Letters to the Editor

Transcapillary escape rate of albumin and extracellular fluid volume in diabetes

Sir,

We read with interest the observations of Fauchald et al. [1] stating that interstitial fluid colloid osmotic pressure is reduced in diabetic patients with long-standing disease. They also noted increased extracellular fluid volume in diabetic patients free of the nephrotic syndrome or heart failure. The latter observation is consistent with reports that total exchangeable sodium (NaE) is increased in such patients [2, 3]. Fauchald et al. suggested that increased transcapillary colloid osmotic gradient may be one factor which prevents frank oedema from developing in these patients. We wonder if Fauchald et al. observed a relationship between the transcapillary escape rate of albumin (TER_{alb}) and extracellular fluid or interstitial fluid volume.

We examined the relationship between TER_{alb} and total exchangeable sodium (NaE) which is predominantly determined by extracellular fluid and sodium volume. TER_{alb} [4] and NaE [3] were measured in 14 diabetic patients who did not have clinically evident diabetic complications or hypertension as these and poor metabolic control increase TER_{alb} [4]. Comparisons were made with non-diabetic patients previously described [3, 4] of similar age, serum albumin concentration, plasma volume and arterial pressure. The diabetic patients had a mean HbA1c of 9.1% (range 7.2–10.8%). TER_{alb} in non-diabetic patients was $5.5 \pm 0.7\%/h$ (SEM $n=12$) and $6.3 \pm 0.7\%/h$ ($n=14$) in the diabetic patients (NS). NaE in controls ($n=42$) was 100 ± 1.6 and $107 \pm 1.5\%$ predicted (by leanness index) in diabetic patients ($p < 0.005$). TER_{alb} correlated with NaE in diabetic patients ($r=0.61$, $p=0.01$, Fig. 1). TER_{alb} and NaE were only measured simultaneously in seven of the non-diabetic controls and no significant correlation was observed.

The relationship between TER_{alb} and NaE in diabetic patients has two possible explanations. Firstly, increased capillary permeability may lead to increased fluid extravasation into the interstitial space which in turn may stimulate sodium retention at the kidney. Alternatively, increased microvascular permeability and increased extracellular fluid volume may have a common determinant where alterations in the systemic microvasculature are coupled with simultaneous structural or functional abnormalities in the renal circulation causing fluid retention. The latter possibility was examined by relating TER_{alb} in the diabetic patients to urine albumin excretion. The 24-h urine albumin excretion was 79 ± 9 mg/24 h in controls and 126 ± 24 mg/24 h in diabetic patients ($p < 0.05$). TER_{alb} correlated with urine albumin excretion ($r=0.65$, $p < 0.005$, Fig. 1b). NaE correlated with urine albumin excretion ($r=0.57$, $p < 0.02$).

These observations suggest that a positive extracellular fluid (and sodium) balance occurs in some diabetic patients before the appearance of overt complications, and that this is related to alterations in capillary permeability and concurrent abnormalities in the kidney.

Sincerely,

J. A. O'Hare and J. B. Ferriss

References

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Fig. 1. a Relationship between transcapillary escape rate of albumin (TER_{alb}) and total exchangeable sodium (NaE), $r=0.65$, ($p < 0.01$). b Relationship between TER_{alb} and urine albumin 24 h albumin excretion, $r=0.65$ ($p < 0.005$)

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Reply from the authors

Sir,

We appreciate the interesting comments by O'Hare and Ferriss. Among our patients [1] no significant correlation could be found between TER_{alb} and extracellular fluid volume or interstitial fluid volume. However, the number of patients was small, with a wide variation in age. The sex differences in extracellular fluid volume could also have contributed to concealing a correlation.

In addition to capillary permeability, TER_{alb} is dependent on capillary hydrostatic pressure [2]. The observations by O'Hare and Ferriss suggest that increased NaE and extracellular fluid volume is caused by primary renal fluid retention. This could lead to increased capillary hydrostatic pressure and contribute to the increased capillary filtration of fluid. Increased net capillary filtration of fluid is necessary to explain our findings of reduced interstitial protein concentration in

diabetic patients. The increased filtration could be due both to increased capillary hydrostatic pressure and to increased capillary filtration coefficient.

Sincerely,
P. Fauchald,
J. Norseth and J. Jervell

References

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