THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (July-August 2012) 62(4):424–428
DOI 10.1007/s13224-012-0299-5

ORIGINAL ARTICLE

Replacing 24-h Albumin Excretion with a Shorter Collection Period in Preeclampsia

Rangasamy Savitha · Rao Arun

Received: 27 October 2009 / Accepted: 7 August 2012 / Published online: 16 October 2012

Abstract
Objectives To evaluate whether the gold standard of 24-h urinary albumin excretion in preeclamptic women could be substituted by a shorter collection period.
Methods From each woman, three spot, two 12-h, and one 24-h urine samples were collected. For each sample, urine albumin concentrations in milligram per liter were analyzed by the immunoturbidimetric method. The albumin concentrations in the spot and 12-h collections (day and night) were compared with the 24-h urine collection.
Results Albumin concentrations in both 12-h collections were fitted closely with the concentrations of the 24-h collection. The median difference between the 24-h collection and the day collection was 43 mg/L and the correlation coefficient was 0.96 ($p < 0.0001$). The median difference between the night collection and the 24-h collection was −31 mg/L and the correlation coefficient was 0.98 ($p < 0.0001$).
Conclusion The gold standard of 24-h urinary albumin concentrations in preeclamptic women can be substituted with a 12-h collection. Spot samples were weaker as compared to the 12-h collection.

Keywords Preeclampsia · Albuminuria · Shorter collection period

Rangasamy S., P G Student · Rao A., Professor
Department of Obstetrics and Gynecology, Kasturba Medical College (Manipal Academy of Higher Education), Mangalore, India

Rangasamy S. (✉), P G Student
Prabhu Polyclinic, 95, New Scheme Road, Pollachi 642002, Tamil Nadu, India
e-mail: savithaprabhuam@hotmail.com

Introduction

Hypertensive pregnancy complicates 7–10 % of pregnancies. The diagnosis of preeclampsia is determined by the presence of hypertension accompanied by proteinuria, evident after 20 weeks of gestation [1, 2]. Albuminuria is an important sign of preeclampsia and repeated urine analysis to test for albuminuria is a part of standard antenatal care. These urine analyses are performed on random spot urine specimens using a test strip assay. If the test strip is positive for protein 2+ or more in the absence of bacteriuria, the next step is usually a 24-h urine collection for quantification of albumin. The purpose of this tedious surveillance is that increased albumin excretion is a sign of aggravation of preeclampsia and reflects serious nephropathy. Massive albumin excretion may result in planned preterm delivery. If the urine collection is not possible, a morning urine sample can be used or as a third option, a semi quantitative test strip. These recommendations are based on the circadian rhythm in urinary albumin excretion [3]. However, for pregnant women, particularly if in the hospital, the circadian variation in albumin excretion is absent [4] and it may therefore be possible to use shorter

collection periods. The aim of this study was to evaluate whether a 24-h urine collection for measuring urinary albumin excretion in preeclamptic women could be substituted by a 12-h collection or spot urine samples.

Methods

Fifty women with preeclampsia admitted to the ward at the department of the government Lady Goshen Hospital, Mangalore were included in the study. The criteria for inclusion were a positive test strip of protein of at least 2+ corresponding to an albumin excretion of 500 mg/L, and a planned 24-h urine collection for quantitative albumin measurement. Women with upper urinary tract infections, defined as a positive urine culture and fever, were not included. Informed consent was obtained from all women. Women admitted to the antenatal ward are usually advised moderate bed rest; that is, that they are advised rest, but are free to move around in the hospital area.

There were 26 nulliparous women and 24 multiparous women. Antihypertensive drugs, primarily Methyldopa and Nifedipine, were prescribed. Five patients were started on a low dose $MgSO_4$ in view of imminent eclampsia. Further details of the participants are given in Table 1.

From each woman, three spot urine samples, two 12-h samples, and one 24-h sample were collected. Urine collection started on the first morning after admission to the hospital and all samples were collected within 25 h (Fig. 1). Before the urine collection, all the women were carefully instructed on the procedure. Urine albumin was analyzed by the Immunoturbidimetric test according to the recommendations of the manufacturer.

As the albumin excretion in the spot urine sample was reported as concentrations in milligram per liter, all values are prescribed as such. The correlation in albumin excretion between the 24-h collection and the shorter collection periods is given in Table 2. Differences in albumin excretions are presented as median differences together with interquartile ranges. Multiple comparisons and the significant value between the 24-h collection and the shorter collection periods are given in Table 3. We considered the interquartile range a better estimate than range when describing dispersion in differences. In Fig. 2, median differences and interquartile range are shown graphically, together with mean differences and ranges.

Table 1 Characteristics of the participants

Parameters	Mean	Standard deviation	Range
Age (years)	26.36	4.38	19–37
Gestational age (weeks)	32.68	2.89	27–37
Systolic blood pressure (mmHg)	154	41	140–200
Diastolic blood pressure (mmHg)	107	7	90–120

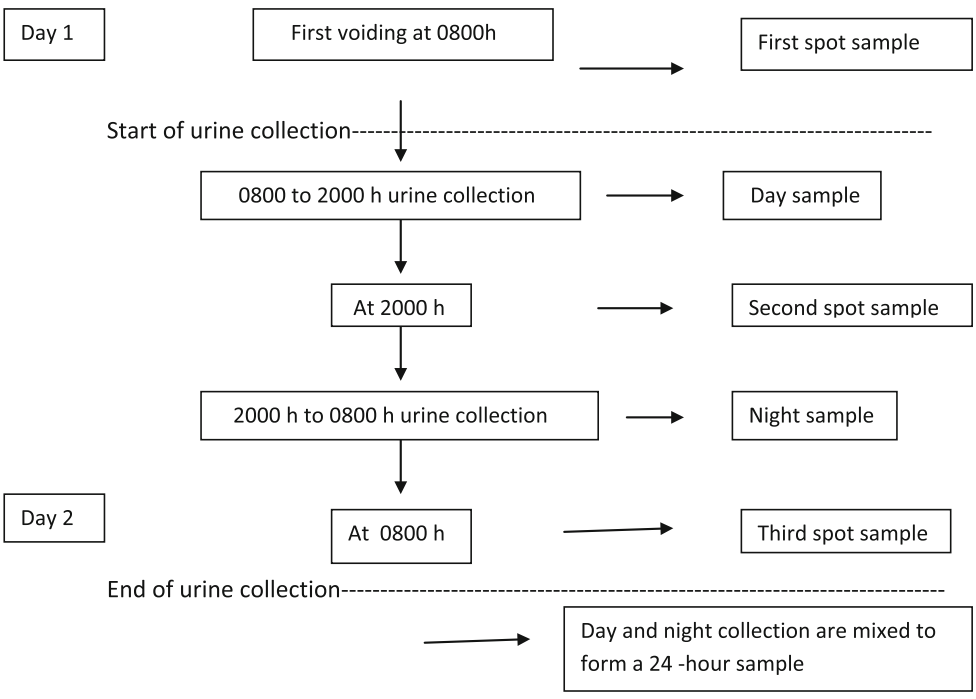

Fig. 1 Flow chart for collection of urinary samples

Table 2 Correlation between other samples with the 24-h sample

Groups	Vs groups	Correlation coefficient (r^2)	*p* value
Spot 1	24 h	0.83	<0.0001
Spot 2	24 h	0.72	<0.0001
Spot 3	24 h	0.71	<0.0001
12 h 1	24 h	0.96	<0.0001
12 h 2	24 h	0.98	<0.0001

Table 3 Multiple comparisons of urine albumin concentration

Groups	Vs groups	Mean difference	Median difference	*p* value
Spot 1	24 h	80.98	−1	0.98
Spot 2	24 h	89.74	−8.50	0.97
Spot 3	24 h	−13.18	22.50	1.00
12 h 1	24 h	−2.68	43.00	1.00
12 h 2	24 h	−25.64	31.00	1.00

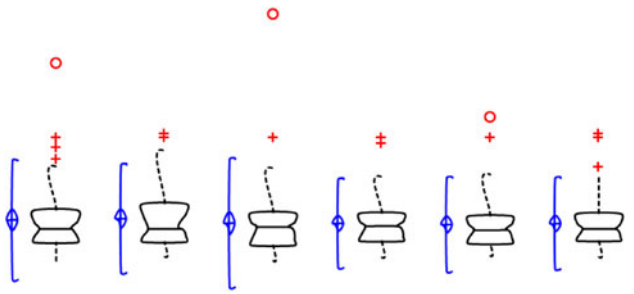

Fig. 2 Comparison of urine albumin concentration for different intervals

Results

The mean 24-h urinary albumin excretion was 957.220 mg/dL (SD 733.64 mg/dL) and the median was 808.500 mg/dL (95 % CI of median 570–924).

In our study, the preeclamptic women who had significant albuminuria were found to have a good correlation between urinary albumin concentrations measured in samples collected for 12 h (day and night samples) and the gold standard 24 h. The median difference between the first 12- and 24-h sample was 43.00 (insignificant 1.00) and the median difference between the second 12- and 24-h sample was −31.00 (insignificant 1.00).The correlation coefficients for both were 0.96 and 0.98, respectively, with *p* value of <0.0001. The median difference between the 24-h sample and the first spot sample was −1 (insignificant 0.98).The median difference between the second and third samples was −8.5 (insignificant 0.97) and 22.50 (insignificant 1.00), respectively. The correlation coefficient for the first, second, and third samples was 0.83, 0.71, and 0.72, respectively, with *p* value of <0.0001 for all. The correlation between spot one, spot two, spot three, the first 12-h, and the second 12-h samples and the 24-h sample is shown in Fig. 3.

Discussion

Proteinuria has been proposed and studied as an indicator of the severity of the disease and as a predictor of outcome in preeclampsia. Many clinicians still make major management decisions based on the degree of proteinuria in such patients. Quantification of a timed collection has been the gold standard for many decades. For a 24-h quantitative specimen, the standard "consensus" threshold value used is >300 mg/24 h- or its extrapolated equivalent in shorter collections. Importantly, this has not been irrefutably established [5].

Currently, the 24-h urine test is the gold standard for the evaluation of proteinuria [6]. A shorter collection period to diagnose would have clinical benefits such as shortened time to delivery and earlier use of antenatal glucocorticoids. An expedient intervention could decrease perinatal morbidity. Certainly, those women without preeclampsia were discharged earlier. Patient compliance with testing may also improve if the test for proteinuria can be simplified or shortened.

In our study, the preeclampsia women who had significant albuminuria were found to have a good correlation between urinary albumin concentrations measured in samples collected for 12 h (day and night) and the gold standard 24-h collection.

We have also been testing the urinary albumin concentrations by the spot urine samples taken at specific times in the morning and in the evening and comparing them against the standard, 24-h excretion. The difference between the 24-h collection and the spot samples was comparable, but weaker as compared to the 12-h collection. Of the spot samples, the first spot sample had a better correlation than the second and third spot samples.

The agreement between albumin concentrations in the 24-h and the second 12-h samples (night sample) was slightly better than that of the first 12-h sample (day sample). The night sample was the one that did not overestimate albumin excretion. Overestimation of albumin excretion may lead to interventions such as planned preterm delivery to be performed earlier than required. Underestimation of albumin excretion, however, may delay detection of severe nephropathy, resulting in damage to the kidneys.

Several investigators have explored other means of quantifying proteinuria in a shorter collection period. The

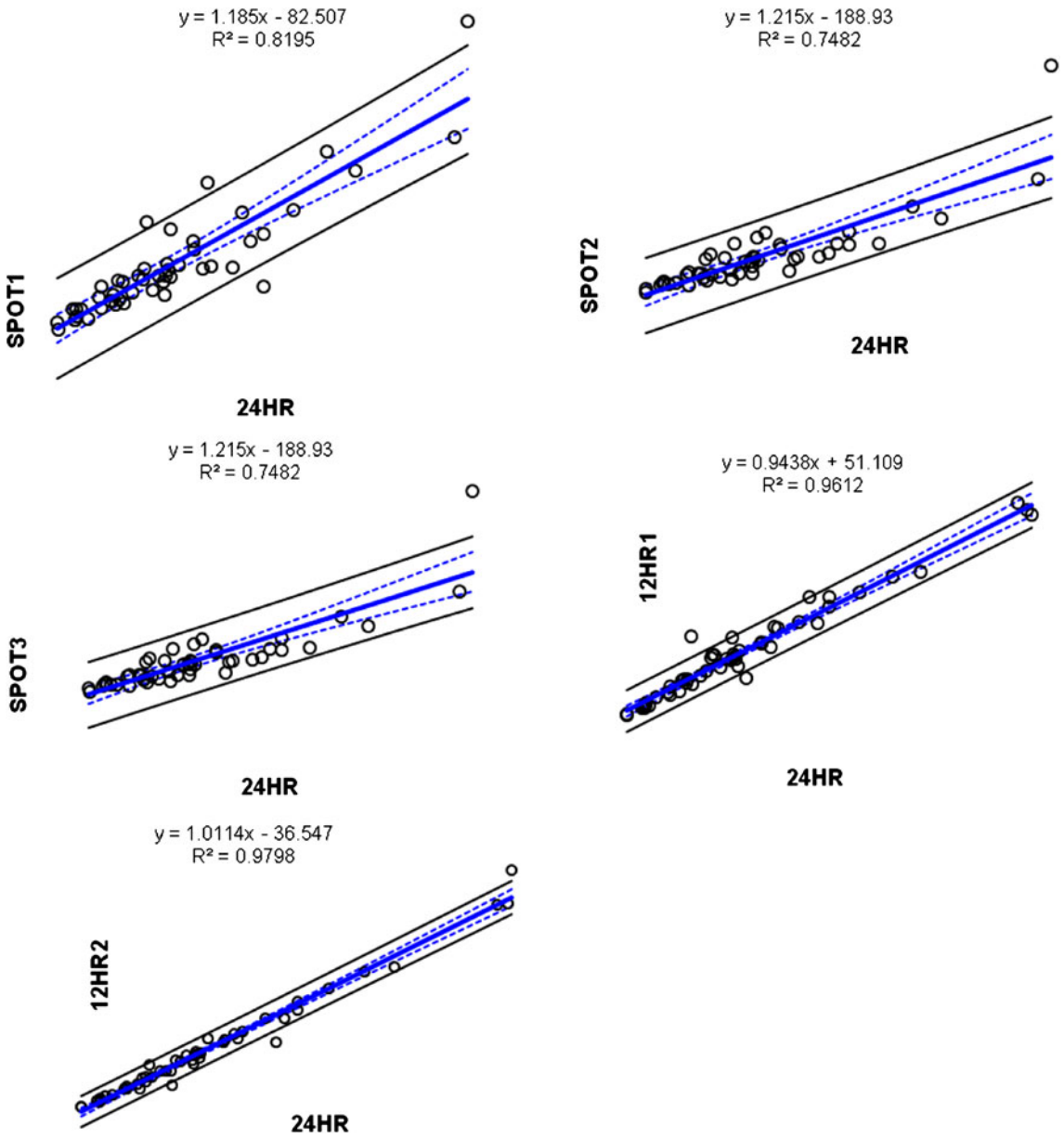

Fig. 3 Correlation between all the samples and the 24-h sample

protein–creatinine ratio of a single urine sample from pregnant women has been shown to correlate significantly with a 24-h collection for patients with protein values of <1 g in 24 h. Above this level, the variation between the samples is increased [7]. The results of urine dipstick for protein have also been shown by Mayer and co-investigators to correlate poorly with the 24-h urine samples for differentiating patients with no disease or severe disease [8].

It is postulated that protein excretion varies throughout the day, which is thought to be secondary to vasoconstriction and vascular spasm producing a fluctuation in protein from moment to moment. Protein excretion tends to increase with ambulation and an upright body position, which produces renal vasoconstriction and altered permeability of the glomerular barrier [9]. These physiologic factors are thought to produce a diurnal variation in protein excretion. It is known that albumin excretion has a circadian rhythm that makes a 24-h collection necessary [3]. The protein excreted in the urine of preeclamptic women is, however, heterogeneous and variable, and in some cases does not even include albumin. Our study did not show a significant pattern of diurnal variation in protein excretion.

Conclusion

Albumin concentrations in a 12-h (day) and 12-h (night) interval collection fitted closely with the 24-h collection.

The association of the 24-h collection and the spot samples was weaker as compared to the 12-h collection.

The study concluded that the gold standard 24-h urinary assessment of albuminuria in preeclamptic women could be substituted with a 12-h collection.

References

1. American College of Obstetricians and Gynecologists. Hypertension in pregnancy. ACOG technical bulletin no. 219. Washington, DC: American college of obstetricians and Gynecologists; 1996.
2. Report of the National High Blood Pressure Education programme working group on high blood pressure in pregnancy. Am J obstet Gynecol. 2000;183:S1–S22.
3. Koopman MG, Krediet RT, Zuyderhoudt FJ, et al. A circadian rhythm of proteinuria in patients with a nephritic syndrome. Clin Sci (Colch). 1985;69(4):394–401.
4. Douma CE, Van der post JA, Van Acker BA, et al. Circadian variation of urinary albumin excretion in pregnancy. Br J Obstet Gynaecol. 1995;102(2):107–10.
5. Pregnancy hypertension, Williams obstetrics, 23rd ed. New York, NY: McGraw-Hill; 2010. pp. 719.
6. Hypertensive disorders in pregnancy, Williams obstetrics, 21st ed. New York: McGraw-Hill; 2001. pp. 567–618.
7. Jascheranky OE, Rosenberg RP, Shalir A, et al. Protein/creatinine ratio in random urine specimen for quantification of proteinuria in preeclampsia obstet. Gynecology. 1990;7:660–6.
8. Meyel NL, Merrer BM, Freedman SA, et al. Urine dipstick protein a poor predictive method for absent or severe proteinuria. Am J Obstet Gynecol. 1994;70:37–41.
9. Highy K, Suitor CR, Phelps JY, et al. Normal values of urinary albumin and total protein excretion during pregnancy. Am J Obstet Gynecol. 1994;171:984–8.