Diamine Oxidase Activity Levels in Anorexia Nervosa

Yoshiyuki Takimoto, MD, PhD*
Kazuhiro Yoshiuchi, MD, PhD
Satoshi Shimodaira, MD, PhD
Akira Akabayashi, MD, PhD

ABSTRACT

Objective: Anorexia nervosa (AN) patients often experience gastrointestinal complications caused by their malnutrition. We hypothesized that intestinal integrity is disturbed in AN. Therefore, the objective of the present study was to investigate serum diamine oxidase (DAO) activity, which is considered to be a clinical indicator of the integrity of the intestinal mucosa, in AN patients.

Method: Thirty-six AN female patients including 21 AN restricting type (AN-R) and 15 AN binge-eating/purging type (AN-BP) were compared with twenty healthy women on serum DAO activity using immunoassay.

Results: DAO levels in AN-R patients were significantly lower than in AN-BP patients and healthy controls.

Discussion: DAO levels were decreased in AN-R patients. This finding suggests the presence of intestinal structural disturbance as one of the physical complications of malnutrition in AN-R patients.

© 2013 Wiley Periodicals, Inc.

Keywords: eating disorder; nutrition; gastrointestinal function

Background

Starvation leads to mucosal atrophy and increased intestinal permeability, which reflects damage to the intestinal barrier. Subsequently, impaired absorption of nutrients and bacterial translocation may also occur.1

Anorexia nervosa (AN) patients exhibit severe malnutrition, which can lead to many of the physical complications of AN, including disturbance of gastrointestinal function.2 The main feature of AN patients, especially those with the AN restricting type (AN-R), is decreased oral food intake and nutrition. Therefore, starvation may cause intestinal mucosa atrophy in these patients, which could lead to impaired absorption of nutrients and bacterial translocation. In fact, systemic sepsis due to bacterial translocation has been previously reported in AN patients.3

In humans and rodents, diamine oxidase (DAO) is specifically localized to the apical end of mature villi with high activity4,5 and its activity reflects the integrity and maturity of the small intestinal mucosa. DAO activity increases in parallel with DAO activity in the villi of the small intestinal mucosa in maturing rats4,6 and correlates with the severity of small intestinal mucosal lesions induced by anti-cancer drugs.6 Several studies of humans and animals have revealed that DAO activity in serum correlates inversely with the intestinal permeability of the small intestine. It has been suggested that serum DAO activity is a reliable indicator of intestinal mucosal integrity and maturation.7–9

Therefore, we hypothesized that intestinal integrity is disturbed in AN, and investigated serum DAO activity to evaluate intestinal function, that is, mucosal maturity and integrity.

Method

Participants

The participants were AN inpatients at The University of Tokyo Hospital who were diagnosed according to The Diagnostic and Statistical Manual of Mental Disorders-IV-TR criteria between 2007 and 2010. Eligible patients were adult female AN patients aged <35 years. Twenty healthy Japanese women <35 years of age were recruited as controls.

Measurement of Serum DAO Activity

Serum DAO activity, as a marker of intestinal mucosal integrity, was measured at admission, by immunoassay.
using ELISA kit (Immundiagnostik, Germany). In the ELISA kit, the intra-assay CV was 1.42% and the inter-assay CV was 7.9%.

Statistical Analysis

Data are expressed as the median [range]. Kruskal Wallis test and Mann–Whitney test with Bonferroni correction were used to compare variables between the AN subgroups and controls. p-values < .016 were considered to be statistically significant.

The study protocol was approved by the Ethics Committee of the University of Tokyo and complied with Declaration of Helsinki. All participants were included in the study after providing informed consent.

Results

Participants Characteristics

Thirty-six AN inpatients, including 21 AN restricting type (AN-R) and 15 AN binge-eating/purging type (AN-BP), were enrolled, and 20 healthy controls were recruited (Table 1).

Age was not different between the AN subgroups patients and controls (AN-R: 21.0 [34–16], AN-BP: 28.0 [34–16], controls: 23.5 [33–20] years). BMI was significantly lower in the AN patients compared with the controls. However, there was no difference in BMI between the AN subgroups (AN-R: 13.5 [16.3–11.0], AN-BP: 14.2 [17.3–10.4], control: 20.8 [24.8–18.8] kg/m²). Their calorie intake measured by Food Frequency Questionnaire (FFQ) were different between the AN subgroups (AN-R: 1456 [2758–443], AN-BP: 2921 [12020–414] kcal/day, p = .001).

Serum Levels of Diamine Oxidase

The serum DAO activity levels in the AN subgroups and controls were 8.2 [14.2–1.8], 12.3 [17.2–3.6] and 12.1 [22.0–8.6] U/l in the AN-R, AN-BP and controls, respectively (Fig. 1). While there were significant differences in AN-R compared with both the AN-BP and controls (p = .01, p < .001, respectively), BMI and duration of illness were not different between the AN-R and AN-BP subgroups.

Discussion and Conclusion

To best of our knowledge, this is the first report of DAO activities in AN patients. In comparing serum DAO activity levels among the AN subgroups and controls, AN-R patients exhibited significantly lower serum DAO activity levels than both AN-BP patients and controls. Because DAO activities reflect intestinal mucosal maturation and integrity,4,5 this suggests that intestinal mucosal atrophy and damage to the intestinal barrier might occur in AN-R patients.

The usage of the intestine in nutrition absorption increases the maturation of the intestinal villi and serum DAO activity.10,11 Frequent dietary-restriction in AN-R patients prolongs the absence of luminal nutrients in the intestinal tract.
compared with AN-BP patients who exhibit binging behavior. Therefore, the intestinal mucosa may undergo atrophy leading to lower serum DAO activity levels in AN-R patients. In contrast, as the gastrointestinal tract in AN-BP patients is regularly used due to their binging behavior, the state of the small-intestinal villi and mucosa may be maintained. There are other possible causes of difference between AN-R and AN-BP in DAO levels. One possibility is the differential nutritional status, because median of calorie intake measured by FFQ was different in the two groups. Another possibility is the difference in histamine intolerance (HIT) because serum DAO activity was reported to reflect HIT.12

The intestinal mucosal immaturity, which is suggested by the low serum DAO activity levels, might be associated with nutrient malabsorption in AN patients. However, it was recently reported that AN patients exhibit preserved intestinal absorption, as indicated by the 13C-labeled triglyceride digestion test.13 Further studies on the association between structural and functional changes in the gastrointestinal tract are needed.

Furthermore, the possibility of damage to the intestinal barrier, as indicated by the low serum DAO activity levels, might reflect increased risk of bacterial translocation14 in AN patients with severe malnutrition.3 Usami et al.15 reported that bacterial translocation occurs more readily when DAO activity is low. Thus, the measurement of serum DAO activity levels might be useful for evaluating risk of bacterial translocation in AN patients with severe malnutrition.

We recognize the following limitations of the present study. First, food intake before admission was not measured. Second, we could not determine whether DAO activity changes after sufficient nutritional recovery. Third, menstrual cycle was not considered in the controls although it has been previously reported that menstrual cycle can affect DAO activity.16 However, there would no influence of the menstrual cycle in AN due to its absence in these patients. Fourth, intensity of restriction could not be exactly evaluated. The analysis of correlation between intensity of restriction and DAO levels is issue in the future investigation. Fifth, our sample size was small. Sixth, “forbidden food” could not be excluded in AN-R. Finally, the medians of DAO in AN subgroups were within normal range. It was thought to be caused by maintaining some degree of food intake in AN patients.

In conclusion, DAO levels were decreased in AN patients. This result suggests the presence of intestinal structural disturbance, as one of the physical complications of malnutrition in AN patients. Therefore, DAO could be a useful marker of nutritional state or gut function in AN, although this should be investigated in further studies.

This work was supported by JSPS KAKENHI Grant Number 20790471.

References