



EVALUATION OF GALECTIN-3 LEVELS IN OBESE ADOLESCENTS

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Abstract

Background: Galectin-3 is a member of the family of soluble beta-galactoside binding lectins, which is involved in inflammation, cell differentiation, adhesion, proliferation, angiogenesis and cancer cell invasion. Increased galectin-3 levels in obese patients have been shown in previous studies. In our study; we aimed to investigate the galectin-3 levels in obese adolescents for the first time in the literature.

Materials and methods: A total of 85 adolescent patients who were admitted to our pediatrics outpatient clinic between December 19th of 2018 and January 31st of 2019 were included in our study. Among those patients 52 were obese and 33 were normal-weighted. Adolescents having body mass index (BMI) 95% percentile and above according to their age and sex were defined as obese. Enzyme-Linked Immunosorbent Assay kit was used for the measurement of galectin-3 in serum. Laboratory tests (Galectin-3, HbA1c, glucose, insulin, HOMA-IR), sex, age and BMI were statistically compared between groups.

Results: We found no statistically significant difference in terms of gender distribution rates, age, glucose or galectin-3 levels among obese adolescent and healthy control groups ($p > 0.05$). The BMI, HbA1c, HOMA-IR and insulin levels of the obese adolescent group were found to be significantly higher than the healthy control group ($p < 0.05$). We found no statistically significant correlation between galectin-3 levels and other parameters in obese adolescent group ($p > 0.05$).

Conclusion: In our study, we did not find any relationship between serum galectin-3 levels and obesity in adolescents. We believe that the effects of galectin-3 levels on obesity in adolescents should be more clearly explained by further investigations, which also measures other biomarkers of the mechanism of action.

Keywords: Galectin-3, obesity, adolescent

List of abbreviations: BMI: Body-Mass Index, CV: Variation coefficient, ELISA: Enzyme linked immunoassay, HOMA-IR: Homeostatic model of assessment-insulin resistance, IL: Interleukin, r: Correlation coefficient, SD: Standard deviation.

Introduction:

Galectin-3 is a member of the family of soluble beta-galactoside binding lectins, which is involved in inflammation, cell differentiation, adhesion, proliferation, angiogenesis and cancer cell invasion (1). The addition of recombinant galectin-3 in vitro induces preadipocyte proliferation (2). Extracellular galectin-3 stimulates apoptosis, while galectin-3 in intracellular compartments protects against apoptosis (3). Galectin-3, produced in various cell types such as epithelial cells, macrophages and adipocytes, is present in every part of the cell. Extracellular galectin-3 plays a role in the relationships between epithelial cells and extracellular matrix (4).

Increased levels of galectin-3 in obese patients have been shown in previous studies (5-7). Various mechanisms have been described before in this increase such as the defected adiponectin activity in obesity eliminates the inhibitory effect and causes an increase in galectin-3 levels or elevated interleukin-6 (IL-6) levels may also increase the galectin-3 levels (5,6). Some studies have reported that galectin-3 plays a protective role in obesity-related metabolic complications and inflammation (8, 9).

There is a low-grade inflammation due to the increase of proinflammatory cytokine levels in obesity characterized by excessive accumulation of lipids and adipose tissue that causes ectopic fat accumulation in different tissues (10, 11). In this study; we aimed to evaluate the levels of galectin-3 in obese adolescents and to investigate their correlations with other parameters.

Material and method:

A total of 85 adolescent patients aged between 10 and 16 years, who were admitted to our pediatrics outpatient clinic between December 19th of 2018 and January 31st of 2019 were included in this study. Among those patients 52 were obese and 33 were normal-weighted. Body mass index (BMI) was obtained by division of weight of the patient in kg to the square of the

height in meters. Adolescents having BMI 95% percentile and above according to their age and sex were defined as obese (12). For insulin resistance, Homeostatic model of assessment mg (HOMA-IR) was calculated with the $(\text{insulin IU / L} \times \text{glucose mg / dL}) / 405$ formula (13). The obese patients with HOMA-IR values of higher than 2.5 were considered to be obese adolescents with insulin resistance and those with a value of 2.5 or less were evaluated as adolescents without insulin resistance.

In obese and control groups, smokers, patients with chronic diseases, infection, metabolic and endocrinologic diseases, those who received drug treatments such as corticosteroids and those with malignancy were not included in the study. In addition, adolescents having normal-weight but insulin resistance were not included in the healthy control group.

The patients who were observed to be in compliance with the inclusion criteria were informed about the study (in addition to routine examinations, an additional 1 tube of blood will be taken for the study). After obtaining informed consent form from the volunteers who wanted to participate in the study, detailed medical histories of the participants were achieved. From the volunteers, while obtaining blood for their routine examinations, only one more biochemistry tube blood was taken for the study. The serum was kept at room temperature for 20 minutes, and then the blood tube was centrifuged at 4000 rpm for 10 minutes and stored at -80 ° C.

On the day of analysis, sera were allowed to dissolve at room temperature. Enzyme-Linked Immunosorbent Assay (ELISA) kits were used for the measurement of Galectin-3 levels in serum (Human Galectin-3 ELISA, Bioassay Technology Laboratory Lot No: E1811005). The analytical (linear) measurement range was 5 - 2000 pg / mL for galectin-3. The minimal detection limit was 2.49 pg / mL. The reported intraassay and interassay CV's were <8% and <10%, respectively.

Hemoglobin A1c (HbA1c) was measured in autoanalyzer (Biorad, Variant II turbo, Japan) with the high performance liquid chromatography method, glucose was measured by colorimetric method, insulin was measured in autoanalyzer with Chemiluminescence immunoassay (Beckman Coulter Brand, AU 5800 model, USA).

Laboratory tests (Galectin-3, HbA1c, glucose, insulin, HOMA-IR), sex, age and BMI were compared between the groups. Correlations between galectin-3 and other laboratory parameters were examined in obese adolescent group.

The present study was approved by the Local Ethics Committee (date:December 18th of 2018; no: 1076) and performed in accordance with the guidelines of the Declaration of Helsinki.

Statistical Analyses: IBM SPSS Statistics 22 (IBM SPSS, Turkey) program was performed for the statistical analyses. The fit of the parameters to normal distribution was evaluated by Shapiro Wilks test. In comparison of two groups, Student t-test was performed to compare the parameters with normal distribution and Mann-Whitney U test was used to compare the parameters that did not show normal distribution. Chi Square test

and Continuity (Yates) correction were performed to compare qualitative data. Pearson correlation analysis was used to examine the relationships between parameters with normal distribution and Spearman’s rho correlation analysis was performed to examine the relationships between parameters which are not compatible with normal distribution. Significance was evaluated as $p < 0.05$.

Results:

The study was carried out with 85 volunteer adolescents, 52 obese patients and 33 healthy control cases with normal weight. Forty three of the obese adolescents were having insulin resistance while 9 did not have insulin resistance. The mean age of the adolescents was 12.83 ± 1.96 years. The mean BMI was 28.28 ± 5.24 kg / m². Demographic and laboratory data of the study groups were compared (Table 1).

We found no statistically significant difference in terms of gender distribution rates, age, glucose or galectin-3 levels among obese adolescent and healthy control groups ($p > 0.05$).

The BMI, HbA1c, HOMA-IR and insulin levels of the obese adolescent group were found to be significantly higher than the healthy control group ($p < 0.05$).

Table 1: Demographic and laboratory data of Obese and Control Adolescent Groups

	Obese Adolescent Group (n:52)	Healthy Control Adolescent Group (n:33)	p
	Mean±SD	Mean±SD	
Age (year)	12.79±2.04	12.88±1.84	¹ 0.848
Gender n (%)			
female	20 (38.4%)	16 (48.4%)	² 0.495
male	32 (61.6%)	17 (51.6%)	
BMI (kg/m ²)	31.29±3.75	23.29±3.09	¹ <0.001*
Galectin-3 (pg/mL) (median)	412.85±616.42 (162.2)	527.41±847.91 (122)	³ 0.853
HbA1c (%)	5.49±0.36	5.2±0.33	¹ 0.002*
Glucose (mg/dL)	89.91±9.47	87.92±8.88	¹ 0.391
HOMA-IR (median)	4.08±2.05 (3.6)	1.84±0.77 (1.6)	³ <0.001*
Insulin (IU/L) (median)	18.29±8.58 (16.8)	8.35±3.17 (7.8)	³ <0.001*

¹Student t test ²Continuity (Yates) correction ³Mann Whitney U test *p<0.05
 BMI: Body-Mass Index, HOMA-IR: Homeostatic model of assessment- insulin resistance, SD: Standard deviation.

Correlations between galectin-3 and other parameters were evaluated in the obese adolescent group (Table 2). We found no significant correlation between galectin-3 levels and other parameters in obese adolescent group (p> 0.05).

Table 2: Correlations between galectin-3 levels and other parameters in obese adolescent group

	Galectin-3 levels	
	r	p
BMI	-0,187	0,229
HbA1c	-0,075	0,632
Glucose	0,157	0,315
HOMA-IR	-0,104 ⁺	0,507
Insulin	-0,112 ⁺	0,475

Pearson’s correlation analysis ⁺Spearman Rho correlation analysis r: correlation coefficient

Discussion

Obesity is a general risk factor for insulin resistance, hypertension, glucose intolerance, hepatic steatosis, atherogenic dyslipidemia and type 2 diabetes mellitus (14). During the development of obesity, macrophages permeate into white adipose tissue and secrete various proinflammatory cytokines and chemokines along with adipocytes (15, 16). Galectin-3 plays an important role in the development of inflammation by interacting with various cytokines and chemokines (17). In an experimental study on Galectin-3 knock-out mice, it was reported that while in vivo galectin-3 administration resulted in glucose intolerance and insulin resistance; in vitro treatment with galectin-3 inhibitors might reduce insulin sensitivity directly on myocytes, hepatocytes and adipocytes (18). In addition, the protective role of galectin-3 has been mentioned in some studies (8, 9). Moreover, galectin-3 binds to advanced glycation end products that cause tissue damage related to the severity of diabetic complications and it has been reported that it protects the tissue damage due to stimulating their breakdown (19).

In our study, we investigated serum galectin-3 levels in adolescents for the first time in the literature. When we looked at the other studies related to this subject, we observed that the studies were generally on the experimental level, while a few studies were conducted in humans. Weigert et al. reported high levels of serum galectin-3 in obese and type 2 diabetic patients (7). In the study of Rhodes et al., they showed that the expression of galectin-3 increased in visceral and subcutaneous adipose tissue in obese mice induced by high fat diet (20). Yilmaz et al. reported that high levels of galectin observed in prediabetes and diabetes resulted in development of diabetes and its complications (21). Li et al. reported that galectin-3 levels were increased in obesity and it was a proinflammatory molecule that would cause insulin resistance (18). In our study, we found that serum galectin-3 levels of obese adolescents were not statistically significantly different compared to normal weighted healthy adolescents. Since this is the first study in the literature evaluating the serum galectin-3 levels in the adolescent patients, we did not have the

opportunity to compare our results directly with previous literature.

In our study, we also investigated the correlations between galectin-3 levels and parameters related to obesity and glucose metabolism. We found no statistically significant correlation between galectin-3 levels and BMI, glucose, insulin or HOMA-IR levels in the obese adolescent group. Weigert et al. reported a positive correlation between galectin-3 levels and BMI in type 2 diabetes mellitus and a negative correlation with HbA1c (7). Dencker et al. reported a positive correlation between galectin-3 levels and BMI in a study on non-obese children (22). Ohkura et al. reported that low galectin-3 levels were associated with insulin resistance (insulin levels and HOMA-IR) in type 2 diabetes but not with BMI (23). A negative correlation was reported between galectin-3 and HOMA-IR levels by Li et al (18). It can be seen that the results of correlation analyzes in the previous studies are contradictory.

To discover the potential relationships between BMI and other markers against galectin-3 at a young age is important because of the increased risk of developing obesity in adulthood and the likelihood of serious short-term and long-term health problems in obese children and adolescents (24,25). In this respect, our study data in adolescents makes it difficult to establish a relationship between the levels of obesity and galectin-3 observed in this group. This may be explained by the difference in the serum galectin-3 pattern in adolescents. Because obese adults are often decompensated by glucose metabolism, but obese children often have an early phase of alteration in glucose metabolism (26). In addition, we did not measure the levels of inflammatory cytokines in this study. Also, we did not analyze the galectin-3 levels at different stages of obesity which are the limitations of this study. Since galectin-3 plays a role in the development of inflammation by interacting with various cytokines (5, 6, 17), we believe that the cytokine pattern in obesity may have a different

effect than the expected on the galectin-3 synthesis, which may also influence our results.

In conclusion, we did not find any correlation between serum galectin-3 levels and obesity in adolescents. We believe that the effects of galectin-3 levels on obesity in adolescents should be analyzed in further investigations, which measures other biomarkers of the mechanism of action.

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