

Efficacy and Safety of Glecaprevir/Pibrentasvir in Combination Therapy in Chronic Hemodialysis Patients with Genotype 2 Hepatitis C Virus Infection

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Abstract

Background: Glecaprevir (nonstructural protein 3/4A protease inhibitor) and Pibrentasvir (nonstructural protein 5A inhibitor) (G/P), a coformulated once-daily, all oral, ribavirin (RBV)-free, direct-antiviral regimen, was evaluated for safety and efficacy in chronic hemodialysis patients with genotype 2 hepatitis C virus infection. **Methods:** In this prospective, observational, single-center study at Masuko Memorial Hospital, between November 2017 and December 2018, a total of 8 HD patients with an HCV infection genotype 2 received G/P combination therapy. Age was an average of 67.1 (61 - 75) years and there were four men and two women. It was FIB4 INDX an average of 2.67 (1.5 - 3.34) before the start of therapy. It was quantity of HCV RNA an average of 4.43 (2.1 - 6.5). HCV RNA levels were measured by real-time RCR-based method (COBAS AmpiPrep/COBAS TaqMan HCV Test). 4 cases 12 weeks were 2 cases eight weeks for dosing period. Patients were excluded if they had evidence of hepatocellular carcinoma. This study was approved by the ethics committee of our hospital, while we obtained written consent from the participants after providing a thorough explanation of the contents and methods of this study. **Results:** 6 patients were available for total dose internal use. As for the HCV RNA of the fourth week, (100%) HCV RNA became negative after administration start of therapy. Rapid virologic response (RVR) achieved all cases. 5 patients achieved 12-week sustained virologic response (SVR12) and were following up the 1 patient. The itching appeared in two cases (33%), but there was symptom improvement in nalfurafine hydrochloride use treatment, and treatment continuation was possible. **Conclusion:** It is thought that G/P can be given to the HD patients' safety, but we will accumulate a case in future, and it is thought to be necessary to examine utility and safety.

Keywords

HCV, RNA, Hepatitis C, Virus Infection, Chronic Hemodialysis, Patients

1. Introduction

Hepatitis C virus (HCV) infects more than 170 million people worldwide and causes liver cirrhosis and hepatocellular carcinoma. Thus, HCV infection is an important health concern [1] [2]. Recent studies have clearly revealed that the prognosis of hemodialysis (HD) patients with an HCV infection is significantly worse compared with dialysis patients not infected with HCV [3]. Death from hepatocellular carcinoma (HCC) and cirrhosis or liver failure is markedly higher in hemodialysis patients with HCV infection than non-infected patients with end-stage renal disease (ESRD) [4]. Patients with chronic kidney disease (CKD) on renal replacement therapy especially HD continue to have a higher prevalence of hepatitis C virus infection than the general population. The prevalence of anti-HCV seropositivity in patients undergoing regular dialysis in developed countries ranges between 7% and 40% [5] [6] [7].

Recently, the Kidney disease Improvement Global Outcome (KIDIGO) and Japanese Society for Dialysis Therapy (JSDT) established the Guideline of Treatment of Hepatitis C Virus infection in dialysis patients [8] [9]. Glecaprevir (nonstructural protein 3/4A protease inhibitor) and Pibrentasvir (nonstructural protein 5A inhibitor)(G/P), a coformulated once-daily, all oral, ribavirin (RBV)-free, direct-antiviral regimen, was evaluated for safety and efficacy in chronic hemodialysis patients with genotype 2 hepatitis C virus infection.

2. Methods

Single-center study at Masuko Memorial Hospital, between November 2017 and December 2018, a total of 8 HD patients showed in **Table 1** with an HCV infection genotype 2 received G/P combination therapy. Age was an average of 67.1 (61 - 75) years and was four men, women two. It was FIB4 INDX an average of 2.67 (1.5 - 3.34) before the start of therapy. It was quantity of HCV RNA an average of 4.43 (2.1 - 6.5). 4 cases 12 weeks were 2 cases eight weeks for dosing period. Patients were excluded if they had evidence of hepatocellular carcinoma. This study was approved by the ethics committee of our hospital, while we obtained written consent from the participants after providing a thorough explanation of the contents and methods of this study.

3. Results

6 patients were available for total dose internal use. 6 patients were available for total dose internal use. As for the HCV RNA of the fourth week, (100%) HCV RNA became negative after administration start of therapy. Rapid virological response (RVR) achieved all cases (**Figure 1**). 5 patients achieve SVR12 and are

following up the 1 patient (**Figure 2**).

The itching appeared in two cases (33%), but there was symptom improvement

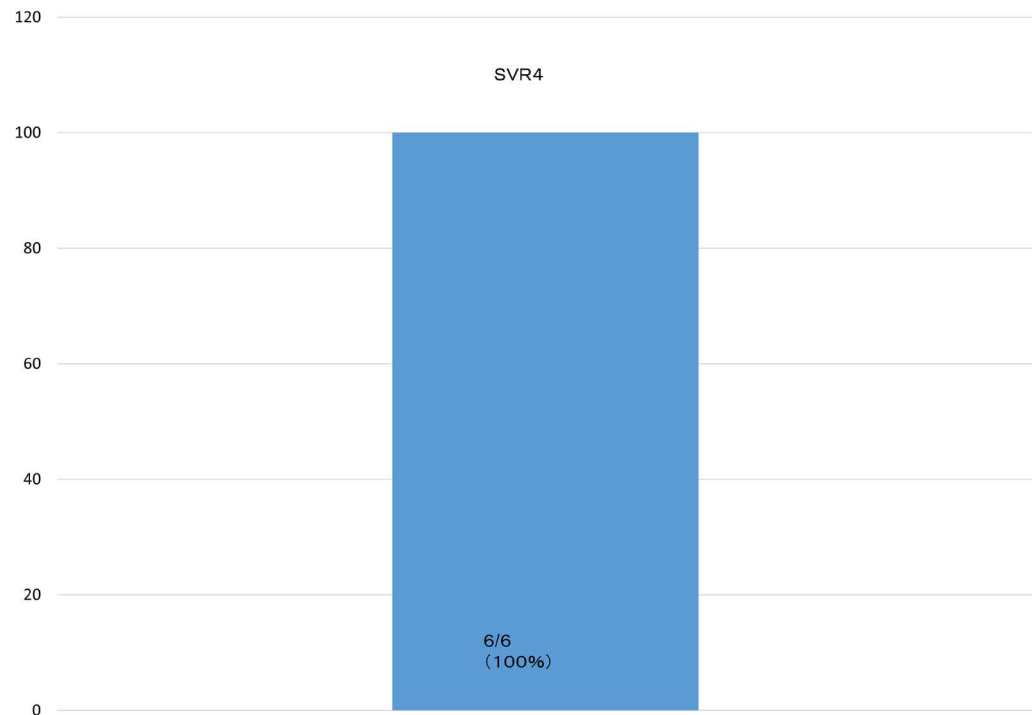


Figure 1. As for the HCV RNA of the fourth week, (100%) HCV RNA became negative after administration start of therapy. Rapid virological response (RVR) achieved all cases.

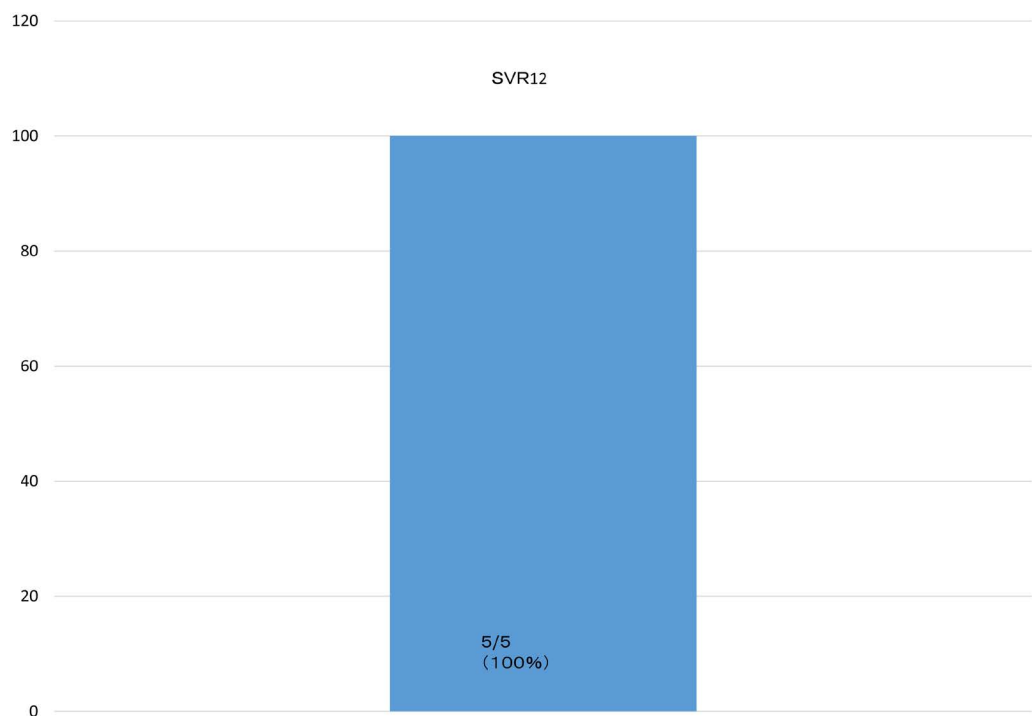


Figure 2. 5 patients achieve rates of sustained virologic response 12 weeks after treatment (SVR12) and are following up the 1 patient.

Table 1. Patient demographic data.

All Patients, n (%)	6 (100)	
Age, Year	Mean 67.1 (Range 61 - 75)	
Gender (%)	Female 2 (34)	Male 4 (66)
FIB4 Index (1.5 - 3, 34)	Mean 2.67	

in nalfurafine hydrochloride use treatment, and treatment continuation was possible.

4. Discussion

In this study, to our knowledge, we are the first to report the effectiveness and safety of G/P combination therapy in chronic hemodialysis patients with genotype 2 hepatitis C virus infection. The genotype 1 report appears, but the report in genotype 2 patients on dialysis is the first time.

Kikuchi *et al.* report the interferon therapy of the patient on dialysis, but an SVR rate is 39% (22 of 56) in a report of REACH Study by peg INF α 2a, [10] that the subject limited to the case that there were few young people and complications without being able to say the enough SVR rate. In addition, the SVR rate of Peg-interferon monotherapy is not high and significant rate of adverse events have been observed. Several oral direct-antiviral drugs (DAAs) for HCV have recently been developed.

An oral agent of the interferon-free (daclatasvir (DCV) and asunaprevir (ASV)) becomes the initiation for the next 2106 years. Indeed, a previous study reported no significant in pharmacokinetics of two drugs between patients with ESRD receiving hemodialysis and those without renal dysfunction. Therefore, these DAAs may be used in patients who are undergoing hemodialysis, with high anti-HCV efficacy expected. Toyoda *et al.* also reported the efficacy and safety of daclatasvir/asunaprevir combination therapy for HCV genotype 1b-infected dialysis patients (overall SVR 12 rate 100%: 28/28), and treatment-related adverse events were similar to those noted among patients with normal renal function [11]; Suda *et al.* [12]. Over all, total of 95.5% (20/21) SVR12 of the patients achieved SVR12. However, DAAs did not have the adaptation to the genotype 2 patients.

Atsukawa *et al.* retrospectively analyzed the safety and efficacy of paritaprevir/ritonavir and ombitasvir in 31 hemodialysis patients with genotype 1b infection. The overall SVR12 rate was 96.8% (30/31). Eleven patients (35.5%) experienced adverse events (AEs). One patient discontinued this combination therapy due to AEs and experienced virological relapse [13]. Also, ribavirin (RBV) can be used with dosage modifications in patients with impaired renal function, the majority of HCV infected patients with ESRD have gone untreated.

Paul *et al.* 20 reported that patients completed 12 weeks of treatment eighteen of the 20 patients achieved SVR12 [14]. Currently, no HCV treatment for genotype 2 is approved in Japan for duration of less than 12 weeks or without RBV.

The elimination of RBV from DAA regimens can improve tolerability and reduce rates of treatment discontinuation due to AEs as RBV is associated with decreases in hemoglobin and elevations of indirect bilirubin.

G/P a coformulated once-daily, all oral, ribavirin (RBV)-free, direct-antiviral regimen, was evaluated for safety and efficacy in chronic hemodialysis patients with genotype 2 hepatitis C virus infection [15] [16].

Oral medicine was able to be given in 6 cases all cases in the examination in this hospital during an adaptation period, respectively. When we used interferon, we might stop treatment for anemia update and leukopenia, but we took G/P without it looking like it and were able to continue. Also, two patients had itching without showing the side effects such as anorexia or the general malaise. Internal use continuation was enabled in acknowledgment of the relief of symptom by using nalfurafine hydrochloride as correspondence to these cases. There is little number of cases, but we will accumulate a case in future and want to examine safety and efficacy now.

5. Conclusion

It is thought that G/P can be given to the HD patients safely, but we will accumulate a case in future, and it is thought to be necessary to examine utility and safety.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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