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Relationship of human plasma leptin concentration with blood cell parameters

No strong relationship between leptin and hematologic values was found in a large series of European patients and control subjects. However a role for high levels of leptin in situations such as obesity or sepsis cannot be excluded, as suggested by the weak correlation between leptin and leukocyte count observed in hospitalized patients.

Sir,

Leptin is expressed by adipocytes and involved in the regulation of body weight and body fat. The characterization of a leptin receptor on $CD34^+$ cells[1-3] and a proliferative effect of leptin on hematopoietic cells in culture[1,2,4,5] suggest a relationship between leptin and hematopoiesis. Our demonstration that bone marrow adipocytes secrete leptin supports this hypothesis.[6]

A negative correlation between leptin and hemoglobin in male Japanese adults has been reported, as has a lack of correlation between leptin and leukocytes.[7] These results appear contradictory with the finding of an association between leptin and leukocytes and erythrocytes in Japanese males aged 15-16 years,[8] and with the observation that, in obese Pima Indians, most of the variance in the leukocytes attributable to body fat could be accounted for by leptin concentration.[9] These contradictory findings concerning particular populations (male adolescents in a narrow age range or constitutionally obese Indians) led us to examine the relationship between leptin and blood cell parameters in a large population of European subjects.

Plasma leptin was determined by radio immunoassay (Linco Research Inc, St Charles, MO, USA) in 300 randomly selected hospitalized patients and 70 healthy normal-weight controls (Table 1). Hospitalized patients had a wider range of leptin concentrations (0.07-147 ng/mL) than control subjects (0.1-16 ng/mL), and levels over 20 ng/mL were observed in 8% of patients. In both populations, leptin concentration was significantly higher in women than in men, even after controlling for body mass index (BMI: kg/m^2), so multiple regression analyses were performed to control for gender. In neither population, was BMI correlated with any hematologic parameters. Leptin was weakly correlated ($p< 0.05$) with leukocytes in hospitalized patients. However, a mean comparison of leukocytes between the patients with leptin >20 ng/mL and the other patients was not significant. In controls, we found no correlation between leptin and leukocytes independently of gender or smoking habit. In neither group, was there any correlation between leptin and erythrocytes, hematocrit, hemoglobin, platelets, or any parameter of the differential analysis.

Table 1. Patient characteristics.

	Men	*Women*	*p value*
Hospitalized patients			
N	146	144	
Age (years)	56±17	53±21	
Weight (kg)	72.9±13.5	60.4±9.4	≤0.01
BMI (kg/m^2)	24.3±3.6	22.8±2.6	
Leptin (ng/mL)	3.52±6.12	11.37±19.43	≤0.0001
Leukocytes ($x10^9$/L)	7.81±2.46	7.51±2.56	
Red blood cells ($x10^{12}$/L)	4.39±0.78	4.29±0.57	
Hemoglobin (g/L)	134±24	128±17	≤0.05
Platelets ($x10^9$/L)	257±114	276±104	
Control subjects			
N	28	42	
Age (years)	35±13	31±12	
Weight (kg)	71.9±8.2	55.8±6.2	≤0.0001
BMI (kg/m^2)	22.5± 2.7	20.9±2.0	≤0.01
Leptin (ng/mL)	1.31±1.25	5.95± 3.48	≤0.0001
Leukocytes ($x10^9$/L)	6.48±1.61	6.49±1.48	
Red blood cells ($x10^{12}$/L)	4.90±0.40	4.52 + 0.26	≤0.001
Hemoglobin (g/L)	150±9	138±8	≤0.0001
Platelets ($x10^9$/L)	217±45	245±51	≤0.05

Values are mean±SD. BMI: body mass index.

Although constituting an heteregeneous group, patients had a normal range of BMI, and their mean leptin was comparable to that of controls and that reported for non-obese subjects.[10] High leptin concentrations are reported in various diseases, such as renal failure and sepsis.[10] Leptin secretion is also influenced by a variety of agents, such as dexamethasone, adrenoceptor agonists, and insulin.[10] In this study, no correlation could be established between leptin concentration and clinical status or treatment regimen. However, many patients were suffering from a critical illness. It was reported that leptin was increased in critically ill septic patients, while its circadian rhythmicity was altered.[10] Thus, it can not be excluded that results from some patients were dependent on the moment of blood sampling.

We found no significant relationship between leptin levels and blood cell parameters in healthy midleaged males and females. However, a role for high concentrations of leptin in situations such as obesity or sepsis cannot be excluded, as suggested by the weak correlation we observed in hospitalized patients. In these situations, leptin could contribute, with other cytokines, to the subtle regulation of hematopoiesis.

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Key words

Leptin, body fat, leukocyte count, hematological parameters

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Erythroid membrane protein defects in hereditary spherocytosis. A study of 62 Spanish cases

We studied the relative prevalences of erythroid cytoskeletal protein defects and their relationship with the clinical course of hereditary spherocytosis (HS) in 62 spanish patients (30 kindreds), 53 cases with familial history (21 kindreds).[1-5] Combined spectrin and ankyrin deficiency was the most prevalent abnormality, as previously described.[2,9,10]

Sir,

Clinical assessment, routine haemocytometry and denaturing electrophoresis (SDS-PAGE) in a continuous system of erythroid ghosts[6,7] with estimation of protein contents - spectrin/band 3 (Sp/B3) and ankyrin/band 3 (Ank/B3) ratios- were performed.

Table 1. Erythroid membrane protein contents and clinical course of hereditary spherocytosis.

HS		Sp/B3 Mean	Sp/B3 SD	Ank/B3 Mean	Ank/B3 SD	Ank/B3 corrected* Mean	Ank/B3 corrected* SD
	Control n=24	1.136 (1.043-1.242)	0.054	0.199 (0.197-0.203)	0.001	0.170 (0.161-0.177)	0.010
Mild	Propositi n=8	1.29 (0.973-1.130)	0.058	0.198 (0.195-0.202)	0.002	0.148 (0.087-0.171)	0.029
	Total n=20	1.032 (0.941-1.194)	0.066	0.197 (0.193-0.202)	0.002	0.154 (0.087-0.171)	0.021
Typical°	Propositi n=16 (s=4)	1.007 (0.934-1.155)	0.062	0.195 (0.188-0.206)	0.004	0.100 (0.014-0.166)	0.046
	Total n=34 (s=15)	1.020 (0.880-1.023)	0.077	0.196 (0.188-0.206)	0.003	0.112 (0.008-0.174)	0.047
Severe	Propositi n=6 (s=2)	0.923 (0.801-0.995)	0.075	0.192 (0.182-0.195)	0.005	0.099 (0.038-0.158)	0.053
	Total n=8 (s=4)	0.935 (0.801-1.023)	0.073	0.194 (0.182-0.203)	0.006	0.166 (0.038-0.176)	0.055

Mild HS: patients with normal hemoglobin and <200x10⁹/L reticulocytes. Typical HS: cases with episodic anemia, no transfusional needs and >200 x10⁹/L reticulocytes. Severe HS: subjects with serious chronic, hemolytic anemia, improving after splenectomy. Sp: spectrin, Ank: ankyrin, B3: band 3 protein, SD: standard deviation. Ranges in brackets. n: number of patients, s: number of splenectomized patients.

**Ankyrin contents corrected for circulating reticulocytes (8) according to the equation:*

% of protein 2.1 to subtract = 0.095 x reticulocytes (x10⁹/L) + 8.744.

°Includes 2 patients with increased spectrin and uncorrected ankyrin contents.

Since reticulocytosis may mask a real ankyrin deficiency, correction of ankyrin contents by reticulocytosis[3,8] was carried out. Statistics (non parametric tests) included a separated analysis of propositi to avoid a prevalence bias by the kindreds sizes.[3]

Clinical features of the HS cases with spectrin and ankyrin protein contents are shown in Table 1. Spectrin contents were lower in mild HS versus controls ($p<0.001$) and in severe versus typical HS ($p<0.01$). Ankyrin contents of patients were decreased versus controls ($p<0.001$). There were no significant differences in spectrin contents between unsplenectomized and splenectomized cases with the same clinical severity, nor in ankyrin contents among patients (exception below). Spectrin and ankyrin deficiencies occurred in 53 (85.5%) and 38 (61.3%) cases respectively, including 27 (90%) and 20 (66%) propositi.

Combined spectrin and ankyrin deficiency was the most prevalent defect (Table 2), increasing with worse clinical course. Isolated spectrin deficiency was the second most prevalent subset, being more frequent in mild disease. However, differences in relative prevalences among HS clinical groups (both propositi) were non-significant (Fisher's test).

Correction for reticulocytosis increased the prevalence of combined spectrin and ankyrin deficiencies and all patients had some ankyrin reduction ($p<0.001$), mainly in typical and severe unsplenectomized cases. Controls yielded even 15% reduction. Mean contents for unsplenectomized patients were 77.2%, 49.6% and 37.6% for mild, typical and severe HS (74.6%, 49.5% and 37.6% for the propositi).