ASSESSMENT OF SERUM β -TRACE PROTEIN (BTP) MEASUREMENT IN THE PREDICTION OF GLOMERULAR FILTRATION RATE. COMPARISON WITH SERUM CYSTATIN C.

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Serum BTP measurement is sometimes believed to be an alternative marker of glomerular filtration rate (GFR) assessment. The aim of the present work was to investigate the correlation between creatinine, cystatin C, and BTP values in sera and to compare the diagnostic efficacy for serum BTP and cystatin C with the glomerular filtration rate estimate. 25 individuals were tested. GFR was estimated from creatinine clearance, serum cystatin C and BTP and urine α -1 microglobulin, albumin, GMT and creatinine were measured. BTP values correlated with cystatin C ($r = 0.75$; $p < 0.01$), creatinine ($r = 0.73$, $p < 0.01$), GFR ($r = -0.46$; $p = 0.02$), urine α -1-microglobulin ($r = 0.66$; $p < 0.01$). The diagnostic efficacy of BTP for reduced GFR was insufficient and the calculation of GFR with BTP was not included in the regression model.

INTRODUCTION

Recent studies have shown that low-molecular weight proteins in serum seem to be better markers for the assessment of reduced glomerular filtration rate (GFR) than the conventional determination of serum creatinine. Several proteins, such as ribonuclease, α -microglobulin, β -microglobulin (B2M), and cystatin C were compared with serum creatinine. Whereas serum creatinine is increased only after a 50 % reduction in GFR, the above proteins, especially cystatin C, are increased within the so-called creatinine-blind range. Recently, another low-molecular weight protein, the β -trace protein (BTP), isolated primarily from cerebrospinal fluid, has been shown to be increased in patients with renal disease. The first information described that BTP may be suitable as an indicator of reduced GFR even in the creatinine-blind range¹.

The aim of our work was to investigate significant correlations between serum cystatin C, BTP and GFR and correlations between BTP and urinary proteins. An additional aim was to compare the diagnostic efficacy of cystatin C and BTP in individuals with reduced GFR values.

MATERIALS AND METHODS

A group of 25 individuals was tested (11 women, 14 men, age 17–80 years). Renal function problems were suspected in all of the patients.

Serum Creatinine (Jaffe), BTP (BNA II, Dade Behring) and cystatin C (Advia 1650, DAKO) and urine albumin (Advia 1650, DAKO), GMT (Advia 1650, Biovendor), α -1-microglobulin (Advia 1650, Biovendor) were tested.

BTP measurement was based on the principle of latex particle-enhanced immunonephelometry using rabbit polyclonal antibodies against BTP. Calibration of the assay is predicated on highly purified BTP from cerebrospinal fluid characterized by amino acid sequencing and quantitative amino acid analysis. For the default sample dilution of 1:100, the basic measuring range is 0.25–15.8 mg/l. The total analytical imprecision of the assay, calculated from two control materials and three serum samples with concentrations of 1.51–7.89 mg/l, was between 2.7 % and 8 %.

Glomerular filtration rate was calculated with standardised method by creatinin clearance with body surface correction $\text{GFR} [\text{ml/s/1.73m}^2] = (\text{Creatinine clearance} / \text{S}) \times 1.73$; where Creatinine clearance $[\text{ml/s}] = (\text{urine creatinine} \times \text{urine volume}) / \text{serum creatinine}$; $\text{S} = 0.0167 \times (\text{m} \times \text{h})^{1/2}$.

Individuals were divided in context with GFR to individuals with reduced GFR ($\text{GFR} < 1.15 \text{ ml/s/1.73m}^2$) and normal GFR values ($\text{GFR} \geq 1.15 \text{ ml/s/1.73m}^2$).

Obtained data were processed by the Medcalc software (Medcalc, Belgium). The value $p < 0.05$ was considered as statistically significant. The comparison of measured marker values was done using Sperman correlation according data distribution. Receiver operating curves for BTP and reduced GFR were performed. All data are expressed as medians and means $\pm$ S.D.

RESULTS

14 individuals had lower GFR values (56 %). Data GFR and BTP distribution were normal (Tab. 1)

Table 1. Basic statistical parameters

Parameter	X	Median	S	Normality
BTP	1.0	0.96	0.38	Yes
Cystatin-C	1.11	1.08	0.23	Yes
Kreat	106.0	104.0	22.4	Yes
Alb/cerat	29.4	4.6	102.8	No
GMT/creat	67.9	59.8	24.1	Yes
A1-MG	7.5	3.7	10.4	No
GFR	1.3	1.2	0.3	Yes

Significant correlations between BTP and cystatin-C ($c = 0.75$; $p < 0.01$), creatinine ($c = 0.73$, $p < 0.01$), GFR (-0.46 ; $p = 0.02$), urine α -1-microglobulin ($c = 0.66$; $p < 0.01$). No additional correlations were found.

Diagnostic efficacy of BTP for reduced GFR was insufficient. Sensitivity of BTP was 57 %, specificity 91 % (cut-off 1.07 mg/l; AUC 0.71; LR+ 6.3; 95 % CI 0.50–0.87). However, the diagnostic efficacy of serum cystatin C was sufficient (AUC 0.8), area under curves of both parameters in lower GFR values did not differ. (Fig. 1)

Fig. 1. Comparison of receive operating curves for serum BTP and cystatin C according to GFR values (AUC 0.71 vs. 0.81; $p = 0.30$)

The stepwise regression incorporated into the model of GFR prediction only cystatin C; BTP was not included.

DISCUSSION

β -TP (synonymum prostaglandin D synthase) is a low-molecular-mass protein belonging to the lipocalin protein family. With its 168 amino acids, the protein has a molecular mass between 23 and 29 kDa depending on the degree of glycosylation. Recently it was verified that β -trace protein was established as an accurate marker of cerebrospinal fluid leakage. It has also been reported recently as a potential marker in detecting impaired renal function, although no more sensitive than cystatin C. The benefit of β TP measurement could be findings that β -trace protein concentrations, in contrast to cystatin C concentrations, are not influenced by glucocorticoid therapy. β TP might be a promising marker in the diagnosis of perilymphatic fluid fistulas²⁻⁶.

BTP is not a useful and reliable analyte to estimate GFR in normal population, in our opinion.

In conclusion, although BTP serum values correlated significantly with serum cystatin C, GFR and urine microproteins, the diagnostic efficacy for GFR estimation in the normal population was insufficient. A partial limitation of our study was the small number of patients and the calculation of GFR with creatinine clearance.

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