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THE VALUE OF DIPSTICK ANALYSIS OF URINARY PROTEIN IN PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

In order to determine the value of dipstick analysis of urinary protein in pregnancy induced hypertension, a prospective study analyzing pregnant patients with a diagnosis of hypertensive disorder was conducted to compare the result of urinary protein dipstick analysis with 24hr. urine protein collection in obstetrical clinics affiliated to Shiraz University of Medical Sciences.

All patients fulfilling the criteria of the American College of Obstetricians and Gynecologists' definitions for establishing a diagnosis of hypertensive disorder on the basis of urinary dipstick measurements were included in the study.

During the study, 102 hypertensive pregnant patients aged from 16-42 years were included in the study. Obtained results showed that the presence of negative value on urinary dipstick with a sensitivity of 100% is a useful method for ruling out significant proteinuria (> 300 mg/24hr). But values of >2+ are not adequate to confirm a diagnosis of severe hypertensive disorder because its positive predictive value is only 22% and values of > trace-although highly suggestive of significant proteinuria (positive predictive value: 78%)-have a false positive rate of 23%; a timed collection of urine for determination of 24-hr protein excretion becomes mandatory in such cases.

The urinary dipstick determination of protein excretion therefore has significant limitations for determination of the presence or severity of proteinuria.

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INTRODUCTION

Pregnancy induced hypertension (hypertensive disorder) is one of the most common medical complications of human pregnancy, responsible in its more severe forms for much maternal and perinatal morbidity and mortality. This is frequently accompanied by proteinuria of glomerular origin which has been described as widely variable from day to day and markedly affected by physical activity. Because proteinuria is postulated to be the result of vasospasm, protein excretion waxes and wanes with vascular spasm, producing a fluctuation in protein leakage from moment to moment. In addition, albumin has a diurnal variation in excretion.[11-16]

Abnormal proteinuria in pre-eclamptic patients has been defined as mild (⩾ 300mg per 24-hours) or severe (⩾4g per 24-hours). On the semiquantitative urinary dipstick the presence of trace or 1+ proteinuria is considered as mild and ⩾2+ as severe, for determination of severity in pre-eclamptic patients.[4]

This study was done to determine the value of dipstick analysis of urinary protein in pre-eclampsia.

MATERIAL AND METHODS

We reviewed the medical records of women with hypertensive disorders of pregnancy (i.e., chronic hypertension, pregnancy induced hypertension and pregnancy aggravated hypertension) admitted to the training hospitals of Shiraz University of Medical Sciences from June 1995 through May 1998.

Unfortunately in many cases of severe hypertensive disorder, pregnancy was terminated according to urinary dipstick protein determination alone. We considered those who had undergone collection of 24-hour urine for determination of urinary protein excretion for our study. Women with a minimum of two urinary dipstick protein determinations at least 6 hours apart, obtained a 24-hour urine collection. These criteria fulfilled the American College of Obstetricians and Gynecologist's definition for establishing a diagnosis of hypertensive disorder on the basis of urinary dipstick measurements.

The diagnosis of chronic hypertension was based on the presence of hypertension prior to onset of pregnancy and no association with edema or significant proteinuria ($\geq$ 300mg/24-hours) during pregnancy. The distinction between mild and severe hypertensive disorder was determined by standard clinical criteria and by 24-hour urinary protein excretion, irrespective of urinary dipstick protein. The medical records of 102 pregnant women with hypertension who met inclusion criteria were identified. Antepartum 24-hour urine samples were collected either as voided or catheterized specimens. Postpartum 24-hour urine samples were excluded from analysis. Samples from the patients with pre-existing renal diseases were excluded also.

Results of at least two consecutive dipsticks were compared with the total protein excretion in a 24-hour urine sample. Only patients who had at least two urinary protein dipstick determinations obtained concurrently with a 24-hour total protein excretion were included. The adequacy of the 24-hour collection was determined by creatinine excretion of 13 mg/kg body weight for nonobese patients and at least 850 mg per 24-hours for obese patients. The number of urinary dipsticks documented in the chart was determined. When more than two urinary dipsticks were recorded in the chart, the most frequently recorded result was used for analysis. When only two urinary dipstick determinations were documented with different results, the higher result was used for analysis.

RESULTS

During the study from June 1995 through May 1998 more than 250 patients diagnosed as a case of hypertensive disorder in pregnancy were identified and their medical reocrds were reviewed. Of these only 130 patients were found who fulfilled the criteria of a 24-hour total urinary protein excretion and at least two concomitant urinary dipstick evaluations. Another 28 of them were omitted due to inadequacy of 24-hour urine collection according to the criteria mentioned above. So the final investigated population consisted of 102 hypertensive pregnant women aged from 16 to 42 years from whom sampling was done at 11 to 42 weeks of gestation. Table I illustrates the characteristics of the population and Table II indicates the range of hypertensive disorders of pregnancy encompassed by the group.

Similar to that shown by Meyer et al. our results revealed also that total urinary protein excretion measured in a 24-hour collection appeared to increase as urinary dipstick proteinuria progressed from semiquantitative values of negative to 3+, but in spite of this, there was an imprecise relationship between semiquantitative urinary dipstick and 24-hour quantitative protein excretion. Of 44 pateints with negative protein on dipstick no one demonstrated clinically significant proteinuria of $\geq$ 300mg per 24-hours (Table III).

Thirty-six patients had 2^+ and 3^+ dipstick proteinuria, which signifies severe hypertensive disorder, but only 8 of them (22%) showed heavy proteinuria ($\geq$4000 mg), 27 (75%) showed significant proteinuria of mild severity (300-4000 mg) and 1 (3%) showed proteinuria of physiologic range. Finally 22 patients had urinary dipstick values of trace and 1^+, of whom 12 (55%) failed to show significant proteinuria; of the 10 remaining patients 8 (36%) had significant proteinuria of mild severity and 2 (9%) showed heavy proteinuria (Table III).

Table III summarizes the relationship between 24-hour urinary protein excretion and dipstick analysis. According to this all 10 patients with heavy proteinuria ($\geq$ 4000 mg/day) had a dipstick proteinuria of $\geq$ 1+. However only 8 (80%) were correctly identified with > 2+ on dipstick, whereas 2 (20%) had 1+ proteinuria on dipstick. Table III also shows that of 57 patients with physiologic range of proteinuria (0-300 mg/24-hours), only 44 (77%) had negative

Table I. Clinical characteristics of the population investigated.

Age	15-19	20-29	30-39	>40
No	12	50	31	9
%	11.8	49	30	8.8
Parity	0	1-3	4-6	7-10
No	40	34	20	8
%	29.2	33.3	19.6	7.8
G/A-wk	0-14	15-28	>28	
No	2	21	79	
%	2	20.6	77.5	

Table II. Hypertensive disorder of pregnancy in the population investigated.

Pregnancy induced HTN	Isolated HTN		Mild hypertensive disorder		Severe hypertensive disorder		Eclampsia		Total No.	%
	No.	%	No.	%	No.	%	No.	%		
	21	20.6	40	39.2	28	27.5	1	0.98	90	88.2
Chronic HTN									8	7.8
Pregnancy aggravated HTN	Superimposed hypertensive disorder				Superimposed eclampsia					
	No.		%		No.		%			
	4		3.9		0		0		4	3.9

Table III. Relationship of urinary dipstick value to 24-hour urine protein.

Urine Protein	Dipstick value					
(mg/24hr)	Negative	Trace	1+	2+	3+	Total
<300	44	8	4	0	1	57
300-3999	0	3	5	20	7	35
>4000	0	0	2	7	1	10
Total	44	11	11	27	9	102

Table IV. Value of dipstick protein in predicting 24-hour urinary protein excretion.

Urinary dipstick	Protein excretion (mg/24hr)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Negative	0.300		77		100
≥Trace	>300	100	77	78	100
≥2^+	>4000	80	70	22	97

values on dipstick and 13 (23%) had dipstick values of trace to 3+.

A urinary dipstick value of ≥2^+ had a positive predictive value of only 22% (8/36). A urinary dipstick value of ≥trace had a positive predictive value of 78% (45/58) for predicting significant (>300mg/24 hours) proteinuria (Table IV).

DISCUSSION

In spite of extensive use of urinary dipstick analysis for determination of severity in pre-eclamptic patients, results from the study presented here document clearly that urinary dipstick analysis is an imprecise test and is not reliable for predicting the range of proteinuria.

Both urinary protein excretion and elevation of blood pressure probably result from vasospasm which display marked variation from hour to hour in pregnancies complicated by hypertension. So protein excretion is highly variable during the day. In addition, urinary dipstick analysis is partially dependent on observer interpretation of slight changes in color and shade.[15,24,25]

Our study showed that although there is a marked increase in the mean 24-hour protein excretion as dipstick protein progresses from negative to 3+, there is wide scatter in the measured value in each group. Dipstick protein values of 1+ were associated with an extremely wide scatter of value for 24-hour protein excretion from 0 to 6250 mg. Although about 64% of these had significant proteinuria of more than 300 mg/24-hours, 36% showed proteinuria of physiologic range. The scatter in the patients with 2^+ proteinuria was great also, being associated with 24-hour excretion ranging from 500 to 8400 mg and 3+ with values ranging from 138 to 5000 mg per 24-hours (Table V).

A negative value was found in 44 of 102 patients, all of whom showed less than 300 mg protein in 24-hour urine. Although a negative value has a specificity of 77% it can be used to rule out significant proteinuria, because its negative

value is 100% (44/44) (Table IV).

Urinary dipstick values of $>2^+$ do not reflect heavy proteinuria and should not be used to diagnose severe hypertensive disorder because its positive predictive value is only 22% (8/36). Urinary dipstick values of > trace had a positive predictive value of 78% (45/58) for predicting significant ($\geq$ 300 mg/24-hours) proteinuria. So this can be useful in identification of significant proteinuria and although it identifies all patients with significant proteinuria (sensitivity 100%), it was nevertheless associated with a 23% false positive rate (specificity 77%) (Table IV).

The results of the current study support the results of Meyer and Sibai et al, who state that urinary dipstick values of > 2+ are not adequate to confirm a diagnosis of severe hypertensive disorder based on proteinuria, because its positive predictive value is only 22%. But in contrast to their observation, our data showed that urinary dipstick values of negative are useful for ruling out significant proteinuria and values of $\geq$ trace are highly suggestive of significant proteinuria, but due to having a 23% false positive rate, a timed collection for quantitation of proteinuria is recommended.[21]

In 1988 Raiston et al. studied 104 samples from 90 patients presenting to the center for Rhematologic diseases. They showed that 24-hr urinary protein was less than 300 mg in all patients with a trace of proteinuria on dipstick testing. The false positive rate for significant proteinuria was 76% in those with 2^+, 7% in those with 3^+ and 0% in those with 4+ proteinuria. They concluded that neither the presence nor the severity of proteinuria could have been confidently predicted by dipstick testing alone. Thus where dipstick readings ranged from 1^+ to 3^+, there was a high incidence of false positivity.[7]

Vanessa et al. assessed the interobserver variability in dipstick analysis of urine samples of known protein content, with the aid of 66 volunteers from the hospital staff and concluded that interobserver variation in assessment of proteinuria by dipstick is high.[8]

Meyer et al. in 1994 compared urinary protein dipstick determinations and concurrent 24-hr urine protein excretion measurement in 300 urine samples obtained from women with hypertension in pregnancy and concluded that there was an imprecise relationship between semiquantitative urinary dipstick and 24-hr quantitative protein excretion.

In another study by Gribble et al. which was performed on 3217 low risk obstetric patients in 1995, routine dipstick proteinuria screening at each visit did not provide any clinically important information regarding pregnancy outcome.[26]

Finally Saudan et al. in 1997 found that dipstick urinalysis had high false positive and false negative rates, casting doubt on the reliability of dipstick urinalysis for detecting true proteinuria in clinical and research practice.[27]

In conclusion urinary dipstick determination of protein excretion has significant limitations for determination of the presence or severity of proteinuria. A negative value with a sensitivity of 100% is a useful method for ruling out significant (> 300 mg/24-hours) proteinuria. In contrast, dipstick values of $\geq$ 2+ should not be used to diagnose hypertensive disorder because their positive predictive value is only 22%. Moreover urine dipstick values of trace and 1+ should not be used for diagnosing mild hypertensive disorder, because about 9% of these were associated with heavy ($\geq$ 4000 mg/24-hours) proteinuria and 55% with a physiologic range of proteinuria, in a 24-hour urine collection. Only the values of $\geq$ trace with a positive predictive value of 78% are useful for predicting significant (> 300 mg/24-hours) proteinuria, however due to having a 23% false positive rate, a timed 24-hour urine collection for detection of these false positive results is required.

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