World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.3748/wjg.v20.i14.4071

World J Gastroenterol 2014 April 14; 20(14): 4071-4075
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

RESEARCH REPORT

Efficacy and tolerability of low-dose interferon-α in hemodialysis patients with chronic hepatitis C virus infection

Kai-Li Wang, Han-Qian Xing, Hong Zhao, Jun-Wei Liu, Deng-Lian Gao, Xue-Hua Zhang, Hong-Yu Yao, Li Yan, Jun Zhao

Kai-Li Wang, Han-Qian Xing, Hong Zhao, Jun-Wei Liu, Deng-Lian Gao, Xue-Hua Zhang, Hong-Yu Yao, Li Yan, Jun Zhao, Department of Blood Purification, 302 Hospital of the People's Liberation Army, Beijing 100039, China

Author contributions: Wang KL and Xing HQ contributed equally to the treatment of patients, analyzing of data, and writing of the manuscript; Zhao H participated in the treatment of patients and collecting of data; Liu JW, Gao DL, Zhang XH, Yao HY, and Yan L participated in data collection and patient follow-up; Zhao J designed the manuscript and edited the final draft.

Correspondence to: Jun Zhao, Professor, Department of Blood Purification, 302 Hospital of the People's Liberation Army, Xisihuan Zhonglu No. 100, Fengtai District, Beijing 100039, China. zhj68@263.net

Telephone: +86-10-66933438 Fax: +86-10-66933434

Received: September 10, 2013 Revised: November 21, 2013
Accepted: January 3, 2014
Published online: April 14, 2014

Abstract

AIM: To evaluate the efficacy and tolerability of low-dose standard or pegylated interferon (PEG-IFN) in hepatitis C virus (HCV)-positive hemodialysis patients.

METHODS: In total, 19 patients were enrolled in this study, of which 12 received PEG-IFNα-2a 67.5 μg 1 time/wk (Group 1) and 7 received standard interferon α-2b subcutaneously 1.5 × 10^6 U 3 times/wk (Group 2). The treatment durations were 48 wk for patients infected with HCV genotype 1 and 24 wk for patients infected with HCV genotype 2/3. All patients were prospectively followed after the completion of therapy. The efficacy and tolerability of the treatment were evaluated based on the sustained virological response (SVR) and treatment-related drop-out rate.

RESULTS: In Group 1, 11 of the 12 patients completed the treatment. Early virological response (EVR) and sustained virological response (SVR) rates were 83.3% and 91.7%, respectively. One patient withdrew from treatment due to an adverse event (leukopenia). The drop-out rate was 8.3% in this group. In Group 2, 5 of the 7 patients completed the treatment with an EVR and SVR of 85.7% and 71.4%, respectively. Two patients withdrew due to treatment-related adverse events (nausea and depression). In this group, the drop-out rate was 28.6%. In total, 16 of the patients attained EVR, and 15 of them completed the treatment. The SVR rate for the patients who attained EVR was 93.7%. Anemia was the most frequent side effect and was observed in 10/19 patients (55.5%), but could be effectively managed with erythropoietin.

CONCLUSION: Low-dose interferon monotherapy, either with PEG-IFNα-2a or standard interferon α-2b, is an effective treatment option for hemodialysis patients with chronic hepatitis C.

Key words: Chronic hepatitis C; End-stage renal disease; Hemodialysis; Hepatitis C virus; Peginterferon

Core tip: The most appropriate treatment for hepatitis C virus (HCV)-positive hemodialysis patients is unknown, and the available treatments have only been assessed in a limited manner. Therefore, this study evaluated the efficacy and tolerability of treatment with low-dose standard or pegylated interferon (PEG-IFN) in HCV-positive hemodialysis patients. The results of the study indicated that low-dose interferon monotherapy, either PEG-IFNα-2a or standard interferon α-2b, is an effective treatment option for HCV-positive hemodialysis patients. Anemia was the most frequently encountered adverse event, but this could be managed with erythropoietin. These results provide important information for clinicians faced with these treatment decisions.

Wang KL, Xing HQ, Zhao H, Liu JW, Gao DL, Zhang XH, Yao HY, Yan L, Zhao J. Efficacy and tolerability of low-dose interferon-α in hemodialysis patients with chronic hepatitis C virus infection. *World J Gastroenterol* 2014; 20(14): 4071-4075 Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i14/4071.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i14.4071

INTRODUCTION

End-stage renal disease (ESRD) is a significant problem worldwide. In China, more than 65000 ESRD patients have received maintenance hemodialysis (HD)[1]. These patients have a higher rate of chronic hepatitis C virus (HCV) infection compared with the overall population[2], with an estimated prevalence and incidence of 3%-80% and 0.33%-2.59%, respectively[2-5]. Moreover, chronic HCV infection might ultimately lead to severe liver lesions, cirrhosis, and hepatocellular cancer, further increasing the morbidity and mortality of ESRD patients[6,7].

Interferon combined with oral ribavirin is the standard treatment for chronic HCV[8]. However, the use of ribavirin is currently contraindicated in dialysis patients[9,10], as the drug is not removed during conventional dialysis and its accumulation causes dose-dependent hemolytic anemia[11,12]. Interferon monotherapy is therefore recommended for the treatment of dialysis patients with chronic hepatitis C[13]. However, experience with monotherapy in ESRD patients is still limited.

The available data suggest that the rate of adverse events and drop-outs in this patient population is high[14-16]. We hypothesized that a lower dose of interferon monotherapy may decrease the incidence of adverse events and drop-outs, thus improving the likelihood of completing treatment. Therefore, the objective of this study was to evaluate the relative efficacy and tolerability of treatments consisting of either 1.5×10^6 U 3 times/wk of standard interferon or 67.5 μg/wk of pegylated interferon (PEG-IFN) α-2a (40 kDa). The treatments lasted for 48 wk in ESRD patients infected with HCV genotype 1 and for 24 wk in ESRD patients infected with HCV genotype 2/3.

MATERIALS AND METHODS

Patients

A total of 19 patients (11 male and 8 female) with a mean age of 37.7 years (range: 27-58 years) were enrolled in this study. The subjects had been undergoing dialysis for an average of 7.3 ± 4.5 (range: 2-16) years. All patients were on a maintenance HD program for ESRD, with 4-h dialysis sessions, 3 times/wk, using high-flux synthetic membranes, and bicarbonate dialysate. All patients were positive for HCV antibodies and had demonstrated detectable HCV RNA by polymerase chain reaction for at least 3 mo. The patients' HCV genotypes were confirmed before treatment. All the treated patients met the criteria for treatment with PEG-IFNα-2a or standard interferon α-2b.

Treatment and follow-up

All patients were recommended to receive intramuscular injections of 67.5 μg PEG-IFNα-2a once/wk after their HD session. For economic reasons, only 12 patients (8 male and 4 female; mean age: 39.4 ± 9.4 years) received this treatment (Group 1). The other 7 patients (3 male and 4 female; mean age: 34.7 ± 6.5 years) received subcutaneous injections of standard interferon α-2b, 1.5×10^6 U 3 times/wk, which was also administered after each HD session (Group 2). The treatment durations were 48 wk for patients infected with HCV genotype 1 and 24 wks for patients infected with HCV genotypes 2/3/6.

All treated patients were prospectively followed until week 96, which corresponded to 48 wk after the completion of the treatment, to assess the long-term efficacy and tolerability of the lower-dose interferon monotherapy. Blood samples were collected weekly to determine blood cell counts, and monthly to determine liver function. The presence of HCV RNA was assessed prior to treatment and then every 3 mo after treatment. Early virological response (EVR), defined as a ⩾ 2 log-fold decrease in HCV RNA from baseline, was evaluated after 12 wk of treatment. The efficacy of the treatment was determined by the achieved end treatment virological response (ETR), defined as the absence of detectable serum levels of HCV RNA at week 48, and sustained virological response (SVR), defined as the absence of detectable serum levels of HCV RNA at week 72. Tolerability was evaluated by assessing the drop-out rates and serious adverse events.

Statistical analysis

The data were analyzed using SPSS software (Windows version 15.0; SPSS, Chicago, IL, United States) and are presented as the means ± SD for parameter variables.

RESULTS

The baseline values of the patients are shown in Table 1, and the outcomes are presented in Table 2.

Efficacy

In Group 1, 11 of the 12 patients completed the treatment, with 1 patient withdrawing from treatment due to an adverse event. In this group, EVR was observed in 10 patients at week 12, and ETR was achieved in 11 patients. The 11 patients who attained ETR also achieved a SVR.

In Group 2, EVR was observed in 6 patients. In total, 5 patients completed the treatment, and ETR and SVR were recorded in all of these patients. In Group 2, 2 patients withdrew from treatment.

The HCV genotype was type 1 in 16 patients, with 13 patients achieving a SVR, yielding a genotype 1 SVR of 81.3%. The 3 patients with HCV genotype 2 all attained a SVR. In total, 16 of the patients attained EVR, and 15 of them completed the treatment. The SVR rate for the patients who attained EVR was 93.7%.

Table 1 Patient baseline characteristics

Case	Sex	Age (yr)	Weight (kg)	HD duration (yr)	Cirrhosis	Genotype	HCV RNA (IU/mL)
1	M	52	62	5	N	1b	4805000
2	F	28	40	10	N	1b	3150000
3	M	28	69	14	N	1b	15840
4	M	38	52	6	N	1b	3600000
5	F	38	54	16	N	1b	3786000
6	F	36	47	2	N	1b	167000
7	F	47	48	14	N	1b	663000
8	M	40	59	9	N	1b	356000
9	M	39	63	13	N	1b	156000
10	M	41	67	2	N	2a	15580
11	F	58	50	6	N	2a	9590
12	M	28	55	2	N	1b	209200
13	M	41	63	3	N	1b	39460
14	M	33	59	6	N	1b	143000
15	F	32	52	7	N	2a	446400
16	M	36	67	6	N	1b	456000
17	F	27	51	4	N	1b	14500
18	F	29	49	4	N	1b	12200
19	M	45	62	11	Y	1b	266000

HCV: Hepatitis C virus; HD: Hemodialysis; F: Female; M: Male.

Table 2 Patient treatment results

Case	IFN-α type	HCV RNA (IU/mL)				
		12 wk	48 wk	72 wk	96 wk	144 wk
1	PegIFNα-2a	405100	Positive	Positive	Positive	Positive
2	PegIFNα-2a	Negative	Negative	Negative		
3	PegIFNα-2a	Negative	Negative	Negative	Negative	Negative
4	PegIFNα-2a	Negative	Negative	Negative	Negative	Negative
5	PegIFNα-2a	Negative	Negative	Negative	Negative	
6	PegIFNα-2a	Negative	Negative	Negative	Negative	
7	PegIFNα-2a	2380	Negative	Negative	Negative	
8	PegIFNα-2a	Negative	Negative	Negative	Negative	
9	PegIFNα-2a	Negative	Negative	Negative		
10	PegIFNα-2a	Negative	Negative	Negative	Negative	
11	PegIFNα-2a	Negative	Negative	Negative	Negative	
12	PegIFNα-2a	Negative	Negative	Negative	Negative	
13	IFNα-2b	Negative	Negative	Negative		
14	IFNα-2b	Negative	Negative	Negative	Negative	
15	IFNα-2b	Negative	Negative	Negative	Negative	
16	IFNα-2b	256000	Positive	Positive		
17	IFNα-2b	Negative	Negative	Negative		
18	IFNα-2b	Negative	Negative	Negative		
19	IFNα-2b	Negative	Positive	Positive		

IFN: Interferon; PEG-IFN: Pegylated interferon; HCV: Hepatitis C virus.

All patients were followed post-treatment, and those who achieved a SVR had undetectable HCV RNA levels at week 96. Notably, 2 patients continued to have undetectable levels of HCV RNA at 144 wk, which was the last follow-up prior to the writing of this manuscript.

Tolerability

In Group 1, 1 patient withdrew from treatment due to significant leukopenia (8.2% drop-out rate). Two patients discontinued the standard interferon α-2b treatment (Group 2) due to treatment-related adverse events; one patient developed nausea (which required treatment cessation after 4 wk of therapy) and the other patient withdrew from treatment at week 20 because of depression (28.6% drop-out rate).

Anemia was one of the treatment-related adverse events observed in both groups. This adverse event was observed in 3 of the 7 (42.8%) patients in the standard interferon group and in 7 of the 12 (58.3%) patients treated with PEG-IFN. In these patients, the erythropoietin dose had to be increased to improve hemoglobin levels. However, the treatment protocol did not have to be discontinued in any patients due to anemia.

Other adverse events included influenza-like symptoms, nausea, poor appetite, leucopenia, and thrombocytopenia, as has been reported in other studies.

DISCUSSION

Interferon monotherapy trials involving small numbers of dialysis patients infected with chronic hepatitis C have previously been reported. In addition, 3 meta-analysis studies have shown that the SVR of ESRD patients infected with chronic hepatitis C and treated with standard IFN monotherapy was approximately 31%-41%[17-19]. However, the corresponding treatment-related withdrawal rate ranged from 20% to 30%[16,17,20]. Similarly, studies have also shown that the SVR and treatment-related withdrawal rates in patients receiving PEG-IFN were 31%-37% and 23%-28%, respectively[17,20,21]. Based on these studies, treatment of patients with either standard interferon or PEG-IFN had similar efficacy and tolerability.

In our study, 7 hemodialysis patients were treated with standard interferon α-2b for 48 wk. Six patients (85.7%) achieved EVR by week 12. In total, 2 patients discontinued treatment because of adverse events (1 due to nausea at week 4 and 1 due to depression at week 20), with both having a high viral load at baseline. At the end of week 72, the SVR rate was 71.4% (5/7 patients), with a drop-out rate of 28.6%. The drop-out rate was similar to that previously described in the meta-analyses. The 11 patients treated with PEG-IFNα-2a completed the treatment, and the EVR and SVR were 83.3% and 91.7%, respectively. For the patients who achieved a SVR, this subsequently remained stable.

Contrary to the concept that HCV genotype 1 is associated with a poor SVR rate in response to interferon monotherapy in HCV patients with normal renal function[22,23] our results showed a good SVR rate in HD patients. Although the 3 patients who dropped out all had genotype 1, the SVR rate for the remaining 16 patients with genotype 1 HCV was 81.3%, higher than that reported for HCV patients with normal renal function. Notably, all of the patients who dropped out had a very high HCV RNA load, which is considered as a negative predictor of a SVR[22,23].

In our study, 16 patients achieved an EVR, and 15 of them achieved a SVR. Therefore, patients with an EVR might be encouraged to continue therapy, as EVR appears to be a good predictor of a SVR. In this respect, our study is in agreement with the current literature.

The overall SVR for the 19 patients in this study was 84.2%, higher than that for interferon therapy in HCV patients with normal renal function. This result may be explained by the fact that the patients in the present study were younger (mean age 37.7 years), had a lower mean weight (55.5 ± 8.7; range 47-67 kg), and had a lower prevalence of cirrhosis (1/19). Being of Asian descent has also been reported to be an independent predictor of SVR in some studies[24]. Some studies have also suggested that hepatitis C dialysis patients usually have a lower viral load[25] and increased endogenous interferon release from circulating white blood cells[26].

Anemia was the most frequently encountered adverse event in both of the present study groups. However, in most cases, it was adequately managed with erythropoietin. The other adverse events observed included fatigue, headache, body ache, fever, nausea, reduced appetite, leucopenia, and thrombocytopenia. Regardless, low-dose interferon monotherapy did not result in a drop-out rate similar to what was expected for standard interferon monotherapy based on the results from non-HD patients.

This study has 2 major limitations: a small sample size and a lack of randomization for the 2 treatment groups, with the latter resulting in the lack of standard controls. Thus, these results may not be broadly extrapolated to the wider HD population.

In conclusion, either PEG-IFNα-2a or standard interferon α-2b monotherapy is an effective treatment option for HD patients with chronic hepatitis C. Anemia was the most frequently encountered adverse event in most cases and was effectively managed with erythropoietin. However, because of the small number of patients in this study, the conclusions of this study cannot be broadly generalized. Studies with low-dose interferon monotherapy are ongoing, and further long-term, large, randomized multicenter studies with larger patients and control populations are needed.

COMMENTS

Background

Hepatitis C virus (HCV) infection remains frequent in hemodialysis patients worldwide. However, the most appropriate treatment for HCV-positive hemodialysis patients is unknown.

Research frontiers

The present study was carried out in hemodialysis patients with chronic hepatitis C. Nineteen hemodialysis patients were included in this study.

Innovations and breakthroughs

The overall sustained virological response (SVR) for the 19 patients in this study was 84.2%, higher than that for interferon therapy in HCV patients with normal renal function.

Applications

This study showed that low-dose interferon monotherapy, either with pegylated interferon α-2a or standard interferon α-2b, is an effective treatment for hemodialysis patients with chronic hepatitis C.

Terminology

SVR indicates sustained virological response, which means sustained (more than 24 wk after treatment) viral clearance from the infected host.

Peer review

The authors investigated the effects and tolerability of low-dose interferon monotherapy for treatment of HCV-positive hemodialysis. The result showed either PEG-IFNα-2a or standard interferon α-2b monotherapy as an effective treatment option for HD patients with chronic hepatitis C.

REFERENCES

1 **Zuo L**, Wang M. Current burden and probable increasing incidence of ESRD in China. *Clin Nephrol* 2010; **74** Suppl 1: S20-S22 [PMID: 20979958 DOI: 10.5414/CNP74S020]
2 **Fabrizi F**, Poordad FF, Martin P. Hepatitis C infection and the patient with end-stage renal disease. *Hepatology* 2002; **36**: 3-10 [PMID: 12085342 DOI: 10.1053/jhep.2002.34613]
3 **Butt AA**, Skanderson M, McGinnis KA, Ahuja T, Bryce CL, Barnato AE, Chang CC. Impact of hepatitis C virus infection and other comorbidities on survival in patients on dialysis. *J Viral Hepat* 2007; **14**: 688-696 [PMID: 17875003 DOI: 10.1111/j.1365-2893.2007.00853.x]
4 **Fabrizi F**, Martin P, Dixit V, Bunnapradist S, Dulai G. Meta-

analysis: Effect of hepatitis C virus infection on mortality in dialysis. *Aliment Pharmacol Ther* 2004; **20**: 1271-1277 [PMID: 15606388 DOI: 10.1111/j.1365-2036.2004.02290.x]
5 **Kao JH**, Huang CH, Chen W, Tsai TJ, Lee SH, Hung KY, Chen DS. GB virus C infection in hemodialysis patients: molecular evidence for nosocomial transmission. *J Infect Dis* 1999; **180**: 191-194 [PMID: 10353878 DOI: 10.1086/314850]
6 **Hou CH**, Chen WY, Kao JH, Chen DS, Yang Y, Chen JJ, Lee SH, Wu DJ, Yang SC. Intrafamilial transmission of hepatitis C virus in hemodialysis patients. *J Med Virol* 1995; **45**: 381-385 [PMID: 7545208 DOI: 10.1002/jmv.1890450405]
7 **Furusyo N**, Hayashi J, Kakuda K, Ariyama I, Kanamoto-Tanaka Y, Shimizu C, Etoh Y, Shigematsu M, Kashiwagi S. Acute hepatitis C among Japanese hemodialysis patients: a prospective 9-year study. *Am J Gastroenterol* 2001; **96**: 1592-1600 [PMID: 11374705 DOI: 10.1111/j.1572-0241.2001.03701.x]
8 **Ghany MG**, Strader DB, Thomas DL, Seeff LB, American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology* 2009; **49**: 1335-1374 [PMID: 19330875 DOI: 10.1002/hep.22759]
9 **Dienstag JL**, McHutchison JG. American Gastroenterological Association medical position statement on the management of hepatitis C. *Gastroenterology* 2006; **130**: 225-230 [PMID: 16401485 DOI: 10.1053/j.gastro.2005.11.011]
10 **Yee HS**, Currie SL, Darling JM, Wright TL. Management and treatment of hepatitis C viral infection: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center program and the National Hepatitis C Program office. *Am J Gastroenterol* 2006; **101**: 2360-2378 [PMID: 17032203 DOI: 10.1111/j.1572-0241.2006.00754.x]
11 **Strader DB**, Wright T, Thomas DL, Seeff LB, American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C. *Hepatology* 2004; **39**: 1147-1171 [PMID: 15057920 DOI: 10.1002/hep.23077]
12 **Heathcote J**, Main J. Treatment of hepatitis C. *J Viral Hepat* 2005; **12**: 223-235 [PMID: 15850462 DOI: 10.1111/j.1365-2893.2005.00600.x]
13 **Asian Pacific Association for the Study of the Liver (APASL) Hepatitis C Working Party**, McCaughan GW, Omata M, Amarapurkar D, Bowden S, Chow WC, Chutaputti A, Dore G, Gane E, Guan R, Hamid SS, Hardikar W, Hui CK, Jafri W, Jia JD, Lai MY, Wei L, Leung N, Piratvisuth T, Sarin S, Sollano J, Tateishi R. Asian Pacific Association for the Study of the Liver consensus statements on the diagnosis, management and treatment of hepatitis C virus infection. *J Gastroenterol Hepatol* 2007; **22**: 615-633 [PMID: 17444847 DOI: 10.1111/j.1440-1746.2007.04883.x]
14 **Berenguer M**. Treatment of chronic hepatitis C in hemodialysis patients. *Hepatology* 2008; **48**: 1690-1699 [PMID: 18972442 DOI: 10.1002/hep.22545]
15 **Perico N**, Cattaneo D, Bikbov B, Remuzzi G. Hepatitis C infection and chronic renal diseases. *Clin J Am Soc Nephrol* 2009; **4**: 207-220 [PMID: 19129320 DOI: 10.2215/CJN.03710708]
16 **Fabrizi F**, Dulai G, Dixit V, Bunnapradist S, Martin P. Meta-analysis: interferon for the treatment of chronic hepatitis C in dialysis patients. *Aliment Pharmacol Ther* 2003; **18**: 1071-1081 [PMID: 14653826 DOI: 10.1046/j.1365-2036.2003.01780.x]
17 **Fabrizi F**, Dixit V, Messa P, Martin P. Interferon monotherapy of chronic hepatitis C in dialysis patients: meta-analysis of clinical trials. *J Viral Hepat* 2008; **15**: 79-88 [PMID: 18184190 DOI: 10.1111/j.1365-2893.2007.00907.x]
18 **Gordon CE**, Uhlig K, Lau J, Schmid CH, Levey AS, Wong JB. Interferon treatment in hemodialysis patients with chronic hepatitis C virus infection: a systematic review of the literature and meta-analysis of treatment efficacy and harms. *Am J Kidney Dis* 2008; **51**: 263-277 [PMID: 18215704 DOI: 10.1053/j.ajkd.2007.11.003]
19 **Fabrizi F**, Martin P, Dixit V, Bunnapradist S, Dulai G. Hepatitis C virus antibody status and survival after renal transplantation: meta-analysis of observational studies. *Am J Transplant* 2005; **5**: 1452-1461 [PMID: 15888054 DOI: 10.1111/j.1600-6143.2005.00864.x]
20 **Russo MW**, Goldsweig CD, Jacobson IM, Brown RS. Interferon monotherapy for dialysis patients with chronic hepatitis C: an analysis of the literature on efficacy and safety. *Am J Gastroenterol* 2003; **98**: 1610-1615 [PMID: 12873587 DOI: 10.1111/j.1572-0241.2003.07526.x]
21 **Zeuzem S**, Feinman SV, Rasenack J, Heathcote EJ, Lai MY, Gane E, O'Grady J, Reichen J, Diago M, Lin A, Hoffman J, Brunda MJ. Peginterferon alfa-2a in patients with chronic hepatitis C. *N Engl J Med* 2000; **343**: 1666-1672 [PMID: 11106715 DOI: 10.1056/NEJM200012073432301]
22 **Heathcote EJ**, Shiffman ML, Cooksley WG, Dusheiko GM, Lee SS, Balart L, Reindollar R, Reddy RK, Wright TL, Lin A, Hoffman J, De Pamphilis J. Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000; **343**: 1673-1680 [PMID: 11106716 DOI: 10.1056/NEJM200012073432302]
23 **Yu ML**, Dai CY, Huang JF, Chiu CF, Yang YH, Hou NJ, Lee LP, Hsieh MY, Lin ZY, Chen SC, Hsieh MY, Wang LY, Chang WY, Chuang WL. Rapid virological response and treatment duration for chronic hepatitis C genotype 1 patients: a randomized trial. *Hepatology* 2008; **47**: 1884-1893 [PMID: 18508296 DOI: 10.1002/hep.22319]
24 **Ge D**, Fellay J, Thompson AJ, Simon JS, Shianna KV, Urban TJ, Heinzen EL, Qiu P, Bertelsen AH, Muir AJ, Sulkowski M, McHutchison JG, Goldstein DB. Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. *Nature* 2009; **461**: 399-401 [PMID: 19684573 DOI: 10.1038/nature08309]
25 **Liao XW**, Ling Y, Li XH, Han Y, Zhang SY, Gu LL, Yu DM, Yao BL, Zhang DH, Jin GD, Lu ZM, Gong QM, Zhang XX. Association of genetic variation in IL28B with hepatitis C treatment-induced viral clearance in the Chinese Han population. *Antivir Ther* 2011; **16**: 141-147 [PMID: 21447862 DOI: 10.3851/IMP1703]
26 **Badalamenti S**, Catania A, Lunghi G, Covini G, Bredi E, Brancaccio D, Salvadori M, Como G, Ponticelli C, Graziani G. Changes in viremia and circulating interferon-alpha during hemodialysis in hepatitis C virus-positive patients: only coincidental phenomena? *Am J Kidney Dis* 2003; **42**: 143-150 [PMID: 12830466 DOI: 10.1016/S0272-6386(03)00417-7]

P- Reviewers: Coffin CS, Forns X, Kato M **S- Editor**: Wang JL
L- Editor: Rutherford A **E- Editor**: Ma S

百世登
Baishideng®

Published by **Baishideng Publishing Group Co., Limited**
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road, Wan Chai, Hong Kong, China
Fax: +852-65557188
Telephone: +852-31779906
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com

ISSN 1007-9327