Microalbuminuria in NIDDM

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OBJECTIVE — To determine an effective screening procedure for microalbuminuria.

RESEARCH DESIGN AND METHODS — The prevalence of microalbuminuria in NIDDM patients whose urine was negative on routine Albustix testing was studied. Microalbuminuria was measured in overnight urine samples from 128 NIDDM patients on at least two of three occasions over a 6-mo period. Patients were tested with Micro-Bumintest or Micral-Test.

RESULTS — Ten of 128 patients had albumin concentrations ≥20 mg/L on two or more occasions, 14 patients had A-C ratios ≥3 mg/M on two or more occasions, and 9 patients had both.

CONCLUSIONS — Neither Micro-Bumintest nor Micral-Test is a useful or feasible screening procedure for microalbuminuria.

Microalbuminuria in NIDDM is predictive of clinical proteinuria and increased mortality (1,2). Microalbuminuria is defined as urinary albumin excretion rates between 20 and 200 μg/min in an overnight or 24-h sample on at least two of three occasions within a 6-mo period (3). With an average fluid intake and a urinary output of 1.5 L/24 h, these excretion rates are approximately equal to 20–200 mg/L or 3–30 mg/M creatinine.

RESEARCH DESIGN AND METHODS

— We studied the prevalence of microalbuminuria in NIDDM patients whose urine was negative on routine Albustix (Miles, Elkhart, IN) testing. Their ages ranged from 45 to 75 yr, with most <60 yr of age. All had been diagnosed with NIDDM for at least 1 yr. Treatment included diabetic diet with or without sulphonylureas and with or without metformin. In addition, some patients received antihypertensive medication, which included angiotensin-converting enzyme inhibitors.

Microalbuminuria was measured in overnight urine samples from 128 patients on at least two of three occasions over a 6-mo period. Urinary albumin was quantitated by immunoturbidimetry with an Encore centrifugal analyzer (Baker, Instruments, Allentown, PA). Calibration solutions were obtained by dilution of Behring N-Protein-Standard Serum (Behringwerke, Marburg, Germany, catalog no. OSAU 06/07). Dako rabbit anti-human albumin (Dako, High Wycomb, U.K., code no. Q328) was diluted 40-fold in PBS containing 40 g/L PEG 6000. Microalbumin was expressed as mg/L and as mg/M of creatinine. Two qualitative assays were tested, Micro-Bumintest (Miles) (4) and Micral-Test (Boehringer Mannheim, Mannheim, Germany; 5). Urine samples were tested as soon as possible after collection but rarely on the same day of collection as recommended for Micro-Bumintest. Urine samples were stored at 4°C pending testing.

RESULTS

— Ten of 128 patients had albumin concentration ≥20 mg/L on two or more occasions. Fourteen patients had A-C ratios ≥3 mg/M of creatinine on two or more occasions, and nine had both albumin ≥20 mg/L and A-C ratio ≥3 mg/M.

We tested 250 urine samples with the Micro-Bumintest and 167 with the Micral-Test (Table 1).

The Micro-Bumintest had a sensitivity of 51% with a specificity of 84%. False/negatives were present in 17 of 35 urine samples with microalbuminuria >20 mg/L. Ten of these had albumins in the 20–30 mg/L range, and 7 had values between 36 and 138 mg/L. Of the 18 true positives, 6 values were between 20 and 30 mg/L.

The Micral-Test had a sensitivity of 63% with a 100% specificity. Among the 20 true positives, four values were between 20 and 30 mg/L.

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NIDDM, NON-INSULIN-DEPENDENT DIABETES MELLITUS; PBS, PHOSPHATE-BUFFERED SALINE; PEG, POLYETHYLENE GLYCOL; A-C RATIO, ALBUMIN-CREATININE RATIO.

Table 1—*Comparison of microalbumin tests*

Test	Urine samples (*n*)	Samples with Microalbumin ≥20 mg/L* (*n*)	True positives	False negatives	False positives
Micro-Bumintest	250	35	18	17	35
Micral-Test	167	32	20	12	0

*by immunoturbidimetry.

False negatives occurred in 12 of 32 urine samples with microalbumin >20 mg/L.

Ten false negatives occurred in the 20–30 mg/L range, with two more occurring at 36 and 66 mg/L.

CONCLUSIONS — The prevalence of microalbuminuria (≥20 mg/L) in our group of patients was 8%. The Micro-Bumintest had false negatives over a wide microalbumin range. It also had an appreciable number of false positives. The Micral-Test had an appreciable number of false negatives in the lower range of microalbuminuria, 20–30 mg/L. Our sensitivity of 63% is lower than that of 83% reported by Jury et al. (6). This degree of interobserver variation is a cause for concern. The test would not, therefore, be feasible at a busy outpatient department where the staff might change from week to week, and simultaneous mass testing would be difficult. We conclude that neither qualitative test is a useful screening procedure for microalbuminuria.

References

1. Mogensen CE: Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. *N Engl J Med* 318:356–60, 1984
2. Jarrett RJ, Viberti GC, Argyropoulos A, Hill RD, Mahmud U, Murrells TJ: Microalbuminuria predicts mortality in non-insulin-dependent diabetes. *Diabetic Med* 1:17, 1984
3. Mogensen CE, Chachati A, Christensen CK, Close CF, Deckert T, Hommel E, Kastrup J, Le Febvre P, Mathieson ER, Feldt-Rasmussen B: Microalbuminuria: an early marker of renal involvement in diabetes. *Uremia Invest* 9:85–95, 1986
4. Schmitz A: Microalbutest: a new screening method for detecting microalbuminuria in diabetes mellitus. *Uremia Invest* 9:79–84, 1986
5. Muller P, Fritzsche E: *Performance of the First Immunometric Dipstick for Rapid and Easy Detection of Microalbuminuria. Evaluation Report Micral-Test.* Mannheim, Germany, Boehringer Mannheim, 1991
6. Jury DR, Mikkelsen DJ, Glen D, Dunn PJ: Assessment of Micral-Test microalbuminuria test strip in the laboratory and diabetic outpatients. *Ann Clin Biochem* 29:96–100, 1992