N-ACETYL – β – GLUCOSAMINIDASE IN THE LOCALIZATION OF THE SITE OF URINARY TRACT INFECTIONS

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ABSTRACT

Excretion of N-acetyl-β-glucosaminidase was measured in 57 patients with urinary tract infections and in 19 normal subjects. The normal range was 0.17 to 1.16 iu/mmol creatinine. The mean NAG/creatinine ratio was 3.11 in 28 patients with upper, and 1.14 in 21 patients with lower urinary tract infection (p=0.0006). However, even among those clinically defined as having lower urinary tract infections, 18% had NAG/creatinine ratios above the normal range. The mean NAG/creatinine ratio of 8 patients with lower urinary tract symptoms who had underlying uronephrological diseases/systemic diseases capable of causing nephropathy was intermediate between the value obtained in patients with upper, and that observed in patients with lower urinary tract infections.

Keywords: A-acetyl-β-glucosaminidase, urinary tract infections.

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INTRODUCTION

Urinary tract infections are common and may be broadly divided into upper and lower urinary tract infections. The distinction is, however, mainly clinical, and although various techniques have been proposed for the accurate localization of the site of infection, none have proved universally acceptable (1). Localization of the site of infection is not purely for the interest of the academic physician, for upper and lower urinary tract infections clearly have different connotations. The present study investigates the value of urinary excretion of N-acetyl-b-glucosaminidase (NAG) in the differentiation between upper and lower urinary tract infections.

Patients and Methods

Fifty-seven patients (12m:45f), aged from 18 to 84 years with a mean of 43.9 years, who had urinary tract infections, were studied. Urinary tract infection was diagnosed when a positive bacterial culture was obtained in the presence of urinary tract symptoms. Those who complained of dysuria, frequency, sense of incomplete emptying with or without gross haematuria and fever but who did not have chills and rigors and who on examination had no tenderness in the loin, were considered as having lower urinary tract infections. Those who had minimal symptoms referrable to the urinary tract but had acute loin tenderness with or without symptoms or signs of bacteraemia were considered as having upper urinary tract infections. When urinary tract infection was suspected, a mid-stream urine was sent for culture and a 2-h urine sample was collected from each patient for the determination of creatinine (picric acid method) and NAG (colorimetric method (2)). The patients were given cotrimoxazole or norfloxacin at random, being subjects of a trial involving the comparison of the two antibiotics. Nineteen normal subjects served as controls for the NAG values. Differences between groups were evaluated with the two sample *t* test or the Mann-Whitney test (if the data were non-parametric) using the Minitab computer programme. A p value of <0.05 was taken as significant.

RESULTS

The clinical data of the patients are given in Table I. Twenty-eight patients had upper urinary tract infections, while 29 had lower urinary tract infections according to clinical criteria. Patients with upper urinary tract infections

Table I
Clinical data of patients with urinary tract infections

	Upper	"Mixed"	Lower
No. of patients	28	8	21
M : F	6:22	5:3	1:20
Age* (years)	46.3 ± 3.8	47.6 ± 6.9	39.4 ± 4.3
Serum creatinine* (umol/1)	96 ± 7	116 ± 13	78 ± 4
Pathogens:			
E. Coli	19	3	16
Klebsiella	4	3	1
Others	5	2	4

* mean ± s.e.m.

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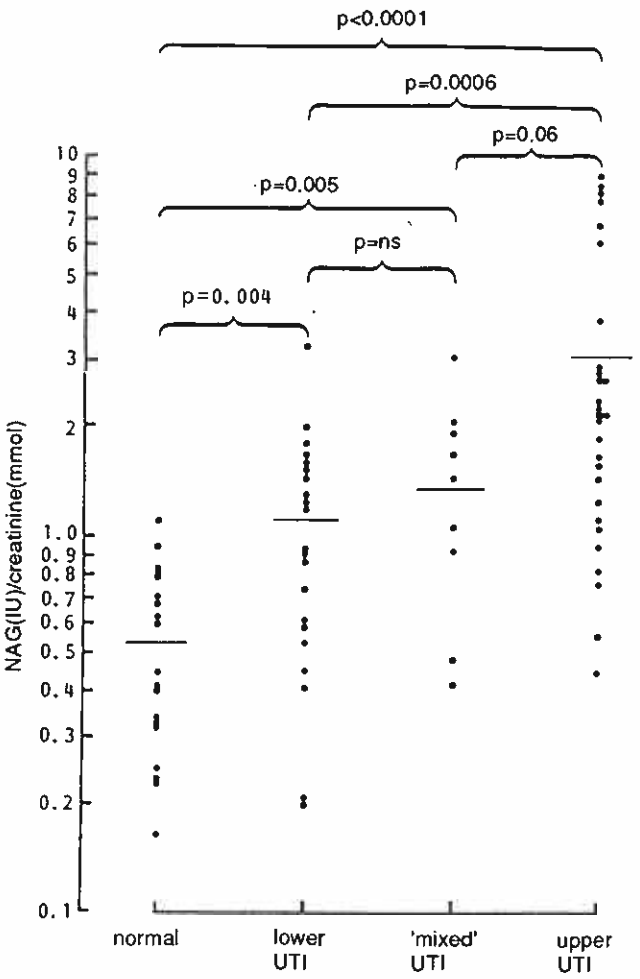
had significantly higher serum creatinine concentrations ($p<0.025$) than those with lower urinary tract infections. The commonest organism isolated was E. Coli while Klebsiella species ranked second. Because of clearly identifiable underlying medical diseases which predisposed to infections or were capable of causing nephropathies (Table II), 8 patients were classified as "mixed" infections despite the fact that clinically they only had symptoms/signs referrable to the lower urinary tract.

Table II
Underlying systemic/uronephrological diseases of patients classified as having "mixed" urinary tract infections

Case No	Sex	Age	Underlying disease	Pathogen
1	M	51	Urethral stricture	E. Coli
2	F	56	Neurogenic bladder	E. Coli
3	M	27	Renal transplant, lymphocoele	Klebsiella
4	F	68	Diabetes mellitus, recurrent urinary tract infections	Klebsiella
5	M	62	Prostatic hypertrophy	Klebsiella
6	M	68	Prostatic hypertrophy	Non haemolytic streptococcus
7	F	28	Renal transplant	E. Coli
8	M	21	Renal transplant	E. Coli

Urinary NAG activities and creatinine were expressed as a ratio and the normal range was from 0.17 to 1.16 iu/mmol creatinine. There was a highly significant difference ($p<0.0001$) between those with upper urinary tract infections and the normal subjects in their urinary NAG/creatinine ratios (Fig 1). Even the difference between those with lower urinary tract infections and the normal was statistically significant ($p=0.004$). From Fig 1, it is evident that those with upper urinary tract infections had the highest urinary NAG/creatinine ratios, while those with lower urinary tract infections had the lowest NAG/creatinine ratios and those with "mixed" infections had the intermediate values. The difference in urinary NAG/creatinine ratios between patients with upper, and those with lower, urinary tract infections was highly significant ($p=0.0006$), even when the arbitrarily defined group of "mixed" infections was incorporated into the lower urinary tract infection group ($p = 0.001$).

Fig 1.
Urinary NAG excretion in patients with urinary tract infections compared to normal controls.



DISCUSSION

NAG is a lysosomal enzyme and its increased urinary excretion has been demonstrated in various situations associated with renal parenchymal damage (3). The major clinical value of measuring urinary NAG excretion is in the monitoring of nephrotoxicity induced by drugs (4) and in detecting renal allograft rejection (5). The use of urinary NAG excretion in the localization of the site of urinary tract infection had been scarcely reported (6). The difficulty in evaluating a relatively new technique for the localization of the site of urinary tract infection lies in the lack of a standard technique of reference. To be absolutely sure, catheterization of both ureters and the bladder for the collection of urine specimens for culture is required. The technique is thus impractical. A lot of interest has been generated by reports that the presence of antibody-coated bacteria indicates upper urinary tract infection (7). Again the technique is not widely applied clinically. The determination of NAG in the urine has several attractions. The enzyme is stable and its colorimetric determination is easy and cheap and can be performed by most laboratories. The simultaneous determination of NAG and creatinine obviates the difficulties in accurate and timed urine collections.

Our results agree with the experience of other investigators that urinary NAG excretion is a useful adjunct in the localization of the site of urinary tract infections. Although in our study, our reference was mainly based on clinical signs and symptoms, there was a highly significant difference in NAG/creatinine ratios between patients with upper, and those with lower, urinary tract infections. In particular, 75% of patients with upper urinary tract infections had NAG/creatinine ratios above the upper limit of the normal range. Slightly unexpected is that 48% of patients with clinically diagnosed lower urinary tract infections had raised urinary NAG/creatinine ratios. It is conceivable that these patients had covert bacterial invasion of the upper urinary tract despite their

clinical symptoms and signs. The fact that the group of patients with "mixed" infections tended to have higher urinary NAG/creatinine ratios than did those with lower urinary tract infections seems to support such a speculation. These "mixed" patients had underlying uronephrological diseases such as diabetes mellitus, neurogenic bladder and prostatic hypertrophy or systemic disease capable of causing nephropathy, eg. diabetes mellitus. In such cases, it is conceivable that urinary NAG excretion will be increased regardless of the site of urinary tract infections and will be of diminished value in the localization of the site of urinary tract infection. Nevertheless, it is reasonable to conclude from our data that in an otherwise healthy patient presenting with urinary tract infection, a raised (ie. >1.0) urinary NAG/creatine ratio probably indicates involvement of the upper tract.

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