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PLASMA SELENOPROTEIN P LEVELS ARE RELATED TO ADIPOSE TISSUE INSULIN RESISTANCE, COMPOSITION OF FREE FATTY ACIDS AND LIVER FIBROSIS IN NON-DIABETIC PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION

Alterations in glucose and lipid metabolism in the setting of insulin resistance (IR) play an important role in the development and progression of Non-alcoholic Fatty Liver Disease (NAFLD) via increased oxidative stress.

Circulating levels of selenoprotein P (Sepp), a selenium carrier protein with antioxidant properties, were found to be higher in obese and diabetic NAFLD subjects compared to controls [1-3]. Moreover, the administration of SeP impaired insulin signaling in hepatocytes while its deficiency in mice leads to an improvement of insulin sensitivity [3].

AIM

The aim of this study were to evaluate the association between plasma Sepp levels and:

1) IR at different sites
2) de novo lipogenesis indices
3) liver damage

in a well characterized group of non-diabetic subjects with biopsy proven NAFLD.

MATERIAL & METHODS

40 subjects with biopsy proven NAFLD underwent tracers studies (6,6D2glucose and D5glycerol) in the basal state (n=40) and after a double tracers 75 g-Oral Glucose Tolerance Test (OGTT)(n=24).

IR components calculation:

- Hepatic IR (Hep-IR) = EGP*insulin
- Adipose tissue (AT)-IR = Glycerol Ra*insulin (AT-IR1) or FFAs* insulin (AT-IR2)
- Peripheral (Per-IR) = EGP/glucose

Gas chromatography mass spectrometry was used to assess FAs composition.

The SCDi and DNLi were derived as the ratio palmitoleic/palmitic acid (16:1/16:0) and palmitic/linoleic (16:0/18:2), respectively.

Plasma Sepp levels was measured using ELISA.

Histology was scored according to Kleiner.

RESULTS

During fasting, plasma Sepp levels were associated with AST and ALT levels (r=0.35, p=0.035 and r=0.32, p=0.050) (**Fig. 1A-B**), with AT-IR1 (r=0.473, p=0.004) and AT-IR2 (r=0.325, p=0.050) (**Fig.1 C-D**), with lipolysis by tracers (r=0.352, p=0.0329) and SCDi (r=0.32, p=0.048) (**Fig.1 E-F**).

Fig. 1

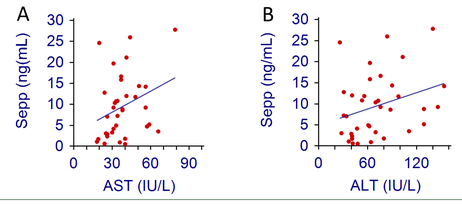
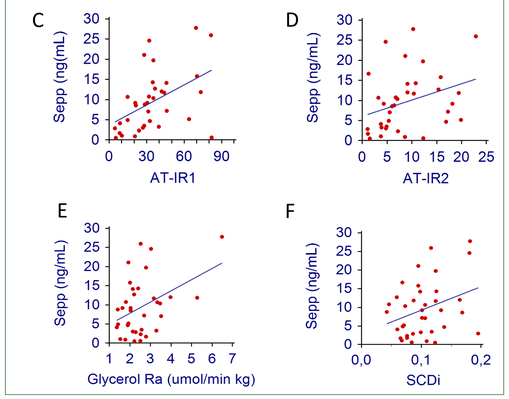


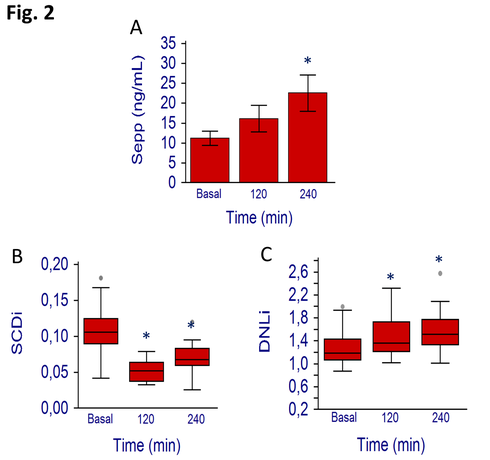
Fig. 1



Following OGTT:

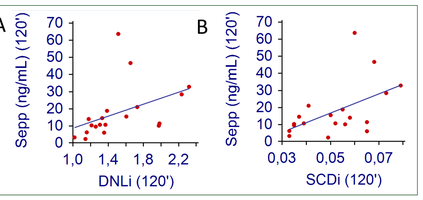
- Sepp levels increased from 11,2 ng/mL at baseline to 17,7 ng/mL at 120' to 23,9 ng/mL at 240' (ANOVA for repeated measures, p=0.008) (**Fig.2A**)
- SCDi decreased from 0.11±0.03 at baseline to 0.06±0.02 at 240' (ANOVA for repeated measures, p<0.001) (**Fig.2B**)
- DNLi increased by 35% (1.23±0.4 at baseline vs 1.66±0.4 at 240' (ANOVA for repeated measures, p=0.016) (**Fig.2C**), indicating an increase in saturated FAs.

Fig. 2



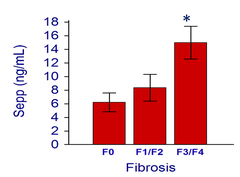
At 120 min OGTT, Sepp levels were directly related to both SCDi and DNLi (r=0.56, p=0.012 and r=0.60, p=0.008) (**Fig.3A-B**) suggesting and increased antioxidant response to increased levels of saturated FAs induced by oral glucose ingestion.

Fig. 3



Among histological features, Sepp levels showed a stepwise increase from F0 to F1-F2 to F3-F4 (Kruskall-Wallis p=0.007), indicating higher scavengers levels in more severe liver damage (**Fig,4**).

Fig. 4



CONCLUSION

In non-diabetic subjects with NAFLD, basal Sepp levels are related to:

- adipose tissue insulin resistance
- FAs composition
- severe liver damage.

Sepp levels increase in response to unfavorable changes in FAs composition induced by the ingestion of a glucose load suggesting that an altered glucose metabolism play a role in the development and progression of NAFLD.

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DISCLOSURES

Nothing to disclose

AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES