

Urine Calcium Excretion in Preeclampsia

PREEKLAMPSİDE İDRAR KALSİYUM EKSKRESYONU

Tufan BİLGİN*, Özer KUTLU**, Yalçın KİMYA*, Şakir KÜÇÜKKÖMÜRÇÜ***, Gürkan UNCU*

* Assoc.Prof.Dr., Dept. of Obstetrics and Gynecology, Uludağ University Faculty of Medicine,

** Dr., Dept. of Obstetrics and Gynecology, Uludağ University Faculty of Medicine,

*** Prof.Dr., Dept. of Obstetrics and Gynecology, Uludağ University Faculty of Medicine, Bursa, TURKEY

Summary

Objective: To determine the urinary excretion of calcium in preeclamptic women and compare with controls.

Institution: Uludağ University Faculty of Medicine, Department of Gynecology and Obstetrics, Bursa.

Materials and Methods: We measured calcium, phosphorus, creatinine and uric acid levels in sera and 24 hour urine specimens of 30 preeclamptic or eclamptic and 34 healthy pregnant controls.

Results: Mean maternal age, gravidity and parity did not differ significantly ($p>0.05$). Mean urine calcium concentration was significantly lower in the preeclamptic group (10.03 ± 0.55 mg/dL), than in the controls (18.18 ± 1.01 mg/dL), ($p<0.001$). Preeclamptic women excreted significantly less total urine calcium (150.1 ± 21.41 mg/24h) than normotensive women (296.0 ± 14.4 mg/24h), ($p<0.001$).

Conclusion: Preeclamptic women excrete less calcium than controls. This parameter would predict preeclampsia earlier in pregnancy.

Key Words: Preeclampsia, calcium, hypocalciuria

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Özet

Amaç: Preeklamptik kadınlarda idrar kalsiyum atılımını saptamak ve kontrol olgularla karşılaştırmak.

Çalışmanın yapıldığı yer: Uludağ Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Ana Bilim Dalı, Bursa.

Materyal ve Metod: Otuz preeklamptik veya eklamptik ve 34 kontrol gebe hastada serum ve 24 saatlik idrarda kalsiyum, fosfor, kreatinin ve ürik asit seviyeleri ölçüldü.

Bulgular: Ortalama maternal yaş, gravidite ve parite arasında anlamlı bir fark yoktu ($p>0.05$). Ortalama idrar kalsiyum konsantrasyonu preeklamptik grupta (10.03 ± 0.55 mg/dL), kontrol grubundan (18.18 ± 1.01 mg/dL) anlamlı olarak daha düşüktü ($p<0.001$). Preeklamptik hastalar (150.1 ± 21.41 mg/24h), normotansif kadınlardan (296.0 ± 14.4 mg/24h) anlamlı olarak daha az idrar total kalsiyumu ekskrete ediyorlardı ($p<0.001$).

Sonuç: Preeklamptik kadınlar kontrollere göre daha az kalsiyum ekskrete etmektedirler. Bu parametre gebeliğin erken döneminde preeklampsiyi öngörmek için kullanılabilir.

Anahtar Kelimeler: Preeklampsi, kalsiyum, hipokalsiüri

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Recent studies have shown that patients with preeclampsia excrete less calcium than normotensives, although some other authors could not find any correlation (1-4). It has been reported that hypocalciuria predicts preeclampsia long before the clinical manifestations exist (5,6).

In this study, we evaluated renal calcium excretion in women with preeclampsia and compared with normotensives.

Materials and Methods

Sixty-four women constituted the study groups. Twenty-five of them were preeclamptic and 5 were eclamptic. Preeclampsia was defined as hypertension, significant proteinuria and edema after 20 weeks of gestation. Blood pressure of more than 140/90 mmHg or a rise of 30 mmHg systolic and 15 mmHg diastolic pressure on at least two occasions 6 hours apart was called hypertension. Proteinuria

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Uludağ Üniversitesi Tıp Fakültesi
Kadın Hastalıkları ve Doğum AD,
16059 BURSA

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was present with urinary protein excretion of more than 300 mg/day quantitatively or "+" on dipstick examination. Generalized edema was the third sign of preeclampsia. Generalized convulsions in a severely preeclamptic patient were regarded as eclampsia.

Patients with hypertension but no significant proteinuria were excluded from the study. Other exclusion criteria were chronic hypertension, superimposed preeclampsia or eclampsia, associated systemic illnesses such as diabetes mellitus, renal disease.

Blood pressure was measured by usual sphygmomanometer from the right arm at left lateral recumbent position at bed rest.

24 h urine specimens were collected from each patient and samples were evaluated for volume, creatinine, total protein, calcium and phosphorus in the routine laboratory. Blood samples were obtained from the antecubital veins at midtime of urine collection. Total serum calcium, phosphorus, creatinine and uric acid were studied at the routine laboratory. Creatinine clearance was calculated. Fractional excretion of calcium was calculated by dividing the calcium clearance by the creatinine clearance.

Patients were assumed to have normal dietary calcium intake and no alterations involving calcium were recommended.

Unpaired Student t test and Kolmogorov-Smirnov two group test were used to compare the

clinical and laboratory findings of the groups. $P < 0.05$ was considered significant.

Results

Table 1 presents the characteristics of the patients. Mean age, gravidity and parity did not differ significantly in the two groups. Patients with preeclampsia delivered at an earlier gestational age ($p < 0.001$). As a result of this, the mean birth weight was significantly lower in the preeclamptic group ($p < 0.001$). As expected, the mean blood pressure in patients with preeclampsia was higher than in the controls ($p < 0.001$).

Urine and serum laboratory findings are listed in Table 2. Women with preeclampsia showed significantly lower urine calcium content ($p < 0.001$) and calcium concentration ($p < 0.001$). Significant proteinuria was observed in preeclampsia. Urine

Table 1. Patient characteristics of the study and the control groups

	Preeclampsia (n=30)	Normotensive (n=34)	P
Age	27.2±1.0	25.6±0.8	NS
Gravidity	2.4±0.4	2.0±0.2	NS
Parity	1.1±0.4	0.6±0.1	NS
Gestational age	34.3±0.8	38.8±0.3	$p < 0.001$
Birth weight	2390±166	3423±69	$p < 0.001$
Mean blood pressure	128.2±3.3	89.3±0.2	$p < 0.001$

NS: Nonsignificant

Table 2. Urine and serum laboratory findings of the study and the control groups

	Preeclampsia (n=30)	Normotensive (n=34)	p
Urine			
Protein (mg/day)	1631±292	-	$p < 0.001$
Ca-concentration (mg/dL)	10.0±0.5	18.2±1.0	$p < 0.001$
Ca-content (mg/day)	150±21	296±14	$p < 0.001$
Phosphorus (mg/day)	0.65±0.08	0.61±0.06	NS
Serum			
Calcium (mg/dL)	10.3±0.1	9.4±0.1	$p < 0.001$
Phosphorus (mg/dL)	4.3±0.2	3.9±0.1	NS
Uric acid (mg/dL)	5.1±0.4	3.4±0.2	$p < 0.001$
Creatinine clearance (mL/min)	111.2±7.8	124.0±2.6	NS
Fractional excretion of calcium(%)	0.98±0.16	1.74±0.09	$p < 0.001$

NS: Nonsignificant

and serum phosphorus levels were similar. Seven of the normotensive patients (20.5%) had urinary calcium contents of less than 195 mg/day. In contrast, only 4 preeclamptic patients (13.3%) had urinary calcium contents of more than 195 mg/day. With the urinary calcium concentration threshold level set at 12 mg/dL, 7 patients with preeclampsia (23.3%) had urinary calcium concentrations of more than the threshold value and 5 normotensives (14.6%) had urinary calcium concentrations of less than 12 mg/dL.

Although there was no significant difference in creatinine clearance ($p>0.05$), mean fractional excretion of calcium was significantly lower in the preeclamptic group ($p<0.001$).

Discussion

A growing number of papers indicate significant hypocalciuria is associated with preeclampsia (7). In most of these studies a 24-hour collection of urine sample at 17-20 weeks gestation predicts preeclampsia earlier (8). Calcium to creatinine ratio is found to be significantly lower in the second trimester and is reported to be an effective marker in predicting preeclampsia (9). Determination of the calcium to creatinine ratio in spot urine samples in the first trimester is found to be limited value for identifying women with an increased risk of preeclampsia (10). The results of our study clearly indicate that preeclampsia is associated with significant hypocalciuria. Urinary calcium excretion increases in normal pregnancy as a result of enhanced intestinal absorption modulated by vitamin D (11). Considering no significant change in creatinine clearance, but a significant decrease in fractional excretion of calcium in the preeclamptic women, hypocalciuria may be due to enhanced tubular reabsorption. The hormones acting on calcium metabolism, i.e parathyroid hormone and calcitonin, do not change in the third trimester and in preeclampsia (12). Considering normal serum and urine phosphorus levels and normal creatinine clearance in preeclampsia, it seems unlikely that increased tubular reabsorption is modulated by parathyroid hormone. Parallel to these conclusions, Frenkel et al. have not been able to find any relation between parathyroid hormone and hypocalciuria in preeclampsia (13). Although other investigators have reported normal serum calcium levels in

preeclamptic patients when compared with normotensives, we have observed a significant relative hypercalcemia (3,12). This alteration may be the result of decreased calcium excretion from the kidneys.

The patients with preeclampsia, in our study, delivered at an earlier gestational age. As a result of this, birth weights were significantly lower. Labor was induced in some patients because of preeclampsia or eclampsia at an earlier time, and premature labor started spontaneously in some others.

Calcium supplementation in order to prevent preeclampsia has been studied in a few randomized trials. It is reported that the administration of low daily doses of linoleic acid and calcium during the third trimester of pregnancy reduced the incidence of preeclampsia significantly in women at high risk (14). In a larger randomized multicenter study from Australia, calcium supplementation during pregnancy reduced the risk of preeclampsia (15). However, in patients with mild preeclampsia, calcium supplementation does not prevent severe preeclampsia (16). Despite these data, in a recently published large series, it is concluded that calcium supplementation during pregnancy does not prevent preeclampsia and pregnancy associated hypertension (17). Differences in study designs, relatively smaller series and differences in dietary calcium intake might be responsible these conflicting results.

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