Enhnced liver fibrosis test in obese children with ultrasound-proven steatosis

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INTRODUCTION

One of the consequences of obesity is the increasing incidence of nonalcoholic fatty liver disease (NAFLD), which affects 2,6-9,8% of children and adolescents. Presently recommended markers of liver steatosis and risk of progression to fibrosis are: ultrasound imaging (US) and liver aminotransferases (ALT, AST). Due to the poor sensitivity of these tests, there is a need to search for biomarkers which could indicate early stages of NAFLD. The enhanced liver fibrosis test (ELF) based on the combination of concentration of serum hyaluronic acid (HA), aminoterminal propeptide of type III procollagen (PIIINP), tissue inhibitor of matrix metalloproteinase type 1 (TIMP-1) was developed as a noninvasive diagnostic tool for estimation of degree of liver fibrosis. Limited number of studies was on performance of ELF test in obese children was done.

AIM OF THE STUDY

To investigate the performance of ELF in obese children.

MATERIAL AND METHODS

The study included 63 obese children. Based on the abdominal ultrasound results the patients were divided into group I with USG proven steatosis and group II without steatosis. Clinical characteristic of the patients is presented in Table 1.

Serum HA, PIIINP and TIMP-1 levels were measured separately on ADVIA Centaur XP using ELF test developed by Siemens Healthcare Diagnostic Inc. (Tarrytown, New York USA). The ELF test results were calculated using following algorithm:

$$ELF = 2.278 + 0.851 \ln(CHA) + 0.751 \ln(CPIIINP) + 0.394 \ln(CTIMP\text{-}1)$$

Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity was determined on VITROS® 5,1 FS (Ortho Clinical Diagnostics) and AST/ALT (*"De Ritis Ratio")* was calculated.

In addition FIB-4 score was calculated using Sterling's formula:

$$FIB\text{-}4 = \text{age [years]} \times \text{AST [IU/L]} / \text{platelet count [expressed as platelets} \times 10^9/\text{L]} \times (\text{ALT}^{1/2}\text{[IU/L]})$$

RESULTS

The mean values of serum HA, PIIINP, TIMP-1 concentrations were higher in children of group I as compared to group II, but the significant differences were noted only for HA and TIMP-1 ($p<0.01$ in both cases) (Fig.1).

The ELF test values in obese children ranged from 7.29 to 10.45 with the mean value of 8,97±0.15 for group I and 8.48±0.09 for group II ($p<0.005$).

In contrast to ELF test results, no statistical differences between two groups studied for FIB-4 score was noted (Fig.2).

The mean value of AST and ALT activity was significantly higher in group I as compared to group II ($p<0.01$) but no difference for AST/ALT ratio between groups was observed. No correlation between ELF test results, enzyme activities, age, BMI and FIB-4 score has been found regardless the group. The cut-off value of ELF test, based on ROC curve, was 9,36 (Fig.3).

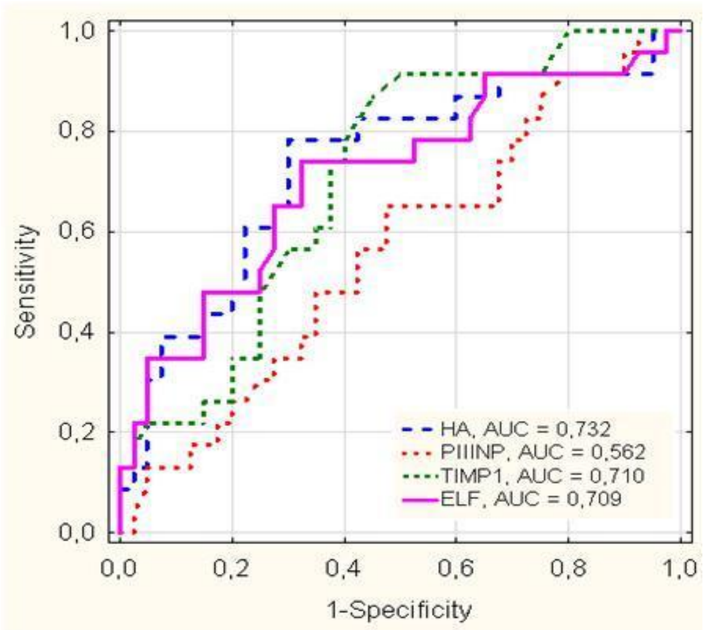

Figure 3. ROC curve with value of AUC for ELF test and its components

STATISTICAL ANALYSIS

The results were expressed using descriptive data (as mean values, SE). Between groups comparisons were performed using one-way analysis of variance (ANOVA) and the Mann-Whitney U-test. The level of statistical significance was established as $p < 0.05$. For ELF test reciever operating characteristic (ROC) curves were created with the area under the ROC curve (AUC). The data were analyzed using Statistica data analysis software system version 10 (StatSoft, Inc. (2011) and PRISM 5.

Table 1. Clinical and Laboratory Characteristic in the Study

Variables	Total (n=63)	Group I (with steatosis) (n=23)	Group II (without steatosis) (n=40)	*p* value
Gender (Male:Female)	29 : 34	9 : 14	20 : 20	
Age (years)	13,99 ± 0,33	14,43 ± 0,41	13,73 ± 0,46	NS
BMI (kg/m^2)	31,46 ± 0,77	33,91 ± 1,52	30,03 ± 0,77	0,028*
AST (U/l)	30,14 ± 1,66	37,42 ± 3,75	25,96 ± 1,06	0,001*
ALT (U/l)	38,87 ± 2,89	50,86 ± 6,59	31,97 ± 1,87	0,010*
AST/ALT	0,85 ± 0,03	0,82 ± 0,04	0,87 ± 0,04	NS
Platelet Count (x10^9/L)	288 ± 8	287 ± 16	288 ± 9	NS

* *P* < 0,05; NS, not significant

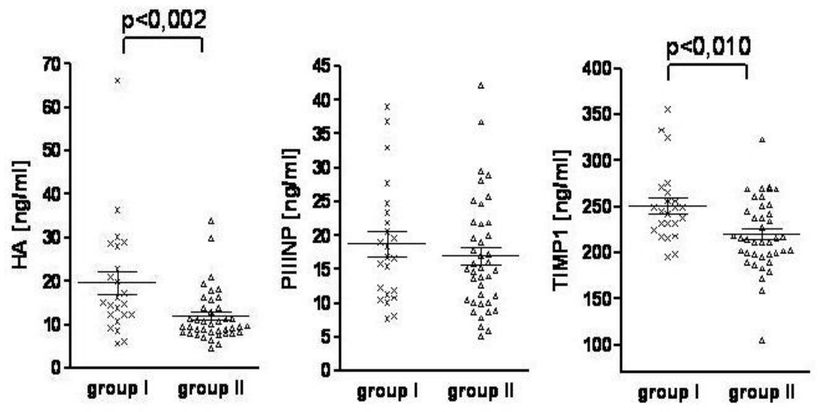

Figure 1. The mean values of serum HA, PIIINP and TIMP-1 (±SE) in obese children with steatosis (group I) and in obese children without steatosis (group II)

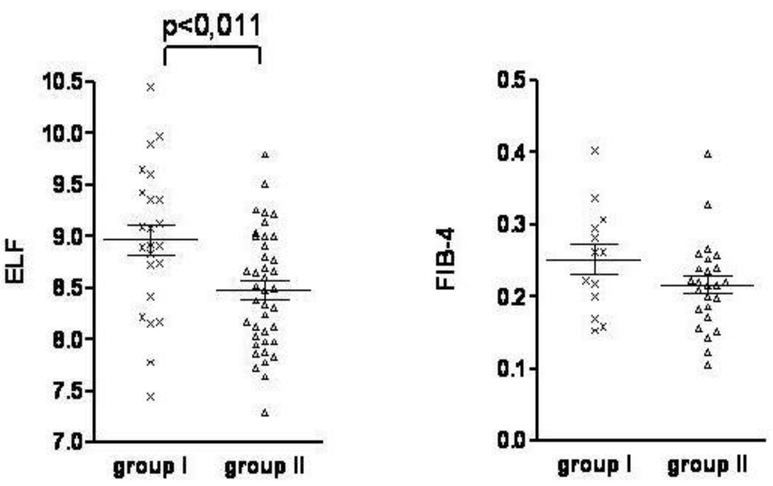

Figure 2.The mean values of ELF test results and FIB-4 score in obese children with steatosis (group I) and in obese children without steatosis (group II)

CONCLUSION

ELF test cannot be used as a single biochemical component for assessing NAFLD in obese children, but can be useful as its predictor. To assess its relationship with insulin resistance parameters further investigations are needed.

Projekt współfinansowany ze środków
Krajowego Naukowego Ośrodka Wiodącego
2012-2017