

COMPARISON OF URINARY PROTEIN CREATININE INDEX IN NORMAL AND HEAVY EXERCISE PERFORMING INDIVIDUALS

Ijen Bhattacharya¹, Anoop Kumar², Akash Gupta¹, Tabassum Yasmin¹, Naved Ahmad³, Mani Goel⁴

¹ Department of Biochemistry, Rama Medical College, Pilakhuwa Hapur, Uttar Pradesh, India

² Department of Biochemistry, Santosh Medical College Ghaziabad, Uttar Pradesh, India

³ Department of Biochemistry, Subharti Medical College, Meerut, India

⁴ Department of Pharmacology, Santosh Medical College Ghaziabad, Uttar Pradesh, India

Correspondence to: Akash Gupta (akash_inspace@yahoo.com)

DOI: 10.5455/ijmsph.2014.050620143

Received Date: 06.05.2014

Accepted Date: 05.06.2014

ABSTRACT

Background: Physical exercise is the performance of some activity in order to develop or maintain physical fitness and overall health. Exercise induce proteinuria is generally benign and a function of the intensity- rather than the duration of the exercise. Quantification using a 24 hours urine collection for protein is being replaced by the urine protein creatinine ration from a random urine specimen, ideally from the first morning void.

Aims & Objective: To compare protein creatinine index between normal and heavy exercise performing individual.

Materials and Methods: Total 40 controls (who were not doing exercise) and 34 subjects) who were doing heavy exercise daily) were selected for the study. Their early morning urine sample was taken for estimating urinary protein by quantitative sulfosalicylic acid method and creatinine by Jaffe's method using colorimetry.

Results: The normal range of the PCI which was stabilized in this study was 62- 220. On comparison of the PCI between the control and the subject, it was found to be significantly elevated in the person who does heavy exercise (controls = 114.64 ± 47.96 and in the person who does heavy exercise = 326.98 ± 117.99) ($p < 0.0001$).

Conclusion: The PCI of a random urine sample can provide a very useful, simple and convenient method for the quantitative assessment of proteinuria to judge the extent of kidney damage and for avoiding the drawback of the 24 hr urine collections.

Key Words: Proteinuria; Protein Creatinine Index (PCI); Physical Exercise

Introduction

Physical exercises are a set of exercises which help us to maintain physical and mental fitness and in some cases help in development of muscle building.^[1] Physical exercise have been classified into three categories viz. Low exercise (person who does light walking up to 3 Km & routine physical activity); Moderate exercise (persons with brisk walking along with outdoor sports activity); Heavy exercise (persons who does jogging more than 3 Km daily with vigorous outdoor sporting activity).

Proteinuria due to exercise is benign in nature. The measure of this type of proteinuria depends mainly on the intensity of the exercise. Athletes of sports which require high intensity exercises will exhibit high proteinuria. The reason for the exercise-induced proteinuria is unclear, but some degree of renal ischemia due to redistribution of blood during exercise has been suggested as a possible mechanism.

Quantification of proteinuria can be useful in the work-up of the patient who has a urine dipstick positive for protein. Quantification using a 24 hours 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.^[2,3] 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.^[4,5] 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 non-diabetic adults.^[6,7]

A normal healthy individual excretes about 20-150 mg/24 hrs protein, of which about half is albumin.^[8] 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.^[9]

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 24 hrs urine collections. Hence, this study was conducted.

Materials and Methods

In our study, a total of 34 individuals belonging to 20 to 40yrs of age, who does heavy exercise were selected from Teerthanker Mahaveer Medical College, Moradabad. Similarly, 40 normal individuals who do not exercise at all but with routine physical activity were taken as control.

Individuals having hypertension, diabetes, thyroid disorder, urinary tract infection, and any other renal disorder which can cause proteinuria, were excluded from the study.

Both the individuals (who do heavy exercise 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.

Heat coagulation test, sulfosalicylic acid test, and heller’s nitric acid test were used qualitatively for the detection of urinary protein.^[10] Semi-quantitative estimation of urinary protein was done by urinary dipstick method. The quantitative estimation of urinary protein was performed by colorimetric sulfosalicylic acid method¹¹. Colorimetric estimation of urinary creatinine was done by modified Jaffe’s method.^[11]

Urinary PCI was calculated by the following equation^[10]:

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

Statistical Analysis: After calculation of the normal urinary PCI range (from normal healthy subjects), the distribution was found to be non-Gaussian. So a non-parametric method was used to determine the normal range taking 95% range (2.5th to 97.5th percentile) as the reference range. The unpaired student’s ‘t’ test was used to compare the PCIs of the normal healthy controls and the individuals doing the exercise.

Results

The urine samples were tested qualitatively and quantitatively for the presence of protein for both the control and the study subject groups. Among the qualitative tests, the heat coagulation test was found to be most sensitive one for the detection of the protein in urine. The dipstick test findings correlated with those of the quantitative analysis results in most of the cases. In few cases, the dipstick analysis showed false negative results in comparison to the results of the quantitative analysis done by the sulfosalicylic acid colorimetric method.

Comparable values of primary creatinine were obtained for the controls and the persons who does exercise. (p = 0.056). It was found that higher amounts of protein were excreted in the urine of person who does exercise, which was found to be statistically highly significant (p < 0.001). Higher Values of PCI were recorded for the persons who do heavy exercise as compared to the controls. These elevated values of PCI in persons who does heavy exercise were found to be statistically highly significant (p<0.001). Out of 34 persons, twenty two persons (who do heavy exercise) were found to have PCI values greater than the established normal range in this group of individuals.

Table-1: Urinary Parameters in control (n = 40) and persons who does heavy exercise (n = 34)

Urinary Parameters	Control	Exercise	p-value
Creatinine (mmol/dl)	0.88 ±0.42	0.72 ±0.25	0.056
Protein (mg/dl)	8.93 ± 3.54	22.55 ±8.37	< 0.001
PCI	114.64 ± 47.96	326.98 ± 117.99	< 0.001

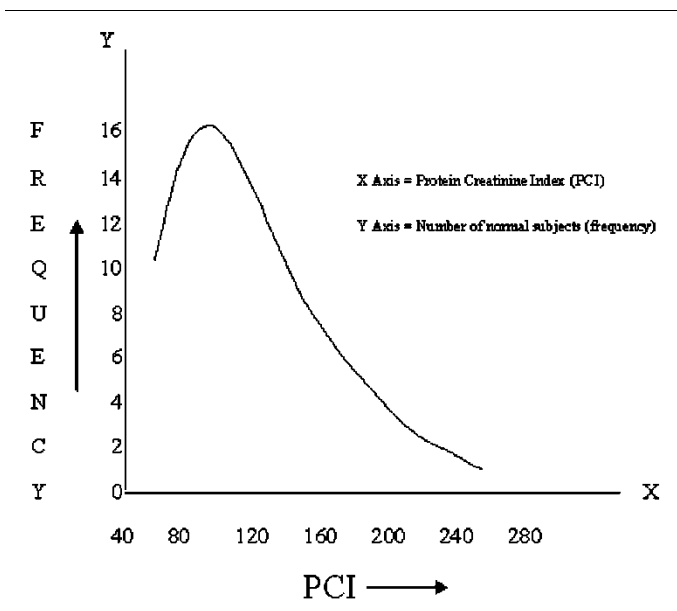


Figure-1: Reference range of PCI in normal individuals

Discussion

The findings show significant differences in protein between the control group and persons who do heavy exercise. Well documented test for the diagnosis of proteinuria has been the timed collection of urine over 24 hrs.^[12] Twenty four hours urine collection is required to nullify the variation in protein excretion throughout the day, since the urinary protein excretion follows a circadian rhythm. However, the 24 hrs urine collection is cumbersome, inconvenient and often incomplete in outpatients.^[13] In an attempt to fulfil the need for a reliable and quick measurement of urinary protein various researchers have proposed the calculation of ratios such as urinary protein/urinary creatinine (UP/UC), urinary albumin/urinary creatinine (UA/AC) and PCI on spot urine samples.^[14] These parameters take into account the fact that creatinine excretion remains fairly constant in the presence of a 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 24 hrs urine sample. But, no 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-hr urine 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. Present study was conducted over a period of 1 year on 34 persons who do heavy exercise and 40 healthy controls. There was no significant difference between the age and sex of the subjects from the two groups.

Urinary Creatinine Excretion: It was found that the amount of creatinine excreted in urine in person who does exercise (0.72 ± 0.25 mmol/dl) was comparable to that in the control subjects (0.88 ± 0.42 mmol/dl).

Urinary Protein Excretion: The mean urinary protein concentration found in the person who does exercise was 22.55 ± 8.37 mg/dl, and in the control group was 8.93 ± 3.54 mg/dl. The protein excretion in spot urine sample in person who does exercise was found to be significantly higher in comparison to the control group with $p < 0.001$. These findings are in concert with the results of previously done studies by various researchers.

In a recent study by Biradar et al (2011), it was indicated that the urinary protein excretion significantly elevated in type 1 and type 2 diabetes mellitus patients. The mean value of 24 hrs urinary protein obtained in their study was 1.6 ± 1.7 gm/day which correlated with P:C ratio 1.27 ± 1.55 .^[16] Price et al reviewed a number of studies and suggested that the P:C ratio can predict the amount of protein excreted in urine.^[12]

Khan et al have suggested in their study that PCI greater than 140 in a random urine sample was indicative of pathological proteinuria.^[17] Khan DA et al in their study shows that the protein creatinine index and Protein: Creatinine ratio of more than 140 and 0.18 respectively in random urine sample indicated pathological proteinuria. An excellent correlation ($r=0.96$) was found between random urine protein: creatinine index/ratio and standard 24 hours urinary protein excretion in these patients ($p < 0.001$). Dipsticks showed moderate correlation ($r=0.52$) and error in interpretation of proteinuria.^[18]

Anoop et al in their study found that higher amount of proteins were excreted in urine in diabetic patients (25.37 ± 12.51 mg/dl) as compared to those in normal subjects (8.93 ± 3.54 mg/dl). And the PCI value was also found to be significantly elevated in the Diabetic patients (373.04 ± 98.53) as compared to controls (114.65 ± 47.97) ($p < 0.001$).^[19]

Shaw et al (1983) 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 (in British subjects) indicated the presence of pathological proteinuria.^[15]

Reference Range for PCI: The data obtained for PCI from normal healthy controls ($n=40$) recruited in this study was found to have a non - Gaussian distribution. Hence, a non-parametric method was used to determine the reference range. The 95% (2.5th to 97.5th percentile) range of PCI was found to be 60-220. The upper limit of normal was found to be higher than that reported by Shaw et al who reported that PCI below 125 in a random urine sample excluded abnormal proteinuria.^[15] Gupta and Gupta reported PCI range to be from 37-247 in Indian subjects which is comparable to the normal range obtained in this study.^[20] Higher values obtained for PCI in this study as compared to Western studies may be on account of comparatively lower value of urinary

creatinine obtained. This leads to an important observation to that PCI in different group of population. The normal reference range for PCI obtained in this study was further used to predict significant proteinuria in person who does heavy exercise.

Urinary PCI: Significantly higher values of PCI were observed in person who does exercise (326.98 ± 117.99) as compared to the control group where PCI was 114.64 ± 47.96 ($p < 0.001$). This indicated that first morning sample urine protein creatinine index serve as baseline predictor of progression of renal diseases. Protein and creatinine are soluble in water so, they will undergo similar changes in dilution or concentration of urine according to the hydration status of the body. Probably this could be the person that the index is independent of errors in urine collection.^[21] 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.

Conclusion

The present study suggests that random urine PCI can be good predictor of significant proteinuria in persons who does heavy exercise. This test could be a reasonable alternative to the 24-hrs urine sample collection for the detection of significant proteinuria in person who does heavy exercise. It is recommended that the PCI should be specially employed for the assessment for microproteinuria in person who does heavy exercise, when in a few instance a negative result may be obtained by the semi-quantitative dipstick test. The simplicity, accuracy and the lower cost of the PCI justifies its preferential diagnostic use. But, since the creatinine excretion is different in different populations, it becomes imperative to establish a normal reference range in a local population, to predict the level of significant proteinuria.

References

- Physical Exercise. Science Daily. Available from: URL: www.sciencedaily.com/articles/p/physical_exercise.htm.
- Schwab SJ, Christensen RL, Dougherty K, Klahr S. Quantitation of proteinuria by the use of protein-to-creatinine ratios in single urine samples. *Arch Intern Med* 1987;147:943-4.
- Houser M. Assessment of proteinuria using random urine samples. *J Pediatr* 1984;104:845-8.
- Assadi FK. Quantitation of microalbuminuria using random urine samples. *Pediatr Nephrol* 2002;17:107-10.
- Nathan DM, Rosenbaum C, Protasowicki VD. Single-void urine samples can be used to estimate quantitative microalbuminuria. *Diabetes Care* 1987;10:414 -8.
- Karalliedde J, Viberti G. Microalbuminuria and cardiovascular risk. *Am J Hypertens* 2004;17:986-93.
- Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA* 2001;286:421-6.
- Ivancic M, Hofmann W, Gurder WG. Development and evolution of a urine protein expert system. *Clin Chem* 1996;42:1214-22.
- Burtis CA, Ashwood ER, Bruns DE. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 4th ed. Philadelphia: Elsevier Saunders; 2006. p. 813.
- Chawla R. *Practical Clinical Biochemistry-Methods and Interpretations*. 3rd ed. Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2003. P. 58-9.
- Gowenlock AH. *Varley's Practical Clinical Biochemistry*. 6th ed. U.K. Butterworth-Heinemann Ltd; 2006. p.436-51.
- Price CP, Newall RG, Boyd JC. Use of protein: creatinine ratio measurements on random urine samples for prediction of significant proteinuria: A systematic review. *Clin Chem* 2005;51:1577-86.
- Koopman MG, Krediet RT, Koomen GM, Strackee J, Arisz L. Circadian rhythm of proteinuria : Consequences of the use of protein : creatinine ratios. *Nephrol Dial Transplant* 1989;4:9-14.
- Keave WF, Eknayan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): A position paper of the National Kidney Foundation. *Am J Kidney Dis* 1999;33:1004-10.
- Shaw AB, Risdon P, Lewis-Jackson JD. Protein creatinine index and Albustix is assessment of proteinuria. *Brit Med J* 1983;287:929-32.
- Matrix HJ, Chi-Yuan HSU, Shaykevich S, Curhan G. Use of albumin/creatinine ratio to detect microalbuminuria : implications of sex and race. *J Am Soc Nephrol* 2002;13:1034-9.
- Biradar SB, Kallaganad GS, Rangappa M, Kashinakunti SV, Retnakaran R. Correlation of spot urine protein-creatinine ratio with 24 - hr urinary protein in type 2 diabetes mellitus patients : a cross sectional study. *JRMS* 2011;16:634-69.
- Khan DA, Ahmad TM, Qureshi AH, Halim A, Ahmed M, Afzal S. Assessment of proteinuria by using protein: creatinine index in random urine sample. *J Pak Med Assoc* 2005;55:428-31.
- Kumar A, Kapoor S, Gupta RC. Comparison of Urinary Protein: Creatinine Index and Dipsticks for Detection of Microproteinuria in Diabetes Mellitus Patients. *JCDR* 2013;7:622-6.
- Gupta RC, Gupta U. Urinary protein/creatinine index. *Clin Chem* 1986;32:914.
- Jafar TH, Chaturvedi N, Hatcher J, Levey SA. Use of albumin creatinine ratio and urine albumin concentration as a screening test for albuminuria in an Indo - Asian population. *Nephrol Dial Transplant* 2007;22:2194-200.

Cite this article as: Bhattacharya I, Kumar A, Gupta A, Yasmin T, Ahmad N, Goel M. Comparison of urinary protein creatinine index in normal and heavy exercise performing individuals. *Int J Med Sci Public Health* 2014;3:986-989.

Source of Support: Nil

Conflict of interest: None declared