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LETTER TO THE EDITOR

Influence of Bacteriuria on the Determination of Urinary Albumin Excretion Rate

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Sir,

Increased urinary albumin excretion rates are associated with increased morbidity and mortality in both diabetic and non-diabetic populations (1–3). In studies of microalbuminuria, it is of crucial importance to exclude other confounding factors that influence urinary albumin excretion. Bacteriuria is considered to be a potential cause of transient increased albuminuria (4, 5). The effect of bacterial growth in vitro has been tested and gross microbiological contamination of urine over a 14 day period at room temperature did not consistently affect albumin concentration (6). However, the impact of in vivo bacterial contamination remains to be elucidated. It is remarkable that patients with bacteriuria are generally excluded from studies on microalbuminuria despite a lack of documentation on the subject. Furthermore, the exclusion criteria used in these studies are highly variable. Some authors demand a sterile urine (7). Others accept small numbers of bacteria (e.g. less than 10^8/l) or an urinary dipstick with a negative test for leukocytes (8). In several studies, the possible influence of urinary tract infection has not been considered. A consensus concerning bacterial growth and urinary albumin excretion would be desirable.

In order to evaluate the influence of bacteriuria on the urinary albumin excretion rate we have examined 524 timed overnight urine samples obtained from 389 patients attending a medical out-patient clinic. Patients with diabetes mellitus, hypertension and renal diseases were not included. Additionally, urine specimens from 48 otherwise healthy subjects with bacteria > 10^8/l were examined before and 3 weeks after antibiotic treatment. Urine was collected in standard plastic containers without additive. The microalbuminuria assay was carried out either in fresh urine samples or after storage for less than one week at 4 °C. Urinary albumin was assayed by immunoturbidimetry using sheep anti-human albumin and a BM/Hitachi 704 analyser (Boehringer Mannheim, Germany). The urine was cultured and bacterial growth was quantified as 10^7, 10^8 or > 10^8 bacteria per litre. Since the data studied were not normally distributed, non-parametric statistics (*Wilcoxon* test) were applied. P values < 0.05 were considered significant.

Tab. 1 Urinary albumin excretion rate related to different categories of bacterial growth in the urine

	No. of urine samples	Urinary albumin excretion rate* [µg/min]
Urine samples with no bacterial growth	433	8.7 (3–194)
Urine samples with bacterial growth:		
total	91	9.9 (3–172)
10^7 bacteria per litre	28	9.0 (3– 95)
10^8 bacteria per litre	27	9.2 (4–106)
> 10^8 bacteria per litre	36	12.1 (3–172)

* Median values (ranges).

Tab. 2 Urinary albumin excretion rate in healthy subjects with more than 10^8 bacteria per litre before and after antibiotic treatment

	No. of urine samples	Urinary albumin excretion rate* [µg/min]
Before treatment	48	11.5 (3–112)
After treatment:		
total	48	6.1 (3– 61)
sterile urine	44	5.9 (3– 13)
urine with bacterial growth	4	17.5 (14– 61)

* Median values (ranges)

The results are summarised in table 1. The median value of urinary albumin excretion rates in urine samples with bacterial growth was significantly higher than in patients with a sterile urine (9.9 v 8.7 µg/min, $p < 0.05$). However, there was no significant difference in urinary albumin excretion rates between urine samples with 10^7 bacteria per litre, 10^8 bacteria per litre and no bacterial growth (9.0 v 9.2 v 8.7 µg/min, $p < 0.2$). Only urine samples with more than 10^8 bacteria per litre had a significantly higher urinary albumin excretion rate than the group without bacterial growth (12.1 v 8.7 µg/min, $p < 0.01$). The results of the healthy subjects with bacteria > 10^8/l are given in table 2. The urinary albumin excretion rate was significantly lower after antibiotic treatment ($p < 0.00001$). The urine specimens were sterile in 44 subjects 3 weeks after treat-

ment and none of these exceeded an urinary albumin excretion rate of 13 μg/min.

Our results indicate that bacterial growth in vivo of more than 10^8 bacteria per litre is associated with increased urinary albumin excretion. Therefore, bacterial growth in vivo should be taken into account in studies of microalbuminuria. We suggested that in patients with bacterial growth, repeated urine cultures should be performed after antibiotic treatment to ensure a sterile urine before urinary albumin excretion is measured.

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