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Calciuria and preeclampsia

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Abstract

Urinary calcium excretion has been reported to be diminished in preeclampsia. The objective of the present study was to determine urinary calcium excretion in pregnant patients with chronic arterial hypertension (CAH) and preeclampsia (PE), and in normotensive patients (N). Forty-four pregnant patients (gestational age, 20-42 weeks; 18 CAH, 17 PE, 9 N) were evaluated for calciuria, proteinuria, plasma uric acid and blood pressure. Patients with PE (82 ± 15.1 mg/24 h) showed significantly lower calciuria ($P<0.05$) than the group with CAH (147 ± 24.9 mg/24 h) and the N group (317 ± 86.0 mg/24 h) ($P<0.05$, Student *t*-test). Plasma uric acid was significantly higher in the PE group (6.1 ± 0.38 mg/dl) than the CAH group (5.0 ± 0.33 mg/dl; $P<0.05$), which also presented higher proteinuria levels, although the difference was not statistically significant. Diastolic and systolic blood pressure did not differ between the PE (164 ± 105 mmHg) and CAH (164 ± 107 mmHg) groups. Calciuria was significantly lower in the group with preeclampsia than in the group with chronic arterial hypertension. We conclude that calciuria can be a further factor for identifying preeclampsia.

Key words
- Preeclampsia
- Hypertension
- Calciuria
- Kidney function
- High-risk pregnancy

Introduction

Hypertension occurs in 5 to 10% of our pregnant patients, corresponding to the major cause of maternal mortality in our midst as well as around the world (1). One way to reduce the impact of arterial hypertension on maternal mortality is to establish the correct diagnosis of preeclampsia, and to proceed with an early intervention when it is diagnosed (2). The classical clinical manifestation of preeclampsia is diagnosed when the pregnant patient presents high blood pressure levels (>140/90 mmHg) after the 20th week of gestation (without a previous history of arterial hypertension) along with the presence of significant proteinuria (>300 mg in 24 h) (3).

Today these clinical signs are considered to be a late manifestation of a disease that has been present since the first trimester of gestation. Due to this "diagnostic delay", many tests have attempted to establish the diagnosis of preeclampsia as early as possible, often even before the patient presents arterial hypertension (4). Tests reported for the early diagnosis of preeclampsia are Doppler ultrasound assessment of maternal and fetal circulation (5-7), uric acid concentration (8), the supine pressure test (9-11), the angiotensin test (12), microalbuminuria (13), plasma fibronectin concentration (14), plasma antithrombin activity (15), calciuria and other tests, all of which are of debatable efficacy and practicality.

One of the difficulties of day-by-day obstetrical practice has been the differential diagnosis of chronic hypertension and pre-

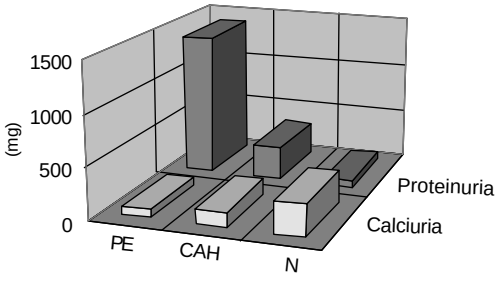

Figure 1 - Distribution of calciuria and proteinuria between groups. PE = Preeclampsia; CAH = chronic arterial hypertension; N = non-hypertensive controls.

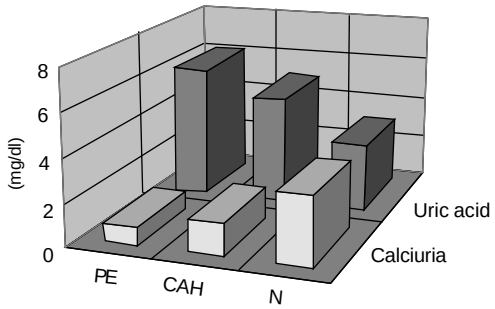

Figure 2 - Distribution of calciuria and uric acid between groups. PE = Preeclampsia; CAH = chronic arterial hypertension; N = non-hypertensive controls.

eclampsia, especially when the hypertensive patient presents proteinuria. Based on the observation that urinary calcium excretion is reduced in pregnant patients with preeclampsia, the authors determined the difference in calcium excretion between pregnant patients with the diagnosis of preeclampsia and pregnant patients with chronic arterial hypertension.

Material and Methods

We carried out an observational, transversal, controlled and prospective study in pregnant patients treated at the maternity clinic of the Hospital de Clínicas de Porto Alegre. Eligible patients had gestational ages from 20 to 42 weeks and arterial hypertension of 140/90 mmHg or higher. Patients who had established concomitant clinical disorders (diabetes mellitus, urinary infection, renal disorder, or epilepsy) as well as twin gestations were excluded from the study. All patients had normal serum creatinine (<0.9 mg/dl).

Patients were allocated to three groups, whose data were crossed and analyzed. Group I consisted of patients with a clinical diagnosis of preeclampsia (PE) while group II consisted of patients with a diagnosis of chronic arterial hypertension (CAH) without preeclampsia. The classification followed the guidelines of the American College of Gynecology and Obstetrics (3). Group III corresponded to a control group of non-hypertensive patients with gestational age from 20 to 42 weeks and with similar criteria for exclusion. The analyzed variables were 24-h urinary calcium, 24-h proteinuria, arterial pressure, and plasma uric acid.

Data were analyzed by the Student *t*-test for independent samples and the Fisher test with the level of significance set at 5%. The results are reported as means ± SEM. Data were stored and analyzed using the EPI-INFO program. The study was approved by the Research and Ethics Committee of the Hospital de Clínicas de Porto Alegre.

Results

The average diastolic and systolic blood pressure levels did not differ significantly between group I (PE) and group II (CAH), although they were higher than in the control group, which did not have arterial hypertension. In group I, the average proteinuria ratio was higher than in group II, although not statistically significant.

The distribution of calciuria and proteinuria between the groups and their inverse relation are shown in Figure 1. Figure 2 shows the inverse relation between calciuria and uric acid.

Plasma uric acid was significantly higher (6.1 ± 0.38 mg/dl) in group I ($P<0.05$) than in group II (5.0 ± 0.33) and group III (3.1 ± 0.15). In group I (PE) the average calciuria ratio (82 ± 15.1 mg/24 h) was significantly lower than the average (147 ± 24.9 mg/24 h) for group II (CAH) (Table 1).

Discussion

Calciuria is a condition which has been

studied in the detection of preeclampsia. Marya et al. (16) point out that urinary calcium excretion tends to increase in all pregnant patients, probably because of the increase in effective glomerular filtration rate. As also observed in the present study, Taufield et al. (17) found a significantly lower mean urinary calcium level in patients with preeclampsia and in hypertensive patients with preeclampsia (42 and 72 mg in 24 h, respectively), than in groups with chronic hypertension, and transitory hypertension and in normotensive patients (223, 248, and 313 mg/24 h, respectively).

Huikeshoven and Zuijderhoudt (18) concluded that the measurement of urinary calcium excretion is of value for the study of pregnant patients with arterial hypertension, both in terms of 24-h excretion and in the calciuria/creatinuria ratio of a single urine sample.

Sanchez-Ramos et al. (19) suggest that patients with preeclampsia present a significantly lower total urinary calcium excretion (129.7 mg/24 h) than that observed for normotensive patients (293.9 mg/24 h) or for patients with pregnancy-induced hypertension (232.2 mg/24 h) (P = 0.0001). These data reflect a higher average than our data. Anai et al. (20) demonstrated that the average urinary calcium excretion is significantly lower in the group of patients with preeclampsia (44.3 mg/24 h) than in the group of patients with fetal growth retardation. Raniolo and Phillipou (21) determined that the calciuria/creatinine ratio was not significantly different between groups of normotensive pregnant patients (0.52 ± 0.32), patients with preeclampsia (0.49 ± 0.32) and patients with pregnancy-induced hypertension (0.57 ± 0.40). The detection of calciuria is often contradictory, reflecting the need for new data.

Table 1 - Calciuria and hypertension in gestation.

PE = Preeclampsia; CAH = chronic arterial hypertension; N = non-hypertensive controls. Data are reported as means ± SEM. *P<0.05 between groups I and II, II and III, and III and I. $^{+}$P<0.01 between groups III and I (Student *t*-test).

	I (PE; N = 17)	II (CAH; N =18)	III (N; N = 9)
Calciuria (mg/24 h)	82 ± 15.1*	147 ± 24.9*	317 ± 86.0*
Proteinuria (mg/24 h)	1395 ± 654.5	326 ± 75.9*	63 ± 18.8*
Uric acid (mg/dl)	6.1 ± 0.38*	5.0 ± 0.33*	3.1 ± 0.15^{+}
Systolic (mmHg)	164 ± 5.2	164 ± 4.2*	115 ± 2.4^{+}
Diastolic (mmHg)	105 ± 3.2	107 ± 3.0*	74 ± 4.1^{+}

Urinary calcium excretion has been already studied as a predictive test of preeclampsia. Sanchez-Ramos et al. (22) found a relative risk of 9.4 of predicting preeclampsia when the patient shows urinary calcium excretion lower than 195 mg/24 h. Baker and Hackett (23) did not find significantly predictive values in the measurement of the albumin/creatinine and/or calcium/creatinine ratio in relation to the diagnosis of preeclampsia. Conde-Agudelo et al. (24) established that urinary calcium excretion produces contradictory and inconclusive findings for the predictive diagnosis of preeclampsia.

The present new results showed lower urinary calcium excretion in the group with preeclampsia than in the group with chronic arterial hypertension. A 24-h calciuria less than 100 mg/24 h may confirm a suspected preeclampsia. Thus, the measurement of calciuria could be used as a further test to differentiate between chronic arterial hypertensive disease and preeclampsia in pregnant patients.

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