TREATMENT OF CHRONIC HEPATITIS C GENOTYPE 6 WITH TRIPLE THERAPY PEG-IFN, RIBAVIRIN AND SOFOSBUVIR: CASE STUDY AND REVIEW OF LITERATURE

Tran Xuan Chuong

Hue University of Medicine and Pharmacy, Vietnam

Abstract

The author presents a case with chronic hepatitis C, genotype 6, treated with triple regimen: Peg-IFN combined to ribavirin and sofosbuvir. After 3 months of therapy and 3 months follow up, patient has clinical and virological response (SVR 12). Some results of similar studies in Vietnam and abroad, especially the studies concerning the new agents DAAs were also presented, analysed and compared with author' s results.

Key words: hepatitis C, treatment, Peg-IFN, ribavirin, sofosbuvir

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1. CASE STUDY

Patient Pham S., 62 years old, retired. Lives in Dong Hoi City, Quang Binh province. From December, 2015, patient has fatigue, anorexia, unsleeping, anxiety. Then urine became yellow, mild jaundice.

Clinical examination in Hue University Hospital (December, 21st 2015): patient fells fatigue, anorexia. Mild jaundice was recognized. Liver was in normal size. In antecedant: patient has not noted liver disease and was not treated by any liver disease.

Paraclinical examination: Blood count: RBC $3,93.10^{12}$/L., Hb 119 g/L:, WBC $5,9.10^{9}$/L. , platelet 130.10^{9}/L, INR 1.16. Biochemistry: AST 245 U/L, ALT 105 U/L, GGT 415 U/L, Bilirubin 37 µmol/L. Quantitative HCV RNA $4,68 . 10^{6}$ copies/mL, genotype 6.

Fibrosis assesment by Acoustic Radiation Force Impulse (ARFI) in Medic clinic, Hue: F2

Diagnosis: Chronic hepatitis C, genotype 6, significant fibrosis (F2).

After consultations with doctors, patient liked to be treated with triple therapy including sofosbuvir, Peg-IFN and ribavirin.

The treatment was started on 30th December 2015 with triple therapy sofosbuvir 400mg daily, Peg-IFN 180 µg subdermal weekly and ribavirin 1000 mg daily.

Clinical evolution: In the first 2 months, the symptoms such as fatigue, anorexia, unsleeping decreased slowly and disappeared after 4 weeks. Mild but not constant epigastric pain was recognized. Patients has losen 2 kg after 2 months.

In the 3rd month after treatment: patient had good appetite, sleeps well, light vertiges. Blood pressure: 130/80 mmHg.

Paraclinical examination in 3 months of treament and after treatment:

Examination	After 2 weeks (12.01.2016)	After 4 weeks (26.01)	After 8 weeks (23.02)	After 12 weeks (22.03). End of treatment	Week 12 after end of treatment (20.06.16)
HCV RNA		positive, under detection 's level		undetectable	undetectable
AST (U/L)	82	79	73	104	42
ALT (U/L)	19	14	11	58	26
GGT (U/L)	311		404	358	127
Bilirubin (µmol/L)	26		19,6		
Hb (g/L)	119	96	85	83	112
WBC (10^{9}/L)	3,62	4,2	3,31	3,2	4,32
Platelet (10^{9}/L)	51,7	78	87	71	128
INR	1.45	1.01		0.9	1.25

- *Corresponding author: Tran Xuan Chuong, email: xuanchuonghue@gmail.com*
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Note: Hemoglobin decreased slowtly in the duration of treatment, from 119 g/L to only 96, 85 and 83 g/L after 4, 8 and 12 weeks after end of treatment 12 weeks, Hb increased to 112g/L. Platelet decreased clearly from 130.000/microlit to only 51.700 after 4 weeks; then elevated mildly to 78.000 and 87.000 at week 4 and 8 and decreased again to 71.000 after 12 weeks.

The noted side effects were low fever, headache, malaise, chills after the first injections of Peg IFN. Besides, sometimes patients has complain about vertiges, nausea ect.

2. REVIEW OF LITERATURE AND DISCUSSIONS

Genotype 6 of HCV is rare in the world but popular in East Asia and South-East Asia. In Thailand, HCV genotype 6 was recognized in about 8 – 18% among HCV infected. In Vietnam and Myanmar, genotype 6 was recognized in about 30 – 40% from HCV infected people and it is the second genotype after genotype 1.

Therefore there are not many reports about treatment's effects of HCV genotype 6. In Vietnam there were some publications of Truong Ba Trung and Pham Thi Thu Thuy related to HCV genotype 6 treatment.

According to the 2015 guideline of American Association for Study of Liver Diseases (AASLD), patients with genotype 5 or 6 should be treated by the combination ledipasvir 90 mg/daily and sofosbuvir 400 mg/daily in 12 weeks. The alternative regimen is triple therapy with sofosbuvir/ Peg-IFN/ ribavirin in 12 weeks [2].

Our patients was treated with the triple therapy in 3 months. The results showed patients had good response just after 4 weeks, HCV RNA level under detection limit (Rapid viral response, RVR). Biochemical response was also acceptable: AST and ALT diminued from 245 U/L and 105 U/L to only 82 and 19 U/L. After 12 weeks, HCV RNA was undetectable (end-of-treatment response), AST 104 U/L, ALT 58 U/L. Only GGT was relatively high (358 U/L).

In 12 weeks after end of treatment, patient felt better, had a good appetite. The controll examination showed HCV RNA undetectable, AST 42 U/L, ALT 26 U/L, GGT 127 U/L. So patient has sustained viral response (SVR 12).

A meta-analysis of Nguyen NH et al (USA) in 2014 shows SVR in patients with HCV genotype 6 infection treated with Peg IFN and ribavirin in 24 and 48 weeks were 59% and 79%, respectively [7]. The similar results of Cai et al were 90.8% and 88.2% [3]

In Vietnam, Pham Thi Thu Thuy et al reported the rate of SVR in patients with HCV genotype 6 infection treated with Peg IFN and ribavirin in 24 and 48 weeks were 60% and 71%, respectively [7]. Truong Ba Trung et al reports the SVR12 in chronic hepatitis C genotype 1 and 6 patients treated with triple therapy sofosbuvir/ Peg-IFN/ ribavirin in 12 weeks was 100% [1].

Recent study (2015) of Gane EJ et al treated HCV genotype 6 patients with sofosbuvir/ledipasvir shows 24/25 has SVR12 (96%) [4]. Lai CL et al treated HCV genotype 6 patients with sofosbuvir/ribavirin shows 100% has SVR12. The noted side effects were fatigue (13%), upper respiratory infection (13%) and anemia (10%) [5].

Zeuzem S et al (Germany) treated HCV genotype 6 patients with the new DAA grazoprevir (NS3/4A protease inhibitor)/ elbasvir (NS5A inhibitor). The results showed 8/10 patients has SVR (80%) [10]. But the sample in this study was too small to evaluate the effect of regimen sofosbuvir/ledipasvir or grazoprevir/elbasvir in treament of these patients.

3. CONCLUSIONS

The new regimens of treatment chronic hepatitis C patients using new DAAs such as sofosbuvir/Peg-IFN/ribavirin or sofosbuvir/ledipasvir have high SVR compared to former regimen Peg-IFN/ribavirin. We need more studies related to the treatment of chronic hepatitis C patients with new DAAs but with bigger samples in Vietnamese patients to have high convince results.

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