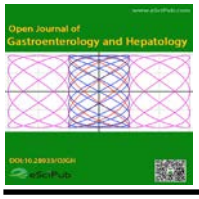
Research Article **OJGH (2019) 2:11**



Open Journal of Gastroenterology and Hepatology
(ISSN:2637-4986)

Study of the effect of sofosbuvir and daklatasivir on respiratory system in patients with chronic hepatitis C

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ABSTRACT

Back ground: The aim is to study effect of sofosbuvir and daklatasivir on respiratory system.

Patient and methods : A randomized study was done after all patients gave an informed consent before the start. The study population consists of 21 patients receiving treatment of HCV coming to the outpatient clinic of beni suef university hospital.

Results : There is no major adverse effect of sofosbuvir and daklatasivir on respiratory system as proved by assessment of pulmonary function and Computed tomography before and after treatment.

Keywords: Hepatitis C- DAAs - Chest.

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How to cite this article:
Alaa Aboud, Laila anwer, Mohammed soliman.Study of the effect of sofosbuvir and daklatasivir on respiratory system in patients with chronic hepatitis C. Open Journal of Gastroenterology and Hepatology, 2019, 2:11

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Introduction

HCV is considered a major health issue in Egypt because of high prevalence as declared by demographic health survey of 2008 that showed a national seroprevalence of 14.7% among those aged between 15 and 59 years, with viremic prevalence of 9.7%in this age group that increased with age and was higher in males than in females in all age groups studied.(Waked et al., 2017)

It is considered major cause of chronic liver disease and has been recognized as a global health problem due to progression into cirrhosis, liver cell failure and HCC, also about 170 million people in world are diseased with HCV and 60 to 80% goes into chronic infection (AA Modi and TJ Liang 2008)

The new direct acting antiviral agents has proved high efficacy in treatment of HCV and so provide promising solution for possibility of HCV eradication, the most important corner stone drug is sofosbuvir (sovaldi).

Sofosbuvir is a nucleotide analog that is a highly potent inhibitor of theNS5B polymerase in HCV. This drug has shown high efficacy in combination with several other drugs with and without PEG-INF, against HCV,it is of special interest among the directly acting antiviral drugs under development, due to its high potency, low side effects, oral administration, and high barrier to resistance, it acts by inhibition of NS5B which is one of the non-structural proteins that is essential for HCV RNA replication.(Harmeet etal.,2014)

Daclalatasvir is also one of the efficient DAAs, it is NS5A inhibitor that is effective against all HCV genotypes with pangenotypic activity , single dosing and is well tolerated and is used in combination with sofosbuvir for prevention of emergence of resistance (osamaetal., 2018)

Interferon was associated with various respiratory complications ranging from mid interstitial pneumonitis to severe acute respiratory distress syndrome up to death and also sarcoid like reactions, bronchiolitis obliterans and asthma exacerbation but New DAAs respiratory effects is not well evaluated.(Dina etal.,2017)

Patients and methods

A randomized study was done after all patients were given an informed consent before the start. The study population consists of 21 patients already receiving treatment of HCV .

Aim of this work is to observe effect of DAAs treatment on respiratory system.

Inclusion criteria:

Patients aged>18years old .

Patients with compensated Liver disease

Exclusion criteria:

Ascites.

Malignancy

End stage organ failure.

All patients were subjected to history taking , clinical examination .

- Abdominal Examination (hepatomegaly, splenomegaly, ascites) .
- Chest Examination

Laboratory investigations including:

Liver synthetic function, AFP,complete blood picture and creatinine.

HCV RNA by PCR.

Liver profile was assessed before , during and after end of treatment.

Imaging in the form of :

abdominal ultrasonography

CT Chest before and after end of treatment

Pulmonary function test before and after end of treatment

Results

In table (1) ages of the patients range from 36 to 72 years with mean age 53 years , 71% of patients were male and 28% of patients were females, 42% of patients were smokers and the major risk of transmission of HCV infection was antischistosomal injections in 42.9% , Previous operations was a risk in 28.6% and there was no obvious risk in 28.6%.

In table(2) there was no symptoms suggestive of decompensated liver disease , by abdominal examination there was hepatomegaly in 42.9% and in 71.4% on ultrasonography. There was splenomegaly in 33.3% on ultrasonography.

In table (3) there was no significant changes in pulmonary functions and imaging in studied patients before and after treatment.

In table 4 fatiguability was the most frequent draw back and to less ex-tent GIT toubles, cough and pruritus in about 4.8% of patients.

Table (1): Demographic data of studied patients

	Total (n=21)	%
Age (Year) Range Mean±SD	 36-72 53.7±10.9	 -
Sex Male Female	 15 6	 71.4 28.6
Smoking	9	42.9
Risk factors No risk Antischistosomal injections Operation	 6 9 6	 28.6 42.9 28.6

Table (2) Clinical and sonographic data of studied patients.

	Total (n=21)	%
Bleeding tendency	0	0
Hematemesis	0	0
Jaundice	0	0
Hepaic encephalopathy	0	0
Liver by exam	9	42.9
Spleen by exam	0	0
Ascites by exam	0	0
Liver sonar	15	71.4
Spleen by sonar	7	33.3
Ascites by sonar	0	0

Table (3): Comparison between pulmonary function test and CT chest of the studied patients before and after treatment

	Pre	Post	P value
FVE1 Range Mean±SD	 71-107 89.1±10.9	 72-109 89.2±10.2	0.934
FVC Range Mean±SD	 66-122 90.2±13.7	 67-124 87.4±13.5	0.157
FEV1/FVC Range Mean±SD	 64-92 77.8±6.9	 55-95 77.3±8.2	0.734
6mw Range Mean±SD	 200-420 347.6±67.9	 210-430 350.6±62.6	0.682
Spo_2 Range Mean±SD	 96-99 97.3±0.9	 96-99 97.6±0.9	0.261
ct chest	0	0	

Table (4): Assessment of side effects of treatment in the studied patients

Side Effect	4 week No.(%)	8 week No.(%)	12 week No.(%)	P value
No side effects	11(52.4)	8(38.1)	9(42.9)	0.858
Fatigue	8(38.1)	11(52.4)	10(47.6)	
GIT Troubles	1(4.8)	1(4.8)	0(0)	
Cough	1(4.8)	1(4.8)	1(4.8)	
Pruritus	0(0)	0(0)	1(4.8)	

Table (5): Comparison between the laboratory data of studied patients during different follow up period

	Time (week)			
	Before	**4 week**	**8 week**	**12 week**
ALT				
Range	22-85	10-54	11-33	11-30
Mean±SD	48.5±17.9	30.1±13.0*	23.8±7.3*+	19.5±6.1*+#
AST				
Range	19-88	10-55	10-36	9-30
Mean±SD	51.0±19.6	29.0±13.2*	23.5±7.7*+	18.2±5.8*+#
HB				
Range	12-16.6	11-16	11-15	10.9-15
Mean±SD	14.3±1.4	13.8±1.4*	13.0±1.3*+	12.8±1.4*+
Bilirubin				
Range	0.5-1.1	0.5-0.9	0.36-0.9	0.4-0.9
Mean±SD	0.7±0.2	0.7±0.1	0.6±0.1	0.6±0.1
Albumin				
Range	3.7-4.9	3.5-4.8	4-4.9	3.7-4.6
Mean±SD	4.4±0.4	4.2±0.3	4.2±0.3	4.2±0.2
PT				
Range	11-13	11-13	11-13	11-13
Mean±SD	12.1±0.8	12.0±0.7	12.1±0.8	12.1±0.8
Creatinine				
Range	0.7-1.1	0.5-1	0.5-1	0.5-1
Mean±SD	0.9±0.1	0.8±0.1	0.8±0.1	0.7±0.2
AFP				
Range	1.4-12.2	-	-	1.5-15
Mean±SD	5.7±3.5			5.5±3.6
TLC				
Range	4300-8900	4600-10000	4700-8300	4700-9000
Mean±SD	6742.9±1479.4	6585.7±1584.7	6033.3±1092.4	6176.2±1317.5
PLT				
Range	150000-350000	164000-432000	154000-316000	150000-265000
Mean±SD	239047.6±60441.3	235761.9±64027.3	210952.4±44894.9	196714.3±30537.1

In table 5 there was no significant change in Bilirubin, PT ,albumin , creatinine, WBC count platelets count and AFP during different weeks of treatment.There was significant decrease of hemoglobin when compared before treatment and during different weeks of follow up.

There was significant normalization of liver enzymes when compared before treatment and during different weeks of follow up.

In table 6 SVR was 90.4% non-responder was 4.8% and relapse was 4.8%.

Table (6) Assessment of efficacy of treatment

Total (n=21)	SVR	Non responsive	Relapse
HCV, no. (%)	19(90.4)	1(4.8)	1(4.8)

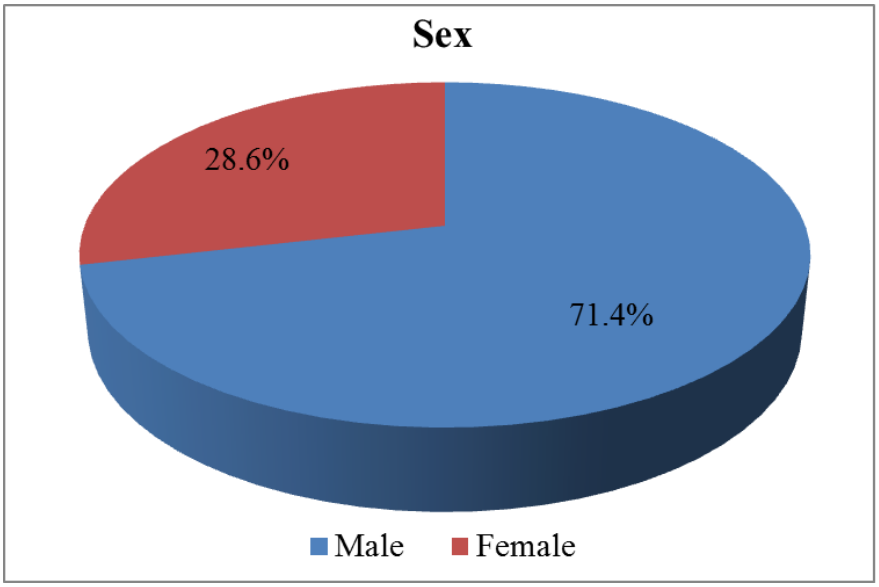

Figure 1a) Sex of the studied patients.

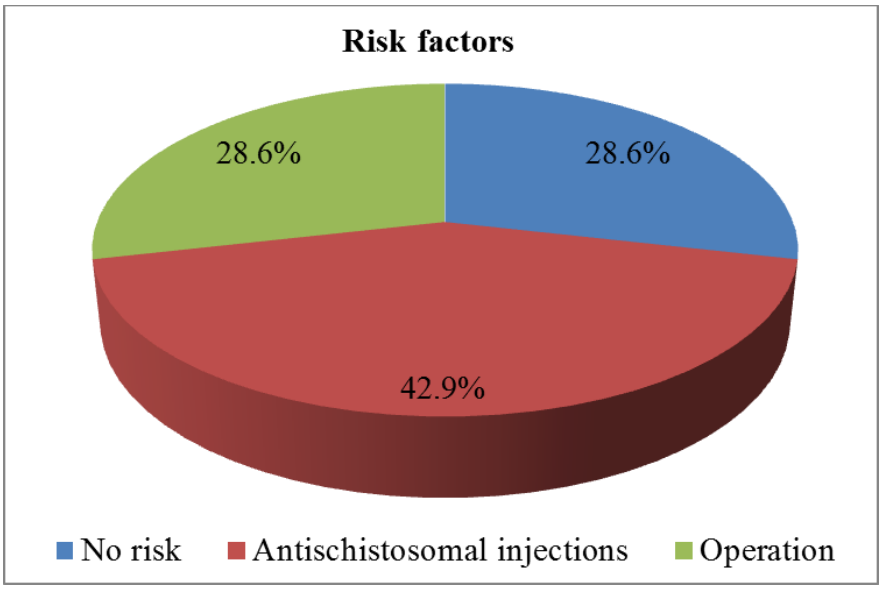

Figure 1b) Risk factors of HCV infection.

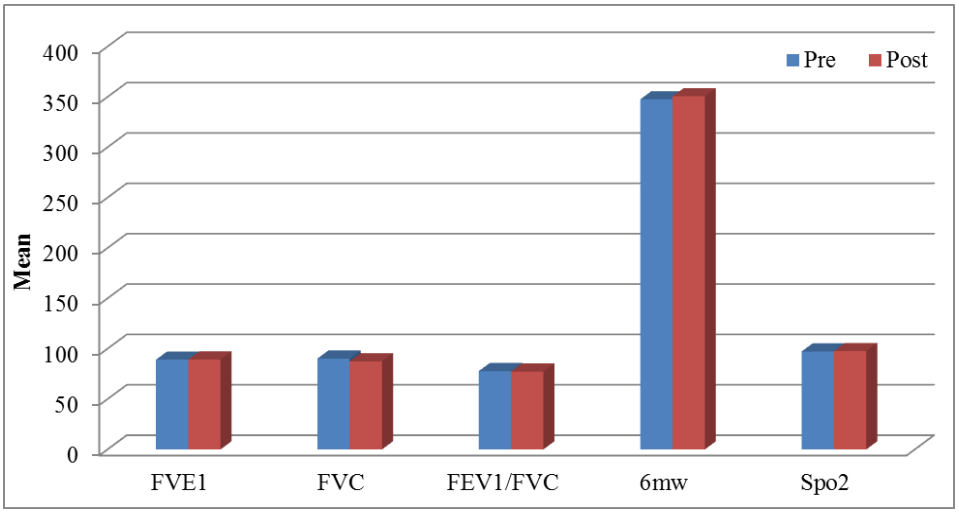

Figure2) Comparison between pulmonary functions before and after treatment

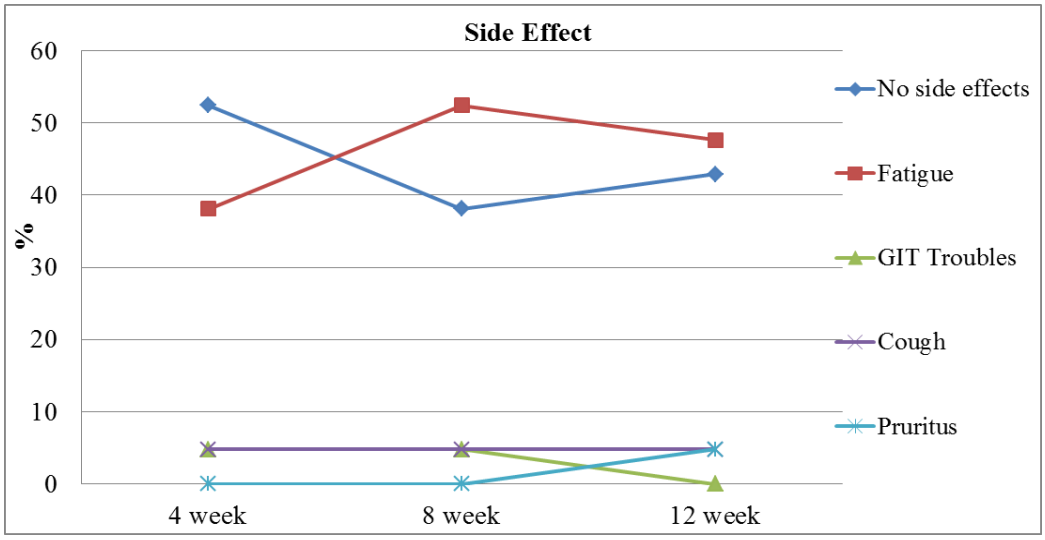

Figure 3) Assessment of side effects of treatment in the studied patients

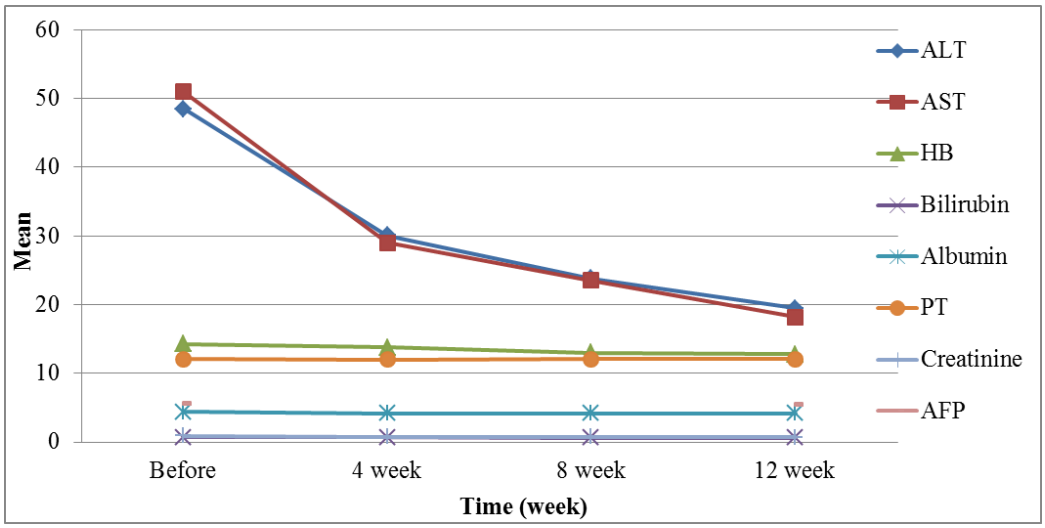

Figure (4a): Assessment of laboratory parameters of studied patients dur-ing different follow up period

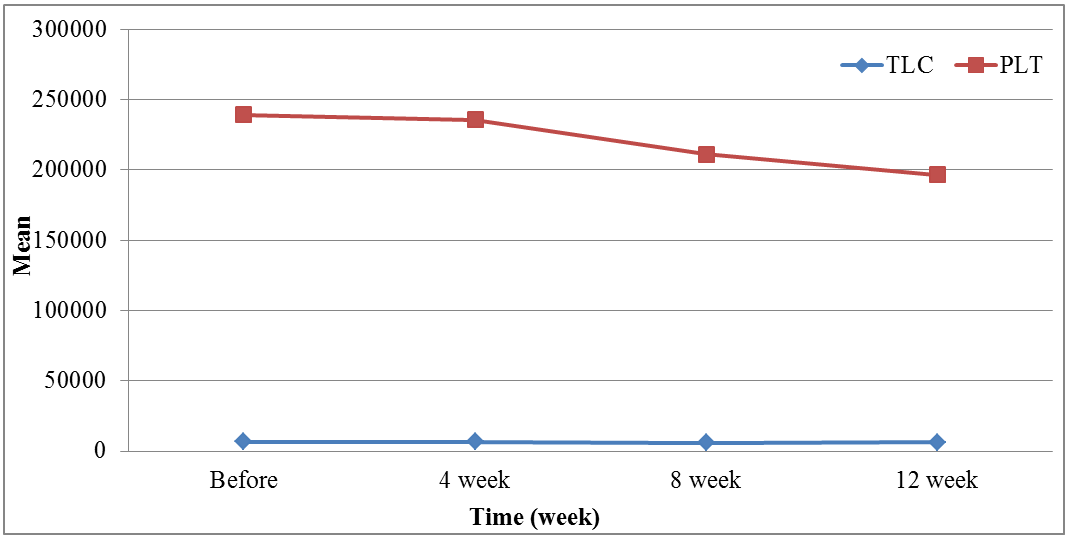

Figure (4b): Assessment of Total leucocytic count and platelets count of studied patients during different follow up period

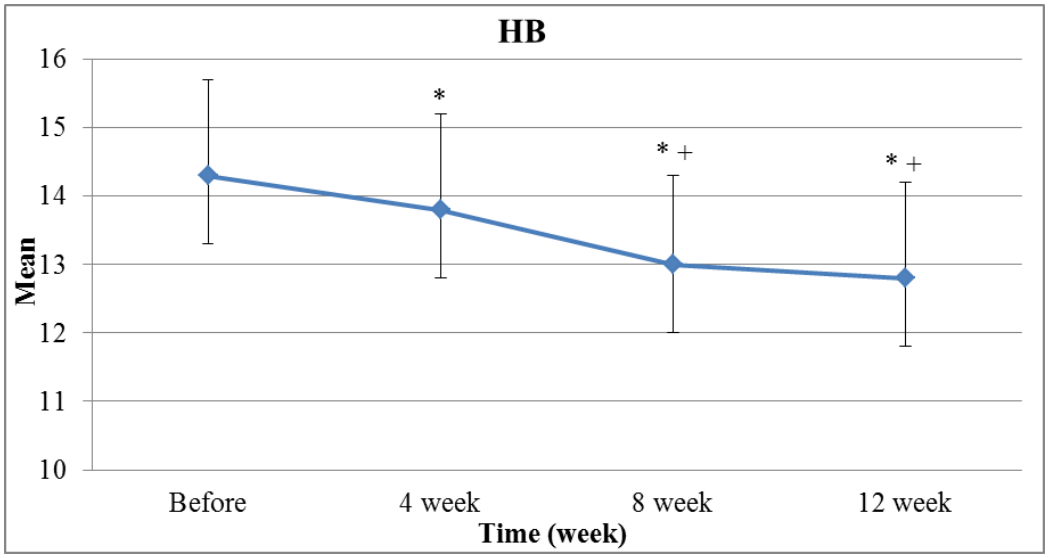

Figure (4b): Assessment of Hemoglobin percent of studied patients during different follow up period

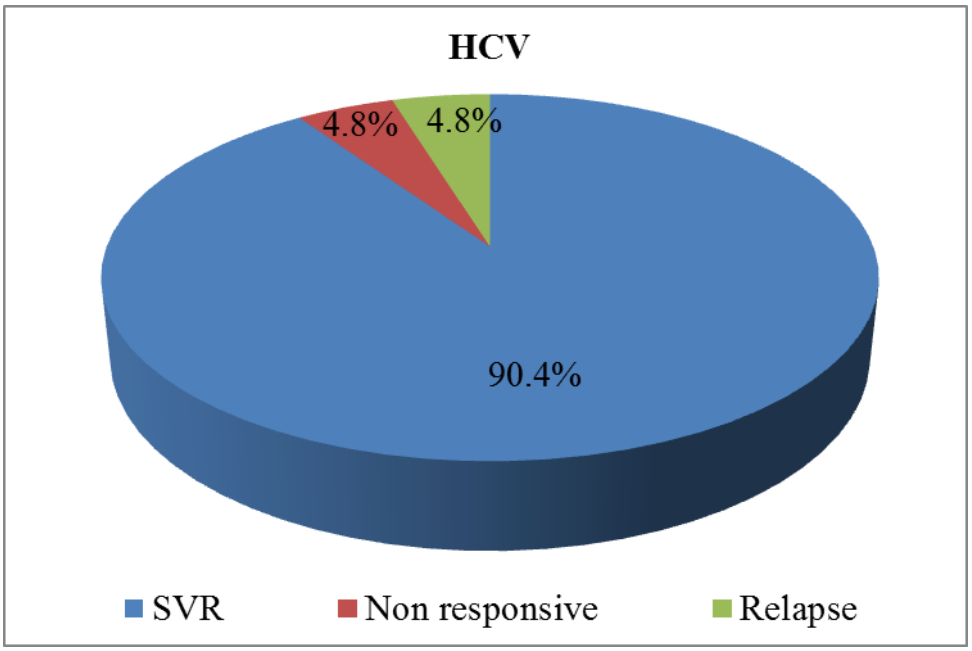

Figure 5) Assessment of efficacy of treatment

Discussion

Egypt ranks 5th amongst all countries for the burden of disease from viral hepatitis, HCV infects more than 170 million people worldwide. Over 80%of infected persons develop chronicity with increased potential to develop cirrhosis and HCC (Hanafiah etal.,2013).

Ages of the patients range from 36 to 72 years with mean age 53 years , 71% of patients were male and 28% of patients were females, 42% of patients were smokers and the major risk of transmission of HCV infection was antischistosomal injections in 42.9% , Previous operations was a risk in 28.6% and there was no obvious risk in 28.6%.

There was no symptoms suggestive of decompensated liver disease , by abdominal examination there was hepatomegaly in 42.9% and in 71.4% on ultrasonography. There was splenomegaly in 33.3% on ultrasonography.

there was no significant changes in pulmonary functions and chest imaging in studied patients

before and after treatment which denotes safety of sofosbuvir and daclatasvir on respiratory system which goes with Dina etal., 2017.

Kohli et al. (2015) studied 20 patients with HCV infection. They were treat-ed by ledipasvir (90 mg) and sofosbuvir (400 mg) as a single combination tablet once per day. Two patients (10%) developed URTI.

Eric Lawitz Studied 20 patients founded that 2patients developed URTI and one patient developed bronchitis received Sofosbuvir plus ledipasvir for8 weeks.

in another study by Kao et al. (2016); 87 patients received treatment with sofosbuvir plus weight-based ribavirin for 12 weeks. URTI occurred in 16%(14/87) of patients.

fatiguability was the most frequent draw back and to less extent GIT toubles,cough and pruritus in about 4.8% of patients.

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