Effect of kidney stone prevention on urinary risk factors for kidney stone formation and new stone formation: a single-centre retrospective cohort study

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Objective: Nephrolithiasis is a highly prevalent and recurrent disease. Prophylactic treatment to prevent recurrent kidney stone formation is recommended. We evaluated the effect of combined preventive measures on the urinary risk factors for kidney stone formation, renal colic rate, stone formation rate and rate of urological interventions in a single-centre retrospective cohort study.

Methods: In all nephrolithiasis (NL) and nephrocalcinosis (NC) patients attending our kidney stone prevention clinic between 22/12/2004 and 31/12/2020, baseline metabolic evaluation was performed and renal colic rate, stone formation rate and urological intervention rate before the first consultation were calculated. Preventive measures were tailored to repeated metabolic evaluation and kidney stone analysis and comprised increasing oral fluid intake, dietary measures including low oxalate, normal calcium, low salt, low protein and low purine intake, calcium supplements with meals, thiazide or thiazide-like diuretics, urinary alkalinization, xanthine oxidase inhibitors, methionine-restricted diet and thiol-binding agents in cystinuria patients and long-term antibiotics and urinary acidification in struvite stone formers. In patients with at least 6 months follow-up, effect of combined preventive measures on urinary risk factors during follow-up was analysed (Wilcoxon signed-rank test). In all nephrolithiasis patients with at least 12 months follow-up, effect of combined preventive measures on renal colic rate, stone formation rate and urological intervention rate during follow-up was evaluated (Wilcoxon signed-rank test).

Results: 835 nephrolithiasis (NL) and nephrocalcinosis (NC) patients (537 males, 298 females, median age 36 yrs (IQR 25-49)) were evaluated at baseline. Median interval between NL/NC diagnosis and first consultation was 3.7 years (IQR 0.4-12.1). 98.4% presented with at least one urinary risk factor (Table 1). In 355 patients with median follow-up of 2.3 years (IQR 1.1-5.0), effect of combined preventive measures on urinary risk factors was evaluated (Table 2). Combined preventive measures significantly reduced median sodium excretion, calciuria, uricosuria and phosphaturia and significantly increased median urinary volume. In patients with hyperoxaluria, increased protein intake, hypocitraturia and low urinary pH at baseline evaluation, combined preventive measures significantly reduced median oxalate excretion and protein intake and significantly increased median citrate excretion and urinary pH, respectively.

Table 1: Urinary risk factors at baseline evaluation (n=835)

Protein intake > 1 g/kg IW/24h, n (%)	643 (77.0)
Sodium excretion > 150 mmol/24h, n (%)	500 (59.9)
Urinary volume < 2000 ml/24h, n (%)	493 (59.0)
Oxaluria > 45 mg/24h, n (%)	305 (36.5)
Urinary pH < 5.5, n (%)	233 (27.9)
Calciuria ≥ 0.1 mmol/kg IW/24h, n (%)	236 (28.3)
Uricosuria > 750 mg/24h in females, > 800 mg/24h in males, n (%)	202 (24.2)
Citraturia ≤ 1500 µmol/24h, n (%)	167 (20.0)
Phosphaturia > 42 mmol/24h, n (%)	128 (15.3)

Table 2: Effect of combined preventive measures on urinary risk factors

	Before prevention	With prevention	P-value
Protein intake (g/kg IW/24h), mean (IQR) (n=355)	1.30 (1.09-1.57)	1.29 (1.08-1.56)	0.23
Sodium excretion (mmol/24h), mean (IQR) (n=355)	178 (135-228)	164 (120-215)	<0.05
Urinary volume (ml/24h), mean (IQR) (n=355)	1950 (1400-2600)	2300 (1790-2850)	<0.0001
Oxaluria (mg/24h), mean (IQR) (n=355)	41 (33-54)	42 (33-53)	0.90
Calciuria (mmol/kg IW/24h), mean (IQR) (n=355)	0.076 (0.046-0.111)	0.068 (0.042-0.094)	<0.0001
Uricosuria (mg/24h), mean (IQR) (n=355)	617 (472-792)	541 (421-693)	<0.0001
Citraturia (µmol/24h), mean (IQR) (n=355)	2688 (1567-4014)	2760 (1710-4290)	0.0533
Phosphaturia (mmol/24h), mean (IQR) (n=355)	28.8 (22.9-37.1)	28.1 (21.1-35.8)	<0.01
Protein intake in patients with increased protein intake before prevention (g/kg IW/24h), mean (IQR) (n=283)	1.37 (1.20-1.65)	1.34 (1.12-1.61)	<0.001
Oxaluria in patients with hyperoxaluria before prevention (mg/24h), mean (IQR) (n=73)	65 (59-73)	46 (36-57)	<0.0001
Citraturia in patients with hypocitraturia before prevention (µmol/24h), mean (IQR) (n=77)	723 (254-1220)	1480 (643-2339)	<0.0001
Urinary pH in patients with low urinary pH before prevention, mean (IQR) (n=86)	5.00 (5.00-5.00)	5.92 (5.00-6.92)	<0.0001

Combined preventive measures significantly reduced median renal colic rate and urological intervention rate (Table 3). Median stone formation rate decreased significantly when the interval between NL/NC diagnosis and first consultation was not adjusted. When this interval was adjusted to a minimum of 5 years, to avoid overestimation of the stone formation rate before start of prevention due to short follow-up before instauration of preventive measures, no effect of combined preventive measures on median stone formation rate could be demonstrated.

Table 3: Effect of combined preventive measures on renal colic rate, urological intervention rate and stone formation rate

	Rate before prevention (/yr), median (IQR)	Rate with prevention (/yr), median (IQR)	Follow-up (yr), median (IQR)	P-value
Renal colic (n=257)	0.09 (0.00-0.40)	0.00 (0.00-0.12)	2.9 (1.7-5.7)	<0.0001
Urological interventions (n=254)	0.00 (0.00-0.20)	0.00 (0.00-0.00)	3.0 (1.7-5.9)	<0.0001
Stone formation (n=142)	0.52 (0.19-1.60)	0.36 (0.00-0.99)	3.1 (1.7-5.5)	<0.01
Stone formation pre 5 yr (n=142)	0.40 (0.19-0.80)	0.36 (0.00-0.99)	3.1 (1.7-5.5)	0.23

Conclusion: Combined preventive measures significantly impact on urinary risk factors for kidney stone formation, especially when tailored to the patient's metabolic evaluation. Additionally, prophylactic treatment significantly reduces symptomatic renal colic rate and urological intervention rate, outcomes that are clinically significant for the patient and will likely reduce kidney stone disease-related health care costs.