Serum Beta-Trace Protein for Assessment of Kidney Function in Neonates

Nastaran Khosravi,[1] Manoochehr Asgari,[1] Nasrin Khalessi,[1] Rozita Hoseini,[2] Niloofar Khosravi[3]

[1]Division of Neonatology, Iran University of Medical Sciences, Tehran, Iran
[2]Division of Pediatric Nephrologist, Pediatric Renal Transplantation and Dialysis Research Center, Iran University of Medical Sciences, Tehran, Iran
[3]Iran University of Medical Sciences, Tehran, Iran

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Introduction. Compared to the conventional methods, serum beta-trace protein (BTP) has been shown to be more helpful for estimating glomerular filtration rate; however, its value is remained unclear in neonates. The present study aimed to investigate the range of serum BTP level in healthy term neonates and its value to estimate glomerular filtration rate.

Materials and Methods. This cross-sectional study was conducted on 50 healthy term neonates without underlying cardiovascular or kidney disorders who were admitted to Ali Asghar hospital in 2013. Serum BTP was measured using an automated nephelometric immunoassay. Glomerular filtration rate was assessed using the Schwartz equation based on serum creatinine level.

Results. The mean age of the neonates was 6.2 ± 3.6 days (range, 2 to 17 days), their mean gestational age was 38.02 ± 0.20 weeks, and their mean height was 49.8 ± 1.7 cm. The mean serum BTP level was 0.41 ± 0.11 mg/L (range, 0.19 mg/L to 0.92 mg/L). The mean serum creatinine level was 0.49 ± 0.16 mg/dL (range, 0.3 mg/dL to 1.0 mg/dL). The mean estimated GFR was 48.90 ± 15.88 mL/min. A positive correlation was observed between the reciprocal concentrations of BTP and GFR (r = 0.383, *P* = .006). Furthermore, the reciprocal concentrations of BTP was associated with the reciprocal concentrations of serum creatinine level (r = 0.365, *P* = .009).

Conclusions. Measurement of serum BTP can be a reliable tool for detecting kidney function in neonates. Further studies are warranted to design a suitable formula for GFR estimation based on serum BTP in neonates.

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INTRODUCTION

Compared to the conventional methods such as measurement of serum creatinine and creatinine clearance, the serum level of low-molecular weight proteins has been shown to be more helpful for estimating glomerular filtration rate (GFR).[1] One of the applicable molecules commonly used in recent decade is cystatin C, a cysteine protease inhibitor produced and secreted by various types of nucleated cells and filtered by the renal glomerula.[2] Another molecule is beta-trace protein (BTP), a glycoprotein from the lipocalin protein family primarily isolated from cerebrospinal fluid,[3] which can be easily filtered through the glomerulus and then completely reabsorbed through the tubules.[4-6] In this regard, the diagnostic application of BTP as a novel serum marker for detection of GFR has been recently suggested.[7,8] This hypothesis was reinforced when it was demonstrated that BTP was not affected by acute-phase reactions, and

also this molecule was completely stable in a wide pH range.[9,10] However, there is little information on the normal range of BTP in neonates and the diagnostic value of this molecule to estimate GFR within neonatal period. Thus, the present study aimed to investigate the relationship between serum BTP and kidney function in healthy neonates.

MATERIALS AND METHODS

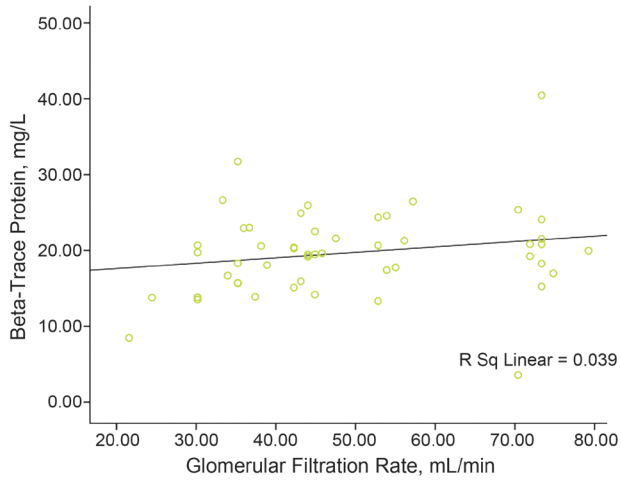
This cross-sectional study was conducted on 50 healthy term neonates without underlying cardiovascular or kidney disorders who were admitted to Ali Asghar Children's Hospital in 2013. Blood samples were taken and after centrifugation (1600 g for 15 minutes), samples of serum were stored at -28°C until analysis. In all neonates, serum levels of creatinine and BTP were simultaneously measured. Serum creatinine concentration was determined by an enzymatic method. Serum BTP was measured using an automated nephelometric immunoassay on a BN ProSpec analyzer (Siemens, Germany). Glomerular filtration rate was assessed by the Schwartz equation from the serum creatinine level with the constant coefficient (K) of 0.44.

The SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc, Chicago, IL, USA) was used for data analysis. *P* values less than .05 were considered significant.

RESULTS

Of the 50 neonates, 56% were boys and 44% were girls. Also, 82% were icteric and the remaining 18% had transient tachypnea of the newborn. The mean age of the neonates was 6.2 ± 3.6 days (range, 2 to 17 days), their mean gestational age was 38.02 ± 0.20 weeks, and their mean height was 49.8 ± 1.7 cm. Only 2 neonates were less than 7 days old with the mean serum creatinine 0.71 mg/dL.

The mean serum BTP level was 0.41 ± 0.11 mg/L (range, 0.19 mg/L to 0.92 mg/L). The mean serum creatinine level was 0.49 ± 0.16 mg/dL (range, 0.3 mg/dL to 1.0 mg/dL). The mean estimated GFR based on the Schwartz equation was 48.90 ± 15.88 mL/min. A positive correlation was observed between the reciprocal concentrations of BTP and estimated GFR (r = 0.383, *P* = .006; Figure). Furthermore, the reciprocal concentrations of BTP was positively associated with the reciprocal concentrations of serum creatinine (r = 0.365, *P* = .009).



Positive correlation between the inverse of beta-trace protein and glomerular filtration rate estimated by the Schwartz equation.

DISCUSSION

Our results emphasized the diagnostic value of serum BTP among neonates to demonstrate kidney function. The presence of association between the reciprocal concentrations of BTP and estimated GFR measured by the conventional method indicated that the measurement of BTP can be considered as a tool to predict kidney function in newborns. A few studies have been published on accuracy of BTP to assess kidney function in neonates and children. However, the main limitations of the present study were the lack of a gold standard method of GFR measurement and the lack of determination of the best cutoff point for BTP to discriminate damage from normal kidney function in neonates; thus, we cannot design a formula for GFR estimation based on serum BTP and cannot predict the validity of BTP to estimate GFR based on standard method results. Also, we did not assess and compare the power of BTP in comparison with conventional methods to assess GFR.

In a study by Priem and colleagues,[11] using the receiver operating characteristic curve analysis, BTP indicated curvilinear behavior in relation to GFR, as did creatinine. Furthermore, there were significant correlations between GFR and the reciprocal concentrations of both creatinine and BTP. In this context, the area under the BTP curve was significantly larger than the areas under the creatinine curve, showing a higher power of discrimination. Similarly, Bhavsar and coworkers[12] showed that the association between higher BTP

level and end-stage renal disease was stronger than those for the other markers. In contrast, some studies could not demonstrate sufficient value of BTP for discriminating impaired from normal kidney condition. Solichova and colleagues[13] showed that the diagnostic efficacy of BTP for reduced GFR was insufficient and the calculation of GFR with BTP was not included in the regression model. One of the main reasons for these paradoxical results is the lack of reliable equation, indicating association between BTP and GFR. To solve this problem, more studies with extended number of cases are required in which measured GFR should be considered as gold standard.

CONCLUSIONS

Inverse serum BTP is associated with estimated GFR level among neonates, and thus, this biomarker can be an applicable marker for assessment of kidney function in this age group. As BTP is a new biomarker of kidney function, especially in neonates, the results of this study are new, more studies are required for demonstration its high power and also its best cutoff point to differentiate normal from impaired kidney function. In addition, studies are needed to determine a new GFR formula based on serum BTP in neonates.

CONFLICT OF INETERST

None declared.

REFERENCES

1. Woitas RP, Stoffel-Wagner B, Poege U, Schiedermaier P, Spengler U, Sauerbruch T. Low-molecular weight proteins as markers for glomerular filtration rate. Clin Chem. 2001;47:2179-80.
2. Randers E, Erlandsen EJ. Serum cystatin C as an endogenous marker of the renal function: a review. Clin Chem Lab Med. 1999;37:389-95.
3. Madero M, Sarnak MJ, Stevens LA. Serum cystatin C as a marker of glomerular filtration rate. Curr Opin Nephrol Hypertens. 2006;15:610-6.
4. Hoffmann A, Nimtz M, Conradt HS. Molecular characterization of b-trace protein in human serum and urine: a potential diagnostic marker for renal diseases. Glycobiology. 1997;7:499-506.
5. Huber AR, Risch L. Recent developments in the evaluation of glomerular filtration rate: is there a place for beta-trace [Comment]? Clin Chem. 2005;51:1329-30.
6. Filler G, Priem F, Lepage N, et al. Beta-trace protein, cystatin C, beta(2)-microglobulin, and creatinine compared for detecting impaired glomerular filtration rates in children. Clin Chem. 2002;48:729-36.
7. Kobata M, Shimizu A, Rinno H, et al. Beta-trace protein, a new marker of GFR, may predict the early prognostic stages of patients with type 2 diabetic nephropathy. J Clin Lab Anal. 2004;18:237-9.
8. Grubb AO. Cystatin C—properties and use as diagnostic marker. Adv Clin Chem. 2000;35:63-99.
9. Astor BC, Shafi T, Hoogeveen RC, et al. Novel markers of kidney function as predictors of ESRD, cardiovascular disease, and mortality in the general population. AmJ Kidney Dis. 2012;59:653-62.
10. Bokenkamp A, Franke I, Schlieber M, et al. Beta-trace protein--a marker of kidney function in children: "Original research communication-clinical investigation". Clin Biochem. 2007;40:969-75.
11. Priem F, Althaus H, Birnbaum M, Sinha P, Conradt HS, Jung K. Beta-trace protein in serum: a new marker of glomerular filtration rate in the creatinine-blind range. Clin Chem. 1999;45:567-8.
12. Bhavsar NA, Appel LJ, Kusek JW, et al; AASK Study Group Comparison of measured GFR, serum creatinine, cystatin C, and beta-trace protein to predict ESRD in African Americans with hypertensive CKD. Am J Kidney Dis. 2011;58:886-93.
13. Solichova P, Novackova L, Ochmanova R, Stejskal D. Assessment of serum beta-trace protein (BTP) measurement in the prediction of glomerular filtration rate. Comparison with serum cystatin C. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2006;150:83-4.

Correspondence to:
Niloofar Khosravi, MD
Iran University of Medical Sciences, Tehran, Iran
E-mail: niloofarkhosravi@rocketmail.com

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