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Efficacy and Safety of Omibtasvir, Paritaprevir and Ritonavir Combination with Ribavirin for Treatment of Chronic Hepatitis C Patients

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Abstract

Background: The highest prevalence of chronic Hepatitis C Virus (HCV) was reported in Egypt. DAAs has been available, with a reported 12 weeks sustained virologic response (12w-SVR) above 95% after treatment for 12 weaks.

Aim of Study: Aim of the current study was to evaluate evaluate efficacy of the 2-DAAs combination of ombitasvir, paritaprevir (co-dosed with ritonavir) with ribavirin in treatment of chronic HCV patients and evaluate correlation between virologic failure and risk factors.

Patients and Methods: Chronic HCV patients (n=100) were enrolled in the current study. All patients received 25mg ombitasvir, 150mg paritaprevir, and 100mg ritonavir orally once daily plus Ribavirin 600-1000mg) for 12 weaks. Response was assessed 12 weeks after end of treatment by SRT-PCR.

Results: The interferon-free regimen of ombitasvir/ paritaprevir/ritonavir + ribavirin for 12 weeks achieved sustained virologic response in 91% of patients.

Conclusion: In conclusion, the 12-week 2-DAA regimen of OBV/PTV/r and DSV achieved an SVR12 rate of 91% in previously untreated patients with HCV infection. Liver Cirrhosis has negative impact on 12 weeks-SVR.

Conflict of Interest: The authors have no conflict of interest related to this publication.

Key Words: *Ombitasvir – Paritaprevir – HCV.*

Introduction

HEPATITIS C Virus (HCV) is a global pathogen estimated to infect between 80 and 185 million people worldwide [1]. Hepatitis C is a health burden because if it remains untreated, it can result in the development of cirrhosis and Hepatocellular Carcinoma (HCC) [2].

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At least a quarter of all cirrhosis and HCC is associated with chronic HCV infection. Additionally, the risk of HCV-induced morbidities such as portal hypertension, hepatic decompensation and associated mortality suggests getting HCV treatment and achieving Sustained Virologic Response (SVR) are critical [2].

Up to 2011, combination of weekly peginterferon-a (pegIFN⁄x) and daily doses of RBV in a 24-or 48-week course was the standard-of-care treatment for chronic hepatitis C [3].

Recently, novel Direct-Acting Antiviral (DAA) regimens have been approved for the treatment of chronic HCV [4].

Subjects and Methods

I- Studied patients:

100 Egyptian patients presented with chronic HCV infection were enrolled in the current study. their age ranged between 18-70 and they were either naïve or experienced (previously treated with Interferon plus ribavirin since at least one year).

All patients tested positive for serum HCV RNA genomic materials by SRT-PCR. The exclusion criteria included decompensated cirrhosis (Child grade B and C), Ascites, hepatic encephalopathy, pregnant females, Hepatocellular Carcinoma (HCC).

II- Medicine administration:

The anti-HCV drugs were administered according to guidelines regarding doses, routes of administration, and duration of therapy. The antiviral therapeutic regimens included 25mg ombitasvir,

150mg paritaprevir, and 100mg ritonavir orally once daily plus Ribavirin 600-1000mg).

III- Monitoring of treatment efficacy:

Quantitative HCV-PCR was measured with a lower limit of detection of 15IU prior to treatment, and 12 weeks after treatment where virologic response was considered when HCV RNA is less than lower limit of detection week 12 post-treatment (SVR12) while treatment failure was defined as confirmed HCV RNA above LLOQ 12 weeks post-treatment.

Treatment of HCV genotype (GT) 1 infection, the 2-DAA combination of ombitasvir (OBV), paritaprevir (co-dosed with ritonavir), with or without ribavirin (RBV) has resulted in high SVR rates in clinical trials [5].

Patients with renal impairment (GFR less than 30ml/minute), those with INR >1.7, serum albumin <2.8g/dl, total bilirubin >3mg/dl or platelet count <50,000/mm^3 were excluded. All patients were submitted to clinical examination, laboratory testing for liver functions, kidney functions, and fasting blood sugar. Pregnancy test was done for female patients in childbearing period. Abdominal ultrasonography was performed to assess hepatic echo pattern of the liver, patency of portal vein, presence of splenomegaly and to exclude hepatocellular carcinoma.

IV- Statistical analysis:

Data were tabulated, computerized and shown in the form of rate (%) and the Standard Deviation (SD). Chi-Square (χ^2) was used where appropriate. The p-value less than 0.05 were considered as statistically significant.

Results

Most of patients were males (55%), the mean age was 47.8 years, the mean BMI of studied patients was 28.1 and the mean viral load was 3.47 (X 10 log6/ml).

All patients were treatment naive, 21% were cirrhotics by ultrasonographic evidence and 8% were diabetic.

Regarding liver biochemical profile, results showed that the mean of ALT, AST, Albumin, S.bilirubin and INR were 29.3U/L, 25.3U/L, 3.9 mg/dl, 0.7mg/dl and 1.04 respectively. Regarding kidney biochemical profile, results showed that the mean of eGFR and s.creatinine were 96.9 and 0.8mg/dl respectively.

This resaults showed no statistical significant difference (p-value >0.05) between responders group and non-responders group as regard demographic data, renal function tests, liver function tests and CBC contents.

This resaults shows highly statistical significant difference (p-value <0.001) between responders and non-responders as regard liver cirrhosis.

Table (1): Baseline data of studied patients.

Baseline data	Studied patients n (100)
Age, yr (mean ± SD)	47.8±13.4
Male n (%)	55 (55%)
BMI kg/m (mean ± SD)	28.1±4.3
Treatment naïve, n (%)	100 (100%)
DM, n (%)	8 (8%)
Liver Cirrhosis, n (%)	21 (21%)
Bilirubin, mg/dl (mean ± SD)	0.7±0.2
Haemoglobin (g/dl) (mean ± SD)	15.2±3.2
Platelets X 1000/mcL, (mean ± SD)	242±82
W.B.Cs X 1000/mcL, (mean ± SD)	5.9±1.8
INR, (mean ± SD)	1.04±0.06
ALT mg/dl (mean ± SD)	32.3±29.8
Albumin mg/dl (mean ± SD)	3.9±0.4
eGFR (mean ± SD)	96.6±25.6
Creatinine, mg/dl (mean ± SD)	0.8±0.2
Viral load X 10^6/ml (mean ± SD)	3.47±9.88
Responders	91 (91%)
Non responders	9 (9%)

Table (2): Comparison between studied groups as regard DM.

Groups / U/S	Responders (N=91)	Non-responders (N=9)	p-value
Normal Liver	76 (83.5%)	3 (33.3%)	<0.001*
Liver Cirrhosis	15 (16.5%)	6 (66.7%)	

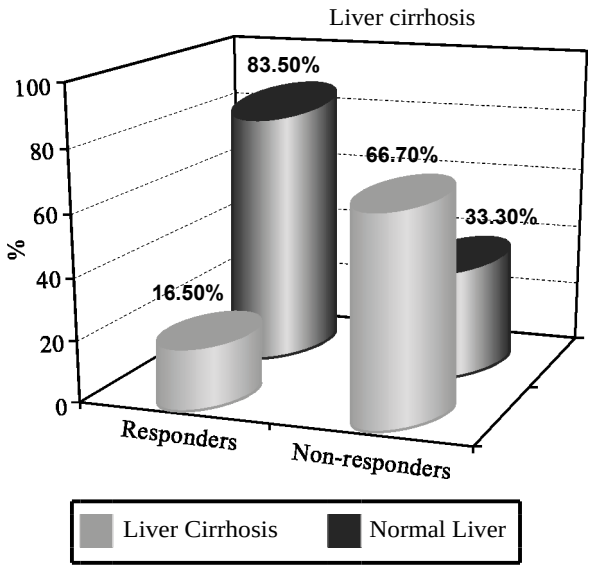

Fig. (1): Comparison between responders and non-responders as regard liver status.

Discussion

The findings of this study showed that the Sustained Virological Response (SVR) was 91% (91/100) overall patients and liver cirrhosis has negative impact on outcome of DAAs therapy.

This results agreed with Hézode et al., (2015), in which 44 treatment-naïve patients with genotype 4 chronic hepatitis C virus infection received the combination of ombitasvir plus paritaprevir plus ritonavir with ribavirin. Rate of SVR was 90.9%. Kumada et al., [4] is a phase 3 trial evaluating the efficacy of a 12-week regimen of co-formulated ombitasvir/paritaprevir/ritonavir for treatment of Japanese hepatitis C virus genotype 1b-infected patients. 215 patients without cirrhosis and 42 with cirrhosis were enrolled. SVR12 rate among patients without cirrhosis was 94.9% (204/215) but SVR12 rate in patients with cirrhosis was 90.5%. This means that L.C has negative impact on efficacy.

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فعالية وآمان عقار الآومبتتسافير والباريتابريفير والريتينوفير مع الريبافيرين فى علاج الإلتهاب الكبدى الفيروسى سى المزمن

الخلفية والآهداف: تم الإبلاغ عن آعلى معدلات لإنتشار فيروس إلتهاب الكبد الوبائى المزمن (HCV) فى مصر. DAAs كانت متاحة، مع ١٢ إسبوعاً ذكرت إستجابة الفيروسية المستمرة (W-SVR 12) فوق ٩٥٪ بعد العلاج لمدة ١٢ يكس.

كان الهدف من الدراسة الحالية هو تقييم فعالية تقييم مزيج من DAA-2 من آومبيتاسفير، باريتابريفير (بالإشتراك مع ريتونافير) مع ريبافيرين فى علاج مرضى إلتهاب الكبد الوبائى المزمن وتقييم العلاقة بين الفشل الفيروسى وعوامل الخطر.

الطريقة: تم تسجيل مرضى إلتهاب الكبد الوبائى المزمن (ن=١٠٠) فى الدراسة الحالية. تلقى جميع المرضى ٢٥ملغ آومبيتاسفير، ١٥٠ملغ باريتابيرفير، و١٠٠ملغ ريتونافير عن طريق الفم مرة واحدة يومياً بالإضافة إلى ريبافيرين ٦٠٠-١٠٠٠ملغ لمدة ١٢ضعفاً. تم تقييم الإستجابة بعد ١٢ إسبوعاً من نهاية العلاج بواسطة SRT-PCR.

النتائج والإستنتاجات: حقق نظام خالى من الإنترفيرون من ribavirin ombitasvir / paritaprevir / ritonavir + لمدة ١٢ إسبوعاً إستجابة فيروسية مستدامة فى ٩١٪ من المرضى.