Erythrocyte Charge, Glycosaminoglycans and Diabetic Nephropathy

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Dear Sir,

In reference to the contribution from the Lambert group [1], we have recently obtained similar data [2,3] also in agreement with Baba et al. [4], but different from those of Mathiesen et al. [5]. In fact, a statistically significant reduction of erythrocyte anion charge (RBCCh) was observed in insulin-independent diabetic (IDD) patients with albuminuria of less than 300 mg/day. Although no linear relationship existed between 24-hour albuminuria and RBCCh, we found a good indirect correlation between RBCCh and the albuminuria peak after inhibition of proximal tubular reabsorption of proteins by the lysine test [6] ($r = -0.77$; $p < 0.001$).

Studying the RBCCh determinants, we observed that, while the sialic acid content was normal, a significant reduction of the RBC membrane content of glycosaminoglycans (GAGs) was present [2, 3]. We think that this anomaly is related to the generalized derangement of the GAG metabolism in diabetes mellitus, which seems to be crucial for the development of diabetic microangiopathy and particularly diabetic nephropathy [7, 8]. The abnormal urinary excretion of GAGs seems to be another marker of this metabolic disorder [9–11]. However, contrary to what was stated by Bernard et al. [11], we believe that the higher urinary excretion of GAGs in diabetes could be an early marker of abnormal glomerular charge permeaselectivity. Actually, patients in our investigation characterized by the greater reduction of RBCCh (which seems to signify a greater abnormality of glomerular charge permeaselectivity) also had a higher urinary excretion of GAGs ($\chi^2 = 9.48$; $p < 0.005$) [unpubl. data]. Moreover, another recent investigation of ours has shown that a lysine provocative test [6] induced a significant pathological urinary excretion of albumin in IDD

patients with abnormal urinary GAGs and albuminuria within the normal range, in contrast to IDD subjects with normal urinary GAGs and albumin [12].

In conclusion, we think these observations support the role of GAG metabolism in the pathogenesis of diabetic nephropathy and the value of abnormal urinary excretion of GAGs as an index of glomerular involvement.

References

- Lauwerys, R.; Ouled, A.; Bernard, B.; Vandeleene, B.; Lambert, A.: Red blood cell electric charge and microalbuminuria in diabetes mellitus. *Nephron* 55:171–172 (1988).
- Gambaro, G.; Cicerello, E.; Mastrosimone, S.; Marzaro, G.; Lavagnini, T.; Del Prete, D.; Borsatti, A.; Baggio, B.: Altera-zione delle cariche anioniche eritrocitarie nella nefropatia diabetica incipiente. *Nefrologia* 1987 Acta Medica Edizioni Con-gressi, Roma 1987, pp. 173–175.

Gambaro, G.; Baggio, B.; Cicerello, E.; Mastrosimone, S.; Marzaro, G.; Borsatti, A.; Crepaldi, G.: Abnormal erythrocyte charge in diabetes mellitus: a link with microalbuminuria. *Diabetes* 37:745–748 (1988).

Baba, Y.; Kai, M.; Setoyama, S.; Otsuji, S.: The lower levels of erythrocyte surface charge in diabetes mellitus. *Clinica chim. Acta* 54:247–249 (1978).

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. *Diabetic Med.* 4:431–433 (1987).

Mogensen, C.E.; Vittinghus, E.; Soiling, K.: Abnormal albumin excretion after two provocative renal tests in diabetes: physical exercise and lysine injection. *Kidney int.* 76:385–393 (1979).

Deckert, T.; Feldt-Rasmussen, B.; Mathiesen, E.; Baker, L.: Pathogenesis of incipient nephropathy: a hypothesis. *Diabetic Nephropathy* 2:83–88 (1985).

Deckert, T.; Feldt-Rasmussen, B.; Djurup, R.; Deckert, M.: Glomerular size and charge selectivity in insulin-dependent diabetes mellitus. *Kidney int.* 33:100–106 (1988).

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9 Baggio, B.; Briani, G.; Cicerello, E.; Gambaro, G.; Brutto-messo, D.; Tiengo, A.; Borsatti, A.; Crepaldi, G.: Urinary glycosaminoglycans, sialic acid and lysosomal enzymes increase in non-albuminuric diabetic patients. *Nephron* 43:187–190 (1986).

Lubec, G.; Legenstein, E.; Pollak, A.; Meznik, E.: Glomerular basement membrane changes, HbA_{1c} and urinary excretion of acid glycosaminoglycans in children with diabetes mellitus. *Clinica chim. Acta* 103:45–49 (1980).

Bernard, A.M.; Ouled, A.; Roels, H.; Lauwerys, R.; Vandeleene, B.; Lambert, A.: Lack of relationship between urinary glycosaminoglycans and indices of tubular or glomerular renal damage. *Nephron* 45:82–83 (1988).

12 Gambaro, G.; Cicerello, E.; Mastrosimone, S.; Lavagnini, T.; Baggio, B.: High urinary excretion of glycosaminoglycans: a possible marker of glomerular involvement in diabetes. *Metabolism* (in press).