protease inhibitors. J Antimicrob Chemother. 2010; 65(10): 2063-2069.
7. Alter MJ. Epidemiology of hepatitis C. Hepatology. 1997; 26(5).
8. Alter MJ. Hepatitis C virus infection in the United States. J Hepatol. 1999; 31: 88-91.
9. Backmund M, Meyer K, Wachtler M, Eichenlaub D. Hepatitis C virus infection in injection drug users in Bavaria: risk factors for seropositivity. Eur J Epidemiol. 2003; 18(6): 563-568.
10. Crofts N, Nigro L, Oman K, Stevenson E, Sherman J. Metha-
done maintenance and hepatitis C virus infection among injecting drug users. Addiction. 1997; 92(8): 999-1005.
11. Diamantis I, Bassetti S, Erb P, Ladewig D, Gyr K, Battegay M. High prevalence and coinfection rate of hepatitis G and C infections in intravenous drug addicts. J Hepatol. 1997; 26(4): 794-797.
12. Galeazzi B, Tufano A, Barbierato E, Bortolotti F. Hepatitis C virus infection in Italian intravenous drug users: epidemiological and clinical aspects. Liver. 1995; 15(4): 209-212.
13. Grassi A, Ballardini G. Hepatitis C infection in injection drug users: It is time to treat. World J Gastroenterol. 2017; 23(20): 3569-3571.
14. Lorvick J, Kral AH, Seal K, Goe L, Edlin BR. Prevalence and duration of hepatitis C among injection drug users in San Francisco, Calif. Am J Public Health. 2001; 91(1): 46-47.
15. Lynch SM, Wu GY. Hepatitis C Virus: A Review of Treatment Guidelines, Cost-effectiveness, and Access to Therapy. J Clin Transl Hepatol. 2016; 4(4): 310-319.
16. Kanda T, Imazeki F, Yokosuka O. New antiviral therapies for chronic hepatitis C. Hepatol Int. 2010; 4(3): 548-561.
17. George SL, Bacon BR, Brunt EM, Mihindukulasuriya KL, Hoffmann J, Di Bisceglie AM. Clinical, virologic, histologic, and biochemical outcomes after successful HCV therapy: a 5-year follow-up of 150 patients. Hepatology. 2009; 49(3): 729-738.
18. Ueno Y, Sollano JD, Farrell GC. Prevention of hepatocellular carcinoma complicating chronic hepatitis C. J Gastroenterol Hepatol. 2009; 24(4): 531-536.
19. Omata M, Kanda T, Yu ML, Yokosuka O, Lim SG, Jafari W, et al. APASL consensus statements and management algorithms for hepatitis C virus infection. Hepatol Int. 2012; 6(2): 409-435.
20. Dolutemeh F, Karimi-Sari H, Rezaee-Zavareh MS, Alavian SM, Behnava B, Gholami-Fesharaki M, et al. Combination of sofosbuvir, pegylated-interferon and ribavirin for treatment of hepatitis C virus genotype 1 infection: a systematic review and meta-analysis. Daru. 2017; 25(1): 11.
21. European Association for Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2015. J Hepatol. 2015; 63(1): 199-236.
22. Aspinall EJ, Corson S, Doyle JS, Grebely J, Hutchinson SJ, Dore GJ, et al. Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis. Clin Infect Dis. 2013; 57 Suppl 2: S80-89.
23. Midgard H, Weir A, Palmateer N, Lo Re V, 3rd, Pineda JA, Macias J, et al. HCV epidemiology in high-risk groups and the risk of reinfection. J Hepatol. 2016; 65(1 Suppl): S33-45.
24. Robaeys G, Christensen S, Lucidarme D, Arain A, Bruggmann P, Kunkel J, et al. Chronic Hepatitis C Treatment in Patients with Drug Injection History: Findings of the INTEGRATE Prospective, Observational Study. Infect Dis Ther. 2017; 6(2): 265-275.
25. Lainini S, Easterbrook PJ, Zumbal A, IPPolito G. Hepatitis C: global epidemiology and strategies for control. Clin Microbiol Infect. 2016; 22(10): 833-838.
26. Gigi E, Sinakos E, Lalla T, Vrettou E, Orphanou E, Raptopolou M. Treatment of intravenous drug users with chronic hepatitis C: treatment response, compliance and side effects. Hip-