Red Cell Surface Charge and Urine Albumin Excretion in Children with Insulin-Dependent Diabetes Mellitus

D.M.		Gibb
M.		Levin
C.		Smith
T.M.		Barratt

Department of Paediatric Nephrology, Institute of Child Health, London, UK

Dr. D. Gibb, Department of Paediatric Nephrology, Institute of Child Health, 30 Guilford Street, London WC1N 1EH (UK)

Dear Sir,

We note with interest the negative relationship which Lauwerys et al. [1] found between red cell surface charge and urine albumin excretion in diabetic adults. We have studied the relationship between red cell surface charge, urine albumin excretion and platelet aggregation in diabetic children and adolescents. We studied 43 diabetic children, mean age 14.3 years and duration of diabetes 6.5 years, and 18 normal children, mean age 12.6 years. Urine albumin concentration was measured by radioimmunoassay and urine albumin excretion was expressed as the geometric mean urine albumin creatinine concentration ratio on 2 overnight urine samples (UA/UC). Red cell surface charge was measured by the binding of the cationic dye Alcian blue 8GX to anionic sites on the cell surface [2]. Platelet aggregation was measured in whole blood using the Ultraflo 100 Whole Blood Platelet Counter and expressed as percentage fall in platelet count after stirring for 2 min at 1,000 rpm at 37 °C [3].

Geometric mean (range, in parentheses), UA/UC in the diabetic children was significantly greater in the diabetic children, 0.69 (0.06–7.6), than in the normal children, 0.32 (0.1–1.02; $p < 0.001$; t test on logged data) and 25% had values above the normal range. Mean (SD) red cell charge, measured by Alcian blue bound, was 87 (4.9) ng Alcian blue/106 RBC in diabetics and 85 (3.9) ($p > 0.05$) in normals. Mean (SEM in parentheses) platelet aggregation was significantly greater in the diabetic 17.8% (1.2) compared to the normal children 12.3% (1.5) ($p < 0.01$).

There was no significant correlation between UA/UC and red cell charge in either the diabetic or the normal children. There was also no relationship between red cell charge and age, hemoglobin A_{1c}, or platelet aggregation, nor was there a correlation between UA/UC and platelet aggregation.

Our findings are at variance with those of Lauwerys et al. [1] who found a significant negative correlation between UA/UC and red cell surface charge. It has been suggested that the albuminuria of early diabetic nephropathy may be due to loss of the charge selectivity of the glomerular basement membrane (GBM). Reduction of heparan sulfate in the GBM has been demonstrated in diabetes [4], and glycation of the GBM and/or albumin may alter charge and therefore the permselectivity properties of the GBM to albumin [5, 6]. However, evidence of loss of charge based on urinary excretion characteristics of differently charged proteins in humans have not been as conclusive as in the minimal change nephrotic syndrome [7, 8].

We note that the amount of Alcian blue bound to red cells found by Lauwerys et al. [1] were much higher than our values. This has also been the experience of other workers and we have previously reported reasons why this might be the case [9]. It is possible that the differences in methodology which exist are responsible for the different relationships reported between red cell surface charge and UA/UC. Our results are in agreement with those of Mathiesen et al. [10] who found no differences in the amount of Alcian blue bound to red cells of normal adult controls compared with those of adult diabetics either with or without nephropathy.

References

Lauwerys, R.; Ouled, A.; Bernard, B.; Vandeleene, B.; Lambert, A.: Red blood cell electric charge and microalbuminuria in diabetes mellitus. *Nephron* 45:171–172 (1988).

Levin, M.; Walters, S.; Smith, C.; Gascoine, P.; Barratt, T.M.: Steroid-responsive nephrotic syndrome: a generalised disorder of membrane negative charge. *Lancet* ii:239–242 (1985). 564

Gibb/Levin/Smith/Barratt

Gibb, D.M.; Dunger, D.; Levin, M.; Shah, V.; Smith, C.; Barratt, T.M.: Early markers of the renal complications of insulin-dependent diabetes mellitus in children (in press).

Schleicher, E.; Wieland, E.: Changes of human glomerular basement membrane in diabetes mellitus. *J. clin. Chem. clin Biochem.* 22:223–227 (1984).

Copeland, K.R.; Yatscoff, W.; Thliveris, J.A.; Mehta, A.; Penner, B.: Non-enzymatic glycation and altered renal structure and function in the diabetic rat. *Kidney int.* 32:664–670 (1987).

Layton, G.J.; Jerums, G.: Affect of glycation of albumin on its renal clearance in normal and diabetic rats. *Kidney int.* 33: 673–676 (1988).

Deckert, T.; Feldt-Rasmussen, B.; Djurup, R.; Deckert, M.: Glomerular size and charge selectivity in insulin-dependent diabetes mellitus. *Kidney int.* 55:100–106 (1988).

Carrie, B.J.; Myers, B.D.: Proteinuria and the functional characteristics of the glomerular barrier in diabetic nephropathy. *Kidney int.* 77:669–676 (1980).

9 Levin, M.; Gibb, D.; Smith, C.; Walters, M.D.S.; Barratt, T.M.: Red blood cell surface charge in nephrotic syndrome. *Lancet* ii: 929 (1986). 10 Mathiesen, E.R.; Smith, C.; Lauritzen, M.;

Hommel, E.; Levin, M.; Parving, H.-H.: Surface charge of red blood cells in insulin-dependent diabetic patients with incipient and overt nephropathy. *Diabet. Med.* 4:431–433 (1987).