Comparison of Clinical Characteristics of Adolescent Women With Different Subtypes of Anorexia Nervosa With First Episode and Without Treatment

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Research article

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Abstract

Background

This study compared whether differences between different anorexia nervosa(AN)subtypes(R-AN,B-AN) in multiple organ complications.

Methods

Peripheral white blood cells (WBCs),thyroid function,etc, were measured in 53 patients (R-AN = 30,B-AN = 23)and compared 55 healthy controls (HCs)

Results

Compared with HCs, significant differences between R-AN in T, P, DBP, SBP WBC, PRL, TT4, TSH, FT3, FT4, TT3, TP, HGB, RBC,, EDI total score and DT, I, ID, IA ,BD, P and MF. Compared with HCs, significant differences between B-AN in DBP, WBC, PRL, TT4, FT3, FT4, TT3, TP, HGB, RBC,, EDI total score, DT, BD, I, ID, and IA and differences in PLT and P. significant differences between R-AN and B-AN in T, P, DBP, SBP, PRL, TSH, B, FT4, and HGB. In R-AN, BMI negatively correlated with amenorrhea, and PRL EDI total score, DT, BD, and P positively correlated with DBP, SBP, HGB and GLB. In B-AN, BMI negatively correlated with amenorrhea, PRL, EDI total score, and DT, and B, BD, positively correlated with T and DBP.

Conclusion

The effects of R-AN and B-AN on T, P, DBP, SBP, PRL TSH, B, FT4, and HGB were different, and BMI played a role in the changes.

Plain English Summary

The purpose of this study was to investigate whether the clinical signs of anorexia nervosa subtypes are different.We also studied the association between body mass index and clinical signs, Eating Disorder Inventory (EDI) scores and eight subscales.In this study, we collected 53 patients diagnosed with anorexia nervosa and 55 healthy controls. Our analysis showed that patients with anorexia nervosa had different clinical features, varying degrees of physical impact, and were associated with body mass index.These findings can help inform interventions that focus on both improving life satisfaction and anorexia nervosa symptoms.

Background

Anorexia nervosa (AN) is a common eating disorder, was officially named by Dr. William Gull in 1873(Vandereycken and Vande,1990), and AN is characterized by self-consciousness and active restriction of food intake and type, resulting in significant emaciation, malnutrition, and a significant decrease in body weight or body mass index (BMI, in kg/m^2). AN may cause damage to various systems, such as amenorrhea, hypothyroidism, leukocytopenia, anemia, bradycardia, hypotension, hypothermia, hypoglycemia, and electrolyte

disturbances. These medical complications are due to malnutrition and weight loss and their associated physiologic compensations(Gibson,etal.,2019). The onset of AN usually occurs in adolescence or young adulthood and more often in women (Treasure,etal.,2010;Udo and Grilo,2018). The World Health Organization (WHO) Expert Committee endorsed the use of BMI to assess thinness in children and adolescents (WHO,1995;De Onis,etal.,2006). Cole et al. proposed the corresponding BMI cutoff for children and adolescents based on the WHO's definition of thinness grade in adults. Cutoffs for children and adolescents 2–18 years old were derived based on a BMI between 16 and 18.5 kg/m2 at 18 years old. Thinness grades 1, 2, and 3 in children and adolescents were 1 (17 to < 18.5 kg/m2), 2 (16 to < 17 kg/m2), and 3 (< 16 kg/m2), respectively, which were consistent with the WHO's adult definitions(Cole,etal.,2007). The degree of reduction was negatively correlated with age and weight(Gibson,etal.,2019). In general, a BMI ≤ 15 kg/m2 indicates a need for hospitalization (Bouquegneau ,etal.,2012).

The most common blood abnormalities in patients with AN are leukopenia and anemia. The incidence of leukopenia in patients ranges from 22–79%, and anemia ranges from 22–83%(Misra,etal.,2004;Sabel,etal.,2013). The possible mechanism is related to bone marrow cellularity and gelatinous marrow transformation(Abella,etal.,2002). The malnutrition and low BMI of AN are associated with reproductive disorders, such as amenorrhea, low fertility and delayed menarche (Castellano,etal.,2005; Castellano,etal.,2010; Pinheiro,etal.,2008;Swenne,2005;Miller,etal.,2005;HermanGiddens,etal.,1997), which may be due to self-starvation that leads to noninflammatory malnutrition and hormonal changes in the body(Germain,etal.,2007)that are an adaptive response of the body to AN (Gibson,etal.,2019). Golden et al found that the recovery of menstruation was related to the restoration of hypothalamic-pituitary-ovarian function (Golden,etal.,1997). Circulating thyroid hormones are sensitive to nutritional status. Low T3, low T4, and normal thyroid stimulating hormone are seen patients with in AN due to the dysfunction of the hypothalamic-pituitary-thyroid (HPT) axis(Gwirtsman,etal.,1983). Starvation (AN) or intermittent dieting bulimia nervosa (BN) reduced sympathetic activity and was clinically associated with hypotension, bradycardia, hypothermia, and depression(Pirke,etal.,1996). This was consistent with the clinical manifestations of AN(Mazurak,etal.,2011).

In the DSM-5 classification, there are two subtypes of AN: restricting AN (AN-R) and binge-purge AN (AN-BP). According to the present literature in the Chinese Han population, we found that the complications caused by AN, Eating Disorder Inventory (EDI) scores and various factors were mostly based on AN subtypes. Therefore, we assumed that the medical complications of AN, EDI score and various factors were different between the two subtypes. The correlation of these complications with the age of onset, course of disease and body weight was further investigated.

Methods

Study population

The study was conducted in accordance with the principles of the Declaration of Helsinki (2013) and approved by the Ethics Committee of Shandong Mental Health Center. Patients were screened from inpatients in Shandong Mental Health Center from January 2016 to June 2020. The adolescent girls and their parents were informed about the nature of the study, and written informed consent was obtained prior to participation. The inclusion criteria and exclusion criteria were as follows:

Inclusion criteria for patients with AN: A diagnosis of AN-R or AN-BP according to the DSM-5 diagnostic criteria, adolescent female aged 12 to 18 years, and Chinese Han ethnicity. To avoid selection bias, we selected only patients with AN who were hospitalized for the first time and without treatment.

Inclusion criteria for healthy controls (HCs): Girls of similar age who underwent a physical examination in our center from January 2016 to January 2020.

Exclusion criteria applied for all groups: A past history of eating disorders, pregnancy, endocrine disorders, metabolic disorders, or other psychiatric, internal or medical comorbidities or medications.

Measurements

All participants were assessed by two child and adolescent physicians. All participants rested in a room with a constant temperature for half an hour before general information was collected, including age, height, weight, course of disease (The time from onset to treatment is calculated in months),blood pressure (in a seated position), temperature, and electrocardiogram. The body mass index (BMI) was calculated as kg/m2. Blood pressure and body temperature were measured at room temperature for 30 minutes at rest

The EDI is a 64-item, self-reporting tool with eight subscales: drive for thinness (DT), bulimia (B), body dissatisfaction (BD), ineffectiveness (IE), perfectionism (P), interpersonal distrust (ID), interoceptive awareness (IA), and maturity fears (MF)(Garner,etal.,1983). EDI-1 was designed to evaluate the psychological and behavioral characteristics associated with anorexia nervosa (AN) and bulimia nervosa (BN)(Franko,etal.,2004). Zhang and his colleagues translated EDI-1 into Chinese, with Cronbach's alpha = 0.95 for the entire EDI (Zhang ,etal.,2004).

Fasting blood was collected in the morning, and blood samples were taken from the participants from 7:00 a.m. to 7:30 a.m. A total of 3 mL of peripheral blood was collected in a vacuum blood collection tube with EDTA anticoagulant, and routine blood testing was performed by an XN-10[B4] (SESSenmekom) automatic blood cell analyzer. A total of 5 mL of fasting venous blood was separated by centrifugation (3000 rpm, 10 min at 20°C) and stored at − 80°C. An AU5800 automatic biochemical analyzer (Beckmann Coulter Trading Co., LTD.) was used to detect the fasting blood glucose in peripheral blood. Albumin, FSH and T3 levels in the peripheral blood were detected by a cl-6000I (Mindri Biomedical Electronics Co., LTD.) automatic chemiluminescence immunoassay analyzer. The above operation was completed according to the manufacturer's instructions.

Statistical analysis

The data were statistically processed by SPSS 20.0 statistical software. The normality test for each variable was the Shapiro-Wilk test. The age of onset, time of treatment, BMI, time of amenorrhea, heart rate, blood pressure, body temperature and EDI score were continuous variables. Continuous data Perform log transformed before assessed for normality with the Kruskal-Wallis test. These continuous variables are expressed as the mean ± standard deviation. Nonparametric Mann-Whitney tests were performed to examine group differences in WBC, HGB, RBC, TSH, TT4 and other hormonal concentrations. Nonparametric Spearman’s rho was used to examine correlations between BMI and the variables. Statistical significance was set at a P-value < 0.05.

Results

A total of 108 women aged 12-18 years old participated in the study, including 53 patients with AN (R-AN=30, B-AN=23) and 55 age-matched healthy controls (HCs). The patient group consisted of 30 patients with R-AN and 23 patients with B-AN.

Comparison of general information

There was no significant difference in age among the three groups; BMI, T, P, DBP and SBP showed significant differences (P<0.01). There was no significant difference in disease course or amenorrhea time between the R-AN and B-AN groups; the disease course was longer than 9 months, and the time of amenorrhea was more than 4 months. T, P, DBP and SBP showed significant differences between the R-AN group and the control group. The same results existed between the R-AN and B-AN groups (P<0.01), while DBP was significantly different between the B-AN group and control group (P<0.01) (Table 1).

Comparison of laboratory data between three groups

There were significant differences in the three groups with regard to WBC, PRL TT4, TSH FT3, FT4 TT3, TP, HGB, RBC and GLB (P<0.01). The same was true for the R-AN and control groups. There was a significant difference between the B-AN and control groups in WBC, PRL, TT4, FT3, FT4, TT3, TP, HGB, RBC, GLB and PLT (P<0.01). There were significant differences in PRL and TSH (P<0.01) and FT4 and HGB (P<0.05) between the two groups. (Table 1).

Table 1 Demographic characteristics and clinical data (Mean ± SD) of patients with anorexia nervosa and healthy controls

	R-AN(n=30)	B-AN(n=23)	HC(n=55)	P	PR-H	PB-H	PR-B
Age (mean±SD)	14.53±0.243	15.04±0.395	15.00±0.217	0.371	0.159	0.916	0.357
BMI	13.567±0.344	15.199±0.471	21.287±0.242	0.000	0.000	0.000	0.009
course of disease	9.9±0.827	11.09±0.616		—	—-	—	0.170
amenorrhea	5.717±0.619	4.948±0.788		—-	—	—	0.272
T	35.723±.0985	36.230±0.075	36.38±.0416	0.000	0.000	0.064	0.002
HR	62.00±1.986	70.826±2.262	72.109±1.060	0.000	0.000	0.684	0.004
DBP	89.33±2.199	97.96±1.973	102.96±1.011	0.000	0.000	0.053	0.007
SBP	56.83±1.423	63.35±1.489	78.76±1.040	0.000	0.000	0.000	0.012
WBC	4.552±0.356	4.507±0.293	6.1605±.1737	0.000	0.000	0.000	0.760
PLT	235.6±13.459	243.09±12.515	213.95±6.229	0.092	0.196	0.033	0.554
HGB	101.387±4.150	110.696±2.874	125.745±1.235	0.000	0.000	0.000	0.043
RBC	3.614±.1107	3.823±.1069	4.238±0.055	0.000	0.000	0.000	0.101
PRL	26.528±3.878	33.657±2.737	8.287±0.5087	0.000	0.000	0.000	0.006
TT4	5.594±.5616	6.055±0.7140	8.173±0.300	0.000	0.000	0.001	0.609
TSH	10.473±1.804	4.424±1.526	3.318±0.380	0.001	0.001	0.15	0.002
FT3	3.007±1.350	2.106±0.169	2.855±0.092	0.000	0.000	0.000	0.106
FT4	0.545±0.043	0.761±0.106	0.860±.0385	0.000	0.000	0.017	0.035
TT3	0.545±0.041	0.654±.055	1.031±.0340	0.000	0.000	0.000	0.167

The comparison of EDI scores

EDI scores were significantly different among the three groups, the total score and DT, ID, and IA were significantly different between the R-AN and control groups, and BD, P, and MF were significantly different between the R-AN and control groups (P<0.01). Total scores and DT, BD, ID, and IA were significantly different between the B-AN and control groups (P<0.01), while differences existed in P (P<0.05). There were only significant differences in the total score and B between the case groups (P<0.01). (Table 2).

Correlation of BMI between case groups

In the R-AN group, BMI was negatively correlated with amenorrhea (r=-0.47, p<0.01), PRL(r=-0.44, p<0.05), EDI total score (r=-0.55, p<0.01), DT (r=-0.67, p<0.01), BD (r=-0.70, p<0.01), and P (r=-0.44, p<0.05) and positively correlated with T (r=0.53, p<0.01) DBP(r=0.26, p<0.05), SBP (r=0.51, p<0.01), HGB (r=0.46, p<0.05), and GLB (r=0.39, p<0.05). In the B-AN group, BMI was negatively correlated with amenorrhea (r=-0.57, p<0.01), EDI total score (r=-0.64, p<0.01), DT (r=-0.43, p<0.05), B (r=-0.42, p<0.05), BD (r=-0.44, p<0.05), and IE (r=-0.60, p<0.01) and positively correlated with T (r=0.56, p<0.01) and DBP (r=0.57, p<0.01). (Table 3).

Table 2: EDI total score and each factor score in anorexia nervosa patients and healthy controls

	R-AN	B-AN	HC	P	PR-H	PB-H	PR-B
TOTA	183.97±2.457	196.3±3.177	137.96±1.252	0.000	0.000	0.000	0.004
DT	28.47±0.851	26.04±1.199	12.95±0.491	0.000	0.000	0.000	0.189
B	9.3±0.304	22.22±0.896	9.69±0.276	0.001	0.396	0.000	0.000
BD	22.7±0.842	23.65±0.951	20.22±0.492	0.003	0.028	0.002	0.45
IE	25.2±0.914	25.57±1.09	20.31±0.504	0.000	0.000	0.000	0.801
P	22.47±0.853	22.7±1.055	19.2±0.75	0.003	0.011	0.022	0.942
ID	21.1±0.961	21.52±1.332	13.11±0.432	0.000	0.000	0.000	0.801
IA	28.3±0.966	28.7±1.438	17.96±0.528	0.000	0.000	0.000	0.950
MF	26.7±0.618	26.35±.0919	24.53±0.545	0.002	0.011	0.103	0.679

Table 3: The correlation between clinical characteristics, EDI score, all factors score and BMI in case group

	R-AN		B-AN	
	r	*P*	*r*	*P*
amenorrhea	-0.474	0.008	-.569	.005
T	0.528	0.003	.557	.005
P	0.267	0.154	.223	.305
DBP	0.263	0.012	.567	.005
SBP	0.513	0.004	.108	.623
WBC	-0.264	0.158	.277	.201
GLU	0.306	0.100	.023	.916
PLT	-0.185	0.327	.143	.156
HGB	0.459	0.011	.209	.338
PRL	-0.443	0.014	.210	.336
TT4	0.261	0.163	.137	.532
TSH	0.098	0.608	.195	.373
FT3	0.145	0.445	.205	.349
TT3	0.316	0.089	.195	.372
EDI:				
TOTA	-0.554	0.000	-0.644	0.001
DT	-0.668	0.000	-0.432	0.04
B	0.021	0.913	-0.416	0.048
BD	-0.698	0.000	-0.437	0.037
IE	0.108	0.568	-0.598	0.003
P	-0.438	0.016	-0.222	0.309
ID	-0.204	0.28	0.083	0.707
IA	0.136	0.474	-0.245	0.259
MF	0.214	0256	0.261	0.229

Discussion

With the growth of China's economy, the incidence of eating disorders in China is increasingly close to that in Western developed countries, but there is a lack of corresponding epidemiological investigations. Jun Tong et al. performed a study based on first-year female students in three universities in Wuhan in 2009 (N = 8,521) and showed that the prevalence rate of AN was 1.05%(Tong ,etal.,2014), while the prevalence rate reported in Western countries ranged from 0.8–4% (UdoandGrilo,2018;Keski-Rahkonen,etal.,2016; Hudson,etal.,2006;Mical,etal.,2017).

However, these studies are focused on adults. Due to a variety of reasons, the incidence and prevalence of childhood-onset AN are still unknown. Only a few studies have shown that the prevalence rate in adolescents is 0.1–0.27%(Keski-Rahkonen,etal.,2007), which is as high as 0.5% in young women (Bentovim,etal.,1990Johnson-Sabine,etal.,1998). Many medical complications in AN may result from excessive dieting, excretion, or exercise, or a combination of these factors.

In our study, it was found that, compared with the normal group, there were significant differences in T, HR, DBP and SBP between them and the R-AN subtype, and such differences also existed between the subtypes, all of which were HCs > R-AN > B-AN. But, the difference between the AN-BP and the control group was only in SBP. BMI is correlated with the T, DBP and SBP of the R-AN group but is correlated with T and DBP in the B-AN group. Previous studies have also shown hypothermia, hypotension, bradycardia and other symptoms in the AN group (Pirke,etal.,1996;Mazurak ,etal.,2011), but no differences between the two subtypes were shown. On the one hand, this may be related to the insufficient intake of food and fluid, resulting in a decrease in blood volume; on the other hand, it may be related to the decrease in sympathetic nerve activity caused by poor nutrition and weight loss in patients (Schneiter,etal.,2009). Due to low caloric intake, the bradycardia mechanism of AN is thought to be a physiological adaptation to increased vagal tone and decreased energy use metabolism (Schneiter,etal.,2009). Decreased glycogen levels and cell atrophy in cardiomyocytes may lead to bradycardia (Kollai,etal.,1994). The adverse change in AN is the effect of fasting, that is, the body adapts to a decrease in nutrition and water intake. This activates the body's reserves and slows down the metabolic process, leading to a hypothermic state where the body temperature drops below 36°C (Vázquez,etal.,2003; Fagher,etal.,1989).

Hypothermia in anorexic patients is usually caused by hormonal disorders, primarily a drop in thyroid hormone levels (responsible for metabolism and calcium and phosphorus balance), and in women, a drop in reproductive hormone levels estrogen and dehydroepiandrosterone (DHEA) can lead to amenorrhea and eventually permanent infertility. A drop in body temperature is also a disorder of the circulatory system (decreased blood flow and blood pressure; bradycardia) and a significant reduction in body fat, the body's main insulator[37]. Equally important, muscle mass and function are reduced due to the loss of electrolytes muscle does work to produce heat energy(Chudecka,etal,2016). Patients with AN compared with those of the normal group and subtypes had a significant decline in white blood cells, red blood cells, hemoglobin, and platelets. In binge eating, only the differences between the group and normal group. A comparison between groups found that the hemoglobin level was lower than in the overeating group. There was no difference between white blood cells, red blood cells and platelets. Correlation analysis found that only hemoglobin and BMI were positively associated with the degree of decline. The most common blood abnormalities of AN are in white blood cells and anemia(Misra,etal,2004;Sabel,etal.,2013). The possible mechanism is related to bone marrow cellularity and gelatinous marrow transformation(Abella,etal.,2002). The platelet count of the AN group was lower than that of the normal control group, but all were within the normal range(Oswiecimska ,etal.,2017).

Except for B, there were differences in EDI between the R-AN and control group in total score and various factors. Case group was the same as control group Bmay be related to the economic development of China and the increase of communication with Western countries, and their pursuit of health and aesthetics is also more and more inclined to Western countriesExcept for MF, there were differences in EDI between the B-AN and control group in total score and various factors. There are some inconsistencies in research with the Mandarin version of the EDI(Tseng,etal.,2014), and the R-AN and B-AN groups differed only in B. In a Japanese study, except for DT, there was no significant difference in scores on the B, BD and P subscales compared with the non-ED control group.

Although the DT score was higher than the control group, it was lower than other ED groups(Pike ,etal.,2005). This is basically consistent with our research.

Conclusions

In this study, differences were observed between the case group and control group in body temperature, heart rate, blood pressure, hematologic examination, EDI total score and factor scores. There were differences in BMI,HR, DBP, SBP, PRL, TSH, FT4, HGB, and B between the R-AN and B-AN groups. In the R-AN group, BMI was negatively correlated with amenorrhea and the PR, total EDI score, DT, BD, and P and positively correlated with DBP, SBP, HGB and GLB. In the B-AN group, BMI was negatively correlated with amenorrhea, PRL, total EDI score, DT, B, BD, and I and positively correlated with T and DBP.

Abbreviations

R- AN,restrictin-anorexia nervosa;B-AN
binge purge-anorexia nervosa; HC, healthy controls; P represents P-value among the three groups; P_{R+H} represents P-value between R-AN and controls; P_{B+H} represents P-value between B-AN and controls; P_{R+B}represents P-value between R-AN and B-AN.BMI:body mass index,T:body temperature,HR:heart rate,DBP□diastolic blood pressure, SBP □systolic blood pressure □WBC□ leukocyte□white blood cell, PLT:blood platelet, TT4:total thyroxin, TSH:thyrotropic hormone, FT3:free tri-iodothyronine, FT4:free thyroxin, TT3:total tri-iodothyronine, HGB:hemoglobin, RBC:red blood cell; erythrocyte,PRL:prolactin

Declarations

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Authors' contributions

HBM andRYZ conceived and designed the study.RYZ, LMY, and DFX were involved in data acquisition. RYZ andDFXprocessed and analyzed the data.

RYZ and LMYdiscussed the results and wrote the manuscript. All authors read and approved the finalized manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This research was approved by the Human Ethics Committee of Shandong

Mental Health Center. All patients were provided with written, informed consent. Participation was voluntary, and participants could withdraw at any time during the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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