All Wales Clinical Biochemistry Audit Group

Urine Microalbumin Testing in Screening for Diabetic Nephropathy

INTRODUCTION

Diabetic nephropathy is an important cause of premature death in diabetics, developing in 40% of Type 1 patients with a disease duration of over 20 years. It is also common in Type 2 patients, especially those of non-European origin. The development of diabetic nephropathy is facilitated by poor long-term control, hypertension, dyslipidaemia and cigarette smoking.

Detection of small increases in urine albumin excretion, defined as "microalbuminuria", is a sensitive marker for the development of diabetic nephropathy. Demonstration of microalbuminuria, especially in individuals with Type 2 diabetes, is also useful as a "surrogate" marker for identifying patients at particularly high risk of vascular complications of diabetes, such as ischaemic heart disease.

A survey of urine microalbumin measurements in use in Wales, presented at an audit meeting in January 1998, showed wide variations in practice. Standards were drawn up and issued in September 1998 in the light of the presentations and discussion at this meeting. A re-audit in April 2002 showed moderate compliance with the standards, although variations in practice were still evident. The following revised standards are recommended, to incorporate recently published NICE guidelines (March 2002).

STANDARDS

1. **Urine Testing for Diabetic Nephropathy**

a) All diabetic subjects should have an annual urinalysis using a dipstick for protein and blood.

b) It is recommended that all diabetic subjects who are dipstick negative for protein should be tested annually for microalbuminuria, except for children aged < 12 years who have had diabetes for < 5 years.

2. Testing for Microalbuminuria

a) Although point-of-care testing (POCT) microalbumin methods are available, advice should be sought from the laboratory before introducing POCT. All POCT devices must comply with guidelines for their use (WSAC, 1995).

b) A timed overnight urine collection is the gold standard for defining microalbuminuria, but may not be a practical screening procedure. Therefore, measurement of the albumin/creatinine ratio in a first voided morning urine sample may be used for screening.

c) To establish microalbuminuria, 2 out of 3 samples, collected over a 3 to 6 month period, should show abnormal urine albumin excretion (see table). Therefore, those diabetic subjects with microalbuminuria on initial screening should be retested, preferably within 1 month (and again if the second sample is negative) to confirm the presence of microalbuminuria.

d) The following urine albumin reference ranges are recommended:

Albumin excretion	Timed overnight albumin excretion rate (µg/min)	Early morning albumin/creatinine ratio (mg/mmol creatinine)
Normoalbuminuria	< 20	< 2.5 (male); < 3.5 (female)
"Microalbuminuria"	20 - 199	2.5 – 29.9 (male); 3.5 – 29.9 (female)
"Macroalbuminuria"	≥ 200	≥ 30

2. Testing for Microalbuminuria (continued)

e) Care should be taken in interpreting single results as there is great variability in albumin excretion rates, which are affected by urinary tract infection, poor diabetic control, physical exercise, uncontrolled hypertension, febrile illness, cardiac failure, vaginal discharge and menstruation. Some diabetic subjects with low level microalbuminuria (< 80 µg/min or < 10 mg/mmol creat.) may revert to normal albumin excretion in 6 to 12 months. "At risk" patients with microalbuminuria are those with higher excretion rates and accompanying hypertension.

3. Urine Albumin Assay Requirements

Each laboratory providing urine albumin assays should ensure that appropriate internal quality control and external quality assessment procedures are in place. Any laboratory consistently unable to meet the following analytical criteria and which cannot change to a superior assay should consider referring samples elsewhere:

a) The precision (expressed as between-batch coefficient of variation) should be less than 8%.

b) It is recommended that the dynamic working range should be at least 5 to 300 mg/l.

c) It is recommended that the assay should have the ability to detect antigen excess.

d) The maximum turn round time should not exceed 1 week.

4. Further Management

a) Patients with established microalbuminuria should be considered for angiotensin-converting enzyme (ACE) inhibitor therapy, aggressive management of risk factors (e.g. hypertension and dyslipidaemia) and assessment by the hospital diabetic clinic.

b) All patients with persistent proteinuria (i.e. macroalbuminuria) have established nephropathy and should be referred to the hospital diabetic clinic for full evaluation and follow-up.

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