Red Blood Cell Electric Charge and Microalbuminuria in Diabetes mellitus

R. Lauwerys
A. Ouled
B. Bernard
B. Vandeleene
A. Lambert

Units of aIndustrial Toxicology and of bDiabetology and Nutrition, School of Medicine, Catholic University of Louvain, Brussels, Belgium

Prof. R. Lauwerys, Faculté de Médecine, Clos Chapelle-aux-Champs 30, B-1200 Bruxelles (Belgium)

Dear Sir,

The glomerular filtration barrier is both size- and charge-selective. Fixed anionic sites within the glomerular basement membrane and on the epithelial cell coat appear to be the basis of the charge selectivity. This charge barrier restricts the passage across the filter of polyanionic macromolecules such as serum albumin [1].

Recently, it has been reported that in children with nephrotic syndrome, a reduction of membrane-negative charge as measured by the binding of the cationic dye, alcian blue (AB), can be detected in red blood cells (RBC) similar to that observed histologically on the glomerular capillary wall in nephrotic patients [2]. The validity of these results has been questioned [3, 4]. However, in rats chronically exposed to cadmium, a well-known nephro-toxin, we have been able to demonstrate, with the AB binding test, a relation between the decrease of membrane-negative charges in RBC and in renal glomeruli and the intensity of the cadmium-induced albuminuria. Furthermore, in cadmium workers a significant decrease of RBC charge was also found which on the average paralleled both the cadmium body burden and albumin excretion [5].

An increased urinary excretion of albumin which is not detectable with conventional tests of proteinuria (microalbuminuria) is an early manifestation of diabetic nephropathy [6]. The initial rate of albumin leakage is due to an enhanced glomerular filtration. Impaired tubular reabsorption of albumin can be excluded because the latter would be associated with an increased urinary excretion of low molecular weight proteins [7] which is not always the case in diabetic nephropathy [8].

Two mechanisms have been suggested as an explanation for the increase filtration of albumin in diabetics: hemodynamic changes in the renal microcirculation [9] which have been linked to rheological changes [10] or a loss of fixed negative charges in the glomerular capillary

250-t

200
n = 69
r = -0.57; p < 0.001
y = 220–19 log x
Fig. 1. Relationship between RBC charge and albuminuria. However, the relationship between rheological changes and microalbuminuria has been refuted by Hill et al. [13]. In the present study, RBC-negative charge was measured by the AB binding test in 69 diabetics, age 19–78 years (30 type I, 7 type II and 32 type III; i.e. diabetics with some residual insulin secretion but requiring insulin treatment). The mean duration of diabetes was 13 years (1–32 years). Nine had a slight degree of renal insufficiency with a serum creatinine between 13.5–27 mg/l. Albuminuria was normal ( < 20 mg/g creatinine) in 32 patients, ranged from 20 to 100 mg/g creatinine in 21 and exceeded the latter value in 16. Increased urinary excretion of retinol-binding protein (> 300 µg/g creatinine), a marker of renal tubular dysfunction, was found in 17 patients (24.5%); 13 of them had also an increased albuminuria. RBC charge was significantly lower in diabetics than in controls (228 ± 28 vs. 191 ± 25 ng/10^6 RBC; p < 0.001). This agrees with the observation of Baba et al. [14]. The RBC charge was not significantly different between patients with or without increased excretion of retinol-binding protein, nor between those with or without retinopathy. There was no statistically significant correlation between the level of glycosylated hemoglobin and RBC charge. There was, however, a high negative correlation (r= -0.57; p < 0.001) between RBC charge and albuminuria (fig. 1). This study supports the hypothesis that the microalbuminuria of diabetic nephropathy mainly results from a loss of glomerular negative charge rather than from Theological changes. Furthermore, the present study and that on cadmium nephropathy [5] suggest that RBC charge, as assayed by the AB method, reliably mirrors the charge on the glomerular capillaries.

References