EFFECT OF INTERFERON-FREE TREATMENT ON LIPID AND GLUCOSE METABOLISM IN HEPATITIS C

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INTRODUCTION

Chronic HCV infection may affect host glucose and lipid metabolism. The virus induces hypocholesterolemia, insulin resistance (IR), diabetes, atherosclerosis and steatosis (1-4). Low density cholesterol (LDL-C) is an atherogenic lipoprotein and its oxidated form (oxLDL) is involved in the formation of atherosclerotic plaques. OxLDL is a biomarker of cardiovascular disease and it is associated with all stages of atherosclerosis, coronary and peripheral arterial disease, acute coronary syndromes and ischemic cerebral infarction (5). Recently several novel highly effective direct acting antiviral agents (DAA) have completely changed HCV treatment (6), but their impact on HCV related metabolic disorders and atherosclerosis has never been studied.

AIM

The aim of this study was to investigate changes of serum lipids (total cholesterol, low and high density cholesterol, triglycerides), oxLDL and IR during and after DAA treatment of HCV.

MATERIALS & METHODS

We enrolled 77 consecutive HCV patients treated with DAA. Diabetic patients were excluded.

Homeostatic model assessment-insulin resistance (HOMA-IR), total, low and high density cholesterol (TC, LDL-C, HDL-C), triglycerides (TG) and oxLDL levels have been evaluated at baseline (T0), end-of-treatment (EOT) and after 12-weeks of follow-up (FU).

Measurements for serum lipids (TC, LDL-C, HDL-C and TG) were performed in our hospital laboratory. HOMA-IR score was calculated as (glucose x insulin)/22.5 using fresh serum glucose and insulin. Serum oxLDL was measured by enzyme-linked immunosorbent assay (ELISA) (Mercodia, Uppsala, Sweden).

Changes in TC, LDL-C, HDL-C, TG, HOMA-IR and OxLDL were assessed by Wilcoxon Test, differences in proportions were assessed by chi-square test.

RESULTS

Table 1: Demographic, clinical, biochemical and virological characteristics of enrolled patients

Parameter	Mean ± SD or %	Parameter	Mean ± SD
Age, years	58.7 ± 11.2	ALT, U/L	87.9 ± 68.9
Gender (Male)	57.1%	Total cholesterol, mg/dL	155.6 ± 34.4
Liver Stiffness, KPa	19.1 ± 9.9	LDL cholesterol, mg/dL	82.4 ± 31.9
Cirrhosis (Yes)	64.9%	HDL cholesterol, mg/dL	49.4 ± 17.6
BMI	24.7 ± 3.8	Triglycerides, mg/dL	119.2 ± 64.08
Steatosis (Yes)	36%	HOMA-IR	4.46 ± 3.08
Metabolic syndrome (Yes)	28%	HCVRNA, Log IU/mL	6.07 ± 0.78

Characteristics of enrolled patients are shown in Table 1. Mean age was 58.7±11.2 years, 57.1% were males, BMI was 24.7±3.9, the prevalence of steatosis and metabolic syndrome was 36% and 28% respectively, 64.9% had cirrhosis. 74% were HCV genotype 1 infected patients with high viral load (6.07 ± 0.78 Log IU/mL).

Patients were treated with different interferon free regimens, 70% of which containing ribavirin (Table 2).

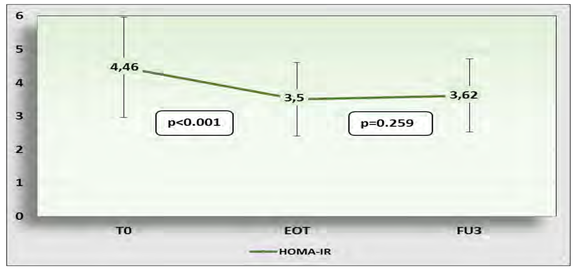
Table 2: Interferon free regimens

DAA Therapy ± Ribavirin	Patients (%)	DAA Therapy ± Ribavirin	Patients (%)
Sofosbuvir + Simeprevir	31.1%	Sofosbuvir + Ribavirin	6.5%
Sofosbuvir + Ledipasvir	27.3%	Paritaprevir/ritonavir, Ombitasvir, Dasabuvir	22.1%
Sofosbuvir + Daclatasvir	13%		

A significant decrease of HOMA-IR occurred during therapy and remained stable during FU (Figure 1).

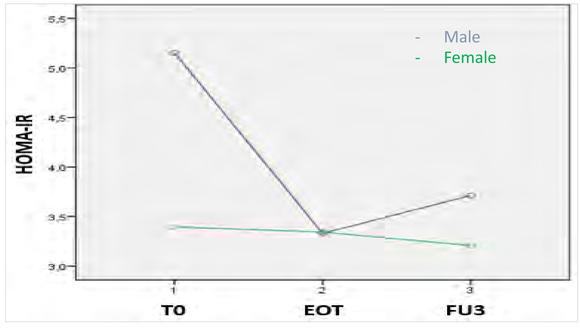
The baseline proportion of patients with HOMA-IR≥4, diagnostic for a pre-diabetic state, was 45.5% and significantly decreased after treatment to 32.5% (p=0.03).

Figure 1: Mean change of HOMA-IR during and after DAA treatment of HCV



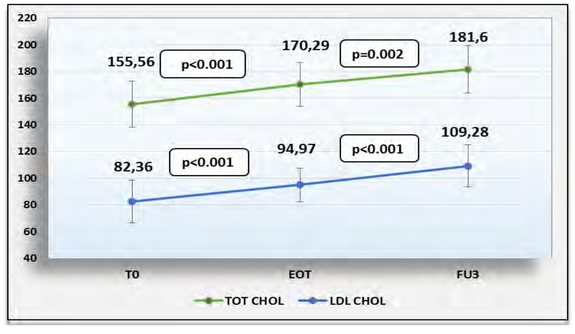
The decline of HOMA-IR during antiviral treatment was gender-related, since men experienced a marked reduction of IR during therapy while women had no changes (Figure 2).

Figure 2: Change of HOMA-IR during and after DAA treatment of HCV according to gender



TC and LDL-C levels significantly increased during antiviral therapy and FU (Figure 3).

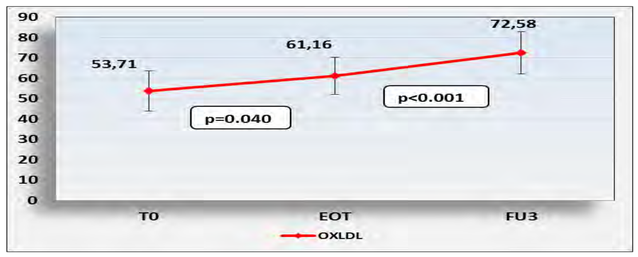
Figure 3: Mean change of Total cholesterol and LDL cholesterol during and after DAA treatment of HCV



The baseline proportion of patients with optimal TC (TC<200 mg/dL) and LDL-C (LDL-C<129 mg/dL) levels significantly decreased during the study period from 88.3% to 70% (p=0.0075) and from 89% to 76.2% (p=0.04), respectively.

Notably also oxLDL levels increased during the study period (Figure 4), while HDL-C did not change and TG levels declined only during treatment.

Figure 4: Mean change of OxLDL (U/L) during and after DAA treatment of HCV



CONCLUSIONS

The improvement of insulin resistance and the significant reduction of the proportion of patients with a pre-diabetic state suggest that DAA treatment might revert HCV related glucose metabolic alterations. The modulation of these changes observed during treatment according to gender is an interesting aspect of the interplay between virus and host and an area of future research.

The rapid and significant increase in total, LDL and oxLDL cholesterol levels observed in patients with advanced liver disease treated with DAA might increase their cardiovascular risk, suggesting the potential benefit of statin co-administration during or immediately after DAA therapy.

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No disclosure to declare in relation to this research

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