SERUM HYALURONIC ACID IN PATIENTS WITH LIVER DISEASE

K.Pelinkova[1]; R.Bruha[2];H.Benakova[1];K.Dvorak[2];T.Zima[1]
[1] Institute of Clinical Biochemistry and Laboratory Diagnostics, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech republic
[2] 4th Department of Gastroenterology and Hepatology; First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech republic

Background

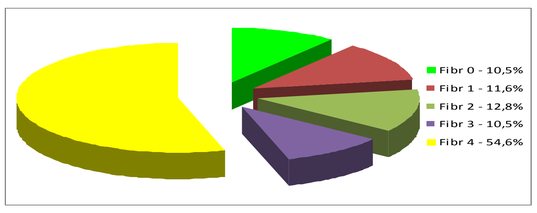
Hyaluronic acid (HA) is a glycosaminoglycan, produced mainly by mesenchymal cells. HA plays a prominent role in the pathogenesis of liver fibrosis; thus serum HA concentrations itself or in combination with other parameters (Hepascore) have been proposed as a non-invasive biomarker of liver fibrosis. The aim of this study was: to assess the correlation of serum HA and Hepascore to the fibrosis in patients with liver disease of different aetiology.

Patients and methods

86 patients, average age 49,6 14,7 years, with chronic liver disease confirmed by liver biopsy were enrolled. The aetiology of liver disease was NASH (16 pat.), HCV (32 pat.), ethylic (30 pat.) and other (9 pat.). Liver fibrosis was determined by METAVIR score. Hepascore was computed as published in literature. Serum samples were collected at the time of biopsy. Serum HA was assayed by the latex agglutination method (Hyaluronic acid LT, Latex Agglutination Method, Wako, Germany), serum GGT (IFCC method at 37°C) and total bilirubin (DPD method) were assayed using a MODULAR SWA (Tokyo, Japan), α2-macroglobulin was measured by nephelometric methods using a IMMAGE nephelometer (Beckman Coulter USA). The MedCalc have been used for the purpose of the statistical evaluation of dates.

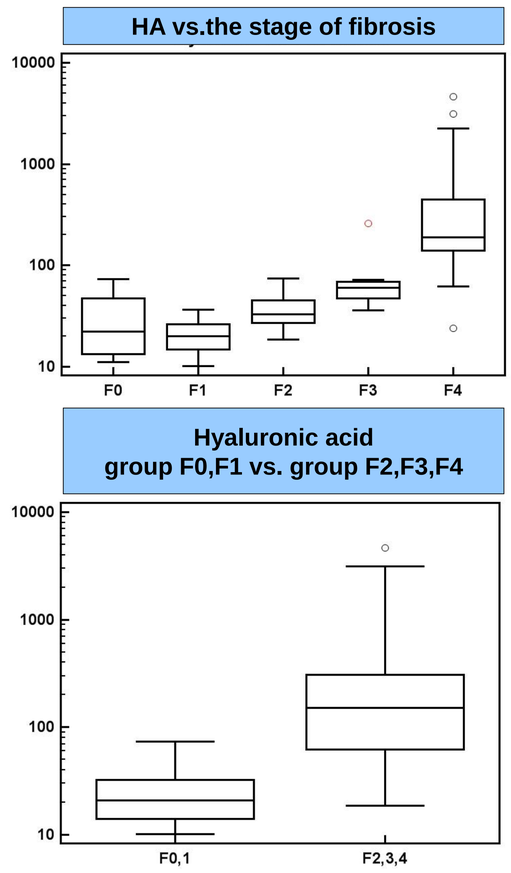
Results

Serum concentration HA (μg/l; median; IQ range) in patients with different stages of fibrosis were: F0 (9 pat):22,4 (13,3-47,3); F1(10 pat.):20,1 (14,8-26,3); F2 (11 pat.):32,7(27,1-45,2); F3 (9 pat.):59,9 (48,1-69,1); F4 (47 pat.): 188,7 (139,6-449,7). Statistically significant differences in HA levels and Hepascore were found between F4 and all other fibrosis stages F0-F3 ($p<0,05$), and between the group F0-F1 and the group F2-F4 ($p<0,05$). However, there were no significant differences in median serum HA levels and Hepascore among the different fibrosis groups. Serum concentration of total bilirubin and GGT did not correlate with fibrosis. In patients with NASH were not significantly elevated serum HA and Hepascore.

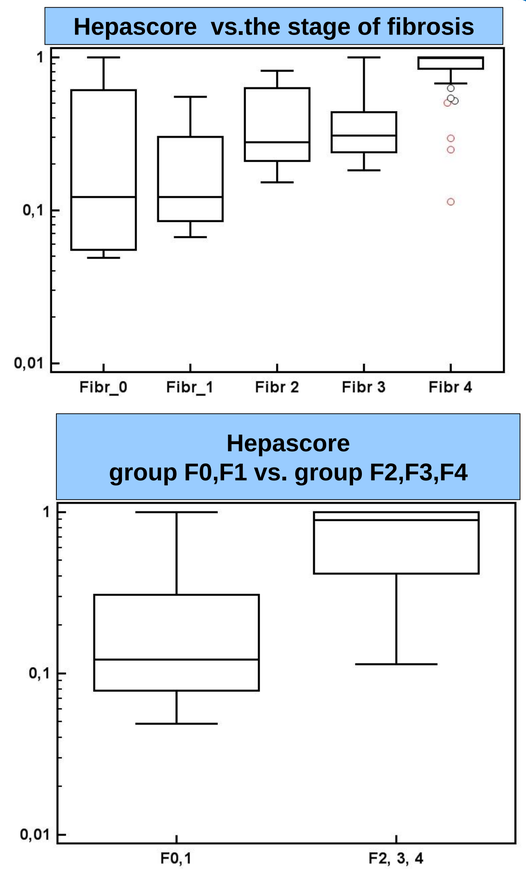


Stage of fibrosis	n (male/ female)	Age ± SD (years)	HA (μg/l) median (IQ range)	Hepascore median (IQ range)	Bili (μmol/l) median (IQ range)	GGT (μkat/l) median (IQ range)
F0	9 (7/2)	47,4±17	22,4 (13,3-47,3)	0,12 (0,05-0,82)	9,5 (5,2-43,4)	3,73 (0,42-7,31)
F1	10 (8/2)	36,1±8	20,1 (14,8-26,3)	0,12 (0,08-0,31)	6,3 (4,5-13,2)	0,86 (0,46-1,85)
F2	11 (6/5)	34,3±11	32,7 (27,1-45,2)	0,28 (0,20-0,68)	9,1 (6,7-14,6)	0,97 (0,37-2,40)
F3	9 (5/4)	50,6±12	59,9 (48,1-69,1)	0,31 (0,19-0,58)	10,6 (7,3-15,2)	1,64 (0,55-5,58)
F4	47 (33/14)	54,6±12	188,7 (139,6-449,7)	0,99 (0,93-1,00)	15,7 (10,6-17,9)	2,23 (1,79-2,93)

HA vs.the stage of fibrosis



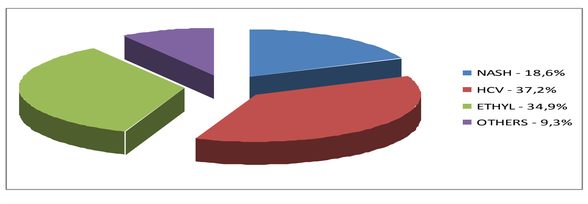
Hepascore vs.the stage of fibrosis



Hyaluronic acid group F0,F1 vs. group F2,F3,F4

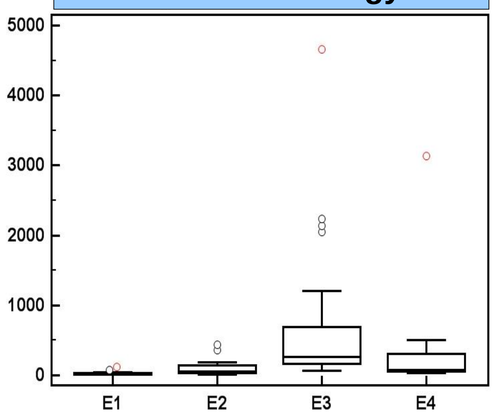
Hepascore group F0,F1 vs. group F2,F3,F4

logaritmic transformation of the data used

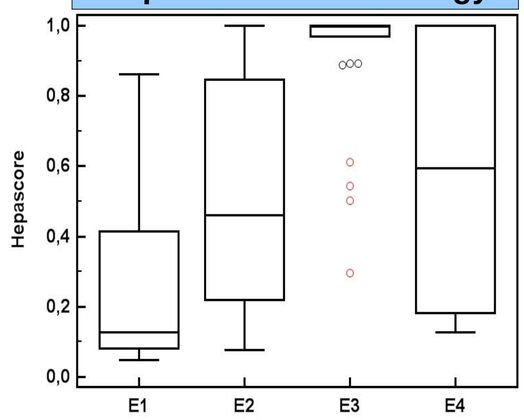


aetiology of liver diseases	n	HA (μg/l) median (IQ range)	Hepascore median (IQ range)	Bili (μ mol/l) median (IQ range)	GGT (μkat/l) median (IQ range)
NASH (E1)	16	22,2 (13,2-30,1)	0,13 (0,08-0,39)	8,3 (5,5-13,6)	2,11 (0,69-3,92)
HCV (E2)	32	59,2 (36,5-90,8)	0,46 (0,26-0,83)	9,7 (7,9-11,5)	1,52 (0,74-1,75)
ETHYL (E3)	30	266,2 (183,9-438,3)	1,00 (0,99-1,00)	19,5 (12,6-39,8)	2,41 (1,82-3,49)
OTHERS (E4)	8	75,7 (48,9-999,3)	0,59 (0,17-1,00)	13,1 (5,2-86,0)	2,03 (0,62-6,92)

HA vs.aethiology



Hepascore vs. aethiology



Conclusion

Serum HA is a useful non-invasive marker of liver fibrosis. Significantly elevated serum HA and Hepascore were detected in patient with marked hepatic fibrosis (F≥2) compared with no fibrosis or mild fibrosis (F0,F1) and between patients with stage of fibrosis F4 and all other fibrosis stages.But these markers are not specific for predicting the different stages of liver fibrosis. These parameters could prove the presence of severe fibrosis without the need for liver biopsy.

Acknowledgement: This Project was supported by the Research Project IGA MZCR: NT 11247