DETERMINATION OF SERUM SCLEROSTIN LEVELS IN WOMEN WITH ANOREXIA NERVOSA

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Introduction:

Anorexia nervosa (AN) is a psychiatric eating disorder with the manifestation of extremely low body weight, amenorrhea and bone loss. Bone metabolism in anorectic patients is affected by several determinants, such as estrogen deficiency, hypercortisolemia, nutritional deficiencies, reduced body mass, and increased physical activity. The consequence is an increased fracture risk. AN is divided into two subgroups, the restricting type (rejection of eating) and the purging type (self-induced vomiting, misuse of laxatives, diuretics, or enemas in addition to denial of eating) [1,2]. However, despite the awareness of these influencing factors, the pathophysiology of bone loss in patients with AN has not been fully established yet.

	Anorexia nervosa (n=19)	Controls (n=29)	P-value
Age (years)	22.6±3.9	25.8±3.4	0.002
Weight (kg)	40.1±3.9	63.2±9.4	0.000
BMI (kg/m²)	14.6±1.1	21.8±2.8	0.000
Sclerostin (pmol/l)	13.91±7.08	17.68±7.70	0.026
Calcium (mmol/l)	2.29±0.14	2.27±0.10	0.514
Phosphate (mmol/l)	1.20±0.25	1.13±0.18	0.448
25-OH-Vitamin D (ng/ml)	22.67±9.55	24.1±11.08	0.774
P1NP (µg/l)	43.76±30.33	63.51±20.18	0.002
CTX (ng/ml)	0.705±0.403	0.302±0.151	0.002
PTH (pg/ml)	37.49±16,09	28.78±16.79	0.145
Cortisol (µg/dl)	17.94±7.45	9.01±3.96	0.000
Estradiol (pg/ml)	17.00±14.08	43.50±45.74	0.128

Table 1: Anthropometrics and Biochemistry in patients with AN and healthy controls shown in means ± SD.

It has been recently recognized that sclerostin (scl), a glycoprotein expressed by osteocytes, regulates bone mass by inhibiting the Wnt signaling pathway and bone formation by inhibiting osteoblastogenesis [3]. Nevertheless, the impact of circulating sclerostin levels in patients with anorexia nervosa and low bone mass is unknown.

Methods:

The aim of the study was to assess serum sclerostin levels in young women with anorexia nervosa and compare serum levels to those of healthy controls. In addition bone turnover markers, cortisol and estradiol levels were analyzed and correlated to scl levels.
Serum sclerostin levels were assessed in 19 patients with AN (mean age 22.6 ± 3.9 ys; mean BMI 14.6 ± 1.1 kg/m²). Subsequently we allocated the AN patients into the restricting type (n=8; mean age 20.8 ± 2.5 ys; mean BMI 14.0 ± 0.9 kg/m²) and the purging type (n=11; mean age 23.9 ± 4.3 ys, mean BMI 15.0 ± 1.1 kg/m²). Women with AN were compared to 29 healthy premenopausal women (mean age 25.8 ± 3.4 ys; mean BMI 21.8 ± 2.8 kg/m²).

	Restricting type (n=8)	Purging type (n=11)	P-value
Age (years)	20.8±2.5	23.9±4.3	0.064
Weight (kg)	38.0±3.3	41.6±3.7	0.043
BMI (kg/m²)	13.95±0.9	15.0±1.1	0.036
Sclerostin (pmol/l)	9.83±2.01	16.48±8.47	0.028
Calcium (mmol/l)	2.35±0.10	2.25±0.16	0.432
Phosphate (mmol/l)	1.08±0.20	1.30±0.26	0.346
25-OH-Vitamin D (ng/ml)	25.96±7.65	20.47±11.33	0.240
P1NP (µg/l)	24.14±20.33	56.80±29.51	0.011
CTX (ng/ml)	0.836±0.550	0.631±0.260	0.352
PTH (pg/ml)	36.26±16.97	36.30±16.95	0.995
Cortisol (µg/dl)	20.23±8.34	17.17±7.01	0.415
Estradiol (pg/ml)	17.04±13.89	13.53±12.53	0.586

Table 2: Anthropometrics and Biochemistry in patients with AN allocated to the restricting type and the purging type shown in means ± SD.

Sclerostin was determined by a quantitative sandwich ELISA assay (Biomedica, Vienna, Austria). Overall comparison was performed using One-way ANOVA (SPSS Version 17.0). In addition linear contrasts were performed to compare scl levels in patients with AN and healthy controls as well as the restricting and purging type.

Results:

Statistically significant decreased sclerostin levels were found in women with AN compared to healthy controls (13.91 ± 7.08 vs. 17.68 ± 7.70 pmol/l, p<0.05). Significant differences between patients with AN and healthy controls were found in P1NP levels (43.76 ± 30.33 vs. 63.51 ± 20.18 µg/l, p<0.005). Furthermore, women with AN showed significantly higher CTX levels compared to healthy controls (0.705 ± 0.403 vs. 0.302 ± 0.151 ng/ml, p<0.005) as well as significantly higher cortisol levels compared to controls (17.94 ± 7.45 vs. 9.01 ± 3.96 µg/dl, p<0.001). Women with AN showed lower estradiol levels compared to healthy controls (17.00 ± 14.08 vs. 43.50 ± 45.74 pg/ml). Nevertheless no significant difference could be shown most likely due to fluctuations of the menstrual cycle.
Patients in the restricting subgroup showed significantly lower scl levels than women in the purging subgroup (9.83 ± 2.01 vs. 16.48 ± 8.47 pmol/l, p<0.05). Women allocated to the restricting type showed a significantly lower BMI (13.9 ± 0.9 vs. 15.0 ± 1.1 kg/m², p<0.05) as well as significantly lower P1NP levels (24.14 ± 20.33 vs. 56.80 ± 29.51 µg/l, p<0.05) compared to the purging type.
No correlations were found between scl levels and bone turnover markers, cortisol and estradiol values.

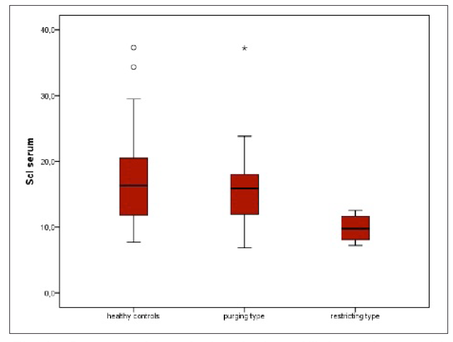

Fig 1: Serum sclerostin levels (pmol/l) in patients with AN allocated to the purging and the restricting type and in healthy controls

Conclusion:

Within anorexia nervosa the restricting type showed the most significant changes in bone turnover markers most likely due to the extensive nutritional deficiencies and the consecutive significantly lower body mass compared to the purging type.
Decreased P1NP values and increased CTX values indicate an uncoupling of bone turnover which might be related to the increased cortisol levels, as it has already been shown in cortisol-induced bone diseases [4].
The markedly decreased sclerostin levels in the restricting type compared to healthy controls may indicate that especially in this patient group sclerostin expression might be suppressed as a rescue mechanism to induce enhanced bone formation.

References

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