
Douglas T. Kurschinski1  
David A. Dennen1  
Maria Garcia2  
Angelo M. Scanu1,3
1 Clin. Labs.  
2 Dept. of Medicine/Lipoprotein Study Unit  
3 Dept. of Biochem. and Molecular Biol.  
The University of Chicago  
Chicago, IL 60637

Concentrations of Neopterin in Serum of Recipients of Renal Allografts

To the Editor:

Determination of neopterin in urine, plasma, and serum is increasingly used in transplantation medicine as a sensitive marker of immunological complications (for reviews, see 1–3).

In a recent Technical Brief, Myara et al. (4) made a significant and important contribution to these issues; showing that, in recipients of heart allografts, simultaneous determination of concentrations of neopterin and of C-reactive protein in serum enables differentiation between bacterial and viral infections.

One of their statements, however, deserves more detailed discussion: They state that concentrations of neopterin in serum are affected by renal dysfunction, and therefore are only of limited use in renal-transplant recipients.

We (5, 6) and others (7–10) have shown that in case of renal impairment it is essential to relate concentrations of neopterin in serum to simultaneously measured concentrations of creatinine in serum if one is to distinguish increases in neopterin due to cell-mediated immune activation from those simply caused by insufficient excretion. Notably, in our study (11) first proposing measurement of neopterin concentrations for diagnosis of rejection of kidney allografts, urine was used, and here, neopterin concentrations are routinely related to urinary creatinine.

It was demonstrated that a strong linear relationship exists between clearance rates of neopterin and creatinine (linear correlation coefficient \( r = 0.863; 95\% \text{ confidence interval } 0.841–0.882 \)) with a regression coefficient of about 1.8 (7). Analogously, in healthy subjects neopterin clearance was found to be about 1.8 (6). Moreover, when serum neopterin concentrations were related to urinary neopterin/creatinine ratios (7), only a weak correlation \( (r = 0.269; 0.190–0.345) \) was found, which was dramatically improved by relating serum neopterin to serum creatinine \( (r = 0.779; 0.750–0.805) \). Similarly, neopterin concentrations in serum were similar in patients with acute tubular necrosis and during acute rejection, but relating them to serum creatinine yielded a clear distinction between both diagnostic categories. Wolf et al. (8) found that the ratio of neopterin clearance and serum neopterin concentrations was superior for differential diagnosis between acute tubular necrosis and graft rejection.

We conclude that it is imperative to relate concentrations in serum to one measure of renal function (most simply to serum creatinine concentration) in all conditions where renal impairment may occur—especially in renal transplantation, where large variability of renal function is met.

References

Gilbert Reibnegger  
Dietmar Fuchs  
Arno Hausen  
Ernst R. Werner  
Gabriele Werner-Felmayer  
Helmut Wachter
Institut für Med. Chem. und Biochem.  
Universität Innsbruck  
Fritz Fregl Strasse 3  
A-6020 Innsbruck, Austria

Immunochemical Test for CK-MB Isoforms

To the Editor:

Puleo et al. (1) recently reported increased concentrations of tissue-specific isoform of CK-MB (CK-MB2), measured by using 1800-V electrophoresis, as early as 1 h after onset of myocardial infarction (MI) and stated that the assay was sensitive, rapid, and specific for diagnosis of MI within 1 to 3 h after its onset. The values for CK-MB2 reported were 7.3 (SD 3.30) U/L for MI and 4.8 (SD 1.9) U/L for normal persons when measurements were made within 3 h of onset of symptoms.

One can measure activities (U/L, 37 °C) of CK-MB2, the serum-specific isoform (CK-MB1), and CK-MB for clinical use with commercially available "IMPRES-MB" (International Immunoassays Laboratories, Inc.) reagents. The test reagents and sample-to-substrate ratios are optimized to increase chemistry analyzer absorbance response by two- to threefold for a given change in activity over what is ordinarily seen. This allows for differentiating CK-MB in the 2–10 U/L range with CVs ranging from about 20% at 2 U/L to 8% at 10 U/L. The following package-insert procedure was used to generate the results reported below. Three 100-µL aliquots of patients' samples were immunoneutralized with 25 µL each of reagents A, B, and C available with the kit. Reagent A removes CK-MM, reagent B removes CK-M subunit (CK-MM +

CLINICAL CHEMISTRY, Vol. 35, No. 10, 1989 2157