



# Treatment with Pegylated Interferon Alfa-2a plus Lower Dose Ribavirin for Hemodialysis Patients with Chronic Hepatitis C

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- **Backgrounds:** Hepatitis C virus infection remains prevalent among patients undergoing long-term hemodialysis. It has a detrimental impact on survival in this population. Antiviral therapy for chronic hepatitis C (CHC) in hemodialysis patient is still challenge to clinicians.
- **Aims:** Research focusing on Pegylated interferon alfa-2a (Peg-IFN- $\alpha$ -2a) plus lower dose ribavirin use in hemodialysis patients with CHC is limited in Ping-Tung. The aim of this study was to evaluate the efficacy and safety for CHC patients undergoing long-term hemodialysis.
- **Methods:** We conducted a retrospective cohort trial with case control study of 13 hemodialysis patients treated with Peg-IFN- $\alpha$ -2a 135 mcg/week with ribavirin, 200 mg daily or tiw. Thirteen CHC patients who did not receive hemodialysis treated with dual therapy were served as control used to match the study group. Clinical parameters and virological responses on treatment were evaluated. Predictive factors of sustained virological response (SVR) were identified.
- **Results:** The pretreatment patient characteristics with presence of hemolytic anemia (69.2% vs. 46.2%,  $P=0.234$ ), 80/80/80 adherence (92.3% vs. 76.9%,  $P=0.277$ ), dose modification (30.8% vs. 46.2%,  $P=0.420$ ) and discontinuation (15.4% vs. 23.1%,  $P=0.619$ ) were comparable between groups with and without receiving hemodialysis. By using ITT and PP analyses, there were no significant differences between both groups for RVR rates (84.6% vs. 100%,  $P=0.141$ , ITT; 76.9% vs. 100%,  $P=0.066$ , PP) and SVR rates (61.5% vs. 69.2%,  $P=0.680$ , ITT; 72.7% vs. 100%,  $P=0.089$ , PP). In multivariate step-wise logistic regression analysis, baseline HCV RNA level <800,000 IU/ml was independently associated with SVR (OR: 6.500; 95% CI: 1.094-38.633;  $P=0.04$ ).
- **Conclusions:** Peg-IFN- $\alpha$ -2a once weekly with lower dose ribavirin dual therapy provides effective and safe therapy for CHC patients undergoing long-term hemodialysis. Pretreatment viral load is a factor predictive of SVR. Further large studies are needed to confirm these findings.

Table 1 Baseline characteristics

Characteristics	Patients with HD (n=13)	Patients without HD (n=13)	p Value
Male gender, n (%)	10 (76.9)	9 (69.2)	<b>0.685</b>
Age (years), mean (SD)	61.8±12.5	62.0±12.2	<b>0.975</b>
Body mass index (kg/m <sup>2</sup> ), mean (SD)	24.2±3.3	24.5±2.7	<b>0.810</b>
Body weight (kg), mean (SD)	63.6±10.4	65.5±12.2	<b>0.620</b>
White blood cell count (x10 <sup>9</sup> /l), mean (SD)	6.6±2.1	5.3±2.3	<b>0.147</b>
Hemoglobin (g/l), mean (SD)	11.3±2.3	13.0±1.8	<b>0.072</b>
Platelet (x10 <sup>9</sup> /l), mean (SD)	168±81	138±60	<b>0.303</b>
ALT quotient (/ULN), mean (SD)	9.2±14.2	2.9±1.5	<b>0.125</b>
ALTxULN $\geq 3$ , n (%)	9 (69.2)	4 (46.2)	<b>0.050</b>
Creatinine (mg/dl), mean (SD)	9.6±3.0	1.1±0.3	<b>&lt;0.001*</b>
APRI score $\geq 1.0$ , n (%)	9 (69.2)	13 (100)	<b>0.030*</b>
HCV RNA level, log <sub>10</sub> IU/mL, mean (SD)	5.9±0.9	5.8±0.7	<b>0.814</b>
RNA level >800000 IU/mL, n (%)	5 (38.5)	5 (38.5)	<b>1.000</b>
Single infection, n (%)	12 (92.3)	13 (100)	<b>0.308</b>
Steatosis, n (%)	9 (69.2)	6 (46.2)	<b>0.234</b>
Cirrhosis, n (%)	1 (7.7)	5 (38.5)	<b>0.663</b>
Genotype, n (%)			<b>0.787</b>
1b	3 (23.1)	3 (23.1)	
2a	9 (69.2)	8 (61.5)	
2b	0 (0)	1 (7.7)	
6	0 (0)	1 (7.7)	
G (2), n (%)	9 (69.2)	9 (69.2)	<b>1.000</b>
Ribavirin dose (mg/kg/day)	3.1±1.2	13.6±4.1	<b>&lt;0.001*</b>
Presence of hemolytic anemia	9 (69.2)	6 (46.2)	<b>0.234</b>
<sup>a</sup> Presence of 80/80/80 adherence	12 (92.3)	10 (76.9)	<b>0.277</b>
Dose modification	4 (30.8)	6 (46.2)	<b>0.420</b>
Discontinuation	<b>2 (15.4)</b>	<b>3 (23.1)</b>	<b>0.619</b>

Data are the no. (%) of patients; SD, standard deviation; AST, aspartate aminotransferase; ALT, almandine aminotranferase; ULN, upper limit of normal; APRI, aspartate aminotransferase to platelet ratio index; <sup>a</sup>80/80/80, Patients who received >80% of expected pegylated interferon, ribavirin doses and completed at least 80% of its expected duration; \* expressed as  $p$  value <0.05.

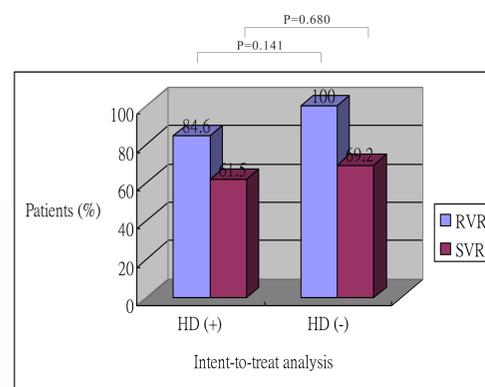


Figure 1 Virological response rates in chronic hepatitis C dialysis patients vs. matching general population with pegylated interferon-2a plus low-dose ribavirin. Intent-to-treat, patients who received at least one dose of the study medication. HD (+), dialysis patients; HD (-), general population. RVR, rapid virological response; SVR, sustained virological response.

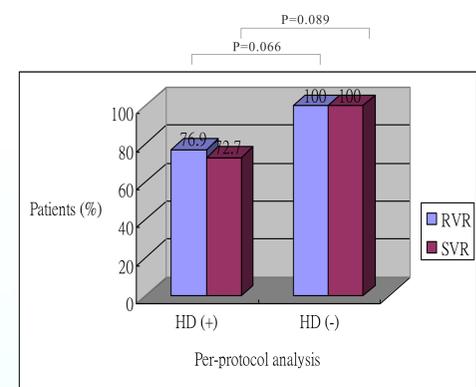


Figure 2 Virological response rates in chronic hepatitis C dialysis patients vs. matching general population with pegylated interferon-2a plus low-dose ribavirin. Per-protocol, patients who completed follow-up of study medication.

Table 2 Univariate and multivariate logistic regression analysis of baseline and on-treatment factors predictive of sustained virological response

Variable	Univariate analysis	Multivariate analysis	
	p Value	OR (95% CI)	p Value
Hemodialysis (presence vs. absence)	0.681		
Gender (male vs. female)	0.695		
Age (<60 vs. >60)	0.135		
BW (<75 vs. >75)	0.663		
Platelet count (>150 vs. <150 x10 <sup>9</sup> /l)	0.875		
ALTxULN (>3 vs. <3)	0.681		
Steatosis (absence vs. presence)	0.324		
Cirrhosis (absence vs. presence)	0.373		
APRI (>1 vs. <1)	0.488		
HCV RNA level (<800000 vs. >800000)	0.04*	6.500 (1.094-38.633)	<b>0.04*</b>
HCV genotype (1 vs. 2)	0.223		
Hemolytic anemia (presence vs. absence)	0.144		
Modification (presence vs. absence)	0.649		
RVR (presence vs. absence)	<b>0.639</b>		

BW, body weight; ALT, almandine aminotranferase; ULN, upper limit of normal; APRI, aspartate aminotransferase to platelet ratio index; OR, odd ratio; CI, confidence interval; RVR, rapid virological response; \* expressed as  $p$  value <0.05.