2형 당뇨환자 미세혈관병증의 지표 : 적혈구 변형성의 점진적인 감소

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Progressive Impairment of Erythrocyte Deformability as Indicator of Microangiopathy in type 2 Diabetic mellitus

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1. Introduction

Erythrocyte deformability is the measurement of the ability of the cells to deform while flowing in large as well as small vessels in cardiovascular system. The major determinants of this include composition of the cell membrane and its cytoskeleton, and internal viscosity (mean cell hemoglobin concentration) (1-3). The contribution of the erythrocyte membrane to the deformability is primarily regulated by the composition and arrangement of its structural constituents.

The measurement of the various structural parameters thus provides information on the changes which are taking place in various constituents of erythrocytes but their overall influence could only be measured through the change in erythrocyte deformability. The precise measurement of this parameter could provide information on the disease process, which is primarily contributing in its deterioration. Based on this, the assessment of the possible changes in the microcirculation could also be made. The measurement of erythrocyte deformability in diabetes and its various diabetes complications forms the objective of the present work which has been carried out by microfluidic ektacytometer, and to establish its correlations with creatinine and glycated hemoglobin, which are considered as the indicators of diabetes complications.

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2. Materials and Methods

The erythrocyte deformability was measured by the microfluidic ektacytometer Rheoscan-D (Sewon Meditech, Korea). The erythrocyte suspension, driven by differential pressure, flows through the disposable microchannel (0.2mm x 4 mm x 40 mm), and is collected in the waste chamber. During flow a laser beam of wavelength 635nm from a laser diode of power 1.5mW passes through the diluted erythrocyte suspension. The diffraction pattern of flowing erythrocytes, at shear stress 3.0 Pa is projected onto the screen and captured by a CCD-video camera, is finally analyzed by an ellipse-fitting- program in a computer. The elongation index (EI) of erythrocytes is defined as (L-W)/(L+W), where L and W are the major and minor axes of the ellipse, respectively. After each measurement the micro-channel was discarded. Further functional details of this technique are given elsewhere (4).

This study was conducted at the Kyungpook National University Hospital as a collaborative project of the Department of Laboratory Medicine and School of Mechanical Engineering of the University. Two hundred and thirty one type 2 diabetic patients participated in this study: Seventy two DM patients without any apparent microvascular disease formed the Group-I. Group-II was comprised of 42 diabetic patients with chronic renal failure (CRF) and fifty one diabetic patients with end-stage renal disease (ESRD) formed the Group-III. Similarly,Group-IV and Group V were

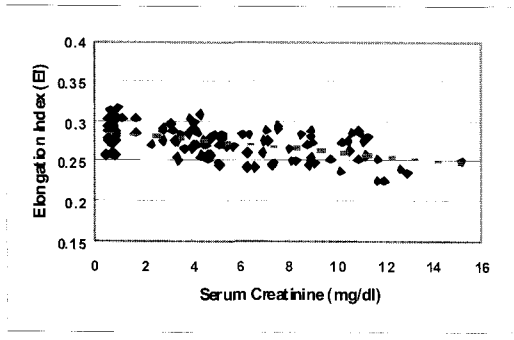

Fig. 1 Correlation between elongation index (EI) of erythrocytes and serum creatinine level

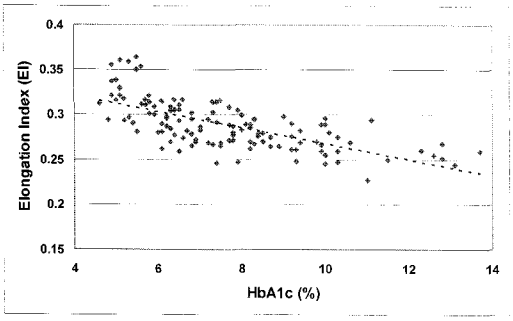

Fig. 2 Correlation between elongation index (EI) of erythrocytes and percentage of HbA1C

consisting of 23 diabetic patients with retinopathy (DMR) and 43 patients with retinopathy and nephropathy (DMR+DMN), respectively. The control group was consisting 49 age-matched subjectswithout any history of DM and associated complications. Patients who had clinically evident cardiovascular diseases were excluded from this study. Serum creatinine levels in Groups II, III and V were higher than 1.5mg/dl. The levels of glucose, creatinine, hemoglobin, HbA1C, LDL and HDL were determined by standard procedures in the Department of Laboratory Medicine at the Hospital.

3. Results

The EI of various blood samples was measured and its variation with the concentrations of creatinine and glycated hemoglobin was analyzed. Fig. 1shows the variation of the EI with the increase of creatinine concentration. Good negative correlation coefficient between these parameters is observed ($r = -0.508$), indicating a decreasing trend of EI with the increase of creatinine level in the plasma. Fig. 2shows the variation of the EI at various concentrations of HbA1C. A strong negative correlation ($r = -0.672$) between these parameters is observed. The EI decreases with the increase of HbA1C.

The variation of EI in diabetes groups and control subjects is shown in Figure 3. The EI is the maximum for control and is decreased significantly ($p<0.0001$) in the Group I. A comparison of the EI erythrocytes of Group II to V with that of Group I further shows a significant reduction ($p<0.0001$) in the EI. The EI is reduced to a minimum in erythrocytes of patients with dual complications due to retinopathy and nephropathy.

4. Conclusions

In conclusion the elongation index is a sensitive parameter in totality to describe the overall effect induced by the diabetic process in erythrocytes. Further significant reduction in the EI in various diabetes complications, as shown in present studies, could directly be taken as indicator of these complications. In contrast to the conventionallevels of plasma and cellular constituents, the EI, in combination with flow related parameters could also provide information on the changes in blood flow through the affected region of the cardiovascular system.

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