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Increased Oxidative Stress In Obese Children

Obez Çocuklarda Artmış Oksidatif Stres

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Aim: Obesity is associated with enhanced lipid peroxidation. Malondialdehyde (MDA), one of several by-products of lipid peroxidation process, is a biomarker that provides an indication of lipid peroxidation level. It was aimed to determine the oxidant damage in obese children.

Materials and Methods: Thirty two children with obesity and 20 age-matched non-obese children were evaluated. None of the subjects were receiving any medication that could affect insulin levels, insulin sensitivity, or oxidative stress. After overnight fasting, blood was drawn from an antecubital vein for determination of biochemical parameters and MDA levels. Insulin resistance was assessed at baseline by using the homeostasis model assessment (HOMA).

Results: Obese group had significantly higher fasting plasma insulin, fasting plasma glucose, plasma cholesterol, LDL-cholesterol and increased blood pressure values as compared to controls ($p<0.05$). Serum MDA levels were significantly increased in obese children (9.856 ± 3.705 μmol/L) when compared with non-obese children (5.43 ± 1.096 μmol/L) ($p=0.001$). Significant positive correlations were observed between HOMA-IR values and body mass index (BMI) ($p=0.0001$) and between HOMA-IR values and MDA levels ($p=0.003$) in all subjects.

Conclusion: These findings suggest that obesity is an important factor for enhanced oxidative stress in children.

Key words: childhood obesity, insulin resistance, malondialdehyde, oxidative stress

Amaç: Obezite artan lipid peroksidasyonu ile ilişkilidir. Lipid peroksidasyon sürecinin birkaç yan ürününden biri olan malondialdehid (MDA), lipid peroksidasyon düzeyini yansıtan biyolojik bir belirteçtir. Bu çalışmada obez çocuklarda oksidan hasarın belirlenmesi amaçladı.

Gereç ve Yöntem: Otuz iki çocuk ve aynı yaş grubunda yirmi obez olmayan çocuk değerlendirildi. Olguların hiçbiri insülin düzeyini, insülin duyarlılığını veya oksidatif stresi etkileyecek ilaç almıyordu. Gece açlığı sonrası biyokimyasal parametreleri ve MDA düzeyini belirlemek için kan alındı. İnsülin direnci HOMA-IR kullanılarak değerlendirildi.

Bulgular: Obez grup kontrol grubuyla karşılaştırıldığında anlamlı olarak yüksek açlık plazma insülin, açlık plazma glukozu, plazma kolesterolü, LDL-kolesterol ve yüksek kan basıncı değerlerine sahipti ($p<0.05$). Serum MDA düzeyi kontrol grubuyla (5.43 ± 1.096 μmol/L) karşılaştırıldığında, obez grupta (9.856 ± 3.705 μmol/L) anlamlı olarak yüksekti ($p=0.001$). Tüm olgularda HOMA-IR değerleri ile vücut kitle indeksi ($p=0.0001$) ve HOMA-IR değerleri ile MDA düzeyleri arasında ($p=0.003$) anlamlı pozitif korelasyon gözlendi.

Sonuç: Bu bulgular çocuklarda obezitenin, oksidatif stres artışında önemli bir faktör olduğunu göstermektedir.

Anahtar Sözcükler: çocukluk çağı obezitesi, insülin direnci, malondialdehid, oksidatif stres

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The cellular defense mechanisms and their influences against many diseases were thought to be related to obesity complications seen in adults. The knowledge about the response to oxidant damage caused by obesity in childhood is limited, compared to adult studies (1). Obesity is associated with enhanced lipid peroxidation. One of the most frequently used biomarkers providing an indication of lipid peroxidation level is the plasma concentration of malondialdehyde (MDA), one of several by-products of lipid peroxidation processes (2). In the present study, we measured the plasma levels of malondialdehyde in obese and nonobese children to investigate the relationship of oxidative stress and insulin resistace. We aimed to determine the oxidant damage in obese children.

MATERIALS and METHODS

The study comprised 32 children with obesity and 20 age-matched non-obese children. Obesity was defined as a body mass index (BMI) greater than the 95th percentile of body mass index BMI for age and sex reported on the BMI tables (3). Signs of diabetes mellitus, thyroid disease, renal failure and liver disease were not present in any of the children. The children were not on a diet and were not participating in physical training programs. some special. None of the subjects were receiving any medication that could affect insulin levels, insulin sensitivity, or oxidative stress.

Anthropometric measurement was carried out by the same investigator. Body weight was determined to the nearest 0.1 cm by standard beam scale. Blood pressure was measured in the supine position after a rest of 5 minutes. Hypertension was defined as systolic and diastolic blood pressure greater than the 95th percentile for age and sex. Written parental consent and child assent were obtained before study.

After an overnight fast, blood was drawn from an antecubital vein for determination of biochemical parameters and MDA levels. Plasma glucose concentrations were determined by the glucose oxidase method. Plasma insulin, cholesterol and triglyceride concentrations were measured with Roche modular systems analyser. Friedwald formula for LDL and VLDL were used in calculations. MDA levels were determined by fluorometric method by using thiobarbituric acid (4)

All of the children were given an oral glucose tolerance test. The test results were evaluated according to the recommendation of the American Diabetes Association (5). Insulin resistance was assessed at baseline by using the homeostasis model assessment (HOMA). The HOMA-IR was derived as estimates of insulin sensitivity. HOMA-IR was calculated using the formula fasting insulin (U/mL) X fasting glucose (mmol/L)/22.5 . Insulin resistance is defined as the levels of the HOMA-IR greater than 3.16 (6).

Metabolic syndrome was defined following according to WHO criteria adapted for children. Metabolic syndrome was defined as having three or more components (7).

Analysis was performed using SPSS version 11.0 software for Windows. Data are reported as means ± SD (range). Unpaired *t*-test were used for comparisons of the variables between the obese and nonobese subjects. Statistical analysis was performed by Mann-Whitney U test. Due to the skewed nature of the indexes, validity was evaluated using Spearman correlation coefficients. $p<0.05$ was considered significant for all the data analyses.

RESULTS

The mean ± SD age was 11±1.7 (year), BMI 26.8±3.5 (kg/m^2) for obese children. The mean ± SD age (year) was 10.3±1.5, BMI 16.06±1.95 (kg/m^2) for non-obese children. None of the participants had diabetes. One child in obese group had impaired fasting glycemia, and another one had impaired glucose tolerance. Metabolic syndrome was absent in obese children.

Body weight, BMI were significantly higher in obese children as compared to the controls. As it was expected, the obese group had significantly higher fasting plasma insulin, fasting plasma glucose, plasma cholesterol, LDL-cholesterol and increased blood pressure values as compared to controls. The fasting HDL-cholesterol and triglyceride level were not significantly different between obese patients and the controls. Table-1 shows the biochemical values, MDA level and anthropometric indices in obese and normal control subjects. Serum MDA levels were significantly increased in obese children compared with non-obese children (Table-1). The plasma levels of MDA were significantly positive correlated with BMI in all (obese and nonobese) subjects ($r=0.506$; $p<0.05$) (Figure 1).

In obese children and non-obese

Table 1. Characteristics of obese and non-obese children (BMI body mass index, BP blood pressure, LDL low-density lipoprotein, HDL high-density lipoprotein MDA malondialdehyde)

	Obese children	Non-obese children
	32	20
Age (months)	132.44±21.74	124.05±19.43
BMI (kg/m^2)	26.85±3.51*	16.06±1.95
Systolic BP (mmHg)	104.69±12.95	95.0±13.95
Diastolic BP (mmHg)	70.94±11.74	61.0±7.18
Fasting glucose (mmol/L)	5.06±0.42*	4.65±0.49
Fasting insulin (U/mL)	15,95±11.01*	5.26±1.59
Cholesterol (mg/dL)	160.09±35.47*	138.05±17.80
LDL-cholesterol (mg/dL)	97.97±27.77*	75.15±17.13
HDL-cholesterol (mg/dL)	43.34±7.8	50.15±15.59
Triglycerides (mg/dL)	89.19±47.47	70.20±24.7
HOMA-IR	3.96±2.72*	1.21±0.55
MDA (Mmol/L)	9.85±3.7*	5.43±1.09

Values are mean s±d. *p<0.05

Table 2 Correlation coefficients (r) among MDA, BMI, and lipid fractions in obese children

(n=32) (A)

	BMI	Cholesterol	LDL-Cholesterol	Triglyceride
MDA	0.506 *	-0.013	-0.15	0.041

*p<0.05

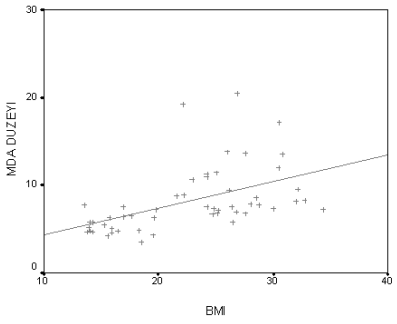

Figure 1: Correlation between the plasma levels of MDA and BMI in all (obese and nonobese) children.

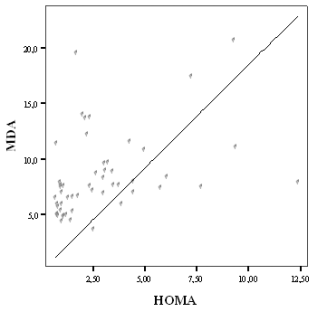

Figure 2.: Correlation between the plasma levels of MDA and HOMA-IR in all (obese and nonobese) children.

children, MDA level didn't correlated with serum cholesterol, LDL-cholesterol, triglyceride levels (Table 2).

We observed strong correlations between insulin concentrations and HOMA-IR values. Significant positive correlations were observed between HOMA-IR values and BMI in all subjects (r=0.592, p=0.0001). Significant positive correlations were observed between the plasma levels of MDA and the serum levels of insulin in all subjects (r=0.484, p=0.0001). Significant positive correlations were observed between HOMA-IR values and MDA level in all subjects (r=0.407, p=0.003) (Figure 2).

Significant negative correlations were observed between HOMA-IR values and HDL cholesterol level (r=-0,323, p=0.0019). Significant positive correlations were observed between HOMA-IR values and VLDL level (r=0.363, p=0.02).

DISCUSSION

The differences between the mean age distribution of the obese and control groups were not statistically significant ($p>0.05$). The similar mean age of groups has eliminated the influence of age on oxidative stress in the study.

Obese subjects are at high risk for atherosclerosis. Some disturbances have been detected in lipid metabolism and pro-oxidant-antioxidant balance in obese subjects (8,9). High serum cholesterol, LDL-cholesterol, and triglyceride and HDL-cholesterol levels have been detected in obese subjects (9-11). When lipid profiles of both groups in our study were compared, although there were significant increases in cholesterol and LDL levels in the obese group, these levels were in normal ranges ($p<0.05$). Lipid peroxidation play an important role in atherosclerosis pathogenesis. Cholesterol is believed to be the main risk factor in atherosclerosis pathogenesis and its pro-oxidant effect has been proved. Plasma lipid peroxide concentrations are high in hyperlipidemic patients (12). Although there were significant increases in lipid levels in obese group, these levels were in normal ranges and this may be the reason for the absence of corelation between MDA level and cholesterol, LDL-cholesterol and triglyceride levels in our study.

The relationship between insulin resistance and fasting lipids can be explained through the effect of insulin on lipoprotein metabolism. Insulin plays a central role in determining triglyceride clearance from the blood via activation of lipoprotein lipase and triglyceride output through effects on the synthesis and secretion of VLDL by the liver. It is thought that in the insulin-resistant state, triglyceride-rich lipoproteins accumulate in the circulation due to decreased activity of lipoprotein lipase, increased lipolysis in adipose tissue, and increased output of VLDL particles from the liver (13-14). The delay in plasma lipoprotein triglyceride clearance allows for cholesterol esters to be passed on from HDL to triglyceride-rich particles, wich results in potentially atherogenic lipoprotein particles (15). Although VLDL and HDL levels were in normal ranges in obese group, we speculate that increased VLDL and decreased HDL with increased HOMA-IR may show the atherogenic activity of insulin resistance in our study.

MDA assay of serum is the most frequently used method in clinical practice because of its sensitivity and simplicity, although several substances interfere with this assay (16). In this study, serum lipid peroxidation was evaluated by measuring MDA level in obese children. Previous studies have shown that the mean MDA levels are higher in obese individuals compared to nonobese healthy controls (17-19). It is also shown that obesity is associated with increases in endogenous lipid peroxides (20) . Recently, Dandona et al. (21) reported that the ratio of oxidative damage to lipids, proteins, and amino acids is increased in obese subjects. Significant decrease in oxidative stress after dietary restriction and weight loss has also been reported in obese subjects (21,22). In our study we also found high MDA levels in obese subjects than in nonobese ones like the general conclusion in these studies which is; obesity caused an oxidative stress by amplifying the lipid peroxidation products.

These findings suggest that obesity is an important factor for enhanced oxidative stress. When the interaction of oxidative stress with obesity complication, hyperinsulinemia and insulin resistnace, is obtained, the risk of life-threating results should be expected. Serious interventions in the childhood period may prevent future obesity-related oxidative damages.

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