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IMPACT OF SUSTAINED VIROLOGICAL RESPONSE OF VIRUS C OUTCOME ON TYPE II DIABETIC PATIENTS INSULIN RESISTANCE AND METABOLIC STATE

By

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ABSTRACT

Background: Diabetes is one of the most prevalent non-communicable diseases throughout the world, affecting 415 million people in 2015 . Hepatitis C virus (HCV) infection is widespread, affecting up to 185 million people worldwide. Interestingly, a systematic review has also shown a significant association between the presence of type 2 diabetes mellitus T2D and the risk of HCV infection . Chronic HCV is associated with hepatic and peripheral insulin resistance (IR) .

Objective: Investigating the impact of SVR12 following combination of Sofosbuvir and Daclatasvir on IR and metabolic state in type 2 D.M.

Patients and Methods: The study was conducted on100 patients. Patients were divided in two groups; group I, that included 30 patients who have both T2D and HCV and did not receive any anti viral drugs, and they served as a control group. Group II, which included 70 patients as a case group who have type 2 DM and HCV and received treatment for 12 weeks according to the Egyptian guidelines using Sofosbuvir and Daclatasvir, and achieved SVR12. All patients were included in the final analysis investigated by fasting and postprandial blood sugar, full lipid profil, HbA1c and microalbuminuria, HOMA- IR , fibroscan and liver enzymes . Serum HCV-RNA was tested at baseline, after 4 weeks, end of treatment, and 12 weeks after the end of treatment. Results showed that cirrhotic patients showed worse metabolic profile as FBS, PPBS, HbA1c, and Homa - IR, serum cholesterol and serum triglycerides compared to non cirrhotic ones at the start of the therapy. Following the achievement of SVR, Group II patients showed a decrease in its mean fasting blood sugar, postprandial blood sugar, HbA1c, albuminuria , Homa - IR score, cholesterol, triglycerides. Group I showed only improvement of cholesterol level. Normalization of SGOT, SGPT, serum bilirubin and serum albumin was recorded only in group II patients, while INR level showed no change from its pretreatment level in both groups. Additionally, fibroscan result improved in group II , while it increased in group I . So, the achievement of SVR in diabetic patients with CHC have a favorable outcome on IR which was more pronounced in non cirrhotic patients.

Conclusion: The achievement of SVR in patients with HCV and diabetes mellitus is associated with improvement in Insulin resistance and metabolic markers. This improvement can lead to stopping of anti-diabetic treatment with additional improvement of albuminuria which reflect improvement of vascular complications of IR.

INTRODUCTION

Diabetes is one of the most prevalent non-communicable diseases throughout the world, affecting 415 million people in 2015 ***(Cho, 2016)*** Hepatitis C virus (HCV) infection is widespread, affecting

up to 185 million people worldwide ***(Lavanchy, 2009)***. Most patients are unaware of their infection but at increased risk of liver cirrhosis, hepatocellular carcinoma (HCC) and liver-related mortality ***(Grebely and Dore, 2011).*** Interestingly, a systematic review has also shown a significant association between the presence of type 2 diabetes mellitus T2D and the risk of HCV infection ***(Younossi et al., 2011).*** The increased risk is likely to be due to the repeated, invasive medical procedures that T2D patients usually undergo, exposing them to blood borne infections if universal precautions are not strictly followed ***(Guo et al., 2013).*** . Chronic HCV is associated with hepatic and peripheral insulin resistance (IR) and the excess diabetes risk in HCV-infected persons is a subject of debate ***(Bose and Ray , 2014).*** The prevalence of IR and T2D in patients infected with HCV has been shown to be high. In one study more than 30% of HCV subjects had glucose abnormalities ***(Milner et al., 2010).*** Meta-analysis found a pooled adjusted odds ratio (OR) for T2D in HCV-infected persons of approximately 1.7 ***(White et al., 2008).*** Furthermore, the dynamics of IR in chronic HCV has shown an increase of hepatic insulin resistance and a decreased peripheral glucose uptake***(Mitsuyoshi et al., 2008*** and ***Smythe et al., 2010) .*** The effect of sustained virological response (SVR) on various clinical outcomes provides another line of evidence linking HCV infection with IR ***(Vanni et al., 2016).*** One clinical trial concurred to demonstrate that SVR was associated with improved IR as measured by HOMA2-IR ***(Delgado-Borrego et al., 2010)*** Another study found a reduction of de novo IR development in following the achievement of SVR compared to non-SVR patients ***(Aghemo et al., 2012).*** Moreover, a reduction of diabetic complications, including renal and cardiovascular complications, ware reported following successful antiviral treatment ***(Hsu et al., 2014).*** Although most of these studies were performed in patients undergoing interferon (IFN)-based therapy, preliminary reports suggests that direct-acting antiviral (DAA) agents are associated with similar improvement of IR after 12 weeks of treatment ***(Pavone et al., 2016)*** , and the persistency of a lower fasting glucose levels at 24 weeks from the end of DAA therapy ***(Fabrizio et al., 2016).***

The present study aimed to investigate the impact of SVR12 following combination of Sofosbuvir and Daclatasvir on IR as assessed by HOMA IR test, fasting and post-prandial blood sugar, full lipid profile, microalbuminurea and HbA1c among diabetic patients infected by HCV.

PATIENTS AND METHODS

This is a single center prospective study that was performed between December 2015 and January 2017 at the department of Internal medicine, Alhossien Hospital, Cairo, Egypt. 105 patients were initially recruited for this study **(Fig**. **1)**. Patients were divided in two groups; group I, that included 30 patients who have both T2DM and HCV . They did not receive any anti viral drugs and they served as a control group. And group II, which included 75 patients as a case group who have both type 2 DM and HCV. They received treatment for 12 weeks according to the Egyptian guidelines using

Sofosbuvir and Daclatasvir and achieved SVR12. Five patients were excluded because they stopped the treatment due to severe side effects or they were non responsive to treatment. In details, one case show tense ascites at one month and stopped treatment while a 2nd case has renal impairment "creatinine >2.5 mg/dl" after 3 weeks of the start of treatment, and the other 3 cases showed failure of treatment. Eventually, 70 patients were included in the final analysis.Fasting and postprandial blood sugar, full lipid profil, HbA1c and microalbuminuria were assessed.

Serum HCV-RNA was tested by the Cobas Ampli Prep/Cobas TaqMan HCV-RNA assay (Roche Diagnostics; Pleasanton, CA, USA) with a lower limit of detection of 15 IU/mL at baseline. It was meassured at week 4, end of treatment, and 12 weeks after the end of treatment **(Wilkins et al., 2010).**

The assessment of IR (HOMAIR) using the standard formula: HOMA-IR = fasting insulin (uU/mL) x fasting glucose (mmol/L)/22**(Hill et al., 2013).**

Fibroscan was done using Fibroscan (M probe, Echosens, Paris) by an experienced examiner in all patients (with at least 6 h of fasting) in left lateral position and the median liver stiffness of the 10 successful measurements fulfilling the criteria (success rate of greater than 60% and interquartile range /median ratio of <30%) and The FibroScan cut-offs proposed by Castéra et al were used to diagnose bridging fibrosis and cirrhosis. The cut-offs for advanced fibrosis (F3 = numerous septa without cirrhosis) and cirrhosis (F4) were ≥9.5 kPa and ≥12.5 kPa respectively **(Nezam , 2012)**

Statistical Analysis

Continuous variables were expressed as means and standard deviation (SD). Categorical variables were presented as frequency and percentage. Comparisons between groups were made by using Student *t* test for continuous variables and the χ^2 or Fisher exact probability test for categorical data. The two-tailed, paired Student's *t*-test was used to test for significance of differences between baseline and post-treatment variables after the achievement of SVR. Multiple ordinal regression analysis to assess factors associated with improvement in Homa IR were assessed. Variables identified by univariate analysis were included in the multivariate analysis by applying backward multiple logistic regression. All the statistical tests were 2-tailed. A P value of <0.05 was considered statistically significant. Data were analyzed using SPSS 19.0 for Windows (SPSS, Chicago, IL).

RESULTS

One handred and five patients were initially recruited for this study. Patients were divided in two groups : Group I included 30 patients who have both T2DM and HCV. They did not receive any anti viral drugs and they served as a control group. Group II, included 75 patients as a case group who have both type 2 DM and HCV. They received treatment for 12 weeks and achieved SVR12. Five patients were excluded because they stopped the treatment due to severe side effects or they were non responsive to treatment (Fig 1).

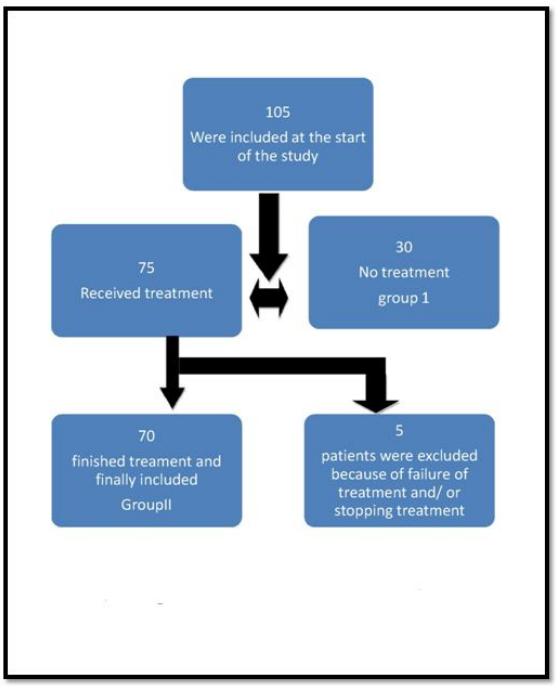

Figure (1) : Studied Groups.

Mean age of group I patients "control" was 50.74±12.80 years, while that of group II, those who received treatment was 49.37±12.65 years (**Table 1**). Males constituted 33.3% of control group, while group II had 42.9% of its members males. Half of group I were cirrhotic, while 44.3% of group II were cirrhotic **(Table 2**).

Group II patients showed improvement of its glycemic control as mean fasting blood showed a decrease from 186.21 ± 82.85 to 132.26 ± 42.20, while that of group I increased from 159.50 ± 65.08 to 172.67 ± 71.85 (p=0.001). Similarly, postprandial blood sugar of group II decreased significantly after achieving SVR12 from 296.79 ± 114.83 to 197.55 ± 48.98 (p=0.001), while that of group I recorded insignificant change from 272.50 ± 104.40 to 285.90 ± 102.19 (p=0.226). Additionally, HbA1c readings showed comparable improvement also in group II as it showed a reduction by about 1 from 7.83 ± 1.60 to 6.86 ± 1.12 (p=0.001). Conversely, group I showed a significant increase of its HbA1c from 6.93±1.25 to 7.41±1.25 (p=0.001). Homa IR score also showed a significant improvement in group II as the score dropped from 3.10±2.18 to 2.20±1.49 (p=0.001). Interestingly, group I showed worsening of insulin resistance as its Homa IR increased significantly from 2.80±1.51 to 3.46±2.22 . Another related improvement was reported in the level of albuminuria . Following SVR, group II showed reduction of albuminuria from 39.42 ± 39.27 to 24.10 ± 25.18 (p=0.001). Unlike group II, group I displayed insignificant change from 34.53 ± 32.01 to 41.90 ± 44.04 (p=0.858). Combined together the variation in albuminuria between the two groups was significant **(Table 3)** .

Blood lipids also showed favorable response to SVR in both groups as regard cholesterol level. Group II patients showed improvement from 275.93 ± 106.93 to 188.77 ± 24.09 , while group I patients showed improvement from 235.18 ± 54.87 to 203.62 ± 33.33 and group II showed lower results than group I (p=0.031) . On the contrary, triglycerides level showed improvement in group II following treatment as compared to group I. A drop from 232.70 ± 151.70 to 148.90±36.31 was reported by group II patients, while group I showed an insignificant change from 177.48 ± 45.54 to 169.74 ± 28.80 (**p=0.689 –Table 3).**

Following SVR, fibroscan results improved in group II as it showed a decline from 11.26 ± 10.87 to 9.54 ± 7.72 (p=0.002), while it increased from 12.91 ±

10.89 to 14.52±13.52 (p=0.213) in group I **(Table 4)** .

Univariate analysis showed that predictive of improvement in Homa IR were FBS (1.694), PPBS (1.471), HbA1c (3.273), INR (2.192), ALT (1.125) and Triglyceride level (1.805). However, multivariate analysis only identified HbA1c and triglycerides (6.068) and (2.699) respectively as of favorable response, Seven patients managed to stop their anti-diabetic drugs as a result of improvement in their IR **(Table 5)**. Patients who eventually stopped anti-diabetic drugs had the following predictive factors; PPBS (1.440) , HOMA IR (1.250) , albuminuria (2.150), and INR (1.859). Multivariate analysis identified PPBS and albuminuruia as the only predictives of response (1.309) and (2.853) respectively **(Table 6**).

Table (1): Comparison of age among studied groups.

Groups / Age (years)	Control group		Cases		Total	
	n	%	n	%	n	%
20-	2	6.8	5	7.1	7	7.0
30-	6	20.0	10	14.3	16	16.0
40-	7	23.3	15	21.4	22	22.0
50-	7	23.3	18	25.7	25	25.0
60-	7	23.3	20	28.6	27	27.0
70	1	3.3	2	2.9	3	3.0
Range	25 - 71		22 - 71		22 - 71	
Mean±SD	50.74±12.80		49.37±12.65		50.71±12.71	
P	0.622					

Table (2): Epidemiology of the studied groups.

Groups / Parameters	Control group		Cases		p
	n	%	n	%	
Sex					
Males	10	33.3	30	42.9	0.373
Females	20	66.7	40	57.1	
Cirrhosis					
Absent	15	50.0	39	55.7	0.599
present	15	50.0	31	44.3	

Table (3): Comparison between the two groups as regard the impact of SVR on glucose and lipid profile metabolism.

Groups / Parameters	Control	Patients	p
Fasting sugar before:	159.50±65.08	186.21±82.85	0.120
Fasting sugar after:	172.67±71.85	132.26±42.20	0.001*
p	0.056	0.001*	
PPS Before:	272.50±104.40	296.79±114.83	0.322
PPS After:	285.90±102.19	197.55±48.98	0.001*
p	0.226	0.001*	
HbAc1 Before:	6.93±1.25	7.83±1.60	0.008*
HbC1 After:	7.41±1.25	6.86±1.12	0.03*
p	0.001*	0.001*	
Albuminuria Before:	34.53±32.01	39.42±39.27	0.549
Albuminuria After:	41.90±44.04	24.10±25.18	0.018*
p	0.858	0.001*	
HOMA Before:	2.80±1.51	3.10±2.18	0.495
HOMA After:	3.46±2.22	2.20±1.49	0.001*
p	0.026*	0.001*	
Cholesterol Before:	235.18±54.87	275.93±106.93	0.0511*
Cholesterol After:	203.62±33.33	188.77±24.09	0.014*
p	0.035*	0.001*	
Triglycerides Before:	177.48±45.54	232.70±151.70	0.054*
Triglycerides After:	169.74±28.80	148.90±36.31	0.007*
p	0.689	0.001*	

*Significant

Table (4): Comparison between the two groups as regard biochemical and radiological parameters.

Groups / Parameters	Control	Patients	p
Fibroscane Before:	12.91±10.89	11.26±10.87	0.588
Fibroscane After:	14.52±13.52	9.54±7.72	0.022*
p	0.213	0.002*	

Table (5): Predictive of improvement in HOMA in response to SVR achievement

Groups / Parameters	Control		Cases		Uni varient		Multi variant	
	n	%	n	%	OR	95%CI	OR	95% CI
Fasting blood sugar:								
70-110	6	20.0	9	12.9			1.014	0.222-4.382
>110	24	80.0	61	87.1	1.694	0.544-5.276		
Post prandial sugar:								
≤200	7	23.3	12	17.1			0.687	0.356-5.940
>200	23	76.7	58	82.9	1.471	0.515-4.203		
HbA1C								
≤6	8	26.7	7	10.0			6.068	0.031-0.863
>6	22	73.3	63	90.0	3.273	1.063-10.07		
HOMA								
≤2	7	23.3	26	37.1				
>2	23	76.7	44	62.9	0.515	0.194-1.366		
Albuminuria								
≤18	10	33.3	35	50.0				
>18	20	66.7	35	50.0	0.500	0.205-1.220		
Prothrombin activity								
<70	20	66.7	57	81.4	2.192	0.83-4.88	0.290	1.138-10.482
70-100	10	33.3	13	18.6				
Serum albumin								
<3.5	13	43.3	20	28.6	0.523	0.22-1.27		
≥3.5	17	56.7	50	71.4				
Total bilirubin								
≤1	16	53.3	42	60.0				
>1	14	46.7	28	40.0	0.762	0.322-1.804		
ALT								
≤45	18	60.0	40	57.1			0.855	0.409-3.347
>45	12	40.0	30	42.9	1.125	0.471-2.686		
AST								
≤45	15	50.0	37	52.9				
>45	15	50.0	33	47.1	0.892	0.379-2.099		
Cholesterol								
≤200	6	20.0	16	22.9				
>200	24	80.0	54	77.1	0.844	0.294-2.422		
Triglycerides								
≤165	11	36.7	17	24.3			2.699	0.126-1.086
>165	19	63.3	53	75.7	1.805	0.718-4.538		
Cirrhosis:								
Negative	15	50.0	39	55.7				
Positive	15	50.0	31	44.3	0.795	0.337-1.873		

Table (6): Predictives of stopping treatment in response to SVR achievement.

Groups / Parameters	Stopped treatment		Continued treatment		Uni varient		Multi varient	
	n	%	n	%	OR	95%CI	OR	95% CI
Fasting blood sugar:								
70-110	2	28.6	13	14.0				
>110	5	71.4	80	86.0	0.406	0.071-2.318		
Post prandial sugar:								
≤200	1	14.3	18	19.4			1.309	0.099-17.383
>200	6	85.7	75	80.6	1.440	0.163-12.72		
HbA1C								
≤6	1	14.3	14	15.1			0.712	0.057-8.879
>6	6	85.7	79	84.9	1.063	0.119-9.519		
HOMA								
≤2	2	28.6	31	33.3			0.901	0.109-7.601
>2	8	71.4	62	66.7	1.250	0.229-6.812		
Albuminuria								
≤18	2	28.6	43	46.2			2.853	0.375-21.680
>18	5	71.4	50	53.8	2.150	0.397-11.65		
Prothrombin activity								
<70	6	85.7	71	76.3	1.859	0.21-16.29	0.390	0.040-3.801
70-100	1	14.3	22	23.7				
Serum albumin								
<3.5	2	28.6	31	33.3	0.800	0.15-4.36		
≥3.5	5	71.4	62	66.7				
Total bilirubin								
≤1	6	85.7	52	55.9				
>1	1	14.3	41	44.1	0.211	0.024-1.826		
ALT								
≤45	6	85.7	52	55.9				
>45	1	14.3	41	44.1	0.211	0.024-1.826		
AST								
≤45	5	71.4	47	50.5				
>45	2	28.6	46	49.5	0.409	0.075-2.214		
Cholesterol								
≤200	2	28.6	20	21.5				
>200	5	71.4	73	78.5	0.685	0.124-3.796		
Triglycerides								
≤165	3	42.9	25	26.9				
>165	4	57.1	68	73.1	0.490	0.102-2.346		
Cirrhosis:								
Negative	6	85.7	48	51.6				
Positive	1	14.3	45	48.4	0.178	0.021-1.535		

DISCUSSION

The epidemiological evidence linking HCV to IR, is rather compelling, although the association seems strongest in at-risk individuals with additional risk factors such as older age and higher BMI***(Khattab et al., 2010) & (Romero-Gomez et al., 2008)*** .There is an accumulating data that the achievement of SVR using DAAs can improve IR***(Pavone et al., 2016 and Fabrizio et al., 2016).***

The results of this study indicate that there is a significant difference between cirrhotic patients and non cirrhotic patients in terms of glycemic control as reflected by FBS, PPBS, HbA1c, and Homa IR which indicate that the development of cirrhosis worsens IR. In addition, the increase of albuminuria level in cirrhotic patients point out that vascular complications of persistent hyperglycemia are more prominent in those patients. Insulin resistance had been reported to be associated with liver cirrhosis (LC) in more than one study ***(Gercia-Compean et al., 2009 and Laure et al., 2013)***. Half of patients with cirrhosis and no previous diagnosis of DM proved to have DM ***(Kayo et al., 2014).*** Malnutrition can contribute to the development of IR which can explain the difference between cirrhotic and non cirrhotic patients***(Kayo et al ., 2014).*** Alternatively, it had been proven that IR can accelerate the progression of liver fibrosis ***(Wree et al., 2013) .*** However, the degree of LC did not affect the extent of IR ***(Kayo et al ., 2014).*** IR-induced hepatic lipid accumulation and generation of ROS can also indirectly activate stellate cells and initiate the cellular signaling cascades triggering hepatic fibrosis ***(Suhag et al., 2016).***

In our cohorts, following successful eradication of HCV, improvement of glucose metabolism was significantly noticed as all FBS, PPBS, HbA1c, and Homa IR were decreased this was strikingly evident by the fact that 7 patients eventually stopped their Anti-diabetic medications. In more than a study, IR had improved significantly following SVR in response to Peg-IFN plus RBV ***(Wedemeyer et al., 2009) and (Khattab et al., 2012)***. Furthermore, this improvement was coupled with changes in adiponectin levels, leptin levels and TNF-α and. Moreover, the speed by which these changes took place was proportionate to the speed of viral clearance as patients who showed EVR at 12 weeks reported more rapid improvement in their IR. More importantly, relapsers showed worsening of HOMA-IR values that returned to baseline in most patients by 24 weeks after stopping therapy***(Grasso et al., 2015).***Indeed the cohorts in our study showed SVR12 which might explain the better responses reported to the degree that some patients stopped treatment. Our data confirm the importance of HCV clearance in management of IR in diabetics which can eventually normalize glucose metabolism.

Kawaguchi and his colleagues reported conflicting results that included no change of Homa IR following SVR, and the researchers rejected the axiom that viral clearance resulted in improvement of Homa IR ***(Kawaguchi et al., 2009)***. However, they admitted a favorable impact of SVR on whole body IR as reflected by improvement of Homa B. To begin with ,the researchers in that study used IFN based treatment and their

diabetic patients were only managed nutritionally but not by drugs which explains the discrepancy between our data and their conclusion**.** In addition, the mechanism of hepatic insulin resistance can be affected by LC which was reported nearly by half of our cohorts unlike those of Kawaguchi study who were all non cirrhotic.

To our knowledge, this is the first study that report stopping anti-diabetic treatment in response to SVR in CHC diabetic patients. This might be explained by multiple factors. Firstly, the shorter duration of treatment and the reported parallel improvement in glucose metabolism took effect early as compared with the previously used IFN based therapy which allowed us earlier reporting of the improvement. Secondly, IFNs have been reported to impair glucose tolerance ***(Huang et al., 2011)***. Consequently, the resultant improvement in IR following its use could have been hampered by the worsening effect of the drug itself**.** The metabolic effect of INF might had attenuated the proposed improvement of IR in response to viral clearance. Finally, the rate of SVR in response to DAAs is higher than that reported in IFN treatment and consequently larger number of patients are experiencing cure with the associated metabolic improvement.

Following SVR and neutralization of the viral replication factor cirrhotic patients had a worse metabolic profile which indicate that cirrhosis is more important than viral replication as a perpetuating factor for IR. Conceptualizing this difference involves the differentiation between the 2 arms of IR. In general, the resultant inflammatory process related to HCV infection with theproduction of cytokines such as TNF-a evokes systemic (primarily muscle) IR ***(Kawaguchi et al., 2009)*** which subsequently impacts Homa B. While cirrhosis which impairs hepatic response to insulin impacts mainly Homa IR which was manifested in our cohorts. However, the analyzed number of patients was small so such conclusion should be taken carefully. In addition, assessment of peripheral IR was not obtained in the current study.

The report that HCV eradication was associated with a reduction in IR in patients infected with genotype 1 but not in those with genotype 2/3 HCV, suggesting a causal relationship between genotype 1 HCV and IR which makes comparison between the results of studies more tricky ***(Thompson et al 2012)*** consequently, special emphasis on the impact of viral genotype on IR should be a subject of scrutiny. However, the favorable impact of eradication of HCV GT-4 had been reported by other researchers ***(Khattab et al., 2012).***

Most studies that investigated the impact of viral clearance on SVR were limited by small sample size and heterogenicity in viral genotypes. ***(Romero-Gomez et al., 2008, Kawaguchi et al., 2009, Khattab et al., 2012 and Grasso et al., 2015).***

Multivariate analysis only identified HbA1c and triglycerides as predictive of improvement in IR. Recently, Multivariate analysis using a logistic regression model showed that baseline HOMA-IR is the only factor associated with the decline in HOMA-IR during and after therapy ***(Chien et al., 2015).*** The dramatic metabolic improvement that was manifested by stopping anti-diabetic treatment was

predicted by PPBS, HOMA IR, albuminuria, and INR using univariate regression analysis. Multivariate analysis identified PPBS and albuminuruia as the only predictives of response.Whether or not this metabolic improvement is solid and not clear. Many studies had evaluated the validity of numerous metabolic markers as predictors of improvement in IR, namely Homa IR, BMI, and Serum Leptin. However none had reported that achieving an SVR can result in stopping anti-diabetic treatment. In fact, all of those studies excluded patients who are under treatment for diabetes and included only those under diet treatment ***(Kawaguchi et al., 2009 , Khattab et al., 2012 , Chien et al., 2015 and Grasso et al., 2015).***

Nevertheless, a clear limitation of the current study is that we only included patients who achieved SVR so it is not clear how unresponsive patients would have responded metabolically to the treatment.

CONCLUSION

The achievement of SVR in diabetic CHC patients have a favorable outcome on IR which is more pronounced in non cirrhotic patients. This improvement can eventually result in stopping anti-diabetic treatment.

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تأثير علاج فيروس س على مرض البول السكرى من النوع الثانى ومقاومة الإنسولين و التغير فى الأيض

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خلفية البحث: مرض البول السكري هو واحد من الأمراض غير المعدية الأكثر إنتشارا في جميع أنحاء العالم، وقد أثر على حوالى ما يقرب من 415 مليون شخص في عام 2015. وعدوى فيروس التهاب الكبد الوبائي س واسعة الإنتشار، وقد أثرت على ما يصل إلى 185 مليون شخص في جميع أنحاء العالم. ومن المثير للإهتمام أنه قد أظهرت مراجعة منهجية أيضا وجود إرتباط كبير بين وجود داء السكري من النوع 2 وخطر الإصابة بفيروس إلتهاب الكبد الوبائي C. ويرتبط فيروس إلتهاب الكبد الوبائي C المزمن بزيادة مقاومة الإنسولين الكبدية والمحيطة .

الهدف من البحث: التحقيق في تأثير علاج فيروس س بعقار سوفوسبوفير و داكلاتاسفير على مقاومة الإنسولين والحالة الأيضية في النوع الثانى من مرض البول السكرى .

المرضى وطرق البحث : أجريت هذه الدراسة على 100 مريض. وقد تم تقسيم المرضى إلى مجموعتين. المجموعة الأولى، شملت 30 مريضا لديهم مرض السكرى النوع الثانى و فيروس التهاب الكبد الوبائي C ولم يتلقوا أي أدوية مضادة للفيروسات، وخدموا كمجموعة مراقبة، والمجموعة الثانية تضمنت 70 مريضا لديهم مرض السكرى من النوع الثانى وفيروس إلتهاب الكبد الوبائي C وتلقوا العلاج لمدة 12 أسبوعا وفقا لمبادئ الجمعية المصرية لعلاج فيروس س بإستخدام سوفوسبوفير وداكلاتاسفير، وحققوا إختفاء للعدد الكمى للفيروس لمدة ثلاثة شهور بعد إنتهاء العلاج. وقد تم تضمين جميع المرضى في التحليل النهائي التحقيق من نسبة سكر الدم صائم وسكر الدم بعد الأكل بساعتين، ونسبة الدهون فى الدم، والسكر التراكمى، والميكرو ألبومينوريا (ألبومين فى البول) ، واختبار هوما ، وفيبروسكان وإنزيمات الكبد. وقد تم اختبار العدد التراكمى لفيروس س في البداية قبل أخذ العلاج وبعد 4 أسابيع من العلاج ، وبعد نهاية العلاج، و12 أسبوعا بعد إنتهاء العلاج. وأظهرت النتائج أن المرضى الذين يعانون من التشمع الكبدى أظهروا حالة أيض أسوأ كما فى السكر الصائم، والسكر بعد ساعتين، والسكر التراكمى، وهوما ، والكوليسترول في الدم والدهون الثلاثية في الدم مقارنة مع تلك

الحالات التى ليس بها تشمع في بداية العلاج. وبعد تحقيق الإستجابة للعلاج ، أظهرت المجموعة الثانية انخفاض في متوسط السكر في الدم الصائم، وسكر الدم بعد الأكل والهيموجلوبين السكرى، وألبومين، وهوما والكوليسترول والدهون الثلاثية. كما أظهرت المجموعة الأولى تحسن فى مستوى الكوليسترول. وتم تسجيل تحسناً فى وظائف الكبد ونسبة الصفراء والألبومين في المجموعة الثانية من المرضى، في حين لم يتغير مستوى البروثرومبين في كلتا المجموعتين. بالإضافة إلى ذلك، تحسنت نتيجة فيبروسكان في المجموعة الثانية، في حين أنها زادت في المجموعة الأولى.

الاستنتاج: تحقيق النجاح فى علاج فيروس س فى المرضى الذين يعانون من إلتهاب الكبد الوبائي ومرض البول السكري يرتبط مع تحسن في مقاومة الإنسولين وعلامات التمثيل الغذائي. وهذا التحسن يمكن أن يؤدي إلى وقف العلاج المضاد للسكري مع تحسن إضافي من الألبومين البولى التي تعكس تحسين مضاعفات الأوعية الدموية لدى هؤلاء المرضى .