Urinary Citrate Excretion in Patients with Urolithiasis

ÜROLİTİYAZİS HASTALARINDA İDRARLA SİTRAT EKSKRESYONU

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SUMMARY

Urinary citrate excretion of 67 patients with urolithiasis and of 31 healthy people determined by colorimetric citrate lyase assay.

A statistically signifant difference was detected between the healthy male (325±75.9 mg/g Cr) and female (453±132 mg/g Cr) ($p<0.05$) and it was seen that mean urinary citrate excretion of patients (172.61±89.27 mg/g Cr) was significantly lower than that of healthy people (391±105.9 mg/g Cr) ($p<0.001$).

There was not a significant difference between the urinary citrate excretions of primer (180.07±90.5 mg/g Cr) and recurrent (172.2±88.18 mg/g Cr) stone formers.

Therefore the decreased citrate excretion is an important factor of stone formation.

Key Words: Citrate, Urolithiasis, Stones

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ÖZET

Ürolitiyazisli 67 hasta ve 31 sağlıklı kişide idrarla sitrat atılımı kolorimetrik sitrat liyaz tayini ile ölçüldü.

Sağlıklı erkekler (325±75.9 mg/g Cr) ve sağlıklı kadınlar (453±132 mg/g Cr) arasında belirgin fark bulundu ($p<0.05$) ve ortalama sitrat atılımının hastalarda (172.61±89.27 mg/g Cr) sağlıklı kişilere göre (391±105.9 mg/g Cr) belirgin düşüklük tespit edildi.

Primer ürolitiyazis hastaları (180.07±90.5 mg/g Cr) ile rekürren taş yapan hastalar (172.2±88.18 mg/g Cr) arasında idrarla sitrat atılımı açısından belirgin fark yoktu.

Bu nedenle taş oluşumunda azalmış sitrat atılımında önemli bir faktördür.

Anahtar Kelimeler: Sitrat, Ürolitiyazis, Taş

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Urolithiasis is one of the ancient diseases. Until the last century, the incidence of bladder stones was very high and they were mainly composed of calcium oxalate or uric acid. In those days, the stones composed of calcium phosphate, magnesium ammonium phosphate and cystine are mostly seen in developing countries and in the industrialized countries. Urinary calculi composed of magnesium ammonium phosphate could be seen only in old men with prostatic obstruction. Simultaneously the incidence of renal calculi composed of calcium oxalate and calcium phosphate or calcium oxalate gradually increases (1).

Urinary citrate is an important determinant for crystallization of calcium salts, and an inhibitor of calcium oxalate (2,3) and calcium phosphate(4) crystal growth. It is frequently lower in calcium stone formers than in normal subjects (5,6). It is also well recognized that women, who usually excrete more citrate than men are less prone to develop calcium stones (6-8) and stone formation was 2 or 3 folds high in men than women (5). It was, also shown that urinary citrate excretion in patients with urolithiasis was low than the normals but that their serum citrate level was equal (9).

Hypocitraturia was seen in all patients with urolithiasis, except in patients with primary hyperparathyroidism (PHPT) and hyperuricosuric patients with calcium oxalate stones (5).

The aim of this study is to investigate urinary citrate excretion in patients with urolithiasis and healthy people.

MATERIALS AND METHODS

The control group (male: 15, female: 16, average age: 45±15) established from the healthy stuff of our hospital after clinical, laboratory and radiological elimination of urinary stones and other diseases. Their creatinine clearances were, also, in normal range. The patients (male: 42, female: 25, average age: 53±17) were selec-

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Table 1. The urinary citrate, calcium, magnesium, and uric acid excretions of controls and patients.

		Citrate (mg/g Cr)	Ca (mg/g Cr)	Mg (mg/g Cr)	Uric Acid (mg/g Cr)
Control	(n:31)	391.00±105.90	150.00±75.00	105.00±42.00	595.0±175
Patients	(n:67)	172.61±89.27*	194.80±48.50	90.01±35.80	545.3±230
Primary Stones	(n:42)	180.07±90.50*	205.90±45.20	95.45±40.50	525.5±255
Recurrent Stones	(n:25)	172.20±88.18*	183.86±50.25	84.58±29.30	565.1±224

*Comparison with the control group p<0.001

ted from the patients with urinary stones admitted to Urology Department of our hospital.

The patient group, also, subdivided according to the recurrence of their disease and there were 42 patients with primary stones and 25 patients with recurrent stones.

All patients had one or more urinary stones. To determine whether hypocitraturia in patients group, caused by renal deterioration, creatinine clearances of all patients were, also detected and it was seen that they were all normal. The urinary calcium, magnesium and uric acid levels determined by Perkin Elmer model atomic absorbtion spectrophotometry and enzymatic uricase methods, respectively. At the time of collection all patients were free of urinary tract infection. None of the subjects had a special diet, except patients who were encouraged to maintain a high fluid intake.

24-hour urine samples were collected adding Penicilline G and streptomycine (10). Citrate determination was performed with an enzymatic method modified by Welshman and Mc Cambridge (11).

RESULTS

The mean 24-hour urinary citrate excretion in control group was 391±105.9 mg/g Cr and in male and female, it was 325±75.9 mg/g Cr and 453±132 mg/g Cr, respectively. When we compared these values of male and female, we detected a statistically significant difference ($p<0.05$).

The mean 24-hour urinary citrate excretion in patients was 172.1±89.27 mg/g Cr male and female, it was 164±70 mg/g Cr and 190±136 mg/g Cr, respectively. However, there was not any significant difference between the values of male and female patients. When we compared the values of patients with the values of healthy people, a significant difference could be determined.

The patients group also, subdivided according to the recurrence of stone formation and the values of patients with primary stone (180.07±90.5 mg/g Cr) didn't show any significant difference than the values of patients with recurrent stones (172.2±88.18 mg/g Cr).

Urinary citrates, calcium, magnesium and uric acid excretions of patients groups and control group were given in Table 1.

DISCUSSION

Urinary calculi is partly a result of physiologic and chemical deterioration of urine and anatomic defect (12). The pathologic changes in urine are; high urinary calcium (13,14), oxalate (15,16) and uric acid (17) excretion, deficiency of protective inhibitors (18) as citrate (19) and super saturation of urine.

Citric acid is freely filtered in the renal glomerulus and is reabsorbed in the proximal renal tubule (20). The presence of citrate in the urine is believed to be beneficial, because citrate chelates calcium, thereby reducing precipitation of calcium salts (21). As calcium chelates with citrate, the concentration of free calcium ions decreases and therefore the supersaturation of urine needed for stone formation decreases.

Reduced urinary citrate excretion in stone formers has been documented in many publications (22,23).

Some of the investigators reported that urinary citrate excretion was higher in women than in men (6,7), which was also found in this study. The reason for the higher citrate excretion in women couldn't be explained. However, it could not be possible to demonstrate a relationship between sex steroids and urinary citrate. Some of the investigators showed no difference between the urinary citrate excretion of men and women (24).

When all of these conflicting previous studies examined, it was seen that no protector added in urine specimens at the time of collection. As urine specimen usually contain bacteria fed with citrate as carbon source, the citrate content of urine specimens gradually decrease, till citrate determination performed. In our study, all urine specimens collected adding Penicilline G and streptomycine as these were known, to be the most effective protectors.

In this study, it was seen, urinary citrate excretion in patients with urolithiasis was significantly low than controls. However, there wasn't any difference between the levels of patients with primary and recurrent disease.

In conclusion, when our results and those of the preliminary studies are taken into consideration, low citrate excretion in patients with urolithiasis shows that the determination of urinary citrate excretion is very important.

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