Fırat Tıp Dergisi 2007;12(1): 37-40

Clinic Research

www.firattipdergisi.com

Relationship Between 24-Hour Urine and Serum Parameters in Patients with Nephrolithiasis

Hüsamettin ERDAMAR [a] , Banu SANCAK, Neslihan BUKAN, Hatice PAŞAOĞLU

Gazi Üniversitesi Tıp Fakültesi Tıbbi Biyokimya Anabilim Dalı, ANKARA

ABSTRACT

Objective: Nephrolithiasis is a common disease, whereas the mechanisms by which stones develop in the kidney are poorly understood. While high levels of oxalate, uric acid, calcium, and phosphate in the urine increase the formation of nephrolithiasis, increased urinary excretion of citrate, magnesium, albumin and alkali urine decrease this process. In this study, we aimed to identify the possible relationship between some serum and 24-hour urinary parameters in patients with nephrolithiasis.

Materials and Methods: Two hundreds thirty-one patients with nephrolithiasis (aged 18-65 years; 143 men, 88 women) were retrospectively examined in this study.

Results: Significant correlations observed between urine and serum levels of creatinine with urine and serum levels of uric acid [r= 0.70, (p<0.01) for urine; r= 0.55, (p<0.01) for serum]; urine levels of phosphorus with urine levels of urea (r= 0.998, p<0.01); urine levels of uric acid with urine levels of calcium (r= 0.488, p<0.001) and between urine levels of chlorine and uric acid (r= 0.547, p=0.00) and creatinine (r= 0.59, p<0.001).

Conclusion: In conclusion, there are some correlations between the values of urine and serum parameters. In patients with nephrolithiasis, 24-hour urine analysis may be helpful for the assessment of stone formation and development. Furthermore these correlations may conduct clinicians determine better treatment strategies. *©2007, Firat University, Medical Faculty*

Key words: *24 Hour Urine Analysis; Nephrolithiasis; Citrate; Oxalate; Phosphate.*

ÖZET

Nefrolitiazisli Hastalarda 24 Saatlik İdrar ve Serum Parametreleri Arasında İlişki

Amaç: Nefrolitiazis yaygın bir hastalık olmasına rağmen, böbrekteki taş oluşum mekanizması tam olarak anlaşılamamıştır. İdrarda yüksek konsantrasyonda oksalat, ürik asit, kalsiyum ve fosfor bulunması nefrolitiazis oluşma riskini arttırırken; sitrat, magnezyum, albumin düzeylerinin yüksekliği ve idrarın alkali olması ise bu riski azaltmaktadır. Bu çalışmada nefrolitiasizli hastalarda serum ve 24 saatlik idrar analizi sonucu elde edilen parametreler arasındaki muhtemel ilişkiyi tespit etmeyi amaçladık.

Gereç ve Yöntem: 231 adet nefrolitiazisli hasta (18-65 yaşları arasında; 143 erkek, 88 kadın)retrospektif olarak incelendi.

Bulgular: İdrar ve serum kreatinin değerleri ile idrar ve serum ürik asit değerleri arasında [sırasıyla r= 0.70, (p<0.001); r= 0.55, (p<0.001)]; idrar fosforu ile idrar üre değerleri arasında (r= 0.998, p<0.001); idrar ürik asiti ile idrar kalsiyum değerleri arasında (r= 0.488, p<0.001); idrar klor değerleri ile hem idrar ürik asi hem de idrar kreatinin değerleri arasında [sırasıyla r= 0.547, (p=0.00);r= 0.59, (p<0.001)] istatiksel olarak anlamı korelasyon bulundu.

Sonuç: Bazı serum ve idrar parametreleri arasında korelasyon vardır. Nefrolitiazisli hastalarda taş oluşumu mekanizmasının daha iyi anlaşılması açısından 24 saatlik idrar analizi faydalı olabilir. Dahası bu korelasyonlar hastaya klinik yaklaşımı yönlendirebilir ve tedavi protokolünü etkileyebilir. *©2007, Fırat Üniversitesi, Tıp Fakültesi*

Anahtar kelimeler: *24 Saatlik idrar analizi; nefrolitiazis; sitrat; okzalat; fosfat.*

Nephrolithiasis is a common cause of morbidity recently. Studies have shown that metabolic causes of nephrolithiasis were hypercalciuria, hypocitraturia, high or low pH of urine, hyperuricosuria, hyperoxaluria, hypomagnesaemia and cystinuria.

Hypocitraturia is seen almost 30% of patients with nephrolithiasis. The importance of citrate in nephrolithiasis stems from the recognition that citrate is a direct inhibitor of calcium phosphate precipitation (1) and the generation of calcium oxalate crystal (2). The ability of citrate to form soluble complexes with divalent cations, such as calcium, is well known. Such complexation may cause some reduction in the urinary saturation of "stone-forming" calcium salts. For these reasons urinary citrate concentrations may have important rolls in renal stone formation. It has also been shown that four of every five patients with nephrolithiasis were male (3). One of the problems with citrate excretion is that it depends on age and sex; it changes with age (4) and is generally higher in women than in man (4-9).

Urine analysis is important in determining urine pH, eliminating probable infection, and the most importantly learning the type of crystals (crystals usually seen during the acute attack). Concentrations of serum electrolytes, calcium, phosphate, creatinine and uric acid have to be measured at the first biochemical investigation of patients with nephrolithiasis. In addition, 24-hour urine volume, creatinine, urea, Na+, Ca++, phosphate, uric acid, oxalate, citrate, urine pH, and serum level of Intact Para Thyroid Hormone (IPTH) may be assessed.

Corresponding Address: Hüsamettin Erdamar , Gazi Üniversitesi Tıp Fakültesi Tıbbi Biyokimya Anabilim Dalı, ANKARA

* 2003 Ekim Klinik Biyokimya Uzmanları Derneği I. Ulusal Kongresi Kapadokya.

Tel: +90 3122026923 e-mail: mdherdamar@yahoo.com

The purpose of this study was to find out the relation between urine and serum parameters that are measured routinely in patients with nephrolithiasis. Then more clarify formation of nephrolithiasis.

MATERIALS AND METHODS

Our study was held in Medical Faculty of Gazi University, Department of Medical Biochemistry, and Central Laboratory on January, February and March in 2004. One hundred forty-three of the patients with nephrolithiasis were male and eighty-eight of them were female, and mean ages were 42.6±12.4 years and 43.4±15.1 years respectively. Whether the patients had nephrolithiasis or not confirmed with each patient's data. The results of analysis of urine oxalate, citrate, uric acid, calcium, phosphate and magnesium, pH of 24 hour urine; serum uric acid, calcium, phosphate and IPTH were reviewed retrospectively.

Urine volume and levels of citrate, oxalate, calcium, creatinine, urea, Na+, Ca++, phosphate, uric acid were measured. Serum electrolytes, calcium, phosphate, creatinine and uric acid levels were also determined. Urinary citrate and oxalate levels were measured spectrophotometrically with enzymatic method by means of using commercially available diagnostic kits (Roche Diagnostics, Darmstadt, Germany and Sigma, St Louis, MO; respectively). Levels of other parameters were measured using Abbott-Aeroset autoanalyzer (USA). IPTH was measured with Abbott Architect 2000 chemiluminescence immunoassay analyzer (USA).

Statistical Analysis:

The results are presented as mean±SD, student's t-test was used for statistical analysis. Pearson test was used for correlation analysis. p values <0.05 were regarded as statistically significant.

RESULTS

The mean values of urinary and serum parameters were shown in Table 1 and 2 respectively. Metabolic analysis showed that in patients with nephrolithiasis 24-hour urine volume, and urinary magnesium and oxalate excretion were higher than normal intervals. The other measured parameters were at normal levels. Although urine excretions of calcium, uric acid were significantly greater in men, excretion of citrate was significantly lower in men.

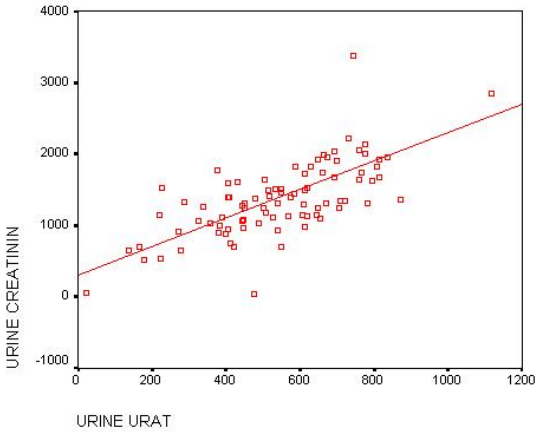

Figure 1. Relationship Between 24-Hour Urinary and Serum Biochemical Parameters
a) Urine levels of creatinine with urine levels of uric acid

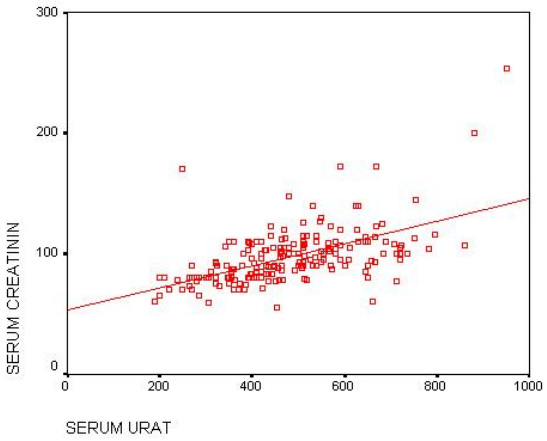

Figure 1. Relationship Between 24-Hour Urinary and Serum Biochemical Parameters
b) Serum levels of creatinine with serum levels of uric acid

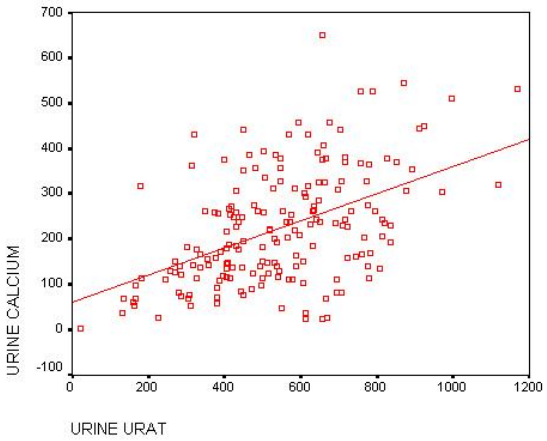

Figure 1. Relationship Between 24-Hour Urinary and Serum Biochemical Parameters
c) Urine levels of uric acid with urine levels of calcium

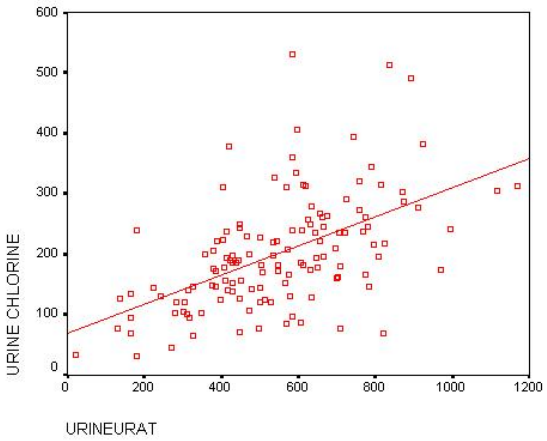

Figure 1. Relationship Between 24-Hour Urinary and Serum Biochemical Parameters
d) Urine levels of chlorine with urine levels of uric acid

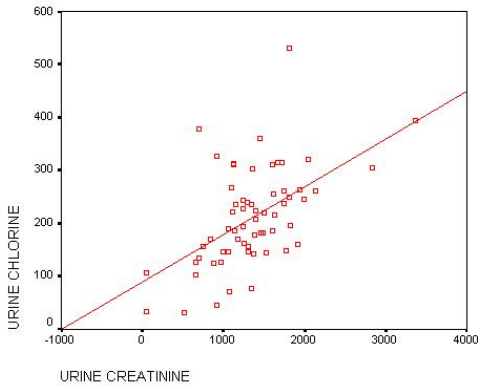

Figure 1. Relationship Between 24-Hour Urinary and Serum Biochemical Parameters Urine levels of chlorine with urine levels of creatinine

As a result of correlation analysis, significant correlations were found between: both urine and serum levels of creatinine with both urine and serum levels of uric acid [r= 0.70 (p<0.01), r= 0.55 (p<0.01) respectively]; urine levels of phosphorus with urine levels of urea [r=0.99 (p<0.01)]; urine levels of uric acid with urine levels of calcium [r=0.48 (p<0.01)] and between urine levels of chlorine with uric acid [r= 0.54 (p=0.00)] and creatinine [r= 0.59 (p<0.01)]. These strong relationships were shown in figure 1.

Table 1. 24-Hour Urinary Excretions of Constituents

	Urine Volume (ml/24 h)	Oxalate (mg/24 h)	Citrate (mg/24 h)	Calcium (mg/24 h)	Uric Acid (mg/24 h)	Phosphate (g/24 h)	Magnesium (mg/24 h)	Sodium (mmol/ 24 h)	Potassium (mmol/L)	Chloride (mmol/L)	Creatinine (mg/dl)
Normal Levels	600-1600	7-44♂ 4-31♀	115-921♂ 250-1152♀	100-300	250-750	0.4-1.3	6-10	40-220	25-125	110-250	600-1800
Patient Men (n=143)	2234±1071.9	92.9±67.3	373.8±228.7	228±123.6	602.1±197.7	0.96±1.83	15.4±47.1	224.6±107.3	57.9±38.5	216.6±95	1578.2±584.5
Women (88)	2283±962.6	72.4±62	490.9±285	192.6±121.1	445±170.1	1.05±3.03	11.7±20.1	197.1±111.6	57.7±70.7	184.9±87.4	1081.9±354.8
P	NS	NS	0.000	0.002	0.000	NS	NS	NS	NS	NS	0.000

NOTE:Values expressed mean ± Standart Deviation
Abbrevation: NS: not significant

Table 2. Values for Serum Chemistry Tests and PTH

	Calcium (mg/dl)	Phosphate (mg/dl)	Uric Acid (mg/dl)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Creatinine (mg/dl)	BUN (mg/dl)	Intact PTH (pmol/L)
Normal Levels	8.2-10.6	2.5-4.5	2.6-7.2	135-146	3.5-5.5	96-108	2.6-7.2	5-25	0.8-5.2
Patient Men (n=143)	9.3±0.6	3.2±0.5	5.3±1.1	142.2±2.1	4.2±0.2	104.3±3.2	1.05±0.2	14.4±5.2	4.1±7.1
Women (88)	9.3±0.6	3.3±0.5	3.9±1.3	141.8±2.2	4.3±0.3	105.3±4.3	0.84±0.1	12.6±4.5	8.7±15.2
P	NS	NS	0.002	NS	NS	NS	0.000	0.002	0.003

NOTE:Values expressed mean ± Standart Deviation
Abbrevation: NS: not significant
IPTH: Intact Para Thyroid Hormone

DISCUSSION

We investigated the correlations between each parameters of 24-hour urine assessed ordinary in patients with nephrolithiasis. In our study we found a different aspect of biochemical values in nephrolithiasis.

It is known that while the raised excretion of oxalate, uric acid, calcium and phosphorus in the urine increase the formation of nephrolithiasis; raised excretion of citrate, magnesium, albumin and alkali urine decrease this process. In our patients with nephrolithiasis the levels of urine citrate, calcium, uric acid, phosphorus, sodium (up limit in men), potassium, chlorine and creatininee were within normal limits but the levels of 24-hour urine volume, and urinary magnesium and oxalate excretion were higher than normal.

Several reports claim that idiopathic stone formers excrete significantly less citrate in their urine than normal subjects (5-7, 9-15). Others, however, have not confirmed this difference (16-19). One of the problems with citrate excretion is that it depends on age and sex; it changes with age (4) and is generally higher in women than in man (4-9). Our results were in agreement with this data.

The levels of all serum parameters were within normal intervals but only IPTH was higher than normal in female patients. Primary hyperparathyroidism is related with stone formation in patients with nephrolithiasis. We also observed positive correlations between urine and serum levels of creatininee with urine and serum levels of uric acid; urine levels of phosphorus with urine levels of urea; urine levels of uric acid with urine levels of calcium and among the urine levels of chlorine with uric acid and creatinine.

Either Fellstrom et al. (20) in patients (n= 467) with calcium lithiasis or Dumoulin et al. (21) in patients (n= 49) with pure and mixed CaOx (calcium-oxalate) lithiasis found out a positive correlation between urine values of uric acid and

oxalate. Although Duranti et al. in patients (n= 30) with calcium lithiasis found a positive correlation between urine values of calcium and phosphorus, they did not find correlation among creatininee, uric acid, urea, chlorine and magnesium excretions (22). Futhermore Conta A et al. (23) and Welshman et al. (4) in patients with CaOx lithiasis found that patients with hypocitraturia also had hypercalciuria. But Menon and Mahle described no significant correlation between calcium and citrate excretion in their controls or patients with stone (14). As a different relationship Oehlschlager et al. (24) found a combination of hypercalciuria and hyperoxaluria in patients (n= 22) after extracorporeal shock wave lithotripsy treatment. Both Tefekli A et al. and Ogava Y et al. found that levels of urine calcium were higher in patients with CaOx stones than normal patients; level of urine citrate, magnesium and creatinine were lower than normal (n= 155 and n= 222) (25,26), but Scholz et al. (27) found out that concentrations of magnesium, uric acid and phosphate were within normal limits in urine. These different results may result from the special characteristics of a particular region (diet, climate, genetics, socio-economic factors, etc.). The dietary differences may be the most important factor to explain the deviation among the various studies.

In conclusion, it is obvious that there are correlations among some urine parameters and this may be clinically useful for a more effective treatment planning.

REFERENCES

1. Parks YJ, Coe LF: The financial effects of kidney stone prevention. Kidney International. 1996; 50: 1706-1712
2. Bisaz S, Felix R., Newman WF, Fleisch H: Quantitative determination of inhibitors of calcium phosphate precipitation in whole urine. Min Electrolyte Metab. 1978; 1:74
3. Tiselius HG: Urinary Excretion of Citrate in Normal Subjects and Patients with Urolithiasis. Plenum Press, New York, 1981
4. Welshman SG, Mc Geown MG: Urinary citrate excretion in stone-formers and normal controls. Br J Urol. 1976; 48: 7-11
5. Hodgkinson A: Citric Acid Excretion of Citrate in Normal Adults and in Patients with Renal Calculus. Clin Sci. 1962; 23: 203-212
6. Elliot JS, Riberio ME: The urinary excretion of citric, hippuric and lactic acid in normal adults and in patients with calcium oxalate urinary calculus disease. Invest Urol. 1972; 10: 102-106
7. Sehwille PO, Scholz D, Paulus M, Engelhardt W, Sigel A:. Citrate in Daily and fasting urine. Invest Urol. 1979; 16: 457-462
8. Robertson WG, Peacock M, Nordin BEC: Activity products in stone-forming urine. Clin Sci.1968; 32: 579-594
9. Welshman SG, Mc Geown MG: A quantitative investigation of the effects on the growth of calcium oxalate crystals of potential inhibitors. Br J Urol. 1972; 44: 677-680
10. Pylypchuk G, Ehrig U, Wilson DR: Idiopathic calcium nephrolithiasis. 1. Differences in urine crystalloids, urine saturation with brushite and urine inhibitors of calcification between persons with and persons without recurrent kidney stone formation. Can Med Assoc. J, 1979; 17: 658-665
11. Butz M: Oxalatsteinprophylaxe durch alkali-theriape. Urologe. 1982; 21: 142-146
12. Rudman D, Kutner MH, Redol SC, Waters WC, Gerron GG, Bleier J: Hypocitraturia in calcium nephrolithiasis. J Clin Endocrnol Metab. 1982; 55: 1052-1057
13. Nicar MJ, Skurla C, Sakhaec K, Pak CYC: Low urinary citrate excretion in nephrolithiasis. Urology. 1983; 21: 8-14
14. Menon M., Mahle CJ: Urinary citrate excretion in patients renal calculi. J Urol. 1983; 129: 1158-1160
15. Millan A, Conte A, Garcia Raso A, Grases F: Determination of Citrate in urine by simple direct photometry. Clin Chem. 1987; 33: 1259-1260
16. Robertson WG, Peacock M, Nordin BEC: Activity products in stone-forming and non stone-forming urine. Clin Sci. 1968; 32: 579-594
17. Robertson WG, Peacock M, Nordin BEC: Calcium oxalate crystalluria and urine saturation in recurrent renal stone-formers. Clin Sci. 1971; 40: 365-374
18. Robertson WG, Peacock M, Heyburn PJ, Marshall DH, Clark PB: Risk factors in calcium stone disease of the urinary tract. Br J Urol.1978; 50: 449-454
19. Marshall RW, Barry HH: Urine Saturation and the formation of calcium Containing Calculi. The effects of various forms of therapy. Karger, Basel 1973
20. Fellstrom B, Backman U, Danielson BG, Johansson G, Ljunghall S, Wikstrom B: Urinary excretion of urate in renal calcium stone disease and tubular acidification disturbances. J Urol. 1982; 127: 589-592
21. Dumoulin G, Haton D, Wolf JP, Henriet MT, Nguyen NU, Mougin C, Saint-Hiller Y, Combes M, Berthelay S: Comparative study of urinary calcium, oxalate and uric acid in calcium oxalate lithiasis. Nephrologie. 1984; 5: 189-191
22. Duranti E, Imperiali P, Badi M, Capiccioni S, Masi MG, Sasdelli M: Study of inhibitor and nucleator activities in calcium stone former. Proc Eur Dial Transplant Assoc. 1983; 20: 445-449
23. Conte A, Roca P, Gianotti M, Grases F: On the relation between citrate and calcium in normal and stone-former subjects. Int Urol Nephrol. 1990; 22: 7-12
24. Oehlschlager S, Albrecht S, Hakenberg OW, Schrodter S, Froehner M, Manseck A, Wirth MP: Early changes of oxalate and calcium urine excretion in those with calcium oxalate stone formation after extracorporeal shock wave lithotripsy. Adult Urology 2003;62: 17-21
25. Tefekli A, Esen T, Ziylan O, Erol B, Armagan A, Ander H, Akinci M: Metabolic Risk factors in pediatric and adult calcium oxalate urinary stone formers: is there any difference? Urol Int. 2003; 70: 273-277
26. Ogawa Y, Yonou H, Hokama S, Oda M, Moruzumi M, Sugaya K: Urinary saturation and risk factors for calcium oxalate stone disease based on spot and 24-hour urine specimens. Front Biosci. 2003; 8: A167-A176
27. Scholz D, Schwille PO, Ulbrich D, Bausch WM, Sigel A: Composition of renal stones and their frequency in a stone clinic: relationship to parameters of mineral metabolism in serum and urine. Urol Res. 1979; 7: 161-170.

Kabul Tarihi: 12.06.2006