

Study of urinary protein creatinine index in hypertensive patient

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Abstract

Objectives: Proteinuria is a hallmark of glomerular diseases. Uncontrolled high blood pressure increases the risk of glomerular disease leading to proteinuria and high urinary creatinine. So an attempt was made to validate the PCI of a random urine sample as a reliable and a convenient test.

Methods: Total of 42 hypertensive patients and 80 controls were selected. Their urinary protein was estimated by urinary dipstick method and colorimetric sulfosalicylic acid method. Urinary creatinine was estimated by modified Jaffe's method. Protein creatinine index was measured for each patients and controls.

Results: It was found that the amount of creatinine in urine in hypertensive patients (0.91 ± 0.29 mmol/dl) was comparable to that in the control subjects (0.86 ± 0.38 mmol/dl).

The mean of urinary protein concentration in the hypertensive patients was 13.66 ± 5.77 mg/dl, and in the controls was 8.13 ± 2.82 mg/dl respectively. Highly significant value of PCI were observed in hypertensive patients (153 ± 59.08) as compared to the controls where PCI was 114.64 ± 47.96 ($p < 0.001$).

Conclusion: PCI of a random urine sample can serve as a reliable and convenient test to replace 24 hr urine protein estimation. It can serve as baseline predictor of progression of renal diseases.

Keywords: Hypertension, PCI, Albumin, Creatinine.

1. Introduction

Hypertension, also referred to as high blood pressure, is a condition in which the arteries have persistently elevated blood pressure. Uncontrolled high blood pressure increases the risk of serious health problems, including heart attack, stroke and renal disease in secondary hypertension. Proteinuria is abnormal protein loss in the urine which is a hallmark of glomerular diseases [1]. From a diagnostic standpoint the clinical finding of proteinuria must first be localized as prerenal, renal, or postrenal[2]. Proteinuria represents a breakdown in early filtering apparatus of the kidney. Albumin the most abundant blood protein - is not charged, and is the protein most likely to pass through the damaged filter. It is this protein that urine tests look for when assessing proteinuria. Some disease states causes the amount of other proteins in the urine -- besides albumin -- to increase, and special tests (PCI or 24hrs urinary protein) are needed to screen for these.

Quantification of proteinuria can be useful in the work-up of the patient who has a urine dipstick positive for protein. Quantification using a 24hrs urine collection for protein is being replaced by the urine protein/creatinine ratio from a random urine specimen, ideally from the first morning void. The urine protein creatinine ratio closely correlates with daily protein excretion that is based on grams per 1.73 m² body surface area[3,4]. This measurement provides a more accurate quantification of proteinuria compared with the urine dipstick and is much less subjects to false negative and false negative reading. As the protein the urine albumin/creatinine ratio correlates well with albumin excretion with a timed urine sample[5,6]. A ratio of greater than 0.03 mg of albumin per milligram of creatinine is considered abnormal. There is increasing evidence that microalbuminuria predicts cardiovascular disease in nondiabetic adults [7,8].

A normal healthy individual excretes about 20-150 mg/24hrs protein, of which about half is albumin [9]. Protein excretion in urine shows considerable biological variability and may be increased by upright posture, exercise, fever, heart failure cold climates and kidney disease. Protein excretion is also higher in adults than children; the protein excretion rate is slightly higher in females. The protein excretion rate is higher in day time than during the night, the sex differences disappear in overnight collection [10]. In this study, an attempt was made to validate the PCI of a random urine sample as a reliable and a convenient test to replace the 24hrs urine protein estimation, in order to overcome the pitfalls which are associated with the 24hrs urine collections. Hence, this study was conducted.

2. Material & Methods

In our study, a total of 42 hypertensive patients belonging to 25 to 60yrs of age, were selected from medicine OPD of Rama Medical College Hospital & RC, Hapur. Similarly, 80 normal individuals were taken as control.

Individuals having diabetes, thyroid disorder, emotion and physical stress, exposure to extremes of climate, urinary tract infection, person who does heavy exercise and any other renal disorder which can cause proteinuria, were excluded from the study. Both the individuals (Hypertensive patients and controls) were instructed to collect early morning sample. Sample was taken at room temperature without adding any preservatives and immediately after collection, the urine sample were analyzed for protein and creatinine.

Heller's nitric acid test, heat coagulation test and sulfosalicylic acid test were used qualitatively for the detection of urinary protein [11]. Semi-quantitative estimation of urinary protein was done by urinary dipstick method. The quantitative estimation of urinary protein was performed by colorimetric sulfosalicylic acid method [12]. Colorimetric estimation of urinary creatinine was done by modified Jaffe's method [12].

2.1 Calculation of protein creatinine index (PCI) [11]

Urinary PCI was calculated by the following equation:

$$\text{Urinary PCI} = \frac{\text{urinary protein (mg/L)}}{\text{urinary creatinine (mmol/L)}} \times 10$$

PCI is estimated by multiplying the protein creatinine ratio (measured in mg/mmol) by a factor of 10 since although daily excretion of creatinine depends on muscle mass, an average figure of 10 mmol creatinine per day can be assumed.

2.2 Statistical analysis

The normal range of the urinary PCI was calculated from the data which was obtained from the urine samples from normal healthy subjects. The unpaired

student's 't' test was used to compare the PCIs of the normal healthy controls and hypertensive patients.

3. Results

The controls and the study subjects (hypertensive patients) were tested qualitatively and quantitatively for the presence of protein in their urine samples. Among the qualitative tests, the heat coagulation test was found to be most sensitive one for the detection of the protein in urine. The finding of the dipstick test matched with those of the quantitative analysis results in most of the cases. In few cases, the dipstick analysis showed false negative results when they were compared with the results of the quantitative analysis which was done by the sulfosalicylic acid colorimetric method.

Comparable value of primary creatinine were obtained for the controls and the hypertensive patients ($p = 0.436$). It was found that the amount of creatinine in urine in hypertensive patients was comparable to that in the control subjects (Table 1).

The mean of urinary protein concentration found in the hypertensive patients was 13.66 ± 5.77 mg/dl, and in the controls was 8.13 ± 2.82 mg/dl (Table no 2). The protein excretion in spot urine sample in hypertensive patients was found to be highly significant in comparison to the controls ($p = <0.001$). Highly significant value of PCI were observed in hypertensive patients as compared to the controls ($p < 0.001$) (Table no 3). Frequency distribution curve for PCI of normal subjects showed a non-Gaussian distribution of observations.

Out of 42 patients, ten persons (hypertensive patients) were found to have PCI values greater than the established normal range in the group of individuals. In our study we found that the range of proteinuria was in upper higher side of normal reference range in hypertensive subjects as compared to control group.

Table 1: Comparison of urinary creatinine between control and hypertensive patients

Parameter	Control group (n=80)	Hypertensive patients (n=42)	p-value
Urinary creatinine (mmol/dl)	0.86±0.38	0.91 ±0.29	0.471

Table 2: Comparison of urinary protein between Control and hypertensive patients

Parameter	Control group (n=80)	Hypertensive patients (n=42)	p-value
Urinary protein (mg/dl)	8.13±2.82	13.66±5.77	($p < 0.001$)

Table 3: Comparison of urinary PCI between control and hypertensive patients

Parameter	Control group (n=80)	Hypertensive patients (n=42)	p-value
PCI	106.82±44.16	153.31±59.08	($p < 0.001$)

4. Discussion

The findings show significant differences of protein between the controls and hypertensive patients. Well documented test for the diagnosis of proteinuria has been the timed collection of urine over twenty four hrs[13]. The use of twenty four hrs urine collection is necessitated by the variation in protein excretion throughout the day, since the urinary protein excretion follows a circadian rhythm. However, the 24hrs urine collection is cumbersome, inconvenient and often incomplete in outpatients [14]. In an attempt to fulfill the need for a reliable and quick measurement of urinary protein various researchers have proposed that the calculation of ratios such as urinary protein/ urinary creatinine, urinary albumin/urinary creatinine and PCI in spot urine samples [15]. These parameters take into the account the fact that creatinine excretion remains fairly constant in the presence of stable GFR, thus eliminating the variation in urinary protein concentration during the day. Good correlation has been found between the results of proteinuria obtained from these parameters and that calculated from 24hrs urine specimen. But, consensus for specific PCI cut-off value has been obtained [15]. In this study an attempt has been made to validate PCI of a random urine sample as a reliable and convenient test to replace 24-hrs urinary protein estimation in order to overcome the pitfalls associated with 24-hrs urine collection. Normal range of PCI in this region has also been established (40-190 mg/mmol). There was no significant difference between the sex and age of the subjects from the two groups.

Shaw *et al* reported that PCI below 125 in a random urine sample excluded abnormal proteinuria and proposed that the protein creatinine index in random urine sample should be used to supplement dipsticks in screening for proteinuria. They concluded that an index of more than 136 (British subjects) indicated the presence of pathological proteinuria[16].

In a recent study by Kumar A *et al*, it was indicated that the urinary protein excretion and PCI value significantly elevated in type 2 diabetes mellitus patients. The mean of urinary protein concentration which was found in the diabetic patients was 25.37 ± 12.5 mg/dl, and in the control group, it was 8.93 ± 3.54 mg/dl. A significantly higher value of the PCI was observed in diabetic patients 373.04 ± 98.53 as compared to that in the control group, where the PCI was 114.65 ± 47.97 ($p < 0.001$)[17].

Price *et al* reviewed a number of studies and suggested that the P:C ratio can predict the amount of protein excreted in urine[13].

Derhaschening U *et al* found his study microalbumin measurement alone and calculation of the albumin/creatinine ratio for the screening of the hypertension patients albumin creatinine ratio values were

not significantly increased ($p = 0.73$) in spot urine sample[18].

According to James MA *et al* median 24 hrs urinary excretion was 15.75 mg. the median 24 hrs albumin creatinine ratio was 1.91 mg/mmol. The closest relation between albumin-creatinine ratio and blood pressure was that between spot albumin-creatinine ratio and clinic systolic blood pressure $r = 0.64$, $p < 0.001$. Albumin-creatinine ratio was generally related to clinic systolic blood pressure, diastolic blood pressure and ambulatory systolic blood pressure. Microalbuminuric subjects had significantly higher level of clinic and ambulatory systolic blood pressure than non-microalbuminuric subjects [19].

Gupta RC *et al*[20] reported that the PCI range to be from 37-247 in Indian subjects which is comparable to the normal range obtained in this study.

5. Conclusion

In this study an attempt has been made to validate PCI of a random urine sample as a reliable and convenient test to replace 24 hr urine protein estimation in order to overcome the pitfalls associated with 24 hrs urinary collection.

This indicates that the first morning sample urine protein creatinine index serve as baseline predictor of progression of renal diseases, The advantages of calculating PCI are that errors due to improper collection of urine sample or inaccuracy in the timing of collection period do not affect the index. The normal range of PCI in this region has also been established.

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