ORIGINAL ARTICLE

Effectiveness of multidisciplinary approach in patients undergoing therapy for chronic hepatitis C

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Abstract

Objective: To assess the effect of a multidisciplinary approach on the outcome of treatment for hepatitis C virus infection.

Methods: This retrospective study was conducted at the gastroenterology division by primary care providers at Phoenix VA Healthcare system in Phoenix, Arizona, United States, and comprised clinical and laboratory data of all hepatitis C patients treated between November 2002 and December 2006. The patients were clinically evaluated to determine whether they were candidates for treatment with pegylated interferon α-2a or α-2b plus ribavirin. Patients were given detailed orientation prior to the therapy, and were closely monitored during the treatment.

Results: Of the 295 patients, 179(60.7%) received pegylated interferon α-2b and ribavirin and 116(39.3%) received pegylated interferon α-2a and ribavirin. Overall, 202(68.47%) had genotype 1 and 93 (31.52%) had non-genotype 1. Age range was 35 to 66 years (mean 51±8.51 and Mean BMI was 28.2±4.22), and the majority was Caucasian males who served in the Vietnam era. The overall sustained virological response was 120(40.7%).

Conclusion: High sustained virological response was achieved among the participants.

Keywords: Hepatitis C, Treatment outcome, Physician extender, Nurse practitioner. (JPMA 67: 1487; 2017)

Introduction

Hepatitis C virus (HCV) is estimated to chronically infect over 3 million people in the United States (US), causing a spectrum of liver diseases ranging from an asymptomatic carrier state to end-stage liver disease.[1,2] However, the prevalence of chronic infection has been estimated to be higher in the US veteran (VA) population, with numbers ranging from 5.4% to 34% depending on the region.[3,4] The reported overall sustained virological response (SVR) with treatment using a combination of pegylated interferon (PEG-IFN) and ribavirin ranges from 42% to 46% for genotype 1 and 77% to 86% for non-genotype 1 virus.[5,6] Such treatment success rates, however, are the result of highly controlled and selected patients within the frame of multicentre studies in both North America and Europe. Unfortunately, the reported SVR for chronic HCV infection in the veteran population has been disappointing with an SVR of16-28%.[7-9] The reasons for this poor response to treatment in the VA population is unknown, but it is believed to be associated with predictors of poor response such as advanced age, associated medical co-morbidities, underlying psychiatric illnesses, poverty and concomitant compliance issues, and alcohol or drug abuse.[7,10,11] In addition, the treatment discontinuation rate in this population has been reported as high as 26.6%.[12]

The current study was planned to assess the effect of a multidisciplinary approach on the outcome of treatment for HCV infection.

Patients and Methods

This retrospective study was conducted at the gastroenterology division by primary care providers at Phoenix VA Healthcare system in Phoenix, Arizona, US, and comprised clinical and laboratory data of all chronic HCV patients treated between November 2002 and December 2006. The patients were clinically evaluated to determine whether they were candidates for treatment with pegylated interferon α-2a (PEG-2a) or α-2b (PEG-2b) plus ribavirin (Riba). All patients also underwent baseline retinal examination, hearing test and psychiatric evaluation. Liver biopsies were performed according to physician's preference based on HCV genotype, patient's acceptance and likelihood of advanced disease. Liver biopsies were classified according to the Metavir score for fibrosis.[13] Approval was obtained from the institutional review board(IRB).

In an effort to improve treatment compliance, the services of two nurse practitioners were used who were experienced in educating patients regarding treatment and side effects and maintained a close follow-up with

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them through office visits and over the phone (by a dedicated phone line) during the entire treatment phase. All patients were followed up for at least 1 year after completion of therapy. All patients were treated by a multidisciplinary team available to patients round the clock over the phone for any questions or concerns. Patients also had follow-ups in outpatient departments (OPDs) every 4 to 6 weeks to see the health provider. Treatment was only started after a comprehensive education session by an experienced, certified nurse practitioner (who had more than 5 years of experience in providing such education, and monitoring HCV therapy).

Descriptive statistics and frequency were noted. Sustained viral response groups were compared by Student's t-test by comparing means. $P<0.05$ was considered statistically significant.

Results

Of the 295 patients, 179(60.7%) received PEG-2b and ribavirin and 116(39.3%) patients received PEG-2a and ribavirin. Age range was 35 to 66 years (mean 51±8.51) and Mean BMI was 28.2±4.22. Overall, 202(68.47%) patients had genotype 1 and 93(31.52%) had non-genotype 1; the ratio of patients with genotype 1 receiving PEG-2b: PEG-2a was 2:1. Moreover, 68(23%) patients [36(20.1%) patients in PEG-2b group and 32(27.6%) patients in PEG-2a group] had a low viral load (< 600,000 IU/mL), and 227(76.9%) patients [143(48.5%) patients in PEG-2b group and 84(28.5%) patients in PEG-2a group] had a high viral load > 600,000 IU/ml). The mean BMI was 28.2±4.22 kg/m^2 (28.4 for those receiving PEG-IFN 2b and 27.9 for those receiving PEG-IFN 2a). The proportion of patients with BMI < 30 and > 30 was similar for both groups (Table-1).

Table-1: Patient's characteristics.

	PEG-2b+ Riba	PEG-2a+ Riba	Total
N	122	77	199
Mean Age (years)	50.8	51.5	51±8.5
Race (%)			
-Caucasian	96	71	167 (83.9%)
-African American	8	0	8
-Hispanic	17	4	21
-Other	1	2	3
Gender M/F (n)	119/3	73/4	192/7
Service (n)			
-Vietnam era	87	50	137
-Pre-Vietnam	1	3	4
-Post-Vietnam	25	21	46
-Persian Gulf	8	2	10
BMI (mean)	28.4	27.9	28.2
<30 (n, %)	75 (63%)	52 (67.5%)	127 (64.8%)
≥30 (n, %)	44 (37%)	25 (32.5%)	69 (35.2%)
Genotypes (n)			
-1	99	43	142 (71.4%)
-Non-1	23	34	57 (28.6%)
-2	12	22	34 (17.1%)
-3	10	12	22 (11.1%)
-4	1	—	1
Viral load (IU/mL)			
-Low (< 600,000)	40/114 (35.1%)	32/68 (47.1%)	72/182 (39.6%)
-High (> 600,000)	74/114 (64.9%)	36/68 (52/9%)	110/182 (60.4%)
Histology [Metavir] (n)	(n=77)	(n=40)	(n=117)
-Mean grade	2.2±0.23	2.2±0.20	2.18
-Mean stage	2.3±0.14	2.0±0.12	2.35
Mean drug dose			
-PEG IFN (ug weekly)	134.4±11.63	180±N/A	N/A
-Ribavarin (mg daily)	1145.8±19.93	1012.9±13.78	

PEG-IFN: Pegylatedinterferon.
M/F: Male/Female.
BMI: Body mass index.

The overall SVR was 120(40.7%), with 66(36.9%) patients in the PEG-2b group and 54(46.6%) in the PEG=2a group (Figure). The overall SVR was significantly higher, i.e. 66(70.9%), for non-genotype 1 than genotype 1 54(26.7%) ($p<0.000001$). This difference between genotypes was maintained with the two types of pegylated interferons [31(72.1%) vs. 35(25.7%) for PEG-2b and 35(70%) vs. 19(26.7%) for PEG-2a]. Overall, there were no significant differences in the SVR between the two pegylated interferon formulations in regards to genotype 1 [36(25.7%) for PEG-2b; 19(28.8%) for PEG-2a] and non-genotype 1 [31(72.1%) for PEG-2b; 35(70%) for PEG-2a].

There was a trend for a higher SVR in patients with BMI < 30 (SVR 58(43.9%) vs. 26(29.9%) ($p=0.06$) in patients with BMI > 30). However, this difference was not seen in those patients treated with PEG-2b [25(33.8%) in patients with BMI < 30 vs. 15(30%) in patients with BMI > 30]. For those treated with PEG-2a who had a BMI < 30, the SVR was significantly higher, i.e. 33(56.9%), than those with BMI > 30, i.e.11(29.7%) ($p= 0.01$). The differences in the SVR for patients with BMI < 30 treated with PEG-2b, 25(33.8%), and PEG-2a, 33(56.9%), were statistically significant ($p=0.008$). The differences in the SVR for patients with BMI > 30 treated with PEG-2b, 15(30%), and PEG-2a, 11(29.7%), were not statistically significant.

Of those with BMI < 30, there was no difference in the SVR for genotype 1 or non-genotype 1 when treated with either PEG formation. Likewise, there was no difference in the SVR rate of those with BMI > 30 and genotype 1 when treated with either PEG type. However, for those with BMI > 30 and non-genotype 1, the SVR was significantly better for those treated with PEG-2b, 11(78.6%), than those treated with PEG-2a, 4(30.8%), ($p=0.02$).

Table-2: Overall SVR and subgroup analysis of SVR per ethnicity, genotype, BMI < or > 30, fibrosis staging, and viral load. All matched superscripts are statistically significant to a p-value of 0.05 or less. Non-response and discontinuation rate.

	PEG-2b + Riba	PEG-2a + Riba	Overall	P value
N	122	77	199	
SVR	36.9% (45)	46.8% (36)	40.7 % (81)	P= n.s
African American (AA)	35.9% (41/114)	--------	40.3% (77/191)	
SVR by Genotype				P< 0.000001
Genotype 1	28.8% (28)*	32.5% (14)*	29.5% (42)*	
African American (AA)	27.9% (26/93)	-----	30.9% (42/136)	
Non-genotype 1	73.8% (17)*	64.7% (22)*	68.4% (39)*	
African American (AA)	71.5% (17/21)	-----	70.9% (39/55)	
SVR by BMI (%)				
BMI < 30	37.3%b (28)	57.7%ab (30)	45.7% (58)	P = 0.008
African American (AA)	40% (28/70)	-----	47.5% (58/122)	
BMI > 30	34.1%(15)	28%a (7)	31.9% (22)	P = n.s
African American (AA)	35.7% (15/42)	-----	32.8% (22/67)	
SVR by Staging (%) [number of biopsies]	N=77	N=40		P = n.s
Stage 1, 2	32.7% (17/52)	46.2% (12/26)	37.2% (29/78)	
Stage 3, 4	40% (10/25)	57.1% (8/14)	46.2% (18/39)	
Overall SVR by viral load (%)				P = n.s
Low load (< 600,000 IU/mL)	57.5% (23/40)c	53.1% (17/32)	55.6% (40/72)c	
African American (AA)	54.1% (20/37)	-----	52.9% (46/87)	
High load (> 600,000 IU/mL)	24.3% (18/74)	38.9% (14/36)	29.1% (32/110)c	
African American (AA)	18.8% (13/69)c	-------	25.9% (27/105)	
SVR by viral load and genotype (%)				
Low viral load (<600,000 IU/mL)				
Genotype-1	50% (15/30)ym	33.3% (5/15)	44.4% (20/45)*n	P = 0.057ym
African American (AA)	46.4% (13/28)	------	41.9% (18/43)	P = 0.7n
Non Genotype-1	80% (8/10)y	70.6% (12/17)	74.1% (20/27)*	P = 0.2wy
African American (AA)	77.8% (7/9)	------	73.1% (19/26)	
High viral load (>600,000 IU/mL)				
Genotype-1	17.5% (11/63)wm	30.4% (7/23)	20.9% (18/86)zn	
African American (AA)	11.9% (7/59)	------	17.1% (14/82)	
Non Genotype-1	63.6% (7/11)w	53.8% (7/13)	58.3% (14/24)z	
African American (AA)	60% (6/10)	------	56.5% (13/23)	
Non-Response n (%)	40 (31.9%)	20 (25.9%)	60 (30.1%)	
Genotype-1	37 (37.4%)	16 (37.2%)	53 (37.3%)	
Non genotype-1	3 (13%)	4 (11.7%)	7 (12.3%)	
Stopped Rx due to side effects n (%)	27 (22.1%)	14 (18.2%)	41 (20.6%)	
Genotype-1	24 (24.2%)	9 (20.9%)	33 (23.2%)	
Non genotype-1	3 (13%)	5 (14.7%)	8 (14%)	
Stopped Rx due to other reasons n (%)	10 (8.2%)	7 (9.1%)	7 (8.5%)	
Genotype-1	10 (10.1%)	4 (9.3%)	4 (9.9%)	
Non genotype-1	0 (0%)	3 (8.8%)	3 (5.3%)	

SVR: Sustained virological response.
PEG-IFN: Pegylatedinterferon.
M/F: Male/Female.
BMI: Body mass index.

Overall, 30(36.1%) patients with fibrosis stage 1 and/or 2 had an SVR and this was not significantly different from those with stage 3 and/or 4, i.e. 18(38.3%). The SVR for genotype 1 and stage 1 and/or 2, 8(18.7%), was similar to stage 3 and/or 4, 5(20.8%), when using PEG-2b and similar to the SVR noted when using PEG-2a (8(38.1%) and 5(35.7%), respectively). Likewise, SVR for non-genotype 1 and stage 1 and/or 2 [(6(85.7%)] was similar to stages 3 and/or 4 [(4(80%)] when using PEG-2b and similar to the SVR found when using PEG-2a (8(66.7%) and 4(100%), respectively). The SVRs for genotype 1 were significantly lower than those for non-genotype 1 irrespective of the

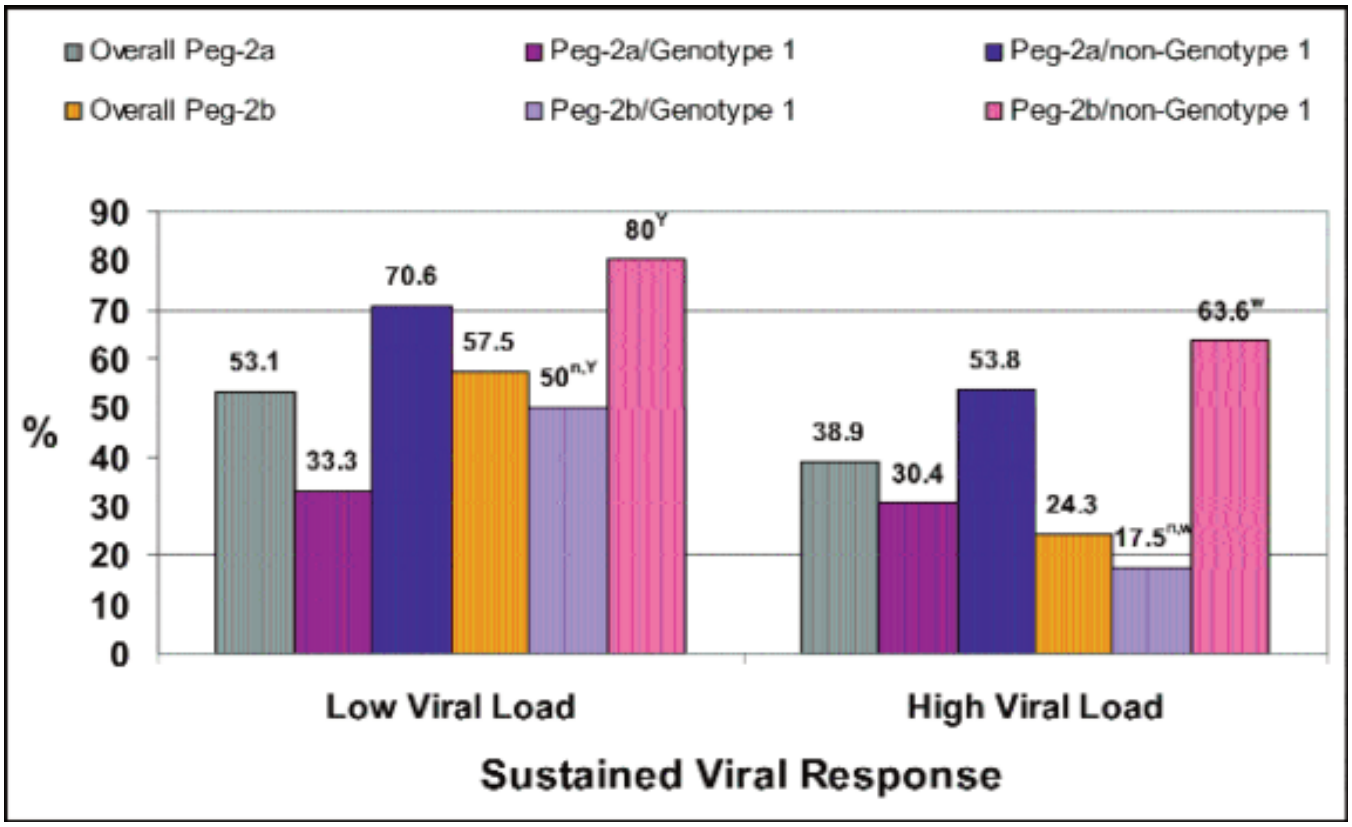

Figure: Sustained virological response (SVR).

stage and the PEG formulation used.

The overall SVR for patients with low viral load (< 500,000 IU/ml) was 37(54.4%) vs. 83(36.6%) for high viral load (> 500,000 IU/ml). The SVR in low viral load group was similar for both pegylated interferon formulations, i.e. PEG-2b 20(55.6%) and PEG-2a 17(53.1%). The SVR in high viral load group was 46(32.2%) for PEG-2b group and 37(44%) for PEG-2a group. The SVR for patients with low viral load treated with PEG-2b was higher [20(55.6%)] than those with high viral load [46(32.2%)]. The SVR for patients with low viral load treated with PEG-2a was similar [17(53.1%)] to those with high viral load [37(54.4%)].

There were no significant differences between SVR for non-genotype 1 with low viral load [16(80%)] and those with high viral load [31(64.6%)] (p= 0.2). The SVR for genotype 1 with low and high viral loads treated with PEG-2b were 7(38.9%) and 14(17.3%), respectively (p=0.057). The SVR for those genotype 1 with low and high viral loads treated with PEG-2a were 5(35.7%) and 12(30%), respectively (p=0.7). There were no significant differences between the two pegylated formulations and SVR regarding low and high viral loads for both genotype 1 and non-genotype 1.

Erythropoietin-α was used in 32(25.2%) patients of those receiving PEG-2b and in 25(26.3%) of those receiving PEG-2a. The use of erythropoeitic growth factor increased the proportion of patients achieving SVR in patients treated with PEG-2b (p=0.03) but not PEG-2a. The difference in the PEG-2b treated group was seen only for genotype 1 infected patients but not in non-genotype 1 (p=0.03). A total of 25(11.3%) patients (19(6%) in the PEG-2b group and 6(24%) in the PEG-2a group required granulocyte colony stimulating factor.

Moreover, 143(48.6%) patients were taking antidepressants that were either started before or during the treatment. Two-thirds of the patients were on a single agent selective serotonin reuptake inhibitors (SSRI's).

Treatment was stopped prematurely due to side effects in 51(17.3%) patients (34(19%) for those treated with PEG-2b and 17(14.7%) in those treated with PEG-2a. The discontinuation rate was 41(20.3%) for those with genotype 1, and 10(10.8%) for those with non-1 genotype. Also, 30(10.2%) patients stopped treatment for reasons other than side effects (work-related issues,

financial issues, incarceration, etc). Three patients stopped treatment due to decompensation of liver disease. There were no differences in terms of side effects between the 2 pegylated interferon formulations. The most common reasons for early discontinuation of treatment due to side effects were ophthalmologic complications (either visual symptoms or abnormal fundoscopic examination), followed by psychiatric disorders (Table-2).

Discussion

The overall prevalence of chronic HCV infection in the US veteran population is far higher (ranging from 5.4% to 34% depending on the US region[3,4] and as high as 44% in the homeless[14]] than the reported 1.8% in the general population.[2,3,4,14] It is also associated with an SVR to treatment of 28%, which is clearly lower than the reported 54% to 56% in the non-VA population.[5,6] The treatment in this population is not only challenging because of the high prevalence of significant co-morbidities, psychiatric conditions, alcohol and drug use, but also because of the high rate (26%) of discontinuation of therapy.[9,11,14,15] In addition, a very important factor is the patient's unwillingness to receive treatment.[9,16] A multi-centre prospective study found that among those patients who are eligible for HCV treatment, 23.8% declined therapy for a variety of non-medical reasons.[9]

In this study, the overall SVR was 38.3% with the use of combination pegylated interferon and ribavirin. In addition, akin to previous reports in the non-veteran population, the SVR was far better in patients infected with non-genotype 1 virus (69% vs. 25%) and in those with low viral loads (54% vs. 34%).We also observed a trend for a better overall SVR in patients with a BMI < 30 compared to those with a BMI $\geq$ 30 (44% vs. 30%, respectively). In contrast to what has been reported in the general non-veteran population, patients with advanced fibrosis (Metavir stage 3 or 4) had similar SVR than those with a lesser degree of fibrosis (Metavir stage 1 or 2) on liver biopsy (38% vs. 36%). The reasons for this finding are uncertain but could be related to higher commitment to treatment given the advanced stage of disease. Another possibility is that of concomitant alcohol/drug use in those patients with lesser degrees of fibrosis, a factor known to ameliorate treatment response.

To start, we found that SVR was significantly better for those patients treated with PEG-2a (46%) compared to PEG-2b (32%). This overall difference, however, may have been confounded by the fact that more patients with genotype 1 (inherently known to have a lower SVR) were present in the group treated with PEG-2b. PEG-2a-treated patients with a BMI < 30 had a significantly better SVR (57%) than patients with a BMI < 30 treated with PEG-2b (34%). For those with BMI > 30, the SVRs for both PEG formulations were the same (30%). In addition, we found a significant difference in SVR among patients with BMI < 30 and $\geq$ 30 treated with PEG-2a but not in those treated with PEG-2b. The latter finding might relate to the fact that PEG-2b dosing is weight based and less likely to fluctuate. As for viral load and SVR among pegylated interferons, we found a significant difference in those with high viral load treated with PEG-2b but not PEG-2a. The difference in SVR when considering the viral load and genotype was seen only in genotype 1 patients treated with PEG-2b but not PEG-2a.

Finally, our overall discontinuation of treatment rate was close to previous reports. However, when considering only those patients that discontinued treatment due to medical reasons, our discontinuation rate was 20.6%, lower than previously reported. Interestingly, the main reason for discontinuation was ophthalmologic complications (4%) followed by psychiatric issues (3%) and intolerance (1.5%). Other reasons included infections, concerns for coronary artery disease (CAD), allergic reactions, and acute renal failure.

The frequently quoted overall SVR of 54% to 56% from the two landmark studies for the treatment of chronic HCV infection with pegylated interferon and ribavirin were obtained in highly selected populations with stringent inclusion/exclusion criteria and intense strict supervision by research personnel.[5,6] These results may not be reproducible and/or applicable to the general or US veteran populations and in our opinion, besides carefully selected patients, it seems to indicate that the role of a research study nurse dedicated exclusively to monitoring treatment was crucial for the successful management and completion of such studies. Therefore, the implementation of a similar approach (a full-time nurse practitioner or physician assistant dedicated to the management of chronic HCV infection with close follow-up) in the clinical practice might increase the treatment outcomes. Gujral et al. had outlined a role of physician assistants and nurse practitioners in their report in 2004.[17] In a recently published report, treatment prescribed by nurse practitioners was as likely to result in SVR as treatment prescribed by doctors of medicine (MDs), even after accounting for patient differences (51% vs. 47%, respectively, p=0.27) without affecting treatment discontinuation rate and haematologic side effects. Authors proposed that engaging more nurse practitioners as HCV treatment providers may allow wider access to HCV treatment.[18] Two other studies have shown increased adherence to treatment for HCV[19] and HIV,[20]

respectively, with the use of multidisciplinary care team.

One of the limitations of our study was that the participants comprised mostly males.

Conclusion

High SVR was achieved in US veterans using PEG-INF (α-2b or α-2a) with ribavirin. We believe that such a high response rate is the result of a multidisciplinary approach and close monitoring by highly trained certified nurse practitioners.

Limitations

Study includes mostly male gender.

Study was performed in an academic setting and replicating this in a private or smaller setting could be a limitation due to scarce resources.

Reason for delayed publication: Presentation of data was delayed due to unavailability of research assistant, however this does not affect the validity of the study. This article was not previously presented or published in any journal, nor under consideration for publication.

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References

References

1. Razavi H, Elkhoury AC, Elbasha E, Estes C, Pasini K, Poynard T, et al.Chronic hepatitis C virus (HCV) disease burden and cost in the United States. Hepatology 2013; 57: 2164-70
2. Ditah I, Ditah F, Devaki P, Ewelukwa O, Ditah C, Njei B, et al.The changing epidemiology of hepatitis C virus infection in the United States: National Health and Nutrition Examination Survey 2001 through 2010. J Hepatol 2014; 60: 691-8.
3. Backus LI, Belperio PS, Loomis TP, Yip GH, Mole LA. Hepatitis C virus screening and prevalence among US veterans in Department of Veterans Affairs care. JAMA Intern Med 2013; 173: 1549-52.
4. Backus LI, Belperio PS, Loomis TP, Mole LA. Impact of race/ethnicity and gender on HCV screening and prevalence among U.S. veterans in Department of Veterans Affairs Care. Am J Public Health 2014; 104: 555-61.
5. Ma P, Yang JM, Hou W, Song SD, Wang L, Lu W. A preliminary study on the efficacy and influencing factors of interferon for the treatment of genotype 1 chronic hepatitis C with different dosage forms. Eur J Gastroenterol Hepatol 2013; 25: 601-5.
6. Zhao S, Liu E, Chen P, Cheng D, Lu S, Yu Q, et al.A comparison of peginterferon ?-2a and ?-2b for treatment-naive patients with chronic hepatitis C virus: A meta-analysis of randomized trials. Clin Ther 2010; 32: 1565-77.
7. Nguyen HA, Miller AI, Dieperink E, Willenbring ML, Tetrick LL, Durfee JM, et.al. Spectrum of disease in U.S. veteran patients with hepatitis C. Am J Gastroenterol 2002; 97: 1813-20.
8. Jensen DM, Cotler SJ, Lam H, Harb G, Shillington A. A comparison of hepatitis C treatment and outcomes at academic, private and Veterans' Affairs treatment centres. Aliment Pharmacol Ther 2004; 19: 69-77.
9. Bini EJ, Brau N, Currie S, Shen H, Anand BS, Hu KQ, et.al. Prospective multicenter study of eligibility for antiviral therapy among 4,084 U.S. veterans with chronic hepatitis C virus infection. Am J Gastroenterol 2005; 100: 1772-9.
10. Gish RG, Afdhal NH, Dieterich DT, Reddy KR. Management of hepatitis C virus in special populations: patient and treatment considerations. Clin Gastroenterol Hepatol 2005; 3: 311-8.
11. Nelson RE, Hoop R, Korner E, DuVall S, Hayden CL, Knippenberg K, et al. Predicting Discontinuation of Pegylated Interferon as a Result of Lack of Efficacy in United States Veterans With Chronic Hepatitis C on Dual Therapy.Ann Pharmacother 2014; 48: 826-36.
12. Getachew Y, Browning JD, Prebis M, Rogers T, Brown GR. Combination therapy for the treatment of hepatitis C in the veteran population: higher than expected rates of therapy discontinuation. Aliment Pharmacol Ther 2004; 20: 629-36.
13. Bedossa P, Poynard T. An algorithm for the grading of activity in chronic hepatitis C. The METAVIR Cooperative Study Group. Hepatology 1996; 24: 289-93.
14. Desai RA, Rosenheck RA, Agnello V. Prevalence of Hepatitis C virus infection in a sample of homeless veterans. Soc Psychiatry Psychiatr Epidemiol 2003; 38: 396-401.
15. Mendenhall CL, Moritz T, Rouster S, Roselle G, Polito A, Quan S, et al. Epidemiology of hepatitis C among veterans with alcoholic liver disease. The VA Cooperative Study Group 275. Am J Gastroenterol 1993; 88: 1022-6.
16. Muir AJ, Provenzale D. A descriptive evaluation of eligibility for therapy among veterans with chronic hepatitis C virus infection. J Clin Gastroenterol 2002; 34: 268-71.
17. Gujral H, Viscomi C, Collantes R. The role of physician extenders in managing patients with chronic hepatitis C. Cleve Clin J Med 2004; 71: S33-7.
18. Backus LI, Belperio PS, Shahoumian TA, Mole LA. Impact of Provider Type on Hepatitis C Outcomes With Boceprevir-based and Telaprevir-based Regimens. J Clin Gastroenterol 2015 Apr; 49: 329-35
19. Rodis JL, and Kibbe P: Evaluation of medication adherence and quality of life in patients with hepatitis C virus receiving combination therapy. Gastroenterol Nurs 2010; 33: 368-373.
20. Horberg MA, Hurley LB, Towner WJ, Allerton MW, Tang BT, Catz SL, et al.Determination of optimized multidisciplinary care team for maximal antiretroviral therapy adherence. J Acquir Immune Defic Syndr 2012; 60: 183-90.