ORIGINAL ARTICLE

Efficacy of pegylated interferon alfa-2a or alfa-2b in combination with ribavirin in the treatment of chronic hepatitis caused by hepatitis C virus genotype 1b

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KEY WORDS

chronic hepatitis, HCV genotype 1b, treatment

ABSTRACT

INTRODUCTION Treatment of chronic hepatitis C (CHC) with pegylated interferon (Peg-IFN) and ribavirin leads to sustained virological response (SVR) in approximately 50% of the patients. SVR depends on hepatitis C virus (HCV) and host factors, including *IL28B* genotypes.

OBJECTIVES The aim of the study was to investigate the therapeutic efficacy of the difficult-to-treat HCV genotype 1b in patients from the south of Poland.

PATIENTS AND METHODS A total of 260 adult patients with CHC and HCV genotype 1b were treated with Peg-IFN alfa-2a or Peg-IFN alfa-2b with ribavirin for 48 weeks. Efficacy was assessed at 12 weeks (early virological response – EVR), 48 weeks (end-of-treatment response – ETR), and at 6 months (SVR). HCV-RNA, alanine transaminase (ALT), and other biochemical parameters were measured in serum at baseline and at 12, 48, and 72 weeks of therapy.

RESULTS HCV-RNA levels were $3.72 \pm 1.17 \times 10^6$ IU/ml at baseline and decreased significantly at 12 weeks ($0.02 \pm 0.17 \times 10^6$ IU/ml); there were no differences between the group treated with Peg-INF alfa-2a and the group treated with Peg-INF alfa-2b. ALT was 94.1 ± 7.6 IU/l at baseline and decreased significantly at 12 weeks (42.5 ± 3.1 IU/l). The overall EVR, ETR, and SVR were achieved by 63.9%, 77.7%, and 48.1% of the patients, respectively. Tolerance of therapy was similar in both groups.

CONCLUSIONS Efficacy of Peg-IFN alfa-2a with ribavirin is not significantly different from that of Peg-IFN alfa-2b with ribavirin, and SVR was achieved in 48.3% and 44.3% of the patients, respectively. Our study confirms that the efficacy of treatment of patients with HCV genotype 1b from the southern region of Poland is similar to that observed in the overall Polish population.

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INTRODUCTION Hepatitis C virus (HCV) infection is a serious global problem affecting from 130 to 210 million people worldwide and about 0.7 million individuals in Poland.[1-3] HCV causes hepatitis, liver cirrhosis, and hepatocellular carcinoma.[4,5] The efficacy of antiviral therapy with pegylated interferon (Peg-IFN) alfa and ribavirin is not satisfactory. Sustained virological response (SVR), defined as undetectable HCV-RNA in the blood for 6 months after a 48-week treatment, is achieved in about 50% of the patients and is lower in so called difficult-to-treat HCV genotype 1 infection.[3-8] To improve SVR, a new class of directly acting antiviral drugs are currently being tested in numerous clinical trials.[9]

The effectiveness of treatment depends on viral factors, such as the genotype and HCV blood levels, and on genetic host factors.[10-17] HCV genotype 1 is the most difficult to eradicate.[18,19] Previous studies have shown that genotype 1b occurs in more than 80% of the Polish patients.[20,21]

The aim of the present study was to investigate the efficacy of Peg-IFN alfa-2a and Peg-IFN alfa-2b in combination with ribavirin in the treatment of patients with chronic hepatitis caused by HCV genotype 1b.

PATIENTS AND METHODS The open-label study included 260 consecutive adult patients with chronic hepatitis induced by HCV genotype 1b. All patients lived in the southern region of Poland and were referred for treatment to the University Hospital in Kraków. They were randomly assigned to 1 of the 2 treatment groups.

The inclusion criteria were as follows: anti-HCV and HCV-RNA in serum and elevated alanine aminotransferase (ALT) levels at least 6 months before the inclusion, chronic hepatitis confirmed by histological examination, body mass index (BMI) below 30 kg/m^2. The exclusion criteria were as follows: decompensated liver cirrhosis, autoimmune liver disease, alcohol abuse, liver cancer, hepatitis B virus or HIV coinfection, any severe chronic disease, diabetes, dyslipidemia, metabolic syndrome, hemochromatosis, and immunosuppressive therapy.

Patients were treated for 48 weeks with: 1) Peg-IFN alfa-2a 180 μg subcutaneously once a week and oral ribavirin 1.0–1.2 g daily (Hoffmann-La Roche Inc., United States), or 2) Peg-IFN alfa-2b 1.5 mg/kg of body weight once a week and oral ribavirin 1–1.2 g daily (Schering-Plough Co, MSD, United States). Patients were followed up for 24 weeks.

The European Association for the Study of the Liver guidelines do not specifically recommend which Peg-IFN alfa should be used in the treatment of chronic hepatitis.[2,22-24]

The study was conducted in accordance with the ethical principles of the 1975 Helsinki Declaration, and was approved by the Bioethical Committee at the Jagiellonian University, Kraków, Poland. Patients provided written informed consent to participate in the study.

Genetic variations of interleukin (IL) 28B, *IL28B*, were studied using a previously described method.[25] Briefly, genomic DNA was isolated from peripheral blood samples. A 190 bp amplification product was obtained using a standard polymerase chain reaction (PCR) with primers: 5'-GCC TCT TCC TCC TGC GGG ACA AG and 5'-GCG CGG GCA AGT ATT CAA CCC T Bsh1236I. After digestion with endonuclease, the resulting products were separated using the agarose gel electrophoresis, and option C was digested with the enzyme. All laboratory procedures were conducted using blinded samples.

Serum anti-HCV, HCV-RNA, ALT, aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin, albumin, international normalized ratio, and morphology were measured. HCV-RNA and HCV genotypes were measured by reverse transcription PCR (Cobas TaqMan HCV Test v. 2.0, Roche Molecular Systems, Inc., United States). HCV-RNA, ALT, and other biochemical parameters were determined at baseline and at 12, 48, and 72 weeks. Early virological response (EVR) was defined as undetectable HCV-RNA or at least a 2-log drop in HCV-RNA at 12 weeks of treatment. End-of-treatment response (ETR) was defined as undetectable HCV-RNA at 48 weeks of treatment.

Liver tissues obtained using a Menghini needle were stained with hematoxylin and eosin; connective tissue was stained using the Masson's trichrome technique. Hepatic inflammation and fibrosis were assessed using the Batts–Ludwig score.[26]

The characteristics of patients are shown in TABLE 1. The majority of patients (62.3%) were men aged 44.0 ±11.6 years (mean ± standard deviation) with an approximate 11.2-year duration of HCV infection established on the basis of medical history and records. There were 30% of patients with C/C genotype *IL28B*, 46.9% with T/C, and 23.1% with T/T. All patients had elevated serum levels of ALT (mean 94.1 ±7.6 IU/l) and AST (mean 62.6 ±4.2 IU/l) and the HCV viral load of 3.72 ±1.17 × 10^6 IU/ml. Histological examination showed that 78.1% of the patients had only minor liver damage (fibrosis stage F0–F2 according to the Batts–Ludwig score).

Statistical analysis The results were analyzed with the parametric *t* test or the nonparametric Mann–Whitney U test and Kruskal–Wallis test using Statistica v. 9.0 (StatSoft, Inc., United States). The results were presented as mean values and standard deviations; *P* values less than 0.05 in a two-sided test were considered statistically significant.

RESULTS HCV-RNA viral load in serum at baseline and at 12 weeks as well as the evaluation of EVR is presented in TABLE 2. Baseline viral load was not significantly different between patients treated with Peg-IFN alfa-2a and ribavirin and those treated with Peg-IFN alfa-2b and ribavirin.

HCV-RNA viral load decreased significantly after 12 weeks of treatment in both groups. In patients receiving Peg-IFN alfa-2a, the serum HCV-RNA level was 0.01 ±0.21 × 10^6 IU/ml and was not significantly different from that in patients on Peg-IFN alfa-2b (0.05 ±0.13 × 10^6 IU/ml, *P* = 0.226). The Spearman's rank correlation coefficient did not show any significant associations between HCV-RNA viral load and ALT activity at baseline or at 12 weeks.

Response to treatment is presented in the FIGURE. We observed no significant differences in EVR, ETR, and SVR between the 2 groups. SVR, which indicates the effectiveness of HCV treatment, was achieved in 49.3% of the patients treated with Peg-IFN alfa-2a and in 44.3% of those treated with Peg-IFN alfa-2b. Tolerance of both treatment methods was similar and independent of the drugs.

There were no significant differences between the 2 groups in ALT, AST, and ALP activity or

TABLE 1 Characteristics of patients with chronic hepatitis C treated with Peg-IFN alfa-2a plus ribavirin or Peg-IFN alfa-2b plus ribavirin

Variable		All patients (n = 260)	Peg-IFN alfa-2a (n = 138)	Peg-IFN alfa-2b (n = 122)	*P*
age, y		44.0 ±11.6	45.2 ±10.5	44.2 ±13.6	NS
women, n (%)		98 (37.7)	58 (42.0)	49 (40.1)	NS
men, n (%)		162 (62.3)	80 (58.0)	73 (59.9)	NS
duration of infection, y		11.2 ±1.3	13.0 ±2.1	10.1 ±1.7	NS
BMI, kg/m^2		24.2 ±1.0	24.5 ±0.9	25.1 ±1.3	NS
IL28B genotypes, n (%)	C/C	78 (30)	39 (28.3)	38 (31.1)	NS
	T/C	122 (46.9)	70 (50.7)	56 (45.9)	NS
	T/T	60 (23.1)	29 (21.0)	28 (23.0)	NS
WBC, ×10^9/l		5.8 ±1.0	5.1 ±0.9	6.3 ±0.8	NS
hemoglobin, mg/dl		13.2 ±1.0	14.6 ±0.9	12.7 ±1.0	NS
platelets, ×10^9/l		171 ±12.4	152 ±10.7	176 ±12.4	NS
INR		1.06 ±0.4	1.01 ±0.26	0.93 ±0.19	NS
ALT, IU/l		94.1 ±7.6	88.0 ±9.5	106.8 ±11.7	NS
AST, IU/l		62.6 ±4.2	58.2 ±3.8	63.0 ±4.2	NS
ALP, IU/l		67.1 ±3.1	63.5 ±3.1	59.6 ±2.1	NS
bilirubin, µmol/l		16.2 ±0.9	16.8 ±0.7	15.1 ±1.1	NS
albumin, g/l		40.6 ±1.9	38.5 ±2.2	41.9 ±2.7	NS
HCV viral load, ×10^6 IU/ml		3.72 ±1.17	4.01 ±2.17	3.45 ±0.92	NS
liver fibrosis[a], n (%)	F0–2	64 (78.1)	35 (72.9)	22 (64.7)	NS
	F3–4	18 (21.9)	13 (27.1)	12 (35.3)	NS

a liver biopsy performed in 48 patients receiving Peg-IFN alfa-2a and 34 patients receiving Peg-IFN alfa-2b

Data are expressed as mean ± standard deviation.

Abbreviations: ALP – alkaline phosphatase, ALT – alanine aminotransferase, AST – aspartate aminotransferase, BMI – body mass index, C/C T/C T/T – genotypes of interleukin 28B, F0–2 – less advanced fibrosis according to the Batts–Ludwig score, F3–4 – more advanced fibrosis according to the Batts–Ludwig score, IL-28B – interleukin 28B, INR – international normalization ratio, NS – nonsignificant, Peg-IFN – pegylated interferon, WBC – white blood count

TABLE 2 Serum HCV-RNA viral level in patients with chronic hepatitis C at baseline and at 12 weeks of treatment with Peg-IFN alfa-2a plus ribavirin or Peg-IFN alfa-2b plus ribavirin

	All patients (n = 260)	Peg-IFN alfa-2a (n = 138)	Peg-IFN alfa-2b (n = 122)	*P* alfa-2a vs. alfa-2b
HCV-RNA level (value × 10^6 IU/ml)				
at baseline	3.72 ±1.17	4.01 ±2.17	3.45 ±0.92	0.106
at 12 weeks	0.02 ±0.017	0.01 ±0.001	0.05 ±0.01	0.226
P	0.001	0.001	0.001	

Data are expressed as mean ± standard deviation.

Abbreviations: see TABLE 1

in serum bilirubin and albumin levels assessed at baseline and at 12, 24, 48, and 72 weeks. We observed a statistically significant decrease in the activity of ALT and AST after 12 weeks of treatment compared with the baseline values (TABLE 3). ALT activity was 89.6 ±9.5 IU/l at baseline and 38.4 ±2.6 IU/l at 12 weeks in the Peg-IFN alfa-2a group and 101.8 ±11.7 IU/l at baseline and 41.7 ±1.9 IU/l at 12 weeks in the Peg-IFN alfa-2b group (TABLE 3). ALP activity and serum bilirubin and albumin levels were not significantly different at 12 weeks compared with the baseline values (TABLE 3).

DISCUSSION Response to standard treatment with Peg-IFN alfa in patients with chronic hepatitis caused by HCV, including genotype 1b, has been widely studied and documented in numerous populations.[27-29] In our study, serum HCV-RNA levels at baseline did not differ significantly between patients receiving Peg-IRN alfa-2a and ribavirin or Peg-IRN alfa-2b and ribavirin, and after 12 weeks of treatment these levels were still similar in both groups. Our findings are generally in line with the results of other studies,[18,21,27-30] although some authors showed higher response rate in patients treated with Peg-IFN alfa-2a.[22-24] These discrepancies might result either from

TABLE 3 Serum ALT, AST, ALP, bilirubin, albumin, and HCV-RNA levels in patients with chronic hepatitis C at baseline and during treatment and response to therapy with Peg-IFN alfa-2a plus ribavirin or Peg-IFN alfa-2b plus ribavirin

	All patients (n = 260)	Peg-IFN alfa-2a (n = 138)	Peg-IFN alfa-2b (n = 122)	*P* alfa-2a vs. alfa-2b
ALT, IU/l				
at baseline	94.1 ±7.6	89.6 ±9.5	101.8 ±11.7	0.090
at 12 weeks	42.5 ±3.1	38.4 ±2.6	41.7 ±1.9	0.105
P	0.001	0.001	0.001	
AST, IU/l				
at baseline	62.6 ±4.2	58.2 ±3.8	63.0 ±4.2	0.125
at 12 weeks	38.2 ±3.6	34.8 ±3.9	39.7 ±3.1	0.075
P	0.001	0.001	0.001	
ALP, IU/l				
at baseline	67.1 ±4.1	63.5 ±7.1	71.9 ±6.1	0.305
at 12 weeks	72.6 ±4.2	65.1 ±6.2	73.3 ±5.8	0.095
P	0.250	0.955	0.550	
bilirubin, µmol/l				
at baseline	16.2 ±0.9	16.8 ±0.7	15.1 ±1.1	0.080
at 12 weeks	24.7 ±0.6	25.8 ±1.1	23.9 ±0.7	0.065
P	0.020	0.035	0.015	
albumin, g/l				
at baseline	40.6 ±1.9	38.5 ±2.2	41.9 ±2.0	0.100
at 12 weeks	41.7 ±2.2	37.9 ±1.6	39.7 ±1.2	0.100
P	0.650	0.800	0.455	

Data are expressed as mean ± standard deviation.

Abbreviations: see **TABLE 1**

ethnical differences or the fact that our population included carefully selected patients with biochemically confirmed activity of chronic hepatitis and high ALT and AST levels. On the other hand, our patients with difficult-to-treat HCV genotype 1 had relatively minor liver damage (more than two-third of the patients had fibrosis stage F0–F2).

Recently, there have been important advances in the understanding of treatment response in patients with HCV genotype 1. Three independent research groups have reported the results of separate genome-wide association studies, supporting the association of SVR in HCV genotype 1 with single nucleotide polymorphisms (SNPs) near the gene region *IL28B* encoding interferon lambda 3.[11-13] In the first study, performed by

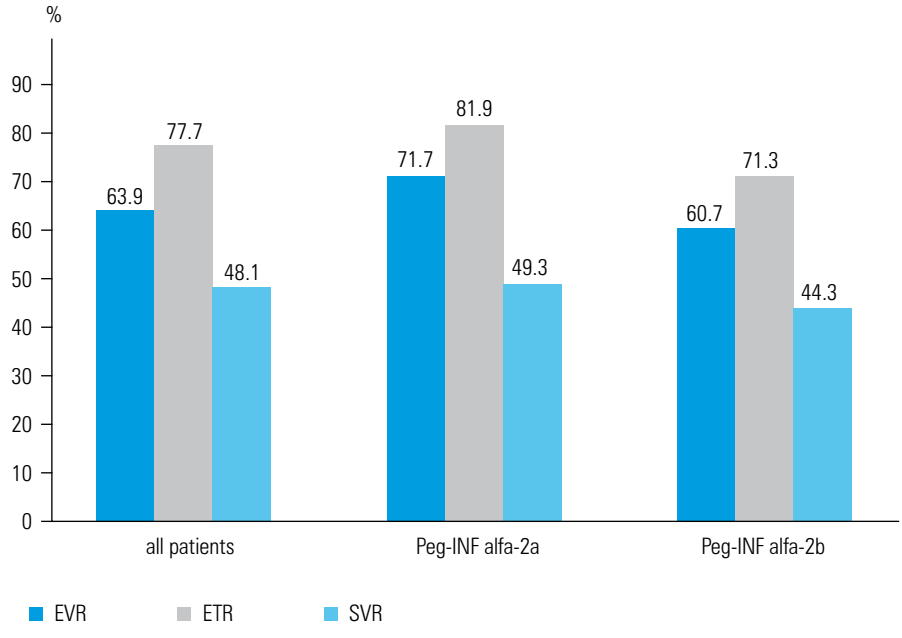

FIGURE Virological response in patients with chronic hepatitis C treated with Peg-IFN alfa-2a plus ribavirin or Peg-IFN alfa-2b plus ribavirin. Data are expressed as percentage of early virologival response (EVR), end-of--treatment response (ETR), and sustained virological response (SVR). SVR vs. EVR in all groups $P < 0.05$, SVR vs. ETR in all groups $P < 0.01$.

Ge et al.,[11] the rs12 979 860 SNP was most strongly correlated with SVR, which is located 3 kilobases upstream of the *IL28B* gene. The minor allele (T) was associated with a lower rate of SVR (26% in patients with TT genotype and 79% in those with CC genotype).[11] Suppiah et al.[12] have shown a significant association between the SNP rs8 099 917 and SVR. Among 63% of the patients who achieved SVR were homozygous for the T allele. Similar findings were also reported in a Japanese study by Tanaka et al.[13] who showed a significant association between treatment response and 2 SNPs (rs12 980 275 and rs8 099 917), both located in the *IL28B* gene region, and the latter being the same SNP found by other researchers. These observations have been recently confirmed by numerous authors. In our previous study, we showed that EVR, ETR, and SVR are achieved, respectively, in 38%, 69.7%, and 44.4% of the patients with chronic hepatitis caused by difficult-to-treat HCV genotype 1b and treated with Peg-IFN and ribavirin.[25] The response rate in patients with C/C genotype *IL28B* was significantly higher (ETR – 92.1%, SVR – 71.1%) compared with T/C genotype (ETR – 67.6%, SVR – 40%) and T/T genotype (ETR – 52%, SVR – 23.5%).[25] Our study confirmed that response to standard treatment of HCV genotype 1b infection in patients from southern Poland depends on the *IL28B* gene polymorphism.

Of note, as few as 30% of the patients in our study had the C/C variant of *IL28B* genotype, which according to the numerous recent publications is closely associated with better response to therapy.[11-17,25,31]

The overall results of EVR, ETR, and SVR are similar to those reported by other investigators.[6,8] In the Peg-IFN alfa-2a group, EVR was achieved by 71.7% of the patients, ETR by 81.9%, and SVR by 49.3%. In the Peg-IFN alfa-2b group, EVR was achieved by 60.7%, ETR by 71.3%, and SVR by 44.3% of the patients. Our results are in line with the results of numerous other publications, including those from the Polish multicenter trials.[18-21,27,30]

Patients with chronic hepatitis caused by HCV often have normal serum ALT levels.[3,5,32-35] Serum ALT and AST levels in our patients exceeded the upper limit of normal values. The levels decreased during treatment with both Peg-IFN alfa-2a and alfa-2b in combination with ribavirin, but there were no significant differences in baseline and on-treatment values between the 2 groups.

Hepatic steatosis is common in patients with chronic HCV infection, and the prevalence is much higher in this group than in the general population.[36] Hepatic steatosis in patients with HCV can be due to alcohol consumption or host metabolic factors such as high BMI, obesity, metabolic syndrome, hyperlipidemia, and diabetes.[36] Nonalcoholic fatty liver disease (NAFLD), which is the most prevalent liver disease in the developed countries, often coexists with HCV infection and might be responsible for the increased activity of aminotransferases in this population. Patients with NAFLD have insulin resistance and metabolic syndrome with its components including obesity and type 2 diabetes.[37,38] It was also shown that HCV hepatitis may modulate chronic inflammatory state in diabetic patients.[37] Therefore, to exclude the effect of metabolic syndrome on treatment response, we included only nonobese and nondiabetic patients into the study.

In conclusion, the overall EVR, ETR, and SVR was achieved, respectively, in 63.9%, 77.7%, and 48.1% of the patients with chronic hepatitis caused by difficult-to-eradicate HCV genotype 1b, who received Peg-IFN alfa-2a with ribavirin or Peg-IFN alfa-2b with ribavirin. Our study confirmed that response to standard treatment of chronic HCV genotype 1b infection is similar in patients from southern Poland and in the overall Polish population and is independent of standard treatment regimen.

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REFERENCES

1 Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. Lancet Infect Dis. 2005; 5: 558-567.

2 EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. J Hepatol. 2011; 55: 245-264.

3 Cieśla A, Mach T. [Chronic viral hepatitis - current epidemiological, clinical and therapeutic challenge]. Przegl Gastroenterol. 2007; 2: 69-73. Polish.

4 Afdhal NH. The natural history of hepatitis C. Semin Liver Dis. 2004; 24 (Suppl 2): 3-8.

5 Czepiel J, Biesiada G, Mach T. Viral hepatitis C. Pol Arch Med Wewn. 2008; 118: 734-740.

6 Fried MW, Hadziyannis MD. Treatment of chronic hepatitis C infection with peginterferons plus ribavirin. Semin Liver Dis. 2004; 24 (Suppl 2): 47-54.

7 Heathcote J, Main J. Treatment of hepatitis C. J Viral Hepat. 2005; 12: 223-235.

8 Manns MP, Wedemeyer H, Cornberg M. Treating viral hepatitis C: efficacy, side effects, and complications. Gut. 2006; 55: 1350-1359.

9 Hofmann WP, Zeuzem S: A new standard of care for the treatment of chronic HCV infection. Nat Rev Gastroenterol Hepatol. 2011; 8: 257-264.

10 Ferenci P. Predictors of response to therapy for chronic hepatitis C. Semin Liver Dis. 2004; 24 (Suppl 2): 25-31.

11 Ge D, Fellay J, Thompson AJ, Simon JS, et al. Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. Nature. 2009; 461: 399-401.

12 Suppiah V, Moldovan M, Ahlenstiel G, et al. IL28B is associated with response to chronic hepatitis C interferon-alpha and ribavirin therapy. Nat Genet. 2009; 41: 1100-1104.

13 Tanaka Y, Nishida N, Sugiyama M, et al. Genome-wide association of IL28B with response to pegylated interferon-alpha and ribavirin therapy for chronic hepatitis C. Nat Genet. 2009; 41: 1105-1109.

14 Thomas DL, Thio CL, Martin MP, et al. Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. Nature. 2009; 461: 798-801.

15 Ahlenstiel G, Booth DR, George J. IL28B in hepatitis C virus infection: translating pharmacogenomics into clinical practice. J Gastroenterol. 2010; 45: 903-910.

16 Thompson AJ, Muir AJ, Sulkowski MS, et al. Interleukin 28B polymorphism improves viral kinetics and is the strongest pretreatment predictor of sustained virologic response in genotype 1 hepatitis C virus. Gastroenterology. 2010; 139: 120-129.

17 Clark PJ, Thompson AJ, McHutchison JG. IL28B genomic-based treatment paradigms for patients with chronic hepatitis C infection: the future of personalized HCV therapies. Am J Gastroenterol. 2011; 106: 38-45.

18 Liu CH, Liu CJ, Lin CL, et al. Pegylated interferon-alpha-2a plus ribavirin for treatment naive Asian patients with hepatitis C virus genotype 1 infection: a multicenter, randomized controlled trial. Clin Infect Dis. 2008; 47: 1260-1269.

19 de Segadas-Soares JA, Villela-Nogueira CA, Perez RM, et al. Is the rapid virologic response a positive predictive factor of sustained virologic response in all pretreatment status genotype 1 hepatitis C patients treated with peginterferon-alpha2b and ribavirin? J Clin Gastroenterol. 2009; 43: 362-366.

20 Juszczyk J, Beniowski M, Berak H, et al. Effectiveness of combined treatment with pegylated interferon α-2a and ribavirin in chronic hepatitis C – study phase summary. Med Sci Monit. 2004; 10 (Suppl 1): 5-11.

21 Juszczyk J, Baka-Ćwierz B, Beniowski M, et al. [Pegylatd interferon-alfa 2a with ribavirin in chronic viral hepatitis C (final report). Przegl Epidemiol. 2005, 59: 651-660. Polish.

22 Ascione A, De Luca M, Tartaglione MT, et al. Peginterferon alfa-2a plus ribavirin is more effective than peginterferon alfa-2b plus ribavirin for treating chronic hepatitis C virus infection. Gastroenterology. 2010; 138: 116-122.

23 Rumi MG, Aghemo A, Prati GM, et al. Randomized study of peginterferon-alpha2a plus ribavirin vs peginterferon-alpha2b plus ribavirin in chronic hepatitis C. Gastroenterology. 2010; 138: 108-115.

24 Awad T, Thorlund K, Hauser G, et al. Peginterferon alfa-2a is associated with higher sustained virological response than peginterferon alfa-2b in chronic hepatitis C: systematic review of randomized trials. Hepatology. 2010; 51: 1176-1184.

25 Mach T, Cieśla A, Sanak M, et al. The importance of IL28B polymorphism in response to pegylated interferon alfa and ribavirin in chronic hepatitis caused by HCV genotype 1b. Przegl Gastroenterol. 2011. [In press].

26 Batts KP, Ludwig J. Chronic hepatitis. An update on terminology and reporting. Am J Surg Pathol. 1995; 19: 1409-1417.

27 Manns MP, McHutchison JG, Gordon SC, et al. Peginterferon alpha-2b plus ribavirin compared with interferon alpha-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomized trial. Lancet. 2001; 358: 958-965.

28 Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. N Engl J Med. 2002; 347: 975-982.

29 Hadziyannis SJ, Sette H Jr, Morgan TR, et al. Peginterferon-alfa-2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. Ann Intern Med. 2004; 140: 346-355.

30 McHutchison JG, Lawitz EJ, Shiffman ML, et al. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. N Engl J Med. 2009; 361: 580-593.

31 Afdhal NH, McHutchison JG, Zeuzem S, et al. Hepatitis C pharmacogenetics: state of the art in 2010. Hepatology. 2011; 53: 336-345.

32 Zeuzem S, Alberti A, Rosenberg W, et al.: management of patients with chronic hepatitis C virus infection and "normal" alanine aminotransferase activity. Aliment Pharmacol Ther. 2006; 24: 1133-1149.

33 Shiffman ML, Diago M, Tran A, et al. Chronic hepatitis C in patients with persistently normal alanine transaminase levels. Clin Gastroenterol Hepatol. 2006; 4: 645-652.

34 Prati D, Shiffman ML, Diago M, et al. Viral and metabolic factors influencing alanine aminotransferase activity in patients with chronic hepatitis C. J Hepatol. 2006; 44: 679-685.

35 Zeuzem S, Diago M, Gane E, et al. Peginterferon alfa-2a (40 kilodaltons) and ribavirin in patients with chronic hepatitis C and normal aminotransferase levels. Gastroenterology. 2004; 127: 1724-1732.

36 Hwang SJ, Lee SD. Hepatic steatosis and hepatitis C: Still unhappy bedfellows? J Gastroenterol Hepatol. 2011; 26 Suppl 1: 96-101.

37 Skowroński M, Zozulińska-Ziółkiewicz D, Juszczyk J, et al. C-reactive protein and chronic hepatitis C virus infection in diabetic patients. Pol Arch Med Wewn. 2010; 120: 491-496.

38 Saryusz-Wolska M, Szymańska-Garbacz E, Jabłkowski M: Rosiglitazone treatment in nondiabetic subjects with nonalcoholic fatty liver disease. Pol Arch Med Wewn, 2011; 121: 61-66.

ARTYKUŁ ORYGINALNY

Skuteczność pegylowanych interferonów PegIFN-α2a lub PegIFN-α2b w połączeniu z rybawiryną w leczeniu przewlekłego zapalenia wątroby wywołanego genotypem 1b wirusa HCV

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SŁOWA KLUCZOWE

HCV genotyp 1b, leczenie, przewlekłe zapalenie wątroby

STRESZCZENIE

WPROWADZENIE Leczenie przewlekłego wirusowego zapalenia wątroby (WZW) typu C pegylowanym interferonem (PegIFN) i rybawiryną powoduje trwałą odpowiedź wirusologiczną (*sustained virological response* – SVR) u około 50% chorych. SVR jest warunkowana czynnikami zależnymi od wirusa zapalenia wątroby typu C (HCV) i osoby zakażonej, włączając genotypy *IL28B*.

CELE Celem badań była ocena skuteczności terapeutycznej trudnego w eliminacji genotypu 1b HCV u chorych z Polski południowej.

PACJENCI I METODY Grupa 260 dorosłych chorych na przewlekłe WZW typu C z genotypem 1b HCV była leczona PegIFN-α2a lub PegIFN-α2b z rybawiryną przez 48 tygodni. Skuteczność leczenia oceniano po 12 tygodniach (wczesna odpowiedź wirusologiczna [*early virological response* – EVR]), 48 tygodniach (*end-of-treatment response* – ETR) i 6 miesiącach (SVR). Oznaczanie stężenia HCV-RNA, aktywności aminotransferazy alaninowej (ALT) i inne testy biochemiczne wykonano przed leczeniem oraz po 12, 48 i 72 tygodniach leczenia.

WYNIKI Stężenie HCV-RNA przed leczeniem wynosiło $3{,}72 \pm 1{,}17 \times 10^6$ IU/ml i po 12 tygodniach leczenia znamiennie się zmniejszyło ($0{,}02 \pm 0{,}17 \times 10^6$ IU/ml); nie stwierdzono różnic pomiędzy grupą leczoną PegIFN-α2a a grupą leczoną PegIFN-α2b. ALT przed leczeniem wynosiła $94{,}1 \pm 7{,}6$ IU/l i po 12 tygodniach znamiennie się zmniejszyła ($42{,}5 \pm 3{,}1$ IU/l). Ogólna EVR, ETR i SVR została osiągnięta odpowiednio u 63,9, 77,7 i 48,1% pacjentów. Tolerancja leków w obu grupach była podobna.

WNIOSKI Skuteczność PegIFN-α2a i PegIFN-α2b z rybawiryną nie różni się znamiennie, a SVR uzyskało odpowiednio 48,3 i 44,3% chorych. Badanie potwierdza, że skuteczność leczenia chorych zakażonych genotypem 1b HCV, pochodzących z regionu Polski południowej, jest zbliżona do efektów obserwowanych w całej polskiej populacji.

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