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Anemia and Its Effect on Cardiovascular Findings in Obese Adolescents

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Abstract

Objective: We assessed the effect of anemia on cardiovascular findings in obese adolescents.

Materials and Methods: We studied 29 anemic, 33 nonanemic obese adolescents, and 33 nonobese healthy adolescents. These three groups were investigated for clinical and laboratory features of anemia and obesity. Echocardiography was used to examine cardiac functions.

Results: The anemia was mild (mean hemoglobin 11.67±0.79g/dL), ferritin level was significantly low, and CRP and fibrinogen levels were significantly high in anemic obese patients. Increased cardiac pulse and echocardiographic findings which may be indicative of early left ventricular diastolic dysfunction were present in these patients.

Conclusion: Anemia may develop due to iron deficiency and chronic inflammation in obese adolescents. Even mild anemia may cause increased heart rate and affect left ventricular diastolic functions. So diet programmes of obese children should be carefully planned to avoid iron deficiency anemia, which may worsen the cardiac events in long term follow-up.

Keywords: Anemia, Cardiac function, Inflammation, Iron deficiency, Obesity

Öz

Amaç: Obez adolesanlarda aneminin kardiyovasküler bulgular üzerine etkisinin araştırılması amaçlanmıştır.

Gereç ve Yöntemler: Çalışmaya 29 anemik, 33 anemik olmayan obez adolesan ve 33 obez olmayan sağlıklı adolesan dahil edildi. Bu üç grup, anemi ve obesitenin klinik ve laboratuvar

bulguları açısından değerlendirildi. Kardiyak fonksiyonları değerlendirmek için ekokardiyografi kullanıldı.

Bulgular: Anemik obez hastalarda anemi hafifti (ortalama hemoglobin 11.67±0.79g/dL), ferritin seviyesi anlamlı olarak düşük, CRP ve fibrinojen düzeyleri anlamlı olarak yüksek bulundu. Bu grupta kardiyak nabız anemik olmayan obez adolesanlarınkine göre anlamlı yüksekti ve ekokardiyografik incelemede anemik obez grupta erken ventriküler diyastolik disfonksiyon göstergesi olabilecek bulgular saptandı.

Sonuç: Obez adolesanlarda demir eksikliği ve kronik inflamasyona bağlı anemi gelişebilir. Hafif anemi varlığı bile kardiyak nabızda artışa ve sol ventrikül diyastolik fonksiyonlarında etkilenmeye neden olabilir. Bu nedenle obez çocuklarda uzun dönemde kalp fonksiyonlarının olumsuz yönde etkilenmemesi açısından diyet programları demir eksikliği anemisini önleyecek şekilde dikkatlice planlanmalıdır.

Anahtar Sözcükler: Anemi, Kardiyak fonksiyon, Inflamasyon, Demir Eksikliği, Obezite

Introduction

The prevalence of childhood obesity has progressively increased in the world for the last decades due to sedentary life style and poor dietary habits (1,2). Childhood obesity is a major risk factor for development of cardiovascular diseases in the adulthood (3-6). On the other hand, anemia is another well-defined risk factor that has negative impact on prognosis of cardiovascular diseases (7-9). The cardiac problems in anemic obese adolescents are not well known. The purpose of this study was to assess the effect of anemia on cardiovascular findings in obese adolescents by means of standard, pulsed wave Doppler (PWD), and tissue Doppler imaging (TDI) echocardiograhy.

Materials and Methods

The adolescent patients admitted to our hospital with exogenous obesity between the ages of 12 to 18 years were included. The study group was divided into two groups as anemic obese (n: 29) and nonanemic obese (n: 33) patients. Those who have endogenous obesity, infection, chronic use of medications, and accompanying other diseases were excluded. Healthy adolescents (n: 33) whose body mass indexes were between the 3rd and 85th percentiles were included as the control group.

Obesity was defined as a body mass index (BMI) at or above the 95th percentile for children and teens of the same age and sex. BMI was calculated by dividing a person's weight in kilograms by the square of height in meters (10). Anemia was defined according to the World Health Organization (WHO) as hemoglobin value ≤ 12 g/dL in women and ≤ 13 g/dL in men (11). Hypertension was defined by a systolic and/or diastolic blood pressure at or above the 95th percentile for children and teens of the same age and sex (12).

Clinical data and results of laboratory measurements of patients including complete blood cell count, renal, liver, and thyroid function tests, serum glucose, insulin, insulin resistance, lipid levels, fibrinogen, C-reactive protein (CRP), iron parameters were obtained from the hospital records.

Echocardiography was performed after 15 min of resting by a pediatric cardiologist. A standardized M-mode echocardiography, PWD, and TDI echocardiography were performed to evaluate the status and functions of the heart (13). By using M-mode echocardiography interventricular septum diastolic diameter (IVSDD), left ventricule end-diastolic diameter (LVEDD), left ventricule posterior wall diastolic diameter (LVPWDD), left ventricule end-systolic diameter (LVESD), ejection fraction (EF), left ventricule mass (LVM), and LVM index (LVMI) were calculated. Early diastolic mitral flow (E-wave), late diastolic mitral flow (A-

wave), and early mitral to late mitral flow ratio (E/A) were found by using PWD. Systolic myocardial velocity (S), late diastolic myocardial velocity (Em), early diastolic myocardial velocity (Am), ratio of early to late diastolic myocardial velocity (Em/Am), isovolumetric relaxation time (IVRT), and myocardial performance index (MPI) were calculated by using TDI echocardiography.

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software version of 15. Differences between groups for categorical variables were compared by chi-square test. Student *t* test and Mann-Whitney U test were used for comparison of continuous variables. One way analysis of variance (ANOVA) and Kruskal-Wallis tests were used for comparison of more than two groups.

Results

Demographic data and clinical features of the groups are given in Table 1. The values of hemoglobin, mean corpuscular volume (MCV), red cell distribution width (RDW), iron parameters, fibrinogen, and CRP are shown in Table 2. Test results including serum glucose, insulin, insulin resistance, renal, liver, and thyroid function tests, and lipid profile didn't differ between the three groups ($p>0.05$).

M-Mode and TDI echocardiographic parameters are given in Table 3 and Table 4. As seen in Table 3, there were significant changes of LVM, LVMI, LVPWDD, and IVSDD in obese patients. PWD measurements demonstrated that E-wave and A-wave showed significant differences between the three groups ($p=0.012$, $p=0.013$) and between anemic and nonanemic obese groups ($p=0.016$, $p=0.039$). E/A ratio was not statistically significant between the three groups ($p=0.751$).

Discussion

In our study, a significant proportion of anemic obese children were found to be on diet to lose weight. Their ferritin level was significantly lower even though there were signs of chronic inflammation, such as high levels of fibrinogen and CRP. Anemia may be seen in the obese population due to poor dietary habits and as a result of chronic inflammatory condition (14-18). In obese patients, adipose tissue secretes proinflammatory cytokines that restrict erythropoiesis (17,18). On the other hand, obesity-associated inflammation is closely linked to iron deficiency and involves impaired duodenal iron absorption associated with low expression of duodenal ferroportin and elevated hepcidin levels (14,19). Iron deficiency and anemia may change mitochondrial and cellular energy homeostasis and increase inactivity and fatigue of obese patients (19).

Anemia may cause hemodynamic changes, cardiomegaly and left ventricular hypertrophy in the long term period (9,20). EF is one of the most commonly used parameters in evaluation of left ventricule systolic function. EF was not impaired in our study. Studies demonstrated that EF does not decrease in early period of obesity (21-23). It has been reported that these changes correlate with degree and duration of anemia (9,20,24). In a recent study, Zhou et al (24) demonstrated that LV remodeling and LV systolic dysfunction occurred in patients with iron deficiency anemia when the hemoglobin level was in the range of 6–9 g/dL. In our study, the mean hemoglobin value was 11.67±0.79 g/dL; it can be concluded that mild anemia in the obese population do not deteriorate systolic dysfunction.

Tachycardia, a well known complication of anemia, develops as a compensatory response of heart to inadequate tissue oxygenation caused by decreased erythroid mass (9). In our study, anemic obese group was found to have significantly higher cardiac pulse rates than the nonanemic obese group, even though the anemia was mild. The changes in E and A

waves seen in PWD might be caused by increased heart rates in our anemic obese group, which may be indicative of early subclinical ventricular diastolic dysfunction (21,23,25,26).

Regarding the cardiac geometry, an increased left venricular mass index (LVMI) has been shown in the obese children (6). Sharpe et al (27) demonstrated that body mass index is directly related with LVMI. An increased LVMI results in ventricular hypertrophy which eventually results in left ventricule diastolic dysfunction (23,25-30). Similarly, in our study, measurements of LVM, LVMI, LVPWDD, and IVSDD were found to be increased in both obese groups, compared to healthy control group.

In this study, the number of patients was relatively low and the anemia was mild, so we recommend further studies with larger samples of obese adolescents with different stages of anemia for more accurate investigation of effects of anemia in obese adolescents. Also follow-up of these adolescents is important to provide prompt therapeutic approach and better outcome.

Conclusion

Anemia may develop due to iron deficiency and chronic inflammation in obese adolescents. Our study suggests that blood pressure, heart rate monitoring, and echocardiographic measurements should be carefully checked in anemic obese adolescents at frequent intervals for early detection of hypertension, tachycardia, and left ventricular diastolic dysfunction. Even mild anemia may cause increased heart rate and change left ventricular diastolic functions in obese adolescents. So diet programmes of obese children should be carefully planned to avoid iron deficiency anemia, which may worsen the cardiac outcome in long term follow-up.

Ethics

Ethics Committee Approval: This study was approved by Dokuz Eylül University Drug and Clinical Investigation Ethics Committee (protokol no 1583-GOA, karar no 2014/23-16).

Informed Consent: Informed consent for study participation was obtained from all patients and their parents.

Authorship Contributions

Concept: Hale Ören; Design: Hale Ören, Nurettin Ünal, Mustafa Kır, Ece Böber, Ayhan Abacı, Nur Arslan, Şebnem Yılmaz, Öner Yıldırım; Data Collection or Processing: Öner Yıldırım, Tülay Demircan, Özgür Kızılca, Pınar Kuyum; Analysis or Interpretation: Hale Ören, Nurettin Ünal, Ayhan Abacı, Mustafa Kır, Özlem Tüfekçi, Öner Yıldırım; Literature Search: Hale Ören, Özlem Tüfekçi, Öner Yıldırım; Writing: Hale Ören, Mustafa Kır, Özlem Tüfekçi, Öner Yıldırım.

Conflict of Interest: The authors of this paper have no conflicts of interest, includingspecific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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Table 1. Demographic and clinical features of the three groups

	ANEMIC OBESE n=29 mean±SD/ median /(min-max)	**NONANEMIC OBESE n= 33 mean±SD/ median /(min-max)**	**HEALTHY CONTROL n=33 mean±SD/ median /(min-max)**	**p**
Age (years)*	13.89±1.39/ 14/(12-17)	14.18±1.28/ 14/(12-16)	14.4±1.42 14/812-17)	0.613
Male/Female (n)	13/16	18/15	18/15	0.683
Fatigue (n/%)	21/72%	24/73%	12/36%	**0.033**
Diet (n/%)	8/28%	1/3%	1/3%	**0.020**
Effort intolerance (n/%)	14/48%	11/33%	5/15%	**0.019**
Weight (kg) *	84.34±17.68/ 80/(65.5-144.8)	86.69±13.1/ 87.5 (59.5-117)	56.08±(9.21) 55.5/(36.8-75)	**0.001** p1:0.326 **p2:0.001** **p3:0.001**
BMI (percentile) *	97.78±1.25/ 98/ (95-99.7)	97.35±1.25/ 97/(95-99.03)	50.83±26.54 57/ (3-88)	**0.001** p1:0.208 **p2:0.001**

				p3:0.001
Cardiac pulse ** (beat/minute)	88.93±14.08/ 88/ (60-116)	84±11.07 84/ (62-109)	77.57±9.69 80/ (48-88)	**0.001** p1:0.225 **p2:0.001** p3:0.070
Hypertension (n/%)	14/48%	14/42%	-	0.644
Systolic blood pressure* (mmHg)	130.55±14.35/ 129/ (107-168)	128.3±10.62/ 130/ (100-164)	111.36±10.62 111/(93-140)	**0.001** p1:0.719 **p2:0.001** **p3:0.001**
Diastolic blood pressure* (mmHg)	80.03±9.76 80/ (68-108)	79.72±10.23/ 80/ (60-104)	68.45±7.37 70/ (52-80)	**0.001** p1:0.938 **p2:0.001** **p3:0.001**

p1: Anemic obese versus nonanemic obese p2: Anemic obese versus healthy control p3: Nonanemic obese versus healthy control

Table 2. Hemoglobin, erythrocyte indexes, **i**ron parameters, fibrinogen and C-reactive protein levels of anemic and nonanemic obese adolescents

	ANEMIC OBESE n=29 mean±SD	**NONANEMIC OBESE n= 33 mean±SD**	**p**
Hemoglobin (g/dL)	11.7±0.8	14.0±1.2	**0.001**
Mean corpuscular volume (fL)	76.1±3.8	83.4±4.1	**0.001**
Red cell distribution width (%)	15.5±5.8	13.6±0.6	**0.001**
Serum iron (µg/dL)	53±36	72±42	0.067
Iron binding capacity (µg/dL)	399±69	375±52	0.791
Transferrin saturation (%)	13.8±10.2	18.2±9.2	0.082
Ferritin(ng/ml)	18.9±14.9	28.18±15.8	**0.023**
Fibrinogen (g/dL)	3.9±0.7	3.5±0.7	**0.045**
C-reactive protein (mg/dL)	8.3±8.4	3.4±4.0	**0.002**

Table 3. Comparison of M-mode echocardiographic parameters between the three groups

	ANEMIC OBESE n=29 mean±SD	**NONANEMIC OBESE n= 33 mean±SD**	**HEALTHY CONTROL n=33 mean±SD**	**p**
EF (%)*	66.70±5.68	67±5.62	66.81±4.78	0.931
LVM (g)	143.09±33.07	145.26±38.07	107.11±25.7	**0.001** **p1:0.977**

				p2:0.001 **p3:0.001**
LVMI (g/m^2)	82.71±19.12	84.12±21.84	68.24±13.76	**0.002** **p1:0.933** **p2:0.002** **p3:0.002**
LVESD (mm)	28.4±3.6	29.8±2.7	28±5.3	0.154
LVPWDD (mm)	9.3±1.1	9.0±1.3	7.9±1.2	**0.001** **p1:0.276** **p2:0.001** **p3:0.001**
LVEDD (mm)	45.9±38	46.8±5.8	45.1±3.8	0.337
IVSDD (mm)	8.9±1.5	9.2±2.4	7.4±1.3	**0.001** p1:0.682 **p2:0.001** **p3:0.001**

p1: Anemic obese versus-nonanemic obese p2:Anemic obese versus healthy control p3: Nonanemic obese versus healthy control

EF: Ejection fraction, LVM: Left ventricular mass, LVMI: LVM index, LVESD: Left ventricular end-systolic diameter, LVPWDD: Left ventricular posterior wall diastolic diameter, LVEDD: Left ventricular end diastolic diameter, IVSDD: Interventricular septum diastolic diameter

Table 4. Comparison of the tissue Doppler image parameters between the three groups

	ANEMIC OBESE **n=29** **mean±SD**	**NONANEMIC OBESE** **n= 33** **mean±SD**	**HEALTHY CONTROL** **n=33** **mean±SD**	**p**
S (cm/s)	10.23±1.66	10.76±2.36	10.91±2.96	0.799
Em (cm/s)	16.37±3.1	16.9±3.87	16.94±3.72	0.791
Am (cm/s)	9.16±2.41	9.46±2.3	8.65±2.51	0.678
Em/Am	1.85±0.41	1.82±0.38	2.03±0.44	0.092
E/Em	5.93±1.15	5.40±1.53	5.29±1.40	0.090
IVRT (ms)	44.06±6.29	44.6±4.6	45.81±4.57	0.530
MPI	0.31±0.04	0.31±0.04	0.31 ±0.04	0.261

p1: Anemic obese versus-nonanemic obese p2:Anemic obese versus healthy control p3: Nonanemic obese versus healthy control

S: Systolic myocardial velocity, Em:Late diastolic myocardial velocity, Am: Early diastolic myocardial velocity, Em/Am: Ratio of early to late diastolic myocardial velocity, E/Em: Early mitral flow to late diastolic myocardial velocity, IVRT: Isovolumetric relaxation time, MPI: myocardial performance index