Evaluation of Subclinical Atherosclerosis by Non-Invasive Radiological Methods along with Soluble Endoglin and Nitric Oxide Levels in Adolescents with Type 1 Diabetes

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The authors declare that there are no conflicts of interest

BACKGROUND

Presumably the same hyperglycemia-induced mechanisms responsible for the occurence of microvascular complications may also be valid for the development of atherosclerosis. Identification of early endothelial dysfunction (ED) in children and adolescents with type 1 diabetes mellitus (T1DM) predicts later development of long-term microvascular complications and further target-organ damage, and as well as related future macrovascular complications leading to cardiovascular diseases.

OBJECTIVE

The aim of this study was to evaluate ED of adolescents with T1DM with respect to the presence of microalbuminuria, as measured flow-mediated dilatation (FMD) of the brachial artery and carotid intima media thickness (CIMT) along with plasma soluble endoglin (S-endoglin) and serum nitric oxide (NO) levels.

METHODS

Fifty-eight adolescents with moderately-poorly controlled T1DM were recruited from Gazi University Hospital, Pediatric Endocrinology Clinic. They were further divided into two groups based on the presence of microalbuminuria, as microalbuminuric group (n=15, age of 16.30±2.17 years, diabetes duration of 7.88±3.4 years) and normalbuminuric group (n=33, age of 15.14±1.55 years, diabetes duration of 6.02±3.2 years). Twenty-nine healthy adolescents (mean age 15.03±1.97 years) were selected as a control group. Serum S-endoglin, plasma NO, FMD and CIMT were evaluated in all subjects.

RESULTS

The three groups did not differ regarding age, gender, height standard deviation score and body mass index standard deviation score ($p>0.05$ for all). No statistically significant difference was found in glycated hemoglobin levels between microalbuminuric and normalbuminuric groups. The NO levels of both microalbuminuric and normalbuminuric groups were higher than that of the control group ($p=0.004$ and $p=0.006$, respectively). Soluble endoglin level was higher in the normalbuminuric group as compared to the control group ($p<0.001$). The FMD percent was lower in the microalbuminuric group as compared to the normalbuminuric and control groups ($p=0.020$ and $p=0.036$, respectively). No statistically significant difference was found in CIMT among all groups ($p=0.443$). Tables 1 and 2 display these results along with p values. No significant correlation between NO, S-endoglin, FMD and CIMT was found.

	Microalbuminuric Group (n=15)	Normalbuminuric Group (n=43)	Control Group (n=29)	p
Sex (F/M)	8/7	17/26	15/14	0.714
Age (years)	16.30 ±2.17	15.14±1.55	15.03±1.97	0.061
Height SDS	0.37±0.53	-0,08±0.91	0.01±0.91	0.059
BMI SDS	0.62±0.53	0.57±0.76	0.26±0.69	0.142
p-HbA1c (%)	9.59±2.24	9.30±2.23	-	0.365*

Data are means ± SE
F: female, M: male, SDS: standard deviation score, BMI: body mass index,
p-HbA1c; mean glycated hemoglobin of the preceding year
*: microalbuminuric group vs normalbuminuric group

Table 1- Characteristics of study and control groups

	Microalbuminuric Group (n=15)	Normalbuminuric Group (n=43)	Control Group (n=29)	p
NO (µmol/L)	47.8±17.6	46.6±20.8	35.6±16.2‡	0.005
S-endoglin (ng/ml)	2.35±0.65	2.68±0.66†	1.97±0.44	<0.001
FMD (%)	7.53±3.29‼	9.93±3.51	10.9±4.01	0.032
CIMT (mm)	0.47±0.08	0.43±0.08	0.43±0.06	0.443

Data are means ± SE
NO: nitric oxide, S-endoglin: soluble endoglin ,FMD: flow mediated dilatation, CIMT: carotid intima media thickness
‡: vs normalbuminuric group and vs microalbuminuric group, p<0.05 for both, †: vs control group, p<0.05
‼: vs normalbuminuric group and vs control group, p<0.05 for both

Table 2- NO, S-endoglin, FMD and CIMT results of study and control groups

CONCLUSIONS

These data suggest that, although structurally not proved, evidence of ED shows that type 1 diabetic patients with microalbuminuria are at an increased risk for premature atherosclerosis as compared to those without and controls. Significantly higher S-endoglin level in the normalbuminuric group relative to the control group may be a marker of ED in the early stage of diabetic process before the emergence of apparent microvascular damage in patients with T1DM. Thus, long-term prospective studies measuring S-endoglin levels periodically in patients with diabetes are needed to better elucidate the relationship of S-endoglin with atherosclerotic process and microvascular complications of T1DM.

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