Serum beta-2-microglobulin estimation as an indicator of the glomerular filtration rate

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Summary

In 56 patients in whom the glomerular filtration rate (GFR) was estimated by the 51Cr-EDTA technique, serum creatinine and beta-2-microglobulin levels were also measured. In the 15 patients with a GFR of $\geq 80$ ml/min, both serum creatinine and beta-2-microglobulin levels were within the reference range. However, the beta-2-microglobulin level was elevated (> 2.3 mg/l) in all 41 patients with a GFR of $< 80$ ml/min, while the serum creatinine level was increased (> 133 $\mu$mol/l) in only 35 patients. In the remaining 6 patients, the creatinine values ranged from 75 to 125 $\mu$mol/l. It would therefore seem that serum beta-2-microglobulin assay is a more sensitive test than creatinine assay for detecting impaired renal function.


A common problem in clinical medicine is the assessment of renal function when renal damage is suspected. Although definitive assessments of glomerular function can be achieved by measuring the glomerular filtration rate (GFR), such methods involve the collection of an accurately timed urine specimen, multiple blood samples and the administration of radioactive substances; these are clearly limitations in terms of cost, time and follow-up procedures. The trend has been towards simpler procedures which give some indication of renal function, and currently serum urea and creatinine levels are widely used for this purpose. Plasma urea levels are influenced by changes in protein intake and in urine flow rate, while creatinine is secreted by the renal tubule and the plasma concentration is also affected by protein intake and dependent on muscle mass. It is evident, therefore, that serum urea and creatinine levels as a measure of renal function have definite limitations. Recently attention has been focused on beta-2-microglobulin levels as a measure of glomerular function in normal circumstances; beta-2-microglobulin is a low-molecular-weight protein (11 800 daltons) and constitutes part of the histocompatibility antigens on cell membranes. It is released at a constant rate in normal subjects and, because of its low molecular weight, is freely filtered by the glomerulus; the filtered protein is almost completely reabsorbed and catabolized by the proximal tubules with only small quantities appearing in the urine.

With normal production rates and given the fact that beta-2-microglobulin is neither excreted nor reabsorbed into the circulation, serum levels should potentially reflect the GFR. To test the validity of this potential, serum creatinine and beta-2-microglobulin levels were measured in patients in whom GFR was estimated with 51Cr-EDTA. The results are reported in this communication.

Patients and methods

The studies were carried out on 56 consecutive patients who were referred by their attending physicians for measurement of the GFR by the 51Cr-EDTA method. Their ages ranged from 20 to 65 years; 19 of the patients were women and the remaining 37 were men. Before commencing with the GFR procedure blood samples were obtained for estimation of serum creatinine and beta-2-microglobulin. All samples were centrifuged within 2 hours and the sera stored at $-20^\circ$C until the day of the assay.

Creatinine was measured by the standard AutoAnalyzer technique, and beta-2-microglobulin by radio-immunoassay (Phadebas; Pharmacia, Uppsala, Sweden). GFR was assessed by means of a single-shot injection of 51Cr-EDTA.

Using double logarithmic scales, correlations were calculated between the serum beta-2-microglobulin value and the GFR and also between the serum creatinine level and GFR over the entire GFR range.

Results

The upper limit of the reference range for serum creatinine and beta-2-microglobulin levels in this laboratory is 133 $\mu$mol/l and 2.3 mg/l respectively. A GFR of $< 80$ ml/min was considered abnormal.

It can be seen in Table I that all 15 patients in whom the GFR was normal ( $\geq 80$ ml/min) had serum creatinine and beta-2-microglobulin levels within the reference ranges. However, in all

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>GFR</th>
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<tbody>
<tr>
<td></td>
<td>&lt; 80 ml/min</td>
</tr>
<tr>
<td>Serum beta-2-microglobulin</td>
<td>41 (100%)</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>35 (85%)</td>
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the remaining 41 patients with a GFR of < 80 ml/min the β₂-microglobulin levels were raised (> 2.3 mg/l), while the serum creatinine level was > 133 μmol/l in only 35 of these 41 patients. This difference was statistically significant at the 5% level. In the remaining 6 patients with a GFR of < 80 ml/min in whom the serum creatinine levels were within the reference range, values ranged from 75 to 125 μmol/l.

Figs 1 and 2 depict the correlations between the serum creatinine levels and the GFR and the serum β₂-microglobulin levels and the GFR. It is clearly evident that there is a highly significant negative correlation between the β₂-microglobulin level and the GFR (r = −0.84; P < 0.001) and also between the serum creatinine level and the GFR (r = −0.80; P < 0.001).

**Discussion**

The significant finding in the present study is that although both serum creatinine and serum β₂-microglobulin levels are correlated to the same degree with the GFR, the β₂-microglobulin levels unfailingly identified those patients with a GFR of < 80 ml/min whereas serum creatinine levels failed to do so in a significant proportion of patients (15%).

These findings therefore support the claim previously made that assay of the β₂-microglobulin level is the preferred test in that it eliminates the blind areas when the creatinine value is used as a measure of glomerular damage. However, one should take cognizance of the fact that increased β₂-microglobulin levels have been reported in liver disease, certain malignant lesions and immune disorders and do not always denote renal disease.

However, in such patients the diagnosis is usually obvious. Since no disorders in which production of β₂-microglobulin is low have been reported thus far, this study would seem to support the claim of Wibell that a normal serum β₂-microglobulin level seems to guarantee a GFR of ≥ 80 ml/min.

In conclusion, it seems that estimation of serum β₂-microglobulin levels would be more useful in assessing renal function than measurement of creatinine levels, and would therefore serve as a useful screening procedure to detect renal impairment if used judiciously.

**REFERENCES**