

EFFECT OF DURATION AND TYPE OF DIABETES ON CEREBRAL HEMODYNAMICS

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SUMMARY – A group of 100 patients aged 48–67 years, with a diagnosis of diabetes mellitus, and control group of 100 healthy subjects were examined by transcranial Doppler sonography, a modern and sophisticated diagnostic method for visualization of hemodynamic changes in basal cerebral arteries in real time. The aim of the study was to determine hemodynamic changes in cerebral arteries in diabetic patients, and to analyze the effect of duration and type of diabetes on cerebrovascular disease. The rate of transcranial Doppler sonography abnormalities was statistically significantly higher in diabetic patients than in control subjects (55% vs. 11%, $\chi^2=$, $p<0.05$). The duration and type of diabetes were found to have an impact on the development of pathologic cerebrovascular changes. Hemodynamic impairments were more common in type 1 than in type 2 diabetes patients (72.5% vs. 43.3%). The study suggested the duration of diabetes to predict for the development of atherosclerotic processes in cerebral vessels. Atherosclerotic changes were found in 34.0% and 71.4% of patients suffering from diabetes for <5 and ≥ 5 years, respectively. In all diabetic patients, signs of cerebral microangiopathy were significantly more commonly recorded than those of cerebral macroangiopathy.

Key words: *Cerebrovascular disorders, etiology; Diabetic angiopathies, complications; Diabetes mellitus, complications; Risk factors; Ultrasonography, Doppler, transcranial*

Introduction

Diabetes mellitus is a major independent risk factor for cerebrovascular disease (CVD), especially for ischemic stroke. After adjustment for age, blood pressure, cigarette smoking and cholesterol level, diabetics have a 3-fold risk for cardiovascular diseases present in nondiabetics. This also applies to cardiovascular death, coronary heart disease and stroke^{1,2}. The National Health Study in USA has shown that about 5% of patients had type 1 (insulin dependent) diabetes, and the remainder had type 2 (non-insulin dependent) diabetes³. Insulin has an important role in the development of atherosclerosis in diabetics, probably because of

metabolic changes. Pathologic changes in diabetics occur as a macrovascular disease (macroangiopathy) or microvascular complications (microangiopathy). Transcranial Doppler sonography (TCD) is a modern and sophisticated diagnostic procedure, which enables visualization of hemodynamic changes in basal cerebral arteries in real time, and recording of changes in cerebral perfusion at various physiological and pathophysiological states⁴⁻⁸.

The aim of the study was to determine hemodynamic changes in cerebral arteries in diabetic patients, and to analyze the effect of duration and type of diabetes on the development of cerebrovascular disease.

Patients and Methods

The study included a group of 100 patients aged 48–67 years, with the diagnosis of diabetes mellitus, and an age- and sex-matched control group of 100 healthy sub-

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jects. Diabetic patients were divided into two subgroups according to the duration (<5 and ≥ 5 years) and type of diabetes (type 1, insulin dependent diabetes, and type 2, non-insulin dependent diabetes).

TCD was performed by leaning a pulsating ultrasound 2 MHz probe against temporal windows, and screening the flow in the blood vessels of the circle of Willis according to standard criteria. A hemodynamic chart was designed, the frequency of the mean blood flow velocity spectra (MBFV; systolic, diastolic and mean) recorded was analyzed, and sound phenomena and flow disturbances in terms of turbulence, stenosis or occlusion were recorded. The findings were analyzed and compared with normal TCD findings⁹. On statistical analysis, the proportion test was used.

Results

TCD investigation shows two specific types of hemodynamic changes in diabetic patients: one type of changes is attenuation of cerebral spectra and deceleration of MBFV in all arteries of the circle of Willis or in most of them, which indicate cerebral microangiopathy; the other type of changes is acceleration of MBFV, turbulence and pathologic sound phenomena in some arteries of the circle of Willis, which indicate atherosclerotic plaques and stenosis of arteries of the circle of Willis or macroangiopathy. We found a statistically significantly higher rate of abnormalities in diabetic patients than in the control group of healthy subjects (55% *vs.* 11%; $p < 0.05$).

Type of diabetes plays a prominent role in the development of cerebrovascular disease in diabetic patients as well as in the character of these lesions. In the group of 40 diabetic patients with type 1 diabetes, nine (22.5%) had signs of macroangiopathy and 20 (50.0%) signs of microangiopathy. In the group of 60 patients with type 2 diabetes, six (10%) had macroangiopathy and 20 (33.3%) microangiopathy. In the control group, macroangiopathy was not observed in any of the subjects, whereas microangiopathy was detected in 11% (Table 2). The results suggested that atherosclerotic lesions were more common in type 1 (72.5%) than in type 2 (43.3%) diabetes, the difference being statistically significant ($p < 0.05$).

Comparison of the duration of diabetes and changes in cerebral hemodynamics in diabetic patients produced interesting results as well. In the group of 44 diabetics with diabetes duration of up to 5 years, signs of macroangiopathy were observed in three (6.8%), and signs of microan-

Table 1. Results of TCD examination

	Diabetic patients (N=100)	Control subjects (N=100)
	n	n
Normal TCD	45	89
Abnormal TCD	55	11

$p = 0.000000000036$

Table 2. Proportion of patients with cerebral hemodynamics impairments according to type of diabetes

	Diabetic patients (N=100)		Control subjects (N=100)
	Type 1 (n=40) (%)	Type 2 (n=60) (%)	(%)
Macroangiopathy	22.5	10.0	0
Microangiopathy	50.0	33.3	11.0
Total	72.5	43.3	11.0

$p = 0.004$

Table 3. Proportion of patients with cerebral hemodynamics impairments according to duration of diabetes

	Diabetic patients (N=100)		Control subjects (N=100)
	<5 years (n=44) (%)	≥ 5 years (n=56) (%)	(%)
Macroangiopathy	6.8	21.4	0
Microangiopathy	27.2	50.0	11.0
Total	34.0	71.4	11.0

$p = 0.00019$

giopathy in 12 (27.2%) patients. In the group of 56 diabetics with diabetes duration of ≥ 5 years, macroangiopathy and microangiopathy were present in 12 (21.4%) and 28 (50.0%) patients, respectively. Pathologic atherosclerotic lesions of cerebral arteries were found in 34% of diabetic patients with diabetes duration of <5 years and 71.4% of

those with diabetes duration of ≥ 5 years. These results yielded a statistically significantly higher rate of pathologic cerebral artery changes in patients with diabetes duration of ≥ 5 years ($p < 0.05$). In the control group, macroangiopathy was not detected at all, whereas microangiopathy was detected in 11% of the subjects (Table 3).

Discussion

According to literature data, diabetes mellitus is one of the most important risk factors for CVD^{1,10}. In the Framingham study, the incidence of stroke in diabetic patients aged 45-74 was 2.5- to 3.5-fold that found in nondiabetics¹⁰. In diabetics, the risk of stroke is twofold that in nondiabetics¹¹, and diabetic patients are at a higher risk of stroke recurrence¹². Diabetes mellitus is a metabolic disease involving all arteries and frequently associated with stroke development along with peripheral vasculopathy and coronary disease^{1,13-16}. The mechanism of atherosclerotic changes in diabetic patients has not yet been fully elucidated, however, the following candidate causes have been proposed: decrease in HDL cholesterol, proliferation of smooth muscle cells, changes in the metabolism of glucosaminoglycans, increased level of thromboxane, decreased prostacyclines, and blood coagulation impairment. Insulin stimulates smooth muscle cell proliferation in the arterial wall and activity of LDL receptors¹⁷⁻²⁰. In our study, we found a significant relationship between the duration of diabetes and cerebral hemodynamics disturbances. In the group of diabetic patients with the disease duration of < 5 years, signs of macroangiopathy were present in 6.8%, and those of microangiopathy in 27.2% of patients. In the group of diabetic patients with the disease duration of ≥ 5 years, the respective rates were 21.4% and 50.0%. Thus, atherosclerotic changes were more common in the group of diabetic patients with a longer disease duration (71.4% *vs.* 34.0%). Also, microangiopathy was found to have more frequently developed than macroangiopathy in both types of diabetes mellitus. Type of diabetes is very important in the development of cerebrovascular disease as well as for the character of changes in diabetic patients. In the group of type 1 diabetics, signs of macroangiopathy and microangiopathy were detected in 22.5% and 50.0% of patients, respectively. In the group of type 2 diabetics, the respective rates were 10.0% and 33.3%. Accordingly, atherosclerotic changes were more common in type 1 than in type 2 diabetics (72.5% *vs.* 43.3%). Also, cerebral microangiopathy

was more frequently present than macroangiopathy in both types of diabetes mellitus.

Conclusion

The results of our study showed the prevalence of cerebral hemodynamics abnormalities to be statistically significantly higher in diabetic patients as compared with healthy control subjects. The duration and type of diabetes play an important role in the development of pathologic changes of cerebral vessels. Hemodynamic impairments were more common in the patients with type 1 diabetes than in those with type 2 diabetes. On the other hand, duration of diabetes was found to predict for the development of atherosclerotic processes in brain vessels. In all our diabetic patients, the signs of cerebral microangiopathy were twice as common as those of macroangiopathy, affecting cerebral perfusion and probably gradually leading to collapse of cerebral autoregulation in these patients.

References

1. OGREM M, HADBLAD B, ISACSSON SO, JANZON L, JUNGQUIST G, LINDELL SE. Non-invasively detected carotid stenosis and ischaemic heart disease in men with leg arteriosclerosis. *Lancet* 1993;342:1138-41.
2. PLOUIN PF. The importance of diabetes as a cardiovascular risk factor. *Int J Clin Pract* 2000;110:3-8.
3. HARRIS MI. National Health Interview Study. *Ann Intern Med* 1996;124:117.
4. DEMARIN V. Transkranijski dopler. In: DEMARIN V, ŠTIKAVAC M, THALLER N, eds. *Dopler sonografija krvnih žila*. Zagreb: Školska knjiga, 1990:89-129.
5. McCARTNEY P, KATHLEEN M, CAMILO R. Introduction to transcranial Doppler. In: McCARTNEY P, KATHLEEN M, CAMILO R, eds. *Handbook of transcranial Doppler*. New York: 1997: 1-5.
6. AASLID R. *Transcranial Doppler sonography*. Vienna: Springer Verlag, 1986.
7. RINGELSTEIN EB. *Transcranial Doppler sonography*. In: POECK K, RINGELSTEIN EB, HACKER W, eds. *New trends in diagnosis and management of stroke*. Berlin: Springer Verlag, 1987:3-28.
8. MARKUS HS. *Transcranial Doppler ultrasound*. *Br Med Bull* 2000;56:378-88.
9. DEMARIN V. Dijagnostika poremećaja moždanog krvotoka. In: DEMARIN V, ed. *Moždani krvotok – klinički pristup*. Zagreb: Naprijed, 1994:103-32.
10. STEGMAYR B, ASPLUND K. Diabetes as a risk factor for stroke. A population perspective. *Diabetologia* 1995;38:1061-8.

11. GOULON-GOEAU C, SAID G. Cerebral arteries and diabetes. In: TCHOBROUTSKY G, SLAMA G, ASSAN R, FREYCHET P, eds. Vascular complications of diabetes. 1994:150-3.
12. SPRAFKA JM, VIRNIG BA, SHAHAR E, McGOVERN PG. Trends in diabetes prevalence among stroke patients and the effect of diabetes on stroke survival: the Minnesota Heart Survey. *Diabet Med* 1994;11:678-84.
13. ORCHARD TJ, STRANDNESS DE. Assessment of peripheral vascular disease in diabetes. *Diabetes Care* 1993;16:1199-209.
14. LECHLEITNER M, BRAUNSTEINER H. Cerebrovascular disorder as a manifestation of generalised disease. *Acta Med Austriaca* 1991;18:47-51.
15. MORRISH NJ, STEVENS LK, FULLER JH, JARRETT RJ, KEEN H. Risk factors for macrovascular disease in diabetes mellitus: the London follow-up to the WHO Multinational Study of Vascular Disease in Diabetics. *Diabetologia* 1991;34:590-4.
16. ADMANI AK, MANGION DM, NAIK DR. Extracranial carotid artery stenosis: prevalence and associated risk factors in elderly stroke patients. *Atherosclerosis* 1991;86:31-7.
17. De SYO D, PODOBNIK-ŠARKANJI S, DESPOT I, FERENČIĆ Ž. Patologija okluzivne cerebrovaskularne bolesti. In: DEMARIN V, ed. Moždani krvotok – klinički pristup. Zagreb: Naprijed, 1994:26-50.
18. PAPOZ L, COSTGLIOLA D, MASSARI V. Epidemiology of the micro- and macrovascular complications of diabetes. In: TCHOBROUTSKY G, SLAMA G, ASSAN R, FREYCHET P, eds. Vascular complications of diabetes. 1994:63-9.
19. MOCKA J, JÄGER K. Rational approach to arterial occlusive disease. *Schweiz Rundsch Med Prax* 1990;79:1553-9.
20. PRIOLLET P. Arterial disease of the lower limbs in the diabetic. In: TCHOBROUTSKY G, SLAMA G, ASSAN R, FREYCHET P, eds. Vascular complications of diabetes. 1994:145-50.

Sažetak

UTJECAJ TRAJANJA I TIPA ŠEĆERNE BOLESTI NA MOŽDANU HEMODINAMIKU

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Transkranijaska doplerska sonografija, vrhunska dijagnostička metoda za prikaz hemodinamskih promjena u bazalnim moždanim arterijama u stvarnom vremenu, primijenjena je u 100 bolesnika u dobi između 48 i 67 godina s dijagnozom šećerne bolesti, te u kontrolnoj skupini od 100 zdravih ispitanika. Cilj istraživanja bio je utvrditi hemodinamske promjene u moždanim arterijama u dijabetičnih bolesnika, te utjecaj trajanja i tipa šećerne bolesti na razvoj cerebrovaskularne bolesti. Nađena je statistički značajno veća zastupljenost patoloških nalaza transkranijaska doplerske sonografije u dijabetičnoj skupini negoli u kontrolnoj skupini ($p < 0,05$). Utvrđeno je da trajanje i tip dijabetesa utječu na razvoj patoloških promjena na moždanim arterijama. Bolesnici s dijabetesom tip 1 češće su imali hemodinamske promjene negoli oni s dijabetesom tip 2 (72,5% prema 43,3%). S druge strane, istraživanje je pokazalo da je trajanje šećerne bolesti značajan predskazatelj razvoja cerebrovaskularne bolesti. Aterosklerotske promjene nađene su u 34% dijabetičara koji su bolovali od dijabetesa kraće od 5 godina, te u 71,4% onih koji su od dijabetesa bolovali 5 godina i duže. U svih dijabetičnih bolesnika znatno su češće nađeni znaci cerebralne mikroangiopatije negoli makroangiopatije.

Ključne riječi: *Cerebrovaskularne bolesti, etiologija; Dijabetične angiopatije, komplikacije; Diabetes mellitus, komplikacije; Rizični čimbenici; Ultrasonografija, doplerska, transkranijaska*