ejpmr, 2017,4(4), 120-127

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

COMPARATIVE STUDY BETWEEN PEG-IFN BASED REGIMEN (PEG-IFN / SOFOSBUVIR / RIBAVIRIN) AND PEG-IFN FREE REGIMENS (SOFOSBUVIR / SIMEPREVIR) - (SOFOSBUVIR / RIBAVIRIN) IN EGYPTIAN PATIENTS WITH CHRONIC HCV INFECTION.

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Article Received on 02/02/2017 **Article Revised on 22/02/2017** **Article Accepted on 14/03/2017**

ABSTRACT

Annually about 150 million people worldwide have chronic hepatitis C viral (HCV) infection. Advances in the molecular biology of the HCV replication life cycle have led to the discovery of several molecules that specifically block various viral proteins and globally called direct-acting antiviral (DAA) agents. We aimed to evaluate of the efficacy and safety of Peg-IFN based triple regimen (Peg-IFN / Sofosbuvir / Ribavirin) versus Peg-IFN free regimens including (Sofosbuvir/Simeprevir) and (Sofosbuvir/Ribavirin) in adult Egyptian patients with chronic HCV genotype 4. We prospectively enrolled 920 patients from Internal Medicine Departments of Ahmed Maher and Al-Hussein University hospitals, Cairo, Egypt, only one hundred and fifty (150) adult patients with chronic hepatitis C virus infection were included in the study. Patients were divided into 3 groups treated with Pegylated interferon plus Sofosbuvir plus Ribavirin (group A), Sofosbuvir plus Simeprevir (group B) and Sofosbuvir plus Ribavirin (group C) respectively. In group A, the percent of patients who achieved SVR12 were 86.5% for naïve, 81.5% for experienced and 84% for the all (naïve and experienced). In group B, the percent of patients who achieved SVR12 were 94% for naïve, 90% for experienced and 92% for the all (naïve and experienced). In group C, the SVR12 rates were 84% for naïve, 72% for experienced and 78% for the all (naïve and experienced). In conclusion, the sustained virological response 12 weeks after treatment among the three studied groups are nearly the same with no statistically significant difference but only group B (Sofosbuvir plus Simeprevir) regimen gave good results with shorter duration and less adverse events compared with other regimens.

KEYWORDS: HCV**,** Hepatitis C Virus; DAAs: Direct Anti-Viral Agents.

INTRODUCTION

HCV is a small enveloped virus with a positive single stranded RNA genome that encodes a large polyprotein of 3010 amino acids (Beaulieu and Tsantrizos 2004). Annually about 150 million people worldwide have chronic hepatitis C virus (HCV) infection, with an additional 3–4 million people becoming newly infected (Lozano et al., 2012*)*. An Egyptian Demographic Health Survey (EDHS) was conducted in 2008 and estimated HCV prevalence to be 14.7%. Accordingly, Egypt has the highest HCV prevalence in the world (El-Zanaty and Way 2009).

Until 2011, the combination of pegylated interferon (Peg IFN)-α and ribavirin for 24 or 48 weeks was the approved treatment for chronic hepatitis C (McHutchison et al., 2009*)*. In 2011, telaprevir and boceprevir were licensed for use in HCV genotype 1 infection. These two drugs are first-wave, first generation direct-acting antivirals (DAAs). Both target the HCV NS3-4A serine protease and are thus referred to as protease inhibitors. However, both direct antiviral agents are no longer be used in patients infected with HCV genotype 1(Poordad et al., 2011).

Advances in the molecular biology of the HCV replication life cycle have led to the discovery of several molecules that specifically block various viral proteins**.** These compounds are globally called direct-acting antiviral (DAA) agents which target different viral non-structural proteins, including the NS3/4A protease, the NS5B polymerase, and the NS5A protein (Pawlotsky et al., 2007*)*. Sofosbuvir is the first available once-daily NS5B polymerase inhibitor (Approved 12/2013 by FDA and 1/2014 by EMA). Simeprevir, NS3/4A hepatitis C protease inhibitor and have already been approved in

2014.The advent of these new direct antivirals quickly changed the face of hepatitis C treatment (Lawitz et al., 2013).

Aimof the work

Evaluation of the efficacy and safety of Peg-IFN based triple regimen (Peg-IFN / Sofosbuvir / Ribavirin) versus Peg-IFN free regimens including (Sofosbuvir/Simeprevir) and (Sofosbuvir/Ribavirin) in adult Egyptian patients with chronic HCV genotype 4.

Patients and Methods

A prospective interventional study was conducted on a convenient sample of 150 Egyptian patients with chronic hepatitis C virus (HCV) infection.The study was carried out in Internal Medicine Departments of Ahmed Maher and Al-Hussein University hospitals, Cairo, Egypt, over a period of nine months from January 2016 till September 2016. Out of nine hundred and twenty patients (920) with chronic liver diseases were received by the hospital over this period, only one hundred and fifty (150) adult patients with chronic hepatitis C virus were included in the study.

Patients were divided into 3 groups: Group (A): includes 50 patients treated with Pegylated interferon alfa-2A with a dose of 180 mcg subcutaneously once a week plus Sofosbuvir 400 mg once daily orally plus Ribavirin 1000/1200 mg orally depending on patient weight for 12 weeks.Group (B): includes 50 patients were treated with sofosbuvir 400 mg once daily orally plus Simeprevir150 mg orally once daily for 12 weeks. Group (C): includes 50 patients were treated with Sofosbuvir 400 mg once daily orally plus Ribavirin 1000/1200 mg orally depending on patient weight for 24 weeks.

All patients were subjected to full medical history, carful clinical examination and routine laboratory tests prior to treatment including complete blood picture, kidney functions, complete liver functions including (AST, ALT, serum albumin, INR, total bilirubin, AFP, HBsAg, HCV RNA quantitative by PCR), ANA, TSH, Pregnancy test (ladies in child-bearing period), abdominal ultrasonography, ECG, fundus examination if diabetic or hypertensive.

In group A and B, the follow up investigation during treatment period were ALT, AST, total bilirubin, CBC at (2, 4, 8 and 12 weeks) and HCV RNA quantitative at (4 and 12 weeks). In group C. the follow up investigation during treatment period were ALT, AST, CBC, total bilirubin at (4, 8, 12, 16, 20 and 24 weeks) and HCV RNA quantitative at (4, 12 and 24 weeks). The follow up investigations after treatment for all groups were ALT, AST, CBC, total bilirubin and HCV RNA quantitative PCR after 12 and 24 weeks from the last day of treatment.

All patients presented with liver cirrhosis (child B or C), Platelet count < 50000/mm^3, combined HCV &HBV infection, patients with HCC or extrahepatic malignancy, GFR less than 30 ml/min, Pregnancy or inability to use effective contraception or Patients who refuse to participate, all are excluded from the current study.

Statistical analysis

The data were processed and analyzed using the statistical package for social sciences **(IBM Corp. Released 2013).** The expression of data in the form of mean, S.D. (standard deviation) for quantitative variables and description of qualitative variables by frequency and percent were used. Student t-test was used to make a Comparison between two groups' quantitative variables. Comparison of more than two groups' quantitative variables was carried out by one way ANOVA test. Chi-square test (Pearson chi-square) was used to compare between qualitative variables.

This study was approved by the Ethical Committee of Azhar University Hospitals, and a written informed consent was obtained from all enrolled participants. The participant consented form was recorded and kept with study documents and the ethics committee approved the consent procedure.

RESULTS

From nine hundred and twenty (920) patients with chronic liver diseases received by the hospital over a period of nine months from January 2016 to September 2016, only one hundred and fifty (150) patients with chronic hepatitis C virus were included in the study.

The number of male patients were 94 (62.5%) and females patients were 56 (37.5%) with a mean age of 54.03 years, table 1. Age and sex distribution among groups, also there was no statistical significant difference between 3 groups regarding the mean of age and sex as shown in table 2.

Table (1): Age and sex of all studied patients,

Age	**Mean**	**±SD**	**Min**	**Max**
	54.03	8.42	24.00	70.00
Sex	Male		No	%
			94	62.5
	Female		56	37.5

Table (1) shows that the mean of age was 54.03± 8.42, there was a higher percentage of male than female (62.5%, 37.5% respectively)

Table (2): Comparison of different groups regarding age and sex.

	Group A	Group B	Group C	ANOVA	P- Value
	Mean ± SD				
Age	51.37 ±7.46	54.17±6.84	53.54±9.81	6.634	0.06
Sex	No (%			χ^2	P- Value
Male	28 (29.5%)	37(40%)	29(30.5%)	4.827	0.090
Female	22(40.4%)	13(22.8%)	21(36.8%)		

Table (2) show that there was no statistical significant difference (P value > 0.05) between 3 groups regarding the mean of age and sex.

In group A (Peg-IFN - sofosbuvir - ribavirin) 80% of which was treatment naïve and 20% was treatment experienced. In group B (sofosbuvir - Simeprevir) 78% of which was treatment naïve and 22% was treatment experienced.In group C (sofosbuvir - ribavirin) in which 76% were treatment naïve and 24% were treatment experienced ,with no statistical significant difference among patients groups regarding history of treatment status as shown in table 3.

Table (3): Comparison of treatment history among studied group.

		Group A	Group B	Group C	χ^2	P-Value
		No (%)				
Treatment status	Naïve	40(34.5%)	39(33.6%)	38(31.9%)	0.287	0.866
	Experienced	10(30.3%)	11(33.3%)	12(36.4%)		

Table (3): shows that there was no statistical significant difference among patients groups regarding history of treatment status (P value > 0.05)

Baseline laboratory data performed among studied groups before starting treatment were shown in table 4.

Table (4): Investigations before treatment among studied groups.

		Group A	Group B	Group C	ANOVA	P-Value
		Mean ± SD				
CBC	TLC	6.52±1.8	5.69±1.91	4.5±1.67	15.924	<0.001**
	ANC	3.3±1.3	2.66±1.09	2.27±1.06	9.886	<0.001**
	HB	14.18±1.2	13.8±1.7	13.2±1.5	4.789	0.010*
	PLT	207 ±64.1	172.1±67.7	120.1±45.5	26.800	<0.001**
LFTS	Albumin	4.05±.36	3.9±.48	3.6±.54	9.306	<0.001**
	INR	1.07±.07	1.12±.11	1.18±.13	10.889	<0.001**
	ALT	57±35.9	51.8±28.9	72.2±48.6	3.787	0.025*
	AST	56.19±38.8	52.27±29.1	71.3±39.8	3.896	0.022*
	total bilirubin	0.73±.23	0.91±.40	1.04±.41	9.372	<0.001**
For DM	HbA1C	6.5±.93	6.47±.94	7.0±.78	1.649	.203
Others	HCV PCR	1.0247E6±2.10	1.1779E6±2.08	7.4256E5±1.06	0.742	.478
	creatinine	0.78±.18	0.85±.22	0.88±.21	2.830	.062
	AFP	8.2±6.1	9.6±11.1	11.2±9.9	1.315	.272

Table (4) shows that there was a statistical significant difference (P value < 0.05) among patients groups regarding the mean of parameter of CBC and liver function tests , however there were no statistical significant difference (P value > 0.05) among patients groups regarding the mean of other parameters (HbA1C, HCV PCR , creatinine, and AFP).

The numbers of patients with cirrhotic liver were 41(27.3%), the numbers of patients with abnormal echopatern by ultrasound imaging were 103 (68.6%) and the numbers of patients with normal imaging by abdominal ultrasound were 6 patients (4%), but there was no statistical significant difference among patients groups regarding the mean of parameter of portal vein diameter, liver echopatern and spleen size as shown table 5.

Table (5): Abdominal ultrasound parameters among studied groups.

		Group A	Group B	Group C	ANOVA	P-Value
		Mean ± SD				
P v (mm)		11.1±1.4	12.1±1.0	11.6±1.1	14.581	.069
		No (%)			χ^2	P-Value
liver	Normal	5(85.7%)	0(0%)	1(14.3%)		

echopatern	Abnormal	39(37.1%)	32(32.4%)	32(30.5%)	14.601	.064
	Cirrhotic	10(24.3%)	15(36.5%)	16(39.0%)		
spleen size	Average	30(35.2%)	26(31.8%)	29(34.1%)	15.886	.067
	Enlarged	21(32.1%)	24(36.9%)	20(30.7%)		

Table (5) shows that there was no statistical significant difference among patients groups regarding the mean of parameter of portal vein diameter, liver echopatern and spleen size (P value > 0.05).

In the current study the mean of haemoglobin level in group A were 14.18±1.22 before treatment and decreased to 11.62±1.20 after treatment with a statistical significant difference among the patients and the percentage of patients who developed anemia (haemoglobin level<11mg/dl) as a result of therapy were 40% (20/50). The mean of platelet count in group A were 207.00±64.10 before treatment and decreased to 182.73±88.80 after treatment with a statistical significant difference among the patients and the percentage of patients who developed thrombocytopenia (platelet count<150000/ml) as a result of therapy was 26% (13/50).The mean of neutrophilic count in group A were 3.30±1.33 before treatment and decreased to 2.07±0.93 after treatment with a statistical significant difference among the patients ,and the percentage of patients who developed neutropenia (neutrophilic count<1500/ml) as a result of therapy was 22% (11/50).

Table (6): Comparison of CBC and liver function tests in group (A) before and 12 week after treatment.

	Before ttt	After 12 w ttt	Paired t test	P- Value
	Mean ± SD			
TLC	6.52±1.81	4.57±1.64	8.408	<0.001**
ANC	3.30±1.33	2.07±0.93	8.730	<0.001**
HB	14.18±1.22	11.62±1.20	15.063	<0.001**
PLT	207.00±64.10	182.73±88.80	23.064	<0.001**
ALT	57.00±35.97	32.47±18.80	4.541	<0.001**
AST	56.19±38.84	34.94±16.55	3.961	<0.001**
TB	0.73±0.23	0.96±0.28	5.602	<0.001**

Table (6) shows that there was a statistical significant difference among patients of group (A) regarding the mean of parameter of TLC,ANC,HB,PLT,ALT,AST and TB before treatment and 12 weeks after treatment (P value < 0.05).

In the current study the mean of haemoglobin level in group B were 13.85±1.78 before treatment and became 13.79±1.82 after treatment with no statistical significant difference among the patients and no anaemia developed as a result of therapy. The mean of platelet count in group B were 172.18±67.71 before treatment and became173.67±69.72 after treatmen twith a statistical significant difference among the patients and the percentage of patients who developed thrombocytopenia (platelet count<100000/ml) as a result of therapy was 14% (7/50). The mean of neutrophilic count in group B were 2.66±1.09 before treatment and became 2.62±0.95 after treatment with no statistical significant difference among the patients (P value > 0.05),and the percentage of patients who developed neutropenia (neutrophilic count<1500/ml) as a result of therapy was 4% (2/50).

Table (7): Comparison of CBC and liver function tests in group (B) before and 12 week after treatment.

	Before ttt	After 12 w ttt	Paired t test	P- Value
	Mean ± SD			
TLC	5.69±1.91	5.53±1.67	.530	.598
ANC	2.66±1.09	2.62±0.95	.212	.833
HB	13.85±1.78	13.79±1.82	2.619	.065
PLT	172.18±67.71	173.67±69.72	18.155	<0.001**
ALT	51.82±28.90	23.86±11.79	7.089	<0.001**
AST	52.27±29.14	26.11±10.81	6.752	<0.001**
TB	0.91±0.40	1.08±0.81	1.554	.127

Table (7) shows that there was a statistical significant difference among patients of group (B) regarding the mean of parameter of PLT,ALT and AST (P value < 0.05), however there were no statistical significant difference among same patients regarding the mean of other parameters HB,TLC,ANC and TB (P value > 0.05).

In the current study the mean of haemoglobin level in group C) were 13.24±1.59 before treatment and decreased to 11.58±1.29 after treatment with a statistical significant difference among the patients and the percentage of patients who developed anemia (haemoglobin level < 11mg/dl) as a result of therapy was 38% (19/50). The mean of platelet count in group C were

120.10±45.53 before treatment and became 127.40±56.62 after treatment with a statistical significant difference among the patients and the percentage of patients who developed thrombocytopenia (platelet count<100000/ml) as a result of therapy was 28% (14/50). The mean of neutrophilic count in group Cwere 2.27±1.06 before treatment and became 2.27±0.73 after treatment with no statistical significant difference among the patients (P value > 0.05),and the percentage of patients who developed neutropenia (neutrophilic count<1500/ml) as a result of therapy was 14% (7/50).

Table (8): Comparison of CBC and liver function tests in group(C) before and 12week after treatment.

	Before ttt	After 12 w ttt	Paired t test	P- Value
	Mean ± SD			
TLC	4.50±1.67	4.21±1.30	1.400	.168
ANC	2.27±1.06	2.27±0.73	.045	.964
HB	13.24±1.59	11.58±1.29	8.720	<0.001**
PLT	120.10±45.53	127.40±56.62	18.644	<0.001**
ALT	72.20±48.62	31.40±15.30	6.345	<0.001**
AST	71.36±39.82	35.90±14.05	6.637	<0.001**
TB	1.04±0.41	1.29±0.40	3.378	0.001**

Table (8) shows that there was a statistical significant difference among patients of group (c) regarding the mean of parameter of HB, PLT, ALT, AST and TB (P value < 0.05), however there were no statistical significant difference among same patients regarding the mean of other parameters TLC and ANC (P value > 0.05).

Table (9): Comparison of Investigations at 12 week after treatment among studied groups.

	Group A	Group B	Group C	ANOVA	P-Value
	Mean ± SD				
TLC	4.57±1.64	5.53±1.67	4.65±1.79	4.967	.008**
ANC	2.07±0.93	2.62±0.95	2.45±1.04	4.354	.015*
HB	11.62±1.20	13.39±1.82	11.50±1.53	23.927	<0.001**
PLAT	182.7±88.8	173.6±69.7	136.20±62.1	5.521	.005**
ALT	32.47±18.80	23.86±11.79	30.62±20.04	3.514	.032*
AST	34.94±16.55	26.11±10.81	35.70±25.23	4.231	.016*
TB	0.96±0.28	1.08±0.81	±0.401.30	4.908	.009**

Table (9) shows that there was a statistical significant difference among patients of studied groups regarding the mean of parameters of CBC (TLC, ANC, HB, and PLT) and liver function tests (ALT, AST, and TB) (P value < 0.05).

Regarding SVR; in group A,the percent of patients who achieved SVR12 were 86.5% for naïve, 81.5% for experienced and 84% for the all (naïve and experienced). In group B, the percent of patients who achieved SVR12 were 94% for naïve, 90% for experienced and 92% for the all (naïve and experienced).In group C , SVR12 percents were 84% for naïve, 72% for experienced and 78% for the all (naïve and experienced). Interestingly, sustained virological response 12 weeks after treatment shows that there was no statistical significant difference among patients groups as shown in table 10.

Table (10): Comparison of SVR12 among studied groups.

		Group(A)	Group(B)	Group(C)	χ^2	P-Value
		No (%)				
SVR12	Relapsed	8(34.8%)	4(17.4%)	11(47.8%)	3.959	0.138
	Treated	42(33.3%)	46(36.4%)	39(30.3%)		

Table (10) shows that there was no statistical significant difference among patients groups regarding SVR12 (P value > 0.05)

DISCUSSION

HCV is the main cause of progressive liver diseases and a public health problem worldwide. It is estimated that approximately 150-180 million people in the world are living with chronic hepatitis, 350.000 of whom die each year from liver damage associated with the infection. About 80% of people infected with HCV develop chronic hepatitis, of which 20%-40% will develop liver cirrhosis or hepatocellular carcinoma (HCC) 20-30 years after infection. As a consequence, chronic HCV infection is the major reason of liver transplantation in developed countries (Razavi et al., 2014)

Until recently, the only therapeutic option was the combination of pegylated interferon-plus ribavirin (pegIFN-RBV).Both drugs are indirect antiviral agents, because they do not target a specific HCV protein or nucleic acid. More importantly (pegIFN-RBV) is characterized by both limited efficacy, and poor tolerability(McHutchison et al., 2009).

Advances in our knowledge of the molecular biology of the HCV replication life cycle have led to the discovery of several molecules that specifically block various viral proteins(Soriano et al., 2011)

These compounds are globally called direct-acting antiviral (DAA) agents and target different viral non-structural proteins, including the NS3/4A protease, the NS5B polymerase, and the NS5A protein.

In this study we evaluated the efficacy and safety of Peg-IFN based regimen(Peg-IFN / Sofosbuvir / Ribavirin) and Peg-IFN free regimens (Sofosbuvir/Simeprevir)-(Sofosbuvir/Ribavirin) in treatment of Egyptian patients with chronic HCV.

In the current study,the mean of age was (51.3±7.4) years in group (A), (54.1±6.8) years in group (B), (53.5±9.8) years in group (C) and 54.03± 8.42 for all groups, these results showed that there was a statistical significant difference between 3 groups regarding the mean of age (P value < 0.05). These findings were close to (Doss et al., 2008) findings who reported that the mean age among HCV cases was 52.8±7.9 years.

In Egypt, a study of prevalence and epidemiological features of HCV was done and revealed that, male patients were 66% while female patients were 34% among 300.000 studied HCV patients (Esmat et al., 2008). These findings were close to findings in our study which revealed that, higher percentage of male than female (62.5%, 37.5% respectively).

In the current study the mean of haemoglobin level in group A (Peg-IFN - sofosbuvir - ribavirin) were 14.18±1.22 before treatment and decreased to 11.62±1.20 after treatment with a statistical significant difference among the patients (P value < 0.05) and the percentage of patients who developed anemia (haemoglobin level<11mg/dl) as a result of therapy were 40% (20/50). These result not concomitant with (Tong et al., 2016) in which percentage of anemia was 69.2% among the patients who used the same regimen.

In the current study the mean of haemoglobin level in group B (sofosbuvir - simeprevir) were 13.85±1.78 before treatment and became 13.79±1.82 after treatment with no statistical significant difference among the patients (P value < 0.05) with no anaemia developed .This result was not far from (Tong et al., 2016) in which the percentage of anemia was 3% among the patients who used the same regimen.

In the current study the mean of haemoglobin level in group C(sofosbuvir - ribavirin) were 13.24±1.59 before treatment and decreased to 11.58±1.29 after treatment with a statistical significant difference among the patients (P value < 0.05) and the percentage of patients who developed anemia (haemoglobin level < 11mg/dl) as a result of therapy was 38% (19/50). This result not agreed with (Tong et al., 2016) in which percentage of anemia was 67.7% among the patients who used the same regimen.

In the current study the mean of platelet count in group A(Peg-IFN - sofosbuvir - ribavirin) were 207.00±64.10 before treatment and decreased to 182.73±88.80 after treatment with a statistical significant difference among the patients (P value < 0.05) and the percentage of patients who developed thrombocytopenia (platelet count<150000/ml) as a result of therapy was 26% (13/50). This results not concomitant with (Chang et al., 2016) in which percentage of thrombocytopenia was 61.5% among the patients who used the same regimen.

In the current study the mean of platelet count in group B (sofosbuvir - simeprevir) were 172.18±67.71before treatment and became173.67±69.72 after treatment with a statistical significant difference among the patients (P value < 0.05) and the percentage of patients who developed thrombocytopenia (platelet count<100000/ml) as a result of therapy was 14% (7/50). This result was close to (Chang et al., 2016) in which percentage of thrombocytopenia was 14.3% among the patients who used the same regimen.

In the current study the mean of platelet count in group C(sofosbuvir - ribavirin) were 120.10±45.53 before treatment and became 127.40±56.62 after treatment with a statistical significant difference among the patients (P value < 0.05) and the percentage of patients who developed thrombocytopenia (platelet count<100000/ml) as a result of therapy was 28% (14/50). This result not agreed with (Chang et al., 2016) in which percentage of thrombocytopenia was 14.5%among the patients who used the same regimen.

In the current study the mean neutrophilic count in group A(Peg-IFN - sofosbuvir - ribavirin) were 3.30±1.33 before treatment and decreased to 2.07±0.93 after treatment with a statistical significant difference among the patients (P value < 0.05),and the percentage of patients who developed neutropenia (neutrophilic count<1500/ml) as a result of therapy was 22% (11/50). This result not agreed with (Huynhet al., 2016) in which percentage of neutropenia was 92.3%among the patients who used the same regimen.

In the current study the mean neutrophilic count in group B (sofosbuvir - simeprevir) were 2.66±1.09 before treatment and became 2.62±0.95 after treatment with no a statistical significant difference among the patients (P value > 0.05),and the percentage of patients who

developed neutropenia (neutrophilic count<1500/ml) as a result of therapy was 4% (2/50).This result was close to (Huynhet al., 2016) in which percentage of neutropenia was 0%among the patients who used the same regimen.

In the current study the mean neutrophilic count in group C(sofosbuvir - ribavirin) were 2.27±1.06 before treatment and became 2.27±0.73 after treatment with no a statistical significant difference among the patients (P value > 0.05),and the percentage of patients who developed neutropenia (neutrophilic count<1500/ml) as a result of therapy was 14% (7/50).This results not concomitant with(Huynhet al., 2016) in which percentage of neutropenia was 19.4%among the patients who used the same regimen.

In the current studythere was a statistical significant difference among patients of studied groups A, B, and C regarding the means of haemoglobin, platelets and neutrophilic count levels at 12 week after treatment (P value < 0.05).This finding concomitant with (Rosinskiet al., 2016) findings who reported that there was also a statistical significant difference among patients of studied groups regarding the means of haemoglobin, platelets and neutrophilic count levels at 12 week after treatment(P value<0.001).

Regarding the baseline of liver function tests parameters before treatment,our study showed that there was a statistical significant difference (P value < 0.05) among patients of studied groups regarding the means of parameters of liver function tests (ALT, AST, and total bilirubin). This result not concomitant with(Tong et al., 2016)in which there was no a statistical significant difference (P value > 0.05) among patients of studied groups regarding the mean of ALT, AST, and total bilirubin.

In this study, in group A (Peg-IFN - sofosbuvir - ribavirin) 80% of which was treatment naïve and 20% was treatment experienced. The percent of patients who achieved SVR12 were 86.5% for naïve, 81.5% for experienced and 84% for the all (naïve and experienced). This result was close to (Esmat et al., 2015) study in which the percent of patients who achieved SVR12 were 78.8% for experienced, 87.5% for naïve and 84.5% for the all (naïve and experienced).

In the present study in group B (sofosbuvir - simeprevir) 78% of which was treatment naïve and 22% was treatment experienced. The percent of patients who achieved SVR12 were 94% for naïve, 90% for experiencedand 92% for the all (naïve and experienced). This result not concomitant with (El Raziky et al., 2015) study in which 57% treatment naïve patients and 43% treatment experienced patients were received the same regimen (sofosbuvir plus simeprevir).The percent of patients who achieved SVR12 were 95 % for experienced, 100% for naïve and 97.5% for the all (naïve and experienced).

In (Doss et al., 2015) study 103 Egyptian patients received sofosbuvir and ribavirin.Among all patients 52% were treatment naïve and 48% were treatment experienced. SVR12 rates were 92% for naïve, 89% for experienced and 90% for the all (naïve and experienced).This result was not concomitant with this study in group C (sofosbuvir - ribavirin) in which 76% were treatment naïve and 24% were treatment experienced. SVR12 rates were 84% for naïve, 72% for experienced and 78% for the all (naïve and experienced).

CONCLUSION

The appearance of direct acting antiviral drugs has radically changed the management of patients with chronic hepatitis C. The high rates of SVR are related with the reduction of the progression to cirrhosis and a lower incidence of complications with established cirrhosis.

HCV therapy is steadily moving to an all oral, well tolerated, short-term, and more efficacious regimen. An IFN-free regimen was available for treatment of all genotypes of HCV. To date, several direct acting antiviral agents (DAAs) have been developed and are currently being evaluated in various combinations in clinical trials.

Sofosbuvir-based therapy regimes are safe and lead to high rates of SVR12.

Sofosbuvir plus Simeprevir regimen for 12 weeks gave good results and less adverse events compared with other regimens such as sofosbuvir plus ribavirin for 24 weeks and sofosbuvir plus pegylated interferon plus ribavirin for 12 weeks. The more recent interferon-free regimens may reduce the unnecessary side effects burden on patients during the course of HCV treatment.

REFERENCES

1. Beaulieu PL and Tsantrizos YS (2004): "Inhibitors of the HCV NS5B polymerase: new hope for the treatment of hepatitis C infections." Curr Opin Investing Drugs, 5: 838-850.
2. Chang PW,Tong MJ, Huynh TT, et al., (2016): "Adverse events associated with ribavirin in sofosbuvir-based therapies for patients with chronic hepatitis C: A community practice experience". Journal of Digestive Diseases, 17: 113–121.
3. DossW, Mohamed MK, El Sayed M, et al., (2008):"Egyptian national control strategy for viral hepatitis, 2008-2012."
4. Doss W, Shiha G, Hassany M, et al.,(2015): "Sofosbuvir plus ribavirin for treating Egyptian patients with hepatitis C genotype 4.", 63(3): 581-585.
5. El Raziky M, Gamil M,Waked I et al., (2015):"Treatment of Hepatitis C Genotype 4 patients with Simeprevir and Sofosbuvir: Preliminary Results from a Phase IIa, Partially Randomised, Open-label Trial conducted in Egypt

(OSIRIS)."AASLDLiverLearning®. 110407: Clinical Trials and Therapeutic Developments.
6. El-Zanaty F and Way A (2009):"Egypt demographic and health survey 2008" (Egyptian Ministry of Health and Associates and Macro International, Cairo).
7. Esmat G, DossW, Mohamed MK, et al., (2008): "Egyptian national control strategy for viral hepatitis; 2008-2012."
8. Esmat G, El-Kassas M and Elbaz T (2015): "New era for management of chronic hepatitis C virus using direct antiviral agents." Journal of Advanced research, 6: 301-310.
9. Huynh TT, Tong MJ, Chang PW,et al., (2016): "Adverse events associated with ribavirin in sofosbuvir-based therapies for patients with chronic hepatitis C: A community practice experience". Journal of Digestive Diseases, 17: 113–121.
10. IBM Corp. Released (2013): IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.
11. Lawitz E, Mangia A, Wyles D, et al., (2013): "Sofosbuvir for previously untreated chronic hepatitis C infection." N Engl J Med, 368(20): 1878-1887.
12. Lozano R, Naghavi M, Foreman K, et al., (2012): "Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010." Lancet, 380: 2095-2128.
13. McHutchison JG, Lawitz EJ, Shiffman ML, et al., (2009): "Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection." N Engl J Med, 361(6): 580-593.
14. Pawlotsky JM, Chevaliez S, McHutchison JG, et al., (2007): "The hepatitis C virus life cycle as a target for new antiviral therapies. Gastroenterology, 132(5):1979-98.
15. Poordad F, McCone J Jr, Bacon BR, et al.,(2011): "Boceprevir for untreated chronic HCV genotype 1 infection SPRINT-2 Investigators." N, Engl J. Med, 364(13): 1195-206.
16. Razavi H, Waked I, Sarrazin C, et al., (2014): "The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm." J Viral Hepat, 21 Suppl 1: 34-59.
17. Rosinski AA,Tong MJ, Chang PW,et al., (2016):"Adverse events associated with ribavirin in sofosbuvir-based therapies for patients with chronic hepatitis C: A community practice experience". Journal of Digestive Diseases, 17: 113–121.
18. Soriano V, Vispo E, Poveda E,et al., (2011):"Directly acting antivirals against hepatitis C virus. J Antimicrob Chemother, 66: 1673-1686.
19. Tong MJ, Chang PW, Huynh TT, et al., (2016): "Adverse events associated with ribavirin in sofosbuvir-based therapies for patients with chronic hepatitis C: A community practice experience". Journal of Digestive Diseases, 17: 113–121.