Concentrations of Brain Natriuretic Peptide in Treated Congestive Heart Failure

To the Editor:

We describe here a significant decrease in brain natriuretic peptide (BNP) concentrations in plasma in seven patients after treatment for congestive heart failure (CHF). We studied five men and two women, ages 35–79 (63.8±6.1, mean±SE) years. Six patients (A, B, C, D, E, and F in Figure 1) had CHF of class IV, classified by New York Heart Association (NYHA) functional criteria; one patient (G) was in class III.

BNP concentration in plasma from each patient was measured by a newly developed radioimmunoassay. In this RIA, the minimum detectable amount of BNP was 0.3 pg/tube, and the cross-reactivity with α-atrial natriuretic peptide (α-ANP), the amino acid sequence of which is remarkably homologous to BNP (I), was <0.001%. The mean concentration of plasma BNP in the seven patients at the start of treatment was 168.3 (SE 67.8) ng/L, which was 29-fold higher than that of normal subjects: 5.9 (SE 0.9) ng/L (n = 5). These results are consistent with those of a recent report in which the plasma concentration of BNP in CHF patients markedly increased (2).

As shown in Figure 1, after treatment with conventional medication (digitalis and diuretics), the plasma BNP concentrations in five patients (A, B, C, D, and E) decreased with accompanying improvement in their symptoms. Plasma BNP concentration increased in two patients (F and G), who took a turn for the worse, although a temporary clinical improvement was observed. These data suggest that plasma BNP concentrations were essentially decreased in clinical improvement, as evaluated by NYHA functional criteria, and that plasma BNP may serve as a potential humoral monitor for clinical improvement in CHF patients treated with conventional medication.

CLINICAL CHEMISTRY, Vol. 37, No. 5, 1991 765

Fig. 1. Plasma concentrations of BNP in patients with CHF, before and after receiving conventional medication

The numbers represent the number of days since the start of treatment (0). The shaded zone at the bottom indicates normal range of plasma BNP concentration.
appropriate control materials. The lower limit of detection for albumin by this method is 0.03 g/L. Electrophoresis of the random specimen and the 24-h urine collection (Figure 1B) on 10% cross-linked sodium dodecyl sulfate-polyacrylamide gel showed no protein of molecular mass similar to that of albumin in the random specimen. However, the sample from the 24-h urine sample obtained on the seventh day of hospitalization showed a well-defined band in the albumin region. Immunofixation electrophoresis (Figure 1A) also identified this protein as albumin. No monoclonal paraproteins were detected, but the presence of lysozyme and transferrin were demonstrated by immunofixation electrophoresis. β_{2}-Microglobulin was not measured.

This case suggests that proteinuria with a transient decrease in albuminuria may occur in patients with similar constellations of medical problems (ischemic cardiac disease and diabetes mellitus) and drug treatment (1, 4). Data from 24-h urine collections and electrophoretic findings for comparison with subsequent urine specimens were not given in other reports (1, 4).

Our patient, however, showed continuing mild proteinuria (based on a urinary protein/creatinine ratio of 0.4 in both the random and the 24-h urine specimens) with a changing composition of urinary proteins. Albuminuria was initially undetectable by immunofixation in this patient, which differs from the findings of others (2). The apparent absence of albumin in this case of proteinuria may be a real but transient finding, possibly related to drug treatment, as suggested by previous reports (1, 2).

References

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Multilayer-Film Bromcresol Green Method for Albumin Measurement
Significantly Inaccurate When Albumin/Globulin Ratio Is <0.8

To the Editor:

Recently we introduced in our "stat" laboratory a Kodak Ektachem 700XR analyzer (Eastman Kodak Co., Rochester, NY). Upon evaluating the chemistries, we observed significant discrepancies between our routine bromcresol purple (BCP) method for measuring albumin and the multilayer-film bromcresol green (BCG) method used by the Ektachem. Using orthogonal regression according to Bablok et al. (1), we calculated from results for 202 samples of unselected hospitalized patients the following regression line: [Alb]_{Kodak} = 0.925 [Alb]_{BCP} + 5.48/g/L (r = 0.93, S_{xy} = 2.2 g/L). Visual inspection of the graphical data revealed large discrepancies for albumin concentrations <25 g/L.

As is well known, BCG methods for measuring albumin in plasma do not always give accurate results, particularly for samples with a low albumin/globulin ratio, as in nephrotic syndrome, burns, and inflammations (2–4). The inaccuracy is particularly significant in methods involving long reaction times (>30 s). The Ektachem BCG-slide method has a reaction time of ~160 s, but was reported to yield satisfactory results in a pediatric population (5), and correlated well with a "fast reading" BCG method (6).

To verify our initial results, we analyzed a further 72 samples, selected to have albumin concentrations ranging from 10 to 50 g/L, and albumin/globulin ratios ranging from 0.26 to 2.5. We measured albumin concentrations with a rate immunonephelometric method (ICS; Beckman Instruments, Mijdrecht, The Netherlands), and compared these concentrations with those obtained with a BCP method (7) in routine use on a Hitachi