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Increased serum sialic acid in diabetic retinopathy of type 1 diabetes

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Foundation item: Marmara University Scientific Research Committee

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Received: 2013-07-10 Accepted: 2013-09-03

1 型糖尿病视网膜病变患者血清唾液酸浓度的增加

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基金项目:马尔马拉大学科学研究委员会资助

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摘要

目的:探讨血清唾液酸和糖尿病性视网膜病变几个阶段之间潜在的关联。

方法:1 型糖尿病视网膜不同程度病变组 40 例。对照组 30 例,对其血清唾液酸水平进行研究。

结果:结果显示,研究组与对照组相比有较高的血清唾液酸浓度(95.95±9.5 *vs* 45.05±19.91mmoL/L, $P=0.0001$)。我们也观察到糖尿病性视网膜病变的水平逐步上升,其浓度升高($P<0.05$),但相关性较弱。血清唾液酸浓度与血糖浓度呈正相关($r=0.67$, $P=0.0001$)。

结论:血清唾液酸浓度的增加与视网膜病变阶段有关。这对确定 1 型糖尿病患者视网膜病变的程度有帮助。但是,仍然需要更详细的研究,以得到更精确的结论。

关键词:糖尿病;糖尿病性视网膜病变;血清唾液酸;糖化血红蛋白

引用:Eraslan M, Yenice O, Kazokoglu H, Yavuz DG, Cerman E, Celiker H. 1 型糖尿病视网膜病变患者血清唾液酸浓度的增加. 国际眼科杂志 2013;13(10):1950-1952

Abstract

• AIM: To investigate the potential association between serum sialic acid and diabetic retinopathy and its several grades.

• METHODS: We studied the level of serum sialic acid in 70 patients. Thirty control *vs* 40 type 1 diabetics and with different levels of diabetic retinopathy as well.

• RESULTS: We found higher levels of serum sialic acid level in diabetics compared to control subjects (95.95±9.5 *vs* 45.05±19.91mmoL/L, $P=0.0001$). We also observed a progressive rise in its concentration as the level of diabetic retinopathy increased ($P<0.05$) but the correlation was weak. Serum sialic acid level correlated positively with blood glucose level ($r=0.67$, $P=0.0001$).

• CONCLUSION: Increase in serum sialic acid levels seems to be related to the stage of the retinopathy and may help us to determine the extent of retinopathy in type 1 diabetic patients. But we think that we need more detailed studies to get a more precise conclusion.

• KEYWORDS: diabetes; diabetic retinopathy; serum; sialic acid; HbA_{1c}

DOI:10.3980/j. issn. 1672-5123. 2013. 10. 02

Citation: Eraslan M, Yenice O, Kazokoglu H, Yavuz DG, Cerman E, Celiker H. Increased serum sialic acid in diabetic retinopathy of type 1 diabetes. *Guoji Yanke Zazhi* (*Int Eye Sci*) 2013;13(10):1950-1952

INTRODUCTION

Sialic acid (SA) is the generic name for compounds derived from neuraminic acid. Serum sialic acid concentration, is a marker of the acute phase response, has been shown to be a strong predictor of cardiovascular disease in the general white population, with raised concentrations being associated with enhanced coronary heart disease and stroke mortality[1-5]. Diabetes mellitus is associated with an increase in sialic acid concentration along with other complications[5]. However, conflicting results regarding the association between serum sialic acid and diabetic micro and macroangiopathy have been presented[6-13]. Additionally serum sialic acid was reported to be involved in the pathogenesis of diabetic microangiopathic complications thus one would expect higher levels of it with increasing levels of microangiopathic complications[14]. In this study, we aimed to investigate the potential association between serum sialic acid and diabetic retinopathy and its several grades.

SUBJECTS AND METHODS

Subjects We included 40 outpatients with type 1 diabetes mellitus. Control group included 30 healthy subjects that came to our clinic for refractive problems. The research followed the tenets of the declaration of helsinki and informed

consent was obtained from the subjects after explanation of the nature and possible consequences of the study and also approved by Institutional Review Board (IRB).

Patients with hypertension, myocardial infarction, cerebrovascular disease, connective tissue disorders and heart failure, who are under treatment with antiaggregants, steroids or other drugs that effect blood pressure and glucose, and cases with serum creatinine >200μmoL/L were excluded from the study.

The ocular fundus was examined by an ophthalmologist after dilation of the pupils and classified with the help of fluorescein angiography. The patients were divided into patients without retinopathy (Group R_0, n:19), with non proliferative retinopathy (Group R_1, n:10) and those with proliferative retinopathy (Group R_2, n:11).

Methods Venous samples were drawn after an overnight fast and serum sialic acid level was determined as follows: Serum sialic acid was measured in serum with a colorimetric method described by Svennerholm with a Shimadzu UV - 1201 spectrophotometer (Shimadzu, Japan) with a wavelength of 525nm. Using N-acetyl neuraminic acid (Sigma catalog no: A 3007) as standard[14]. Intra assay and inter assay coefficients of variations were 6.6% and 9.2% for 1mmol/L sialic acid respectively.

HbA_{1C} (reference range 4.4% - 6.0%) was measured by a turbidimetric inhibition immunoassay technique (Roche Diagnostics, USA).

Statistical Analysis Nonparametric tests (Mann - Whitney U) were used in comparing diabetic patients to control subjects and Kruskal - Wallis test was used in subgroups of diabetics. Analysis of covariance was used to calculate means adjusted for diabetes duration and to assess differences between trends in adjusted means. Correlation analysis was performed with Spearman rank test. The results were given as mean±SD. SPSS/PC 10.0 (SPSS Inc., Chicago, IL) was used. $P<0.05$ was considered as statistically significant.

RESULTS

The clinical characteristics of the study groups are shown in Table 1. Results of laboratory parameters are shown in Table 2. Serum cholesterol, triglyseride and HDL levels were not statistically different between diabetic patients and control subjects. The fasting blood glucose level was significantly higher in the diabetic patients ($P=0.0001$).

When we compared the serum sialic acid level between control patients and diabetic subjects, the results were 45.05±19.91 *vs* 95.95±9.5 correspondingly and the difference between them were statistically significant ($P=0.0001$) (Table 3).

Fasting blood glucose and HgA_{1c} levels were not different in subgroups of diabetic population. Diabetes duration were 3.94±2.41, 10.2±4.34 and 15±6.14 in Group R_0, Group R_1 and Group R_2 correspondingly and the difference between groups were statistically significant ($P=0.0001$). After adjusting for diabetes duration, blood glucose and HgA_{1c}, we observed a progressive rise in serum sialic acid concentration as the degree of diabetic retinopathy increased ($P=0.019$).

Table 1 Demographic characteristics of the study groups

Parameter	Control group $n=30$	Diabetic patients $n=40$
Age (a)	29.52±8.7	27.13±6.30
M/F	18/12	19/21
Duration of diabetes(a)	-	8.32±6.12

Table 2 Laboratory parameters of the study groups

Parameter	Control group	Diabetic patients
Fasting blood glucose (mg/dL)	100±26	215±116
HbA_{1c}(%)	4.75±0.82	7.75±1.34
Cholesterol (mg/dL)	180±43	192±56.66
Triglycerides (mg/dL)	121±45	134±37
HDL (mg/dL)	49±8	45±7

Table 3 Serum sialic acid concentrations in nondiabetic control subjects and Type 1 diabetic patients

Groups	Serum sialic acid (mmoL/L)
Control subjects	45.05±19.91
Type I diabetic patients	
Group R_0	97.22±4.30
Group R_1	90.68±16.39
Group R_2	98.54±16.39

Table 4 Simple linear regression analysis of serum sialic acid concentration and demographic and laboratory parameters

Independent variables	Correlation coefficient	P
Age(a)	-0.24	0.8
Diabetes duration (a)	-0.25	0.12
HbA_{1c}(%)	-0.05	0.91
Fasting blood glucose(mg/dL)	0.67	0.0001
Cholesterol (mg/dL)	0.03	0.81
Triglycerides (mg/dL)	0.34	0.7
HDL (mg/dL)	0.23	0.92

$P<0.05$ is statistically significant.

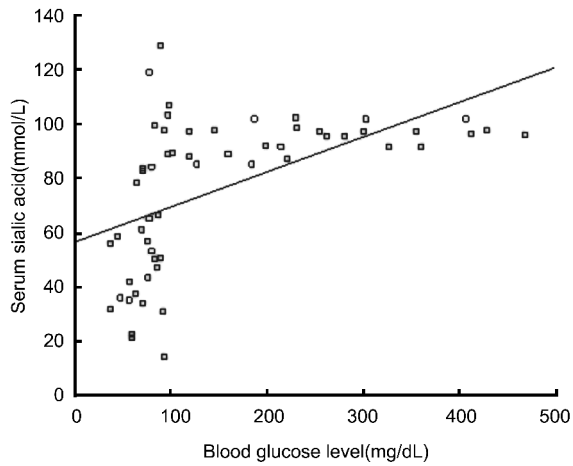

Figure 1 The correlations between serum sialic acid age and fasting blood glucose; serum sialic acid level correlated significantly with blood glucose level ($r=0.67$, $P=0.0001$).

When we looked at the correlations between serum sialic acid age and laborotary parameters (HbA_{1C}, cholesterol, fasting blood glucose, Triglycerides, HDL); serum sialic acid level correlated significantly only with blood glucose (Figure 1) level ($r=0.67$, $P=0.0001$) and others were not significant ($P>0.05$) (Table 4).

DISCUSSION

The associations between various markers of inflammation and the incidence of diabetes and its complications have been reported previously[14,15]. Studies of Nayak *et al*[15] shows the significant increase in serum sialic acid levels in diabetics with complications compared to non diabetic controls or diabetics without complications. A relationship between serum sialic acid levels and diabetic retinopathy has also been observed before[8,10,12,15]. On their study Kurtoglu *et al*[16] found that serum TSA/TP ratio might be an indicator as an index of diabetic complications.

Our cross-sectional study additionally revealed progressive raise in serum sialic acid concentrations with increasing diabetic retinopathy levels suggesting an effect per se of the diabetic state. This result has been also reported by Roozbeh *et al* and Nayak *et al* for diabetic nephropathy[7,16-20].

In this study, the association between sialic acid and blood glucose most likely follows from the association between sialic acid and microvascular complications. Plasma sialic acid is a marker of the acute phase response, acute phase glycoproteins with sialic acid as a component of the oligosaccharide side chain being produced by the liver, stimulated by pro-inflammatory cytokines. Thus increase in serum sialic acid level in type 1 diabetics with retinopathy lesions can be explained with the production of local cytokines by macrophages of the vessel endothelium or throughout the body due to diabetic process itself.

In conclusion, we found higher levels of serum sialic acid in patients with higher levels of diabetic retinopathy. This result can not result from diabetes duration, HgA_{1c} level and blood glucose, as after adjusting for these confounding factors serum sialic acid level still were increasing in the diabetic group as the degree of retinopathy increased. Thus increase in serum sialic acid levels seems to be related to the stage of the retinopathy and maybe able to determine the extent of retinopathy in type 1 diabetic patients. We also agree with the other study about diabetic nephropathy, and think that sialic acid may be involved in the pathogenesis of lesions that are observed in diabetic retinopathy. But we think that we need more detailed studies to get a more precise conclusion.

REFERENCES

1 Duncan BB, Schmidt M, Pankow JS. Low grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. *ADA* 2003;52:1799-1805

2 Soedamah-Muthu SS, Chaturvedi N, Pickup JC, Fuller JH. Relationship between plasma sialic acid and fibrinogen concentration and incident micro- and macrovascular complications in type 1 diabetes. The EURODIAB Prospective Complications Study (PCS). *Diabetologia* 2008;51:493-501

3 Soedamah-Muthu SS, Fuller JH, Mulnier HE. High risk of cardiovascular disease in patients with type 1 diabetes in the U.K.: a cohort study using the general practice research database. *Diabetes Care* 2006; 29:798-804

4 Knuiman MW, Watts GF, Divitini ML. Is sialic acid an independent risk factor for cardiovascular disease? A 17-year follow-up study in Busselton, Western Australia. *Ann Epidemiol* 2004;14:627-632

5 Laing SP, Swerdlow AJ, Slater SD. Mortality from heart disease in a cohort of 23,000 patients with insulin-treated diabetes. *Diabetologia* 2003;46:760-765

6 Browning LM, Jebb SA, Mishra GD. Elevated sialic acid, but not CRP, predicts features of the metabolic syndrome independently of BMI in women. *Int J Obes Relat* 2004;28:1004-1010

7 Rahman I, Malik SA, Bashir M, Khan R, Iqbal M. Serum sialic acid changes in non-insulin-dependant diabetes mellitus (NIDDM) patients following bitter melon(Momordica charantia) and rosiglitazone (Avantia) treatment. *Phytomedicine* 2009;16: 401-405

8 Sabzwari MJ, Ahmad M, Majeed MT, Riaz M, Umair M. Serum Sialic acid concentration and type 2 diabetes mellitus. *Professional Med J* 2006; 13(4):508-510

9 Khurshid MU, Us I. Sialic acid as a predictor of type 2 diabetes mellitus. *Professional Med J* 2008;15(2):273-275

10 Crook MA, Khanhadia S, Lumb P, Ridha A, Hussain A. No differences in serum sialic acid in type 2 diabetic patients from the United Arab Emirates with and without diabetic retinopathy. *Diabetes Res Clin Pract* 2000;47:147-150

11 Nayak BS, Duncan H, Lalloo S, Maraj K, Matmungal V, Matthews F, Prajapati B, Samuel R, Sylvester P. Correlation of microalbumin and sialic acid with anthropometric variables in type 2 diabetic patients with and without nephropathy. *Vascular Health and Risk Management* 2008;4(1):243-247

12 Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. *Diabetes Care* 2004;27:813-823

13 Varki A. Sialic acids in human health and disease. *Trends in Molecular Medicine* 2008;14(8):351-360

14 Crook MA, Pickup JC, Lumb PJ, Georgino F, Webb DJ, Fuller JH. Relationship between plasma sialic acid concentration and microvascular complications in type 1 diabetes. *Diabetes Care* 2001;24:316-321

15 Nayak BS, Bhakta G. Relationship between Sialic acid and metabolic variables in Indian type 2 diabetic patients. *Lipids Health Dis* 2005;4: 15-17

16 Kurtoglu S, Atabek ME, Muhtaroglu S, Keskin M. The association of serum total sialic acid/total protein ratio with diabetic parameters in young type 1 diabetic patients. *Acta Diabetol* 2006;43:1-5

17 Roozbeh J, Merat A, Bodagkhan F, Afsharian R, Yarmohammadi H. Significance of serum and urine neuroaminidase activity and serum and urine level of sialic acid in diabetic nephropathy. *Int Urol Nephrol* 2011; 43:1143-1148

18 Giordano M, Ciarambino T, Gesue` L, Castellino P, De Simone M, Rinaldi G, D'Amora M, Zito G, Paolisso G, Coppola L. The ratio between kidney volume and function increases with the progression of nephropathy in Type 2 diabetes. *Clin Nephrol* 2009;72(4):247-251

19 Nayak BS, Roberts L. Relationship between inflammatory markers, metabolic and anthropometric variables in the Caribbean type 2 diabetic patients with and without microvascular complications. *J Inflamm (Lond)* 2006;3:17-22

20 Phillip MH. Prevention of progression in diabetic nephropathy. *Diabetes Spectrum* 2006;19:18-24