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ORIGINAL ARTICLE

Prospective Study

Interferon-λ polymorphisms and response to pegylated interferon in Iranian hepatitis C patients

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Informed consent statement: Informed consent was obtained from all patients participating in the study.

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Abstract

AIM: To evaluate the efficacy of pegylated interferon in Iranian chronic hepatitis C patients in relation to interferon-λ (IFNL) polymorphisms.

METHODS: This study enrolled patients with chronic hepatitis C referred to the Tehran Blood Transfusion Hepatitis Clinic in 2011. Patients were included in the study if they had no concomitant hepatic illness, were negative for human immunodeficiency virus antibodies, and had no prior history of treatment with any type of

pegylated interferon. Patients were treated with 180 μg pegylated interferon alpha-2a (Pegaferon®) weekly and 800-1200 mg ribavirin daily for 24 or 48 wk depending on weight and hepatitis C virus (HCV) genotype. Blood samples were collected from patients to obtain DNA for determination of *IFNL* rs12979860 and rs8099917 polymorphisms. The virologic response in patients was then evaluated and compared between the different *IFNL* genotypes.

RESULTS: A total of 152 patients with a mean age of 41.9 ± 10.0 years were included in the study, of which 141/152 were men (92.8%). The most frequent HCV genotype was type-1, infecting 93/152 (61.2%) patients. Sustained virologic response (SVR) was achieved in 81.9% of patients with HCV genotype-1 and 91.1% of patients with HCV genotype-3. Treatment success was achieved in 91.2% (52/57) of patients with the *IFNL* rs12979860 CC genotype and 82.1% (78/95) in those with other genotypes. Similar treatment response rates were also observed in patients with rs8099917 TT (39/45; 86.7%) and non-TT (61/68; 89.7%) genotypes. Univariate analyses identified the following factors which influenced treatment response for inclusion in a multivariate analysis: age, HCV RNA level, stage of liver fibrosis, rs12979860 CC genotype, and aspartate transaminase level. A logistic regression analysis revealed that only the rs12979860 CC genotype was significantly associated with achievement of SVR (OR = 6.2; 95%CI: 1.2-31.9; P = 0.03).

CONCLUSION: The rs12979860 CC genotype was associated with SVR in patients receiving pegylated interferon plus ribavirin, however, the SVR rate in other rs12979860 genotypes was also relatively high.

Key words: Chronic hepatitis C; Pegylated interferon; rs12979860; rs8099917; Sustained virologic response

Core tip: Chronic hepatitis C-infected Iranian patients treated with pegylated interferon and ribavirin showed relatively high rates of sustained virologic response. Treatment success was not influenced by hepatitis C virus genotype. However, a comparison of treatment success related to *IFNL* polymorphisms (also known as *IL28B* polymorphisms) using a logistic regression analysis revealed that the interferon-λ rs12979860 CC genotype was significantly associated with achieving a sustained virologic response.

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INTRODUCTION

Chronic infection with the hepatitis C virus (HCV) is a serious condition that can lead to cirrhosis or hepatocellular carcinoma. An estimated 150 million people worldwide are chronically infected with HCV, which is responsible for 350000 liver-related deaths annually[1]. In Iran, the prevalence of chronic HCV infection is approximately 0.5%[2]. With the advent of new potent drugs such as direct acting oral agents, recommendations for chronic hepatitis C treatment in adults is rapidly changing. Although these new agents are more effective and have fewer side effects they are offered at very high prices, making pegylated interferon (Peg-IFN) plus ribavirin the only affordable treatment option for a large group of patients, especially those in developing countries[3]. Until recently the Peg-IFN regimen was the mainstay of chronic hepatitis C treatment, and resulted in a sustained virologic response (SVR) in 33%-80% of patients[4,5]. However, data regarding the response rate of Iranian patients to Peg-IFN is limited, with the reported success rates ranging from 50%[6] to 61%[7]; although these studies were not restricted to the evaluation of treatment-naïve patients.

Treatment outcome can be affected by various factors, including single nucleotide polymorphisms (SNPs) of interferon-λ (*IFNL*) (located near the *IL28B* gene and thus also known as *IL28B* polymorphisms) such as rs12979860 and rs8099917[8]. These SNPs are also associated with spontaneous clearance of HCV[9,10]. Studies have shown that rs12979860 "CC" and rs8099917 "TT" genotypes are significantly associated with preferred treatment outcome[11,12]. Thus, to further investigate the role of these SNPs, the success of Peg-IFN-alpha-2a plus ribavirin treatment in Iranian patients with chronic HCV infection was evaluated with respect to host genetics and HCV genotypes.

MATERIALS AND METHODS

Study population

Adult patients with chronic HCV infection (defined as the presence of HCV RNA in serum for > 6 mo) referred to the Tehran Blood Transfusion Hepatitis Clinic between March 2011 and August 2013 were enrolled in the study. Patients with no concomitant hepatic illness, negative results for human immunodeficiency virus antibody and hepatitis B surface antigen, and no history of prior antiviral therapy for HCV infection were included in the study. A majority of the patients underwent percutaneous liver biopsy, for which specimens were evaluated according to the modified Knodell score grading and staging system by Ishak *et al*[13].

Treatment regimen

Patients received weekly subcutaneous injections of Peg-IFN-alpha-2a (180 μg/mL Pegaferon®; Pooyesh Darou, Tehran, Iran) and daily oral ribavirin (Ribabiovir®;

Bakhtar Bioshimi, Kermanshah, Iran): 800 mg for HCV genotype-3 and 1000-1200 mg according to the patient's weight (< or ⩾ 75 kg) for HCV genotype-1.

Treatment duration was 24 wk for those infected with HCV genotype-3, or 48 wk for infection with HCV genotype-1, but could be shortened or extended depending on the patient's response and compliance.

The patients were closely monitored throughout the treatment course, with monthly complete blood cell count and liver enzyme tests, and HCV RNA level assessment before treatment, at weeks 4, 12, 24, at the end of treatment, and 24 wk after treatment completion. Informed consent was obtained from all participating patients. The study conformed to the ethical guidelines of the 1975 Declaration of Helsinki, and was approved by the Ethics Committee of the Iranian Blood Transfusion Organization.

Laboratory assessments

Quantitative assessment of HCV RNA was performed using the COBAS TaqMan HCV Test v2.0 (Roche Diagnostics, Basel, Switzerland) according to the manufacturer's instructions and a detection limit of 10 IU/mL. HCV genotyping was performed using HCV genotype-specific primers[14].

The *IFNL* SNPs were assessed using the PCR-restriction fragment length polymorphism method[15]. Briefly, genomic DNA was extracted from patients' peripheral blood using the QIAamp DNA Blood Mini Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions. The PCR was performed using Accupower PCR PreMix (Bioneer Corp., Daejeon, South Korea) with the following conditions: 94 ℃ for 5 min, 35 cycles of 94 ℃ for 20 s, 66 ℃ for 20 s, and 72 ℃ for 20 s, followed by 72 ℃ for 5 min. Primers used for the reaction included: rs12979860, 5'-GCGGAAGGAGCAGTTGCGCT-3' and 5'-GGGGCTTTGCTGGGGGAGTG-3'; or rs8099917, 5'-CCCACTTCTGGAACAAATCGTCCC-3' and 5'-TCTCCTCCCCAAGTCAGGCAACC-3'. The PCR amplicons were then digested for ⩾ 1 h with 10 U of restriction endonuclease: *Bst*UI for rs12979860 or *Bsr*DI for rs8099917 (Fermentas of Thermo Fisher Scientific, Waltham, MA, United States). The digested PCR products were separated on 3% agarose gels revealing the following sized fragments: rs12979860, 196 and 45 bp for the CC genotype, 241, 196, and 45 bp for the CT genotype, or 241 bp for the TT genotype; rs8099917, 552 bp for the TT genotype, 552, 322 and 230 bp for the GT genotype, and 322 and 230 bp for the GG genotype.

Assessment of treatment response

Therapeutic responses were categorized as: rapid virologic response (RVR; HCV RNA undetectable after 4 wk of treatment), early virologic response (EVR; HCV RNA undetectable or ⩾ 2 log decreased at 12th wk of treatment), or sustained virologic response (SVR; HCV RNA undetectable at 6 mo after the end of treatment). Achievement of SVR was considered as treatment success, and thus used to describe patients as responders or non-responders. HCV breakthrough was used to describe cases where HCV RNA was detected during treatment after a previous period where it was undetectable, and resistant infections were cases where HCV RNA was detectable at all times. If HCV RNA was undetectable at the end of therapy, but then detected 6 mo later, this was considered a relapse[16].

Statistical analysis

Statistical analyses were performed using SPSS v16.0 software (SPSS Inc., Chicago, IL, United States). The association of each nominal variable with SVR achievement was evaluated with cross tabulation and χ^2 testing. Independent sample Student's *t* tests were used for continuous variables with a normal distribution, otherwise the Mann-Whitney *U* test was used. All baseline variables that had a $P < 0.2$ in univariate tests were entered into a logistic regression model, and $P < 0.05$ was considered statistically significant. The statistical methods used in this study were reviewed by Maryam Sharafkhah, MS, of the Biostatistics in Digestive Diseases Research Institute.

RESULTS

Patient characteristics

A total of 152 patients (141 men and 11 women; mean age 41.9 ± 10.0 years) with chronic HCV infection were included in this study. The mean HCV RNA level was 3920258 ± 6856760 IU/mL (interquartile range: 4420288 IU/mL). A larger proportion of patients (93/152; 61.2%) were infected with HCV genotype-1 (1a: *n* = 86; 1b: *n* = 7), and the remaining patients were infected with HCV genotype-3a (*n* = 56), a mixed genotype-1a/3a (*n* = 2), or mixed genotype-1a/4 (*n* = 1).

The frequencies of *IFNL* rs12979860 CC, CT, and TT genotypes were 37.5%, 47.3%, and 13.2%, respectively, and were 60.2%, 37.2%, and 2.7% for rs8099917 TT, GT, and GG genotypes, respectively. There were no significant differences in rs12979860 and rs8099917 subtype frequencies with respect to HCV genotype.

Liver biopsies were performed in 99/152 (65.1%) patients, indicating stage 0 (*n* = 8), stage 1 (*n* = 23), stage 2 (*n* = 26), stage 3 (*n* = 27), or stage 4 (*n* = 4) fibrosis, or cirrhosis (*n* = 11).

Treatment response

Treatment duration was reduced to < 48 wk for 24/94 (25.5%) patients with HCV genotype-1 infection (15 with shortened treatment course, two as a result of non-compliance, and seven following treatment failure), and to < 24 wk in one non-compliant HCV genotype-3 subject. Treatment was prolonged up to

Table 1 Treatment outcomes *n* (%)

Hepatitis C virus genotype	Virologic response				Resistant	Breakthrough	Relapse
	Rapid	Early	End of treatment	Sustained			
Type-1[1] (*n* = 94)	42 (44.7)	86 (91.5)	85 (90.4)	77 (81.9)	6 (6.4)	3 (3.2)	8 (8.5)
Type-3 (*n* = 56)	47 (83.9)[b]	49 (89.1)[2]	56 (100)	51 (91.1)	0 (0)	0 (0)	5 (8.9)
Mixed type-1 and -3 (*n* = 2)	1 (50.0)	2 (100)	2 (100)	2 (100)	0 (0)	0 (0)	0 (0)
Total (*n* = 152)	90 (59.2)	137 (90.7)[2]	143 (94.1)	130 (85.5)	6 (3.9)	3 (2.0)	13 (8.6)

[1]Includes one patient with mixed hepatitis C virus genotype-1a/4; [2]Data from one patient was missed; [b]$P < 0.01$ *vs* type-1.

Table 2 Baseline variables according to treatment response

Variable	All subjects		HCV genotype-1		HCV genotype-3	
	R (*n* = 130)	NR (*n* = 22)	R (*n* = 77)	NR (*n* = 17)	R (*n* = 51)	NR (*n* = 5)
Age (yr)	40.9 ± 9.4[a]	47.7 ± 11.5	41.7 ± 9.0	47.9 ± 11.9	40.0 ± 10.1	46.8 ± 8.9
HCV RNA (× 10^5 IU/mL)	35.6 ± 55[a]	60.1 ± 99.5	37.9 ± 48.6	70.1 ± 111.6	32.4 ± 64.9	26.3 ± 16.8
Liver fibrosis stage	2.2 ± 1.5	3.0 ± 1.7	2.3 ± 1.5	3.0 ± 1.8	1.8 ± 1.3	3.0 ± 0.0
ALT (IU/L)	71.9 ± 57.7	100.9 ± 108.7	74.2 ± 63.9	77.9 ± 63.7	70.1 ± 47.9	198.7 ± 203.6
AST (IU/L)	44.5 ± 26.4	71.2 ± 66.8	44.9 ± 28.7	58.5 ± 47.6	44.4 ± 23.3	125.2 ± 113.5
BMI (kg/m^2)	26.9 ± 4.0	25.8 ± 3.4	27.2 ± 3.5a	25.1 ± 3.0	26.2 ± 4.6	29.5 ± 3.7

Data are presented as mean ± SD; [a]$P < 0.05$ *vs* NR. ALT: Alanine transaminase; AST: Aspartate transaminase; BMI: Body mass index; HCV: Hepatitis C virus; NR: Non-responder; R: Responder (achieved sustained virologic response).

72 wk in 14/94 (14.9%) patients with HCV genotype-1 infection because of cirrhosis or the continued presence of HCV RNA at 12 wk. Similarly, 10 patients with HCV genotype-3 infection required an extended 48-wk therapy course. Treatment course was withdrawn in 1 subject due to attempted suicide. The 11 patients with cirrhosis did not show signs of ascites or thrombocytopenia, and treatment was therefore administered.

The treatment outcomes for all patients and according to HCV genotypes are shown in Table 1. Although the rates of EVR and SVR did not differ between the HCV genotype-1 and genotype-3 groups, the rate of RVR was significantly higher in patients with HCV genotype-3 than in patients with HCV genotype-1 ($P < 0.01$). Furthermore, 44/62 (71.0%) patients who did not demonstrate RVR and 7/14 (50.0%) patients who did not show EVR eventually achieved SVR. Therefore, overall, RVR and EVR were significantly related to treatment success ($P < 0.01$).

Predictors of treatment response

The age, baseline HCV RNA level, liver fibrosis stage, serum alanine and aspartate transaminase levels, and body mass index were compared among treatment responders and non-responders within the HCV genotype groups (Table 2). Patients with mixed HCV genotypes were excluded from analyses due to the small sample size. The baseline characteristics did not differ between HCV genotype groups, although responders were significantly younger ($P < 0.01$), and had lower HCV RNA levels ($P = 0.04$) than non-responders. These differences were not significant within the HCV genotype subgroups. In contrast, body mass index did not differ within the entire cohort with regard to treatment response, however, responders with HCV genotype-1 infection had a significantly higher body mass index than non-responders ($P = 0.03$).

Table 3 shows the prevalence of rs12979860 and rs8099917 genotypes with respect to treatment response. Among subjects with rs12979860 CC genotype, 91.2% (52/57) responded successfully to treatment, whereas 82.1% (78/95) of patients with a non-CC genotype responded. Treatment success occurred in 86.7% (39/45) of patients with the rs8099917 TT genotype, and in 89.7% (61/68) of those with a non-TT genotype. Univariate analyses revealed that there were no differences in the prevalence of the *IFNL* genotypes between responders and non-responders for either polymorphism. However, among patients with HCV genotype-1 infection, the rs12979860 CC genotype was significantly related to treatment success (94.1% *vs* 75.0%; $P = 0.02$). This was not observed in the HCV genotype-3 group.

Patients with the rs12979860 CC genotype had significantly higher HCV RNA levels compared to those with a non-CC genotype ($60.9 \times 10^5 \pm 81.8 \times 10^5$ IU/mL *vs* $26.4 \times 10^5 \pm 45.7 \times 10^5$ IU/mL, $P = 0.01$). Further analyses also revealed that RNA levels of HCV

Table 3 Prevalence of single nucleotide polymorphisms *n* (%)

Hepatitis C virus genotype	rs12979860 genotype		rs8099917 genotype[1]	
	CC	Non-CC	TT	Non-TT
Type-1				
Responders	32 (41.6)	45 (58.4)	32 (59.3)	22 (40.7)
Non-responders	2 (11.8)	15 (88.2)	3 (33.3)	6 (66.7)
Type-3				
Responders	20 (39.2)	31 (60.8)	28 (63.6)	16 (36.4)
Non-responders	3 (60.0)	2 (40.0)	4 (100)	0 (0)
Mixed type-1 and -3				
Responders	0 (0)	2 (100)	1 (50.0)	1 (50.0)
Non-responders	0 (0)	0 (0)	0 (0)	0 (0)
Total				
Responders	52 (40.0)	78 (60.0)	39 (39.0)	61 (61.0)
Non-responders	5 (22.7)	17 (77.3)	7 (53.8)	6 (46.2)

[1]Data missing for 39 patients.

genotype-1 were significantly higher in patients with rs12979860 CC *vs* other genotypes ($71.6 \times 10^5 \pm 88.1 \times 10^5$ IU/mL *vs* $28 \times 10^5 \pm 40.2 \times 10^5$ IU/mL, $P < 0.01$). However, this was not the case for patients in the HCV genotype-3 group. In addition rs12979860 CC and rs8099917 TT genotypes were significantly related to achievement of RVR (both $P < 0.05$), but not EVR. RVR was also significantly associated with rs12979860 CC and rs8099917 TT genotypes in patients infected with HCV genotype-1 ($P = 0.01$).

Logistic regression analysis of treatment success was conducted according to age, categorical HCV RNA level, stage of liver fibrosis, rs12979860 CC genotype, and aspartate transaminase level (variables identified by $P < 0.2$ in univariate analyses). The results showed that only rs12979860 CC genotype was a predictor of SVR achievement ($P = 0.03$). Table 4 shows the results of multivariate analysis.

Table 4 Predictive factors of treatment success

Baseline variable	*P* value	Odds ratio	95%CI
Age	0.18	0.96	0.91-1.02
AST	0.55	0.99	0.98-1.01
HCV RNA level (categorical)	0.30	0.53	0.16-1.75
Stage of liver fibrosis	0.22	0.77	0.50-1.17
rs12979860 CC genotype	0.03[1]	6.23	1.22-31.88

[1]Significant association with SVR achievement. AST: Aspartate transaminase; HCV: Hepatitis C virus; SVR: Sustained virologic response.

DISCUSSION

A wide range of response rates has been reported for Peg-IFN and ribavirin treatment of chronic HCV infection, reflecting the various settings and patient selections. For example, these values range from 7% in patients with HCV genotype-1 and high viral load[17] to 80% in patients with HCV genotype-2 and -3[5,18]. Although recently more effective treatments for chronic hepatitis C have been introduced, the high cost of these treatments has made the Peg-IFN plus ribavirin regimen the only affordable treatment option in many developing countries[3]. Jabbari *et al*[19] reported a high success rate with this regimen in Iranian patients with HCV genotype-3 compared to genotype-1 (95% *vs* 67%), and another Iranian study reported an 83.8% success rate in patients with HCV genotype-3 and 72.6% in those with HCV genotype-1[20]. Moreover, Alavi Moghaddam *et al*[21] reported an excellent treatment success rate of 95.6% in 45 younger hemophiliac patients (mean age 30.4 ± 12.6 years) with HCV genotypes-1 and -3. The results from these Iranian studies are in line with our results presented herein. Studies on the success rate of this treatment regimen in neighboring countries are rare and comparing the results of the existing ones is also difficult due to different HCV genotype distributions. A study from Turkey reported SVR rates of 48.6% and 35.1% in a group of patients with HCV genotype-1 treated with Peg-IFN-alpha-2a or Peg-IFN-alpha-2b, respectively[22].

A report by Muir *et al*[23] found that responses to Peg-IFN varied among ethnicities regardless of the HCV genotype, with the lowest rates (22%) in African Americans, and the highest (59%) in Asian Americans. Another study reported an SVR rate of 76% in Asian patients *vs* 36% in Caucasians[24]. Thus, ethnic differences may explain the higher success rates in the Iranian patients reported here and elsewhere[21].

Another interesting finding in our study was the same treatment success rate in HCV genotype- 1 and -3 patients. Lin *et al*[25] showed that patients younger than 40 with HCV genotype-1 had a treatment response similar to HCV genotype-2 infection. Moreover, a study by Gheorghe *et al*[26] showed that patients with HCV genotype-1 and mild hepatitis had a high rate of SVR similar to those with other HCV genotypes, young age and low level of viremia and significant hepatocytolisis were found to be independent predictors of SVR. These findings can explain the similar SVR achievement rates between the 2 HCV genotype groups in our study regardless of IFNL polymorphism. It is also possible that apart from ethnic differences, the relatively younger age of the participants and their high compliance (3.6% dropout rate) in our study accompanied by the fact that we only included treatment-naïve patients contributed to the observed high treatment success rate.

The identification of rs12979860 and rs8099917 genotypes has been recommended prior to treatment of patients infected with HCV genotype-1 or -4 due to the possibility of a more favorable outcome[8]. Although a meta-analysis performed by Belgian scientists demonstrated that favorable *IL28B* genotypes are associated with higher RVR and SVR rates in HCV genotype-2 and -3 patients, but as their impact on SVR was slim, they did not recommend *IL28B* genotyping before therapeutic interventions in these patients[11].

The findings reported herein indicate that only the rs12979860 CC genotype significantly affects SVR, which is consistent with another previous Iranian study on 48 patients infected with HCV genotype-1, where the SVR rate was higher in those with the rs12979860 CC genotype in comparison to those with rs12979860 TT genotype[27]. Nevertheless, in the present study, both rs12979860 and rs8099917 were related to RVR, but not EVR achievement, regardless of HCV genotype. The distributions of rs12979860 and rs8099917 SNPs observed in this study were concordant with previous reports[28,29].

As we only included 152 subjects in our study and had a high treatment success rate, only 22 patients failed to achieve SVR, therefore a larger sample size with more subjects in the non-responder group may have confirmed these results with more certainty. Although in this study reaching RVR and EVR were both significantly related to treatment success, SVR was still achieved in more than half of the patients that initially had failed to reach RVR or EVR (71% and 50%, respectively).

The results of the present study also show that patients with the rs12979860 CC genotype had more than two times the HCV RNA level than non-CC genotypes, which has been reported for various HCV genotypes throughout the various courses of infection (acute, early chronic, and chronic)[30-33]. Bucci *et al*[34] reported similar results in 201 HCV genotype-3 patients from the United Kingdom, this study showed that favorable IL28B polymorphisms (rs8099917) are associated with a marked increase in baseline viral load and RVR achievement, but not SVR. Domagalski *et al*[32] also confirmed the association between favorable rs12979860 CC genotype and higher baseline viral loads in patients with HCV genotype 1 and 4. Abe *et al*[35] reported more severe inflammation and fibrosis in the homozygous bearers of major IL28B alleles questioning their benefit outside the treatment context. It is suggested that different IL28B polymorphisms induce different cytokine profiles that can cause different inflammatory or biochemical results in the course of chronic HCV infection. This apparent paradox between higher baseline HCV RNA level, which has been linked to treatment failure in many studies[36,37], and higher response rate in patients with the rs12979860 CC genotype requires further investigation.

More large scale multi-centric studies are needed to reliably evaluate the response rate of patients in different ethnical or geographical parts of the world and to identify the responsible factors for high success rates in specific populations to improve the treatment outcome for all patients with chronic hepatitis C.

In conclusion, this study shows that the SVR achievement rate is high in Iranian treatment-naïve patients regardless of HCV genotype. Although the rs12979860 CC genotype showed a strong relationship with SVR achievement, the comparatively high level of SVR achievement with Peg-IFN and ribavirin in patients with other rs12979860 genotypes indicates that the Iranian patient's *IFNL* polymorphism should not alter treatment decisions.

COMMENTS

Background

Chronic hepatitis C virus (HCV) infection is a major public health problem that can result in cirrhosis and lead to hepatocellular carcinoma or even death. For the past decade, Pegylated interferon (Peg-IFN) has been the primary therapeutic intervention for chronic HCV infection, although its efficacy is influenced by many factors, including single nucleotide polymorphisms in or near the *IL28B* gene.

Research frontiers

Many studies have reported wide ranging efficacies for Peg-IFN and ribavirin in the treatment of chronic HCV infection. Although patient age, viral load, and ethnicity can substantially affect treatment success, the role of host genetic factors, such as single nucleotide polymorphisms in relevant genes, are becoming more apparent. Thus, further understanding of the influence of these factors will help improve patient outcome.

Innovations and breakthroughs

The high response rate to Peg-IFN and ribavirin is an important finding of this study, and may support the decision to accept treatment by many patients with chronic HCV infection, particularly those in developing countries. The high response rate of Iranian patients to Peg-IFN and ribavirin in this study highlights that the conventional dual therapy can still be considered the first-line treatment for these patients.

Applications

The results of this study show that the rs12979860 CC genotype is a strong predictor of treatment response. Thus, patients with this rs12979860 genotype can achieve greater benefit from Peg-IFN and ribavirin treatment.

Terminology

Interferon-λ is a cytokine that is involved in host defense against viral infections, such as hepatitis C. Single nucleotide polymorphisms are genetic variations within the DNA that are common within a population.

Peer-review

The authors carried out a cross-sectional multivariate analysis to describe positive predictive factors for response to HCV treatment with Peg-IFN alpha-2a plus ribavirin in a naïve Iranian cohort. Special attention is given to *IL28B* polymorphisms as a target to predict sustained viral response. They observed a similar finding to previous reports showing a relationship between the *IFNL* rs12979860 CC genotype and a higher sustained virologic response probability. The patient cohort demonstrated a high sustained virologic response rate overall, which could be related to ethnic factors that render the Iranian population more sensitive to Peg-IFN plus ribavirin treatment.

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