Danish general practitioners’ estimation of urinary albumin concentration in the detection of proteinuria and microalbuminuria

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SUMMARY

Background. Microalbuminuria may predict proteinuria and increased mortality in non-insulin dependent diabetic patients. Early detection of microalbuminuria may therefore be essential.

Aim. The primary objective of this study was to describe the association between the presence of albuminuria in diabetic patients as detected by general practitioners using conventional reagent strip dipstick tests for albumin, and the urinary albumin concentration as measured in a hospital laboratory.

Method. A total of 675 newly diagnosed diabetic patients aged 40 years or over were included in the Danish study, diabetes care in general practice. Data for urinary albumin concentration from a morning urine sample and the results of three consecutive dipstick tests for albumin were collected for 417 patients.

Results. When defining elevated urinary albumin concentration as 200 mg l\(^{-1}\) or more (proteinuria) the finding of at least one positive test out of the three dipstick tests for albumin had a diagnostic sensitivity of 73% and a specificity of 89%. When the microalbuminuric range (15.0 to 199.9 mg l\(^{-1}\)) was added to the definition of renal involvement, the sensitivity of the dipstick test became as low as 28% with a specificity of 96%.

Conclusion. It is essential for general practitioners to be able to identify proteinuric patients. To achieve this by means of the conventional dipstick test, general practice procedures need to be improved. As it is becoming increasingly well-documented that microalbuminuric non-insulin dependent diabetic patients may benefit from pharmacological treatment of even slight arterial hypertension and heart failure, it seems reasonable to suggest that the use of dipsticks for albumin in general practice be replaced by laboratory quantitative determination of urinary albumin concentration in a morning urine sample.

Keywords: urologic diseases; proteinuria; non-insulin dependent diabetes; urine dipstick testing.

Introduction

In Denmark most non-insulin dependent diabetic patients are managed in general practice.1 In these patients there is already a high prevalence of renal involvement at diagnosis.2,4 General practitioners usually assess renal involvement by measurement of serum creatinine and by semi-quantitative estimation of urinary albumin concentration using reagent strip dipstick tests with a detection limit between 150 mg l\(^{-1}\) and 200 mg l\(^{-1}\). There is, however, evidence to suggest that levels of urinary albumin in the microalbuminuric range between 15 mg l\(^{-1}\) and 200 mg l\(^{-1}\), predict clinical proteinuria2 and increased mortality.5,6 It is generally believed that a better prognosis may be achieved through optimized control of blood glucose and blood pressure. Therefore, general practitioners should be able to identify the microalbuminuric patients among their diabetic patients.

The objective of this sub-study of the Danish study, diabetes care in general practice, was to describe the association between the presence of albuminuria detected by general practitioners using up to three consecutive dipstick tests for albumin for each patient and the concentration of urinary albumin as measured in a hospital laboratory.

Method

Patients

At the end of 1988, 487 general practitioners from all over Denmark volunteered for the study.5 During a two-year period the doctors in the intervention group included all 675 patients on the practice list aged 40 years or over with newly diagnosed diabetes mellitus. The three-monthly follow ups included a dipstick test for albumin on a random urine sample, if the general practitioner found this was indicated. At the yearly examination a dipstick test for albumin was compulsory. Once a year, urinary albumin concentration was determined from a freshly voided morning urine sample.

Urinary albumin concentration assessment

The estimation of urinary albumin concentration in the practices was performed without quality assessment. The practices used their routine urinary dipstick material. The results of three consecutive tests were recorded by the general practitioner as either positive or negative.

Urinary albumin concentration was measured by a polyethylene-glycol radioimmuno-assay10 at Medical Department M, Århus Kommunehospital, Århus.4

Analysis

For each patient the three results of the dipstick test for albumin that were closest to the day of urine sampling for the urinary albumin concentration were included where the interval between two dipstick tests was no more than 365 days and where the interval between diagnosis of diabetes and the first test result was no shorter than 183 days. The arbitrary limit of 183 days was chosen in order to avoid the period of poor metabolic control close to the time of diagnosis. Only one set of urinary albumin concentration dipstick test results was used for each patient.

Results

A set of data for the urinary albumin concentration results of three consecutive dipstick tests was collected for 417 diabetic patients. The median age of the group was 65.5 years and the male: female ratio was 1:1.00. This compares with a median age
of 65.5 years and a ratio of 1: 0.86 in the intervention group as a whole (675 patients). The three dipstick tests were carried out on a median of 0, 92 and 152 days, respectively, from the day of urine sampling for measurement of urinary albumin concentration.

As the number of positive dipstick test results increased, so the power of the dipstick tests to detect renal involvement (as expressed by urinary albumin concentration) increased (Table 1). Even so, 26.7% of diabetic patients with proteinuria (urinary albumin concentration > 200.0 mg l⁻¹) and 76.8% of patients with microalbuminuria (urinary albumin concentration 15.0-199.9 mg l⁻¹) did not have any positive results from their three consecutive dipstick tests for albumin. Among patients with pronounced microalbuminuria (100.0-199.9 mg l⁻¹) the proportion of patients with at least one positive dipstick test result out of three was comparable with that of patients with proteinuria.

Calculations for diagnostic sensitivity, specificity and positive predictive value are shown in Table 2, including data from the 344 patients who had a sample sent for urinary albumin concentration on the same day as a dipstick test was carried out, 23 of whom had a positive dipstick test result. When the cut-off point for proteinuria was 200.0 mg l⁻¹ or more, the diagnostic sensitivity for a positive dipstick result was 73%, and the specificity was 89%. When the cut-off point was lowered to include the microalbumuric range (15.0 mg l⁻¹ or more) the sensitivity of one positive dipstick test result was 28% and the specificity was 96%. When the analysis was confined to the 344 patients who had a dipstick test and urine sample taken on the same day, specificity improved but sensitivity decreased.

### Table 1. Overnight urinary albumin concentration (UAC) and results of the three consecutive dipstick tests for albumin in 417 diabetic patients.

<table>
<thead>
<tr>
<th>Results of 3 dipstick tests</th>
<th>No. of pts with UAC (mg l⁻¹)</th>
<th>% of pts with dipstick test result with UAC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;15.0</td>
<td>15.0-99.9</td>
</tr>
<tr>
<td>3 negative</td>
<td>240</td>
<td>111</td>
</tr>
<tr>
<td></td>
<td>(66.7)</td>
<td>(30.0)</td>
</tr>
<tr>
<td>1 positive, 2 negative</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>(25.0)</td>
<td>(50.0)</td>
</tr>
<tr>
<td>2 positive, 1 negative</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>(14.3)</td>
<td>(35.7)</td>
</tr>
<tr>
<td>3 positive</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>(0)</td>
<td>(26.6)</td>
</tr>
<tr>
<td>Total</td>
<td>251</td>
<td>136</td>
</tr>
<tr>
<td></td>
<td>(60.2)</td>
<td>(32.6)</td>
</tr>
<tr>
<td>One or more positive tests</td>
<td>11</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>(19.3)</td>
<td>(43.9)</td>
</tr>
</tbody>
</table>

### Table 2. Diagnostic sensitivity, specificity and predictive value of a positive dipstick test result among all 417 patients, 57 of whom had at least one positive result, and among all 344 patients who had a sample sent for measurement of urinary albumin concentration (UAC) on the same day as a urinary dipstick test, 23 of whom had a positive result.

<table>
<thead>
<tr>
<th>Sensitivity (%)⁴</th>
<th>Specificity (%)⁵</th>
<th>Positive predictive value (%)⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one positive dipstick test result</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UAC ≥200.0 mg l⁻¹</td>
<td>73</td>
<td>89</td>
</tr>
<tr>
<td>UAC ≥15.0 mg l⁻¹</td>
<td>28</td>
<td>96</td>
</tr>
<tr>
<td>Positive result on same day as UAC sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UAC ≥200.0 mg l⁻¹</td>
<td>58</td>
<td>95</td>
</tr>
<tr>
<td>UAC ≥15.0 mg l⁻¹</td>
<td>15</td>
<td>99</td>
</tr>
</tbody>
</table>

*Proportion of patients with UAC who had a positive dipstick test (true positive divided by true positive plus false negative). *Proportion of patients without UAC who had a negative dipstick test (true negative divided by true negative plus false positive). *Proportion of all patients with a positive dipstick test who had UAC (true positive divided by true positive plus false positive).

**Discussion**

The presented data had not been collected with the specific purpose of evaluating the quality of urinary dipstick tests for albumin in general practice. However, this sub-study aimed to describe how dipstick tests were currently used in Danish general practice.

The 675 patients in the intervention group constituted a representative sample of newly-diagnosed predominantly non-insulin dependent diabetic patients.⁴ The two patient samples presented — all those with three dipstick results and a urinary albumin concentration value, and those who had a dipstick test performed on the same day as a sample was sent for urinary albumin concentration measurement — accounted for 62% and 51% of the total intervention group, respectively. Data were missing because the application of a dipstick test for albumin was compulsory only at the yearly examinations; for many patients the yearly follow up had not yet progressed far enough to fulfil the data selection criteria; approximately 7% of patients die within the first two years of follow up; approximately 3% of patients are persistently haematuric;⁵ and because of low patient motivation for carrying through follow-up examinations. The biased selection of the final patient sample is not likely to have had any serious impact on the main results, as there is no reason to suggest any influence of sex, age and patient motivation on the methodological problems discussed.

A single urinary albumin concentration was used to evaluate the degree of renal involvement in diabetic patients. Although the intra-individual comparable variability of albumin excretion is approximately 40%,⁶ single measurements of urinary albumin

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concentration have proved to predict both more severe renal involvement and increased mortality.6,7,12-14 When classified according to urinary albumin concentration, approximately 4% of the patients in the present study were proteinuric (200.0 mg l\(^{-1}\) or more) and 36% were microalbuminuric (15.0–199.9 mg l\(^{-1}\)).

The importance of microalbuminuria is highlighted by its ability to predict proteinuria and increased mortality in non-insulin dependent diabetic patients.8,9 Furthermore, it has been documented in normotensive non-insulin dependent diabetic patients with microalbuminuria that angiotensin-converting enzyme inhibition has a long-term stabilizing effect on plasma creatinine and on albumin excretion rate.10 Although the therapeutic consequences of the finding of microalbuminuria need further elucidation, there are many indications for starting pharmacological treatment of even slight degrees of arterial hypertension or congestive heart failure in those patients who are microalbuminuric. Consequently, the general practitioner should be able to identify the microalbuminuric diabetic patients on the practice list.

Even through evaluation of three consecutive, conventional dipstick tests for albumin in this group of predominantly non-insulin dependent diabetic patients, general practitioners were only able to identify 73% of the proteinuric and 23% of the microalbuminuric patients. The figure of 75% may have resulted from insufficient quality of the dipstick itself or the handling of it, and much may thus be gained through improvement of the procedures and techniques employed. The figure of 23% is primarily a simple derivation of the detection limit of the commonly used dipstick methods for albumin.

In conclusion, it seems reasonable to suggest that the use of urine dipstick tests for albumin in general practice is replaced by the use of either the now available semi-quantitative dipstick methods for use in the range as low as 15 mg l\(^{-1}\) or,11,16 preferably, quantitative determination of urinary albumin concentration in a freshly voided morning urine sample.

References


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