



**Karolinska
Institutet**

Department of Woman and Child Health

**Endocrine and metabolic disorders in bulimic women and effects
of antiandrogenic treatment**

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i
Skandiasalen, Astrid Lindgrens Barnsjukhus, Karolinska Universitetssjukhuset Solna

Onsdagen den 20 december 2006, kl. 09.00

av

Sabine Naessén

Leg. Läkare

Handledare:

Docent Angelica Lindén Hirschberg
Institutionen för Kvinnors och Barns
Hälsa, Karolinska Institutet

Fakultetsopponent:

Docent Marie Bixo
Institutionen för klinisk vetenskap
Umeå Universitet

Betygsnämnd:

Professor Ingemar Engström
Institutionen för klinisk medicin
Örebro Universitet

Docent Lisa Juntti-Berggren
Institutionen för molekylär medicin och kirurgi
Karolinska Institutet

Professor Britt-Marie Landgren
Institutionen för Klinisk Vetenskap,
Intervention och Teknik (CLINTEC)
Karolinska Institutet

Stockholm 2006

ABSTRACT

Endocrine and metabolic disorders in bulimic women and effects of antiandrogenic treatment

Sabine Naessén, MD

Department of Woman and Child Health, Division of Obstetrics and Gynecology
Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden

Background: Bulimia is a mental disorder frequently associated with menstrual disturbances and low estradiol levels although most bulimic women are of normal weight. Low bone mass has also been reported in these women. Furthermore, increased androgen levels and polycystic ovaries (PCO) have been described in bulimic women. Little is known about the mechanisms of these hormonal disturbances and the role of sex hormones in the etiology of the disease has not been fully explored. Androgens may promote bulimic behavior by influencing food craving or impulse control.

Aims: The specific aims of this work were to compare women with bulimia to healthy controls with respect to: 1) menstrual disturbances and the occurrence of polycystic ovary syndrome (PCOS) 2) endocrine and nutrition-related factors predicting bone mass 3) estrogen receptor (ER) β polymorphism in view of the potential role of estrogen signalling in bulimic disease 4) effects of an antiandrogenic oral contraceptive (OC) on appetite and eating behaviour.

Methods: Seventy-seven bulimics and 59 controls were investigated with respect to menstrual status, PCO, symptoms of hyperandrogenism, bone mineral density (BMD), sex hormone levels and ER β polymorphism. Meal-related appetite response and bulimic symptoms were evaluated in 21 women with bulimia nervosa before and after three months of treatment with an antiandrogenic OC.

Results: 1) Bulimics had a higher occurrence of menstrual disturbances, hirsutism and PCOS than controls. Positive correlations between hirsutism and levels of biologically active testosterone were found in bulimics but not in controls. 2) Bulimics had a lower spinal BMD and higher frequency of osteopenia in the total body than controls. Subgroups of bulimics with a history of amenorrhea or previous anorexia nervosa had the lowest BMD values, whereas those without such history did not differ from controls. Multiple regression analysis including significant endocrine and nutrition-related variables, revealed previous anorexia nervosa to be the strongest determinant of spinal BMD in bulimic women. 3) An association was found between two common polymorphisms in the ER β gene and bulimic disease. A novel variant changing the primary structure of ER β protein was identified in one bulimic patient, but an initial characterization of this variant did not reveal any differences compared to the wild type protein. 4) Antiandrogenic OC treatment reduced meal-related hunger and gastric distention in women with bulimia nervosa and improved bulimic behavior in relation to reduced testosterone levels.

Conclusions: 1) Our study supports an increased frequency of PCOS in bulimic women. This endocrine disorder may be of importance for the development of bulimia. 2) Low bone mass in bulimics could be explained by previous anorexia nervosa, whereas bulimia *per se* does not influence bone mass negatively. 3) Genetic variation in ER β may play a role in the etiology of bulimic disease. 4) An antiandrogenic OC may develop into a new strategy for treatment of women with bulimia nervosa not responding to conventional therapy and particularly in those with hyperandrogenic symptoms.

Key Words: Bulimia nervosa, anorexia nervosa, polycystic ovary syndrome, bone mineral density, estrogen receptor β , appetite, oral contraceptives.