

Renal Manifestations in Inflammatory Bowel Disease: Lithogenic Factors and Tubulointerstitial Involvement

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Introduction

Renal involvement in patients with inflammatory bowel disease (IBD) can occur either as an extra-intestinal manifestation of disease or as a side-effect of the therapies used, mainly 5-aminosalicylate drugs, often in those with severe long-standing disease. The most common manifestation in these patients is kidney stones, but tubulointerstitial abnormalities are being reported more frequently and are not uncommon in autopsy studies. Tubulointerstitial involvement, once thought to represent a consequence of therapy, is now being pointed as a consequence of disease.

Objective: The aim of this study was to evaluate patients with the diagnosis of IBD with respect to: 1) prevalence of nephrolithiasis and lithogenic factors and 2) prevalence of tubular dysfunction, using an early marker of tubular injury, N-acetyl-beta-D-glycosaminidase (beta-NAG).

Methods

A point prevalence study was performed in 45 consecutive outpatients with IBD. Clinical and laboratory data were collected, including routine indices of kidney function (serum creatinine, creatinine clearance, urinary pH, urinary density and urinary electrolytes in 24h samples), as well as urinary concentration of beta-NAG, also in a 24h sample.

History of symptomatic renal colic, exposure to 5-aminosalicylate drugs in previous 6 months and severity of disease were assessed by questionnaire and clinical file consultation. Disease severity was defined according to the number of risk factors, namely history of bowel surgery, need for hospital admission or need for immunosuppression (azathioprin or monoclonal antibodies), ranging from zero risk factors to 3 risk factors.

Results

Table 1. Baseline characteristics of the population.

Patients (n=45)	
Males	17 (38%)
Mean age (years)	43±15
Mean time of disease (years)	9.5±6.8
Type of IBD – Crohn Disease	30 (67%)
Ileal involvement	18 (40%)
History of nephrolithiasis	9 (20%)
Aminosalicylates in previous 6 months	32 (71%)
Mean creatinine (mg/dl)	0,74±0,18
Mean creatinine clearance (ml/min)	118,8±44

Table 2. Differences between patients with and without history of nephrolithiasis.

	History of nephrolithiasis (n=9)	No history of nephrolithiasis (n=36)	p
Urinary density	1024±7,9	1022±6,7	0,396
Urinary oxalate mmol/24h			
Males (0,08-0,49)	0,63±0,21	0,44±0,15	0,086
Females(0,04-0,32)	0,32±0,13	0,33±0,15	0,858
Urinary citrate mmol/24h			
Males (0,6-4,8)	1,8±1,2	2,0±1,4	0,848
Females (1,3-6,0)	1,2±1,4	2,4±1,6	0,117
Serum uric acid mg/dl (2,7-6,8)	4,63±1,35	4,66±1,12	0,961
Urinary uric acid g/24h (0,25-0,75)	0,60±0,21	0,53±0,15	0,234
Urinary calcium mmol/24h (1,25-7,50)	6,63±3,63	3,41±2,15	0,001
Urinary phosphorus mmol/24h (12,9-48)	29,432±11,3	24,71±9,07	0,192
Urinary magnesium mg/24h (73-122)	82,33±53,79	64,36±31,04	0,192
Urinary potassium mmol/24h (25-125)	62,56±28,50	58,92±20,59	0,663

There was no difference in the prevalence of symptomatic nephrolithiasis between the two types of IBD; in patients with history of nephrolithiasis, ileal involvement was more prevalent.

	Crohn's Disease	Ulcerative Colitis	p
History of nephrolithiasis	7 (23,3%)	2 (13,3%)	0,429

	Ileal involvement	No ileal involvement	p
History of nephrolithiasis	6 (33,3%)	2 (7,7%)	0,003

Beta-NAG was not different between the groups defined below, except for a tendency to be higher in patients with lower creatinine clearance.

	Aminosalicylates in previous 6 months	No aminosalicylates in previous 6 months	p
Beta-NAG (median; interquartile range)	2,51 (1,64 – 5,38)	2,54 (2,16 – 4,0)	0,423

	Creatinine clearance >90ml/min	Creatinine Clearance <90ml/min	p
Beta-NAG (median; interquartile range)	2,30 (1,70 – 3,80)	3,60 (2,80 – 6,60)	0,110

	Crohn's Disease	Ulcerative Colitis	p
Beta-NAG (median; interquartile range)	2,53 (1,78 – 4,0)	2,34 (1,57 – 5,82)	0,656

Number of risk factors for disease severity	Beta-NAG (median; interquartile range)	p
0	2,84 (0,76 – 5,33)	p=0,753
1	3,05 (1,78 – 6,32)	
2	2,34 (2,18 – 3,45)	
3	2,50 (1,94 – 4,72)	

Conclusions

As previously reported, ileal involvement in IBD has a significant relationship with the occurrence of nephrolithiasis. Elevated levels of urinary oxalate and low levels of urinary citrate are potential lithogenic factors, and we found an interesting gender difference in our study population considering these parameters. Patients with a previous history of symptomatic nephrolithiasis had a significantly higher calcium urinary excretion, but no differences were found considering other potential lithogenic factors.

Beta-NAG was elevated in a small number of patients and was not related to any patient or disease characteristics, and so its clinical implications are yet unknown. Prospective studies with more patients and possibly other markers of tubular injury are warranted to clarify this issue.

