Research Article

Effect of Direct-Acting Antivirals on Lipid and Glucose Metabolism in Chronic HCV Patients

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Abstract
Introduction: Hepatitis C virus (HCV) infection is a global public health burden, total global HCV prevalence is estimated at 2.5% (177 million of HCV infected adults), Considerable differences are present among different populations. For example, the HCV prevalence in Egypt is 10-15%. **Aim of the study:** The aim of this study is to determine the effect of treatment with DAAs on serum lipids (total cholesterol, low and high density cholesterol, triglycerides, ox LDL) and Insulin Resistance (HOMA_IR) in chronic HCV patients. **Patients and Methods: Study design:** Our Prospective study aimed to determine the effect of treatment with Direct Acting Antivirals (DAAs) on lipid and glucose metabolism in chronic hepatitis C patients. **Results:** Eighty six chronic hepatitis c patients were included in this study, the patients were consecutively from admitted and/or attendant of out patient's clinic of Tropical Medicine Department, Minia University Hospitals. The main results of the study were summarized in the following tables and figures. **Conclusion:** The DAAs therapy is highly effective in treatment of chronic hepatitis c patients especially (SOF/DAC) regimen, reaching about 100% SVR.
Keywords: Direct-Acting Antivirals, Chronic HCV

Introduction
Hepatitis C virus (HCV) infection is a global public health burden, total global HCV prevalence is estimated at 2.5% (177 million of HCV infected adults), Considerable differences are present among different populations. For example, the HCV prevalence in Egypt is 10-15%. Chronic HCV infection is often associated with the development of liver cirrhosis, liver cell failure, hepatocellular cancer, and death.[(1)]

Chronic HCV infection is associated with metabolic complications, including insulin resistance, hepatic steatosis, hypobetalipo-proteinemia, and hypocholesterolemia.[(2)]

Clinical metabolic complications of HCV infection improve after successful treatment of HCV (sustained virologic response, or SVR), implicating a causative role of ongoing viral replication[(3)].

HCV is known to utilize host lipid metabolic pathways during replication Viral assembly and envelope acquisition during hepatocyte budding require the VLDL biosynthetic pathway, and circulating HCV is complexed with VLDL in lipoviral particles containing host apolipo-proteins, including APOB, APOE, and APOC3[(4)].

Upregulation of the MTTP gene, whose protein product modulates VLDL production, is observed in HCV infected liver, and a high association of HCV virions with LDL and VLDL particles and is correlated with increased viral infectivity[(5)].

HCV infection is also associated with intrahepatic transcriptional upregulation of SREBP genes, master transcriptional regulators of fatty acid metabolism, leading to enhanced HCV lipid droplet association and viral assembly[(6)].

Aim of the study
The aim of this study is to determine the effect of treatment with DAAs on serum lipids (total cholesterol, low and high density cholesterol, triglycerides, ox LDL) and Insulin Resistance (IR) in chronic HCV patients.

Patients and Methods
Study design:
Our Prospective study aimed to determine the effect of treatment with Direct Acting

Antivirals (DAAs) on lipid and glucose metabolism in chronic hepatitis C patients.

Study setting and population:
One hundred thirty CHC patients who attended the virology unit Minia university hospitals in the period between February 2018 and December 2018 were enrolled in our study, only 86 patients met the inclusion criteria. The inclusion criteria were:

- **Age:** 30 -45 years old
- **BMI:** 23 -27
- **HCV PCR:** positive
- **Treatment:** naïve
- **Ultra sound:** non cirrhotic liver

The exclusion criteria were:-

- Patients known to have diabetes mellitus.
- Patients who are taking cholesterol lowering agents.
- smokers.
- obesiety.
- Cardiovascular patients.
- Patients who were contraindicated for DAAs therapy:-

- Total serum bilirubin > 3 mg.
- Serum albumin < 2.8 g/dl
- INR ≥ 1.7.
- Platelet count < 50,000/mm3.
- Serum creatinine >2.5mg/dl. If creatinine is between 1.5 and 2.5 mg/dl, eGFR should be calculated and should exceed 30ml/min with favorable nephrological consultation.
- Extra-hepatic malignancy except after two years of disease-free interval.
- Pregnancy or inability to use effective contraception.

Results

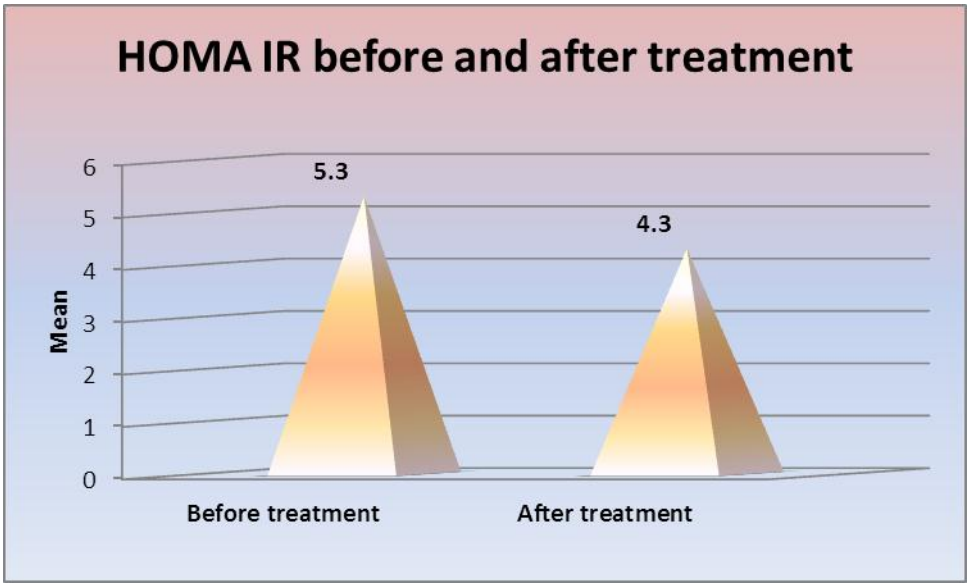
Eighty six chronic hepatitis c patients were included in this study, the patients were consecutively from admitted and/or attendant of out patient's clinic of Tropical Medicine Department, Minia University Hospitals. The main results of the study were summarized in the following tables and figures.

The study included 86 patients, 36males (41.9%) and 50femles (58.1%) with the mean age 38years old and a range from (31-45) years and the mean of BMI was 24.9 and the range was 23-27% Table (1) and figure (1).

Insulin and glucose changes before and after treatment.

Laboratory data	Before	After	P value
RBS			
Range	0 - 169	88 – 143.5	<0.001*
Mean ± SD	133.3 ± 26.5	112.7 ± 13.7	
Serum insulin			
Range	0.4 – 1.5	0.64 – 1.4	0.780
Mean ± SD	0.86 ± 0.19	0.85 ± 0.13	
HOMA-IR			
Range	3.4 – 8.9	2.9 – 7.3	<0.001*
Mean ± SD	5.3 ± 1.06	4.3 ± 0.85	

* Paired sample t test was used to compare before and after treatment
*There is significant difference (P-value <0.05).



Lipid profile before an after HCV treatment.

Laboratory data	Before	After	P value
LDL			
Range	50 - 135	63.5 - 161	<0.001*
Mean ± SD	83.6 ± 18.9	106.9 ± 23.9	
HDL			
Range	3 - 52	35 - 57	<0.001*
Mean ± SD	39.9 ± 7.8	45.6 ± 5.3	
Triglyceride			
Range	60 - 129	100 – 200.5	<0.001*
Mean ± SD	97.6 ± 14.7	144.7 ± 22	
Cholesterol			
Range	110 - 192	138 - 241	<0.001*
Mean ± SD	144.1 ± 17.6	180.8 ± 22.2	
Oxidized LDL			
Range	768 - 5640	1182 - 5640	<0.001*
Mean ± SD	1726.2 ± 777	2925.8 ±866.2	

* Paired sample t test was used to compare before and after treatment
*There is significant difference (P-value <0.05).

Discussion

The development of DAAs for treatment of viral hepatitis continues to generate much interest, Meissner EG, et al., 2015 and Mauss S, et al., 2016 examined the changes in lipid profile and IR, associated with the use of such therapy for infection with hepatitis C. the study reached an SVR-12 of100% of the treated cases the changes in lipid profile after therapy represented an interesting finding, as recently reported with the use of DAAs.

HCV is known for its metabolic effects on glucose metabolism and insulin resistance. chronic liver disease associated with insulin resistance called hepatogenous diabetes[7]. Although the pathogenic mechanism is still unclear, but insulin thought to exert many

biological effects through insulin receptor substrate(IRS)1 and (IRS)2. Disruption of IRS1 results in insulin resistance but not DM because of compensatory hyperinsulinemia[8], [9].

In our study, using the HOMA-IR model, we found significant decrease in insulin resistance after achieving sustained virological response (SVR) using the new Direct acting antiviral drugs (DAAs).

Hui Et al., 2003 reported that the HOMA model has been validated and widely used for determining the degree of IR in epidemiological studies.

Hsu et al., 2008, reported a correlation between HCV-RNA levels and HOMA-IR score. Even in nondiabetic patients.

Conclusion

The DAAs therapy is highly effective in treatment of chronic hepatitis c patients especially (SOF/DAC) regimen, reaching about 100% SVR. DAAs therapy has a significant effects in HOMA-IR lead to improvement of insulin resistance. Monitoring of lipid profile especially OX LDL level after treatment is important to decrease risk of hyperlipidemia.

Recommendations

1. Monitoring of lipid changes during and after DAAs treatment for long term.
2. Administration of statin during or immediately after DAAs treatment.

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