EP787

Reduced expression of chemerin in visceral adipose tissue associates with hepatic steatosis in obese patients

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BACKGROUND

- The growing epidemic of obesity has led to a simultaneously increased prevalence of non-alcoholic fatty liver disease (NAFLD).
- NAFLD is a chronic liver disease that encompasses a broad histopathological spectrum, of which pathophysiology is still incompletely known.
- Emerging data indicate that an impaired release of adipose tissue-derived adipokines could play a pivotal role in the development of NAFLD.

AIMS

To evaluate whether circulating levels or visceral adipose tissue (VAT) expression of recently described adipokines associate with the histopathological disease severity.

METHODS

- 81 morbidly obese patients with biopsy-proven NAFLD and 18 lean control subjects undergoing abdominal surgery were recruited
- Serum levels of omentin, chemerin, monocyte chemoattractant protein-1 (MCP-1) and secreted frizzled-related protein (SFRP) 4 were measured using enzyme-linked immunosorbent assay (ELISA)
- VAT expression of these adipokines was assessed with real-time PCR analysis
- Histopathological grading of NAFLD was scored using the NAFLD activity score (NAS) as verified by Kleiner *et al.* [1]. According to NAS, NAFLD patients were subdivided into patients with simple steatosis (SS; NAS 1-2), borderline NASH (NAS 3-4) and NASH (NAS 5-8)

Table 1: General characteristics of NAFLD patients and healthy controls

Parameter	Healthy controls (N=18)	NAFLD patients (N=81)	P
M/F	18/0	55/26	0.001
T2D	0 (0%)	20 (25%)	0.017
Age, years	44 ± 12	45 ± 10	0.899
BMI, kg/m²	24 [22-26]	41 [38-44]	< 0.001
Glucose, mmol/L	5.44 [4.63-5.84]	5.33 [4.78-6.31]	0.693
Insulin, pmol/L	25.7 [21.1-40.4]	92.9 [57.5-150.9]	< 0.001
Triglycerides, mg/dl	156.0 [111.5-204.9]	185.0 [144.0-241.0]	0.075
HOMA-IR	0.87 [0.60-1.47]	3.21 [1.92-6.10]	< 0.001
AST, IU/L	22.0 [17.8-33.0]	28.0 [20.0-40.0]	0.169
ALT, IU/L	11.3 [8.5-29.5]	25.0 [14.5-36.5]	0.020
GGT, U/l	22.2 [16.0-29.2]	30.0 [19.5-50.5]	0.027
CRP, mg/L	1.05 [0.60-2.20]	3.00 [1.10-5.35]	0.026

Data are presented as mean ± SD or median [interquartile range] and were analyzed using Mann-Whitney U test and Chi-square test for categorical variables. ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CRP, C-reactive protein; GGT, gamma-glutamyltransferase; M/F, male-to-female ratio; T2D, type 2 diabetes

RESULTS

- NAFLD patients had higher serum chemerin levels (P=0.020) and higher VAT expression of omentin and SFRP4 (P=0.043 and P<0.001; respectively) as compared to lean controls
- Neither adipokine serum levels, nor VAT expression differed according to NAS stage
- HOMA-IR was higher in NAFLD patients and was associated with NAS, independent of age and BMI (β=0.282; P=0.020)
- Serum adipokine levels were neither associated with histopathological severity, nor with their VAT expression
- Chemerin VAT expression was negatively associated with NAS (r=-0.331; P=0.022) and steatosis grade (r=-0.335; P=0.020), independent of age, BMI and HOMA-IR

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Table 2: Adipokine serum levels and VAT expression in patients with simple steatosis, borderline NASH and NASH

Adipokines	Simple steatosis (N=32)	Borderline NASH (N=24)	NASH (N=25)	P
Serum levels				
Omentin, ng/ml	363.4 [301.8-492.5]	430.3 [313.5-519.7]	353.3 [293.5-437.9]	0.234
Chemerin, ng/ml	203.0 [154.0-271.5]	195.9 [147.6-255.7]	202.4 [139.9-232.2]	0.759
MCP-1, pg/ml	282.7 [239.9-396.9]	319.9 [274.2-408.5]	300.7 [263.3-381.3]	0.531
Sfrp4, pg/ml	4725.7 ± 1414.3	4273.4 ± 1754.7	4939.9 ± 2167.4	0.673
VAT expression, AU				
Omentin	16.78 [3.59-36.15]	5.28 [1.59-26.11]	5.87 [1.63-10.86]*	0.166
Chemerin	0.88 [0.65-1.25]	0.97 [0.66-1.07]	0.69 [0.56-0.92]	0.260
MCP-1	0.52 [0.32-2.18]	0.54 [0.32-1.35]	0.66 [0.40-1.43]	0.896
SFRP4	3.78 [1.85-4.59]	2.54 [1.68-3.96]	2.99 [2.07-4.38]	0.484

* vs simple steatosis. Data are presented as mean ± SD or median [interquartile range] and were analyzed using Mann-Whitney U test.

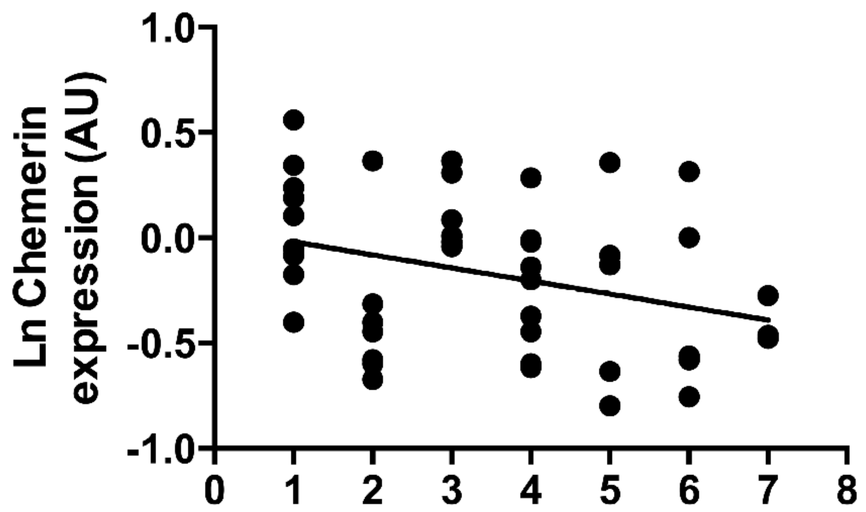

Figure 1 The inverse relationship between disease severity, presented as the NAFLD activity score (NAS), and ln-transformed chemerin VAT expression (N=63) in biopsy-proven NAFLD patients.

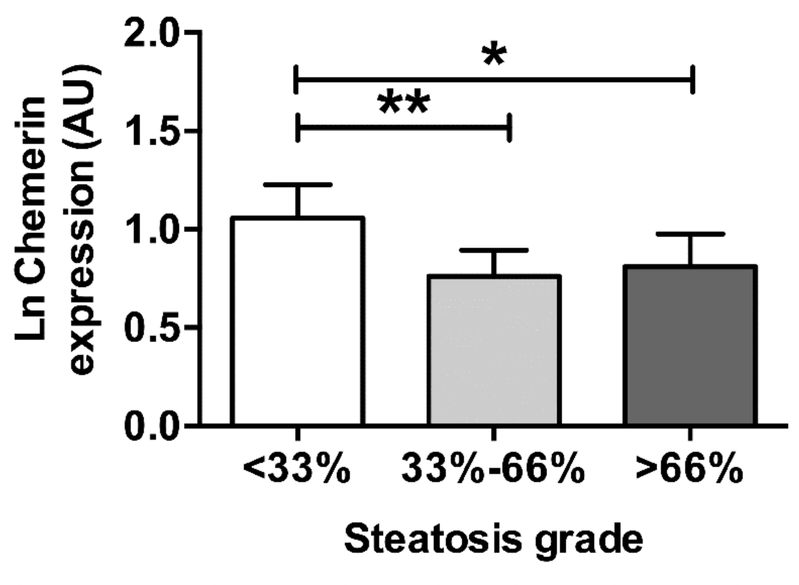

Figure 2 Chemerin VAT expression was highest in patients with < 33% of steatosis and was lower in patients with moderate (33-66%) to severe (> 66%) steatosis grade. * P < 0.05; ** P < 0.01.

CONCLUSION

No differences in adipokine serum levels were found between obese patients with varying degrees of NAFLD. However, our findings suggest that lower VAT expression of chemerin in obese patients may be involved in the pathophysiology of hepatic steatosis.

References:

[1] Kleiner DE *et al*. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology 2005; 41: 1313-1321.

ECE 2016 787--EP

Obesity

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Poster presented at: ECE2016 28 – 31 May 2016 MUNICH, GERMANY 16th EUROPEAN CONGRESS OF ENDOCRINOLOGY

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