당뇨병성 혈관 합병증과 적혈구 변형성의 연관성 연구

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Association of impairment of red blood cell deformability with diabetic vascular complications

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1. Introduction

RBCs have ability to undergo large deformations when subjected to stresses, which allows the RBCs to pass through capillaries narrower than resting RBC diameter. RBCs are biconcave discs typically 6-8 mm in diameter and 2mm in thickness; in mammals the cells are non-nucleated and consist of a concentrated hemoglobin solution enveloped by a highly flexible membrane. A slight decrease in red cell deformability may cause important disturbances in the blood circulation of micro-vessels.

Recent clinical observations have reported that reduced RBC deformability accompany diabetes, hypertension, sickle cell anemia and other circulation disorders.[1~2] The chronic consequences of such diseases exclusively, or to a great extent, afflict the microcirculation and cause vascular complications. Diabetic nephropathy, which is one of theserious microvascular complications of diabetes mellitus, is the major cause of renal diseases including chronic renal failure (CRF) and end-stage renal disease (ESRD). The progressive mechanism of these vascular complications has been rarely known.

Recently, our previous study[3] developed a new disposable-slit ektacytometer (Rheoscan-D), which is capable of continuously measuring RBC deformability over broad range of shear stresses. Therefore, the objective of the present study is to investigate the correlation of the reduced RBC deformability with progressive development of diabetic nephropathy and retinopathy using the disposable ektacytometry.

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2. Method and Materials

One hundred and sixty one diabetic patients, divided into three groups according to serum creatinine concentration. Forty-nine (normal, healthy), fifty-five (CRF) and fifty two (ESRD) nondiabetic patients served as controls. The detailed statistical data are available in Table 1 including group designation, patient's demographics, and clinical data. Group-I comprised 72 diabetic patients whose serum creatinine was less than 1.5mg/dL. Group-II comprised 39 diabetic patients with renal insufficiency (CRF) whose serum creatinine ranged from 2 to 6 mg/dL and Group-III comprised of 50 diabetic patients with ESRD whose serum creatinine ranged from 7to 16 mg/dL. In nondiabetic cohort, 49 healthy controls having normal renal function, 55 patients with CRF and 52 with ESRD were controls for diabetic groups I, II and III, respectively. No patients in the nondiabetic group have clinically evident cardiovascular diseases.

The basic apparatus of the slit ektacytometer[4], containing the laser, a CCD video camera, screen, vacuum generating mechanism and pressure driven slit rheometry. Typical tests are conducted as follows: At time t = 0, the vacuum generating mechanism is connected with the slit element, which allows the fluid to flow through the slit and to be collected in the waste sample chamber as driven by

Table 1 Patient demographics and clinical features

	Healthy (n=49	Normal renal function (n=72)	Chronic renal failure (n=94)		End stage renal disease (n=102)	
	Group 0 Healthy (49)	Group I Diabetic (72)	Group II Diabetic (39)	Control Non-Diabetic (55)	Group III Diabetic (50)	Control Non-Diabetic (52)
Age	56.2 ± 8.3	58.3 ± 11.8	58.2 ± 11.3	52.8 ± 15.4	54.4 ± 12.5	54.0 ± 13.9
Gender (male/female)	22/27	42/30	25/14	26/24	34/21	32/20
Serum Creatinine (mg/dL)		0.82 ± 0.2	4.87 ± 1.91	4.25 ± 2.06	9.08 ± 2.62	9.74 ± 2.71
		< 1.5	2 < x < 6		> 7	

the differential pressure.

While the blood is flowing through the slit, a laser beam emitted from the laser diode traverses the diluted RBC suspension and is diffracted by the RBCs in the volume.

3. Results and Discussion

Figure 1 shows the comparison of RBC deformability for healthy and diabetic groups. The diabetic group with normal renal function (group I) shows a substantially greater impairment in red blood cell deformability compared with normal healthy control (P= 0.004). Subsequently, a further impaired RBC deformability was found with renal function loss, in diabetic patients with renal insufficiency (group II) when compared with diabetic subjects with normal renal function (P= 0.008). In addition, there shows a slight further reduction of RBC deformability when renal function loss progress from CRF (group II) to ESRD (group III). These subsequent decreases of RBC deformability imply that the RBC deformability impairment play a significant role in the progress of diabetic renal diseases. When microvascular vessels are exposed to flowing less deformable RBCs for long period of time, there might cause mechanical damages on the vessel walls and result in either narrowing or hardening process of vessel wall.

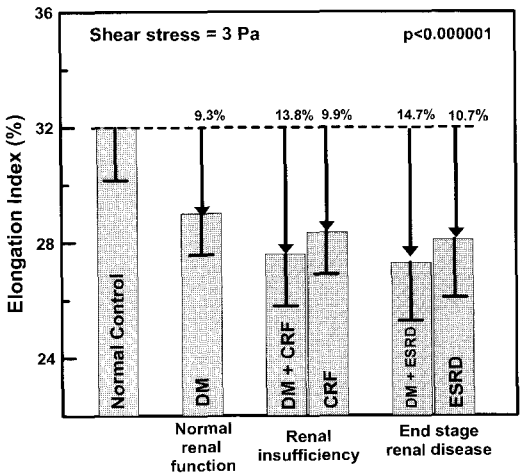

Fig. 1 Comparison of red blood cell deformability of diabetes and diabetic nephropathy.

Acknowledgment

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Reference

(1) Brown, C., Ghali, H., Zhao, Z., Thomas, L. and Friedman, E., 2005, Association of reduced red blood cell deformability with diabetic nephropathy, Kidney International, 67, 295.

(2) Usami, S., Chien, S. and Bertles, J.F., 1975, Deformability of sickle cells as studied by microsieving, J. Lab. Clin. Med., 86, 274.

(3) Shin, S., Ku, Y.H., Park, M.S., Jang, J.S., 2005, Rapid cell-deformability sensing system based on slit-flow laser diffractometry with decreasing pressure differential,Biosensor and Bioelectronics, 20, 1291.