Incidence of symptomatic urinary tract infections in HIV seropositive patients and the use of co-trimoxazole as prophylaxis against *Pneumocystis carinii* pneumonia

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Abstract

Objectives—To determine the incidence of symptomatic urinary tract infections in HIV seropositive patients and to assess whether this varies with stage of disease, risk group or the use of co-trimoxazole as prophylaxis against *Pneumocystis carinii* pneumonia.

Methods—A retrospective case note review of 175 HIV-infected patients attending The Royal London Hospital between July 1988 and December 1992 was performed. A urinary tract infection was defined as a pure culture of $\geq 10^5$ colony forming units in a mid-stream specimen of urine from a patient with symptoms consistent with a urinary tract infection.

Results—Urinary tract infections occurred in 10 (5.7%) of 175 patients, with an incidence of 1.49 per hundred patient years. Urinary tract infections were significantly more common in patients with AIDS or a CD4 lymphocyte count below $0.2 \times 10^9/l$ (or both) when compared to those without AIDS and a CD4 lymphocyte count above $0.2 \times 10^9/l$ (5.4 vs. 0.5 urinary tract infections per hundred patient years, $p = 0.00005$). Women with AIDS or a CD4 count below $0.2 \times 10^9/l$ (or both) had an incidence of urinary tract infection of 18.5 per hundred patient years. No significant difference was found between the incidence of urinary tract infections in those taking co-trimoxazole as *Pneumocystis carinii* pneumonia prophylaxis and those taking alternative or no prophylaxis (2.6 vs 6.4 per hundred patient years, $p = 0.39$).

Conclusions—Urinary tract infection represents a considerable health problem amongst HIV infected patients. Our data show that urinary tract infections are more common in patients with advanced compared with early HIV infection. Co-trimoxazole, when taken by patients as prophylaxis against *Pneumocystis carinii* pneumonia did not appear to reduce the incidence of urinary tract infection.

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Introduction

Bacterial infections are a common cause of morbidity and mortality in HIV positive indi-

viduals. Recent reports suggest that the incidence of urinary tract infection (UTI) is increased in HIV positive patients.^{1,2} Furthermore, there is evidence that bacteriuria is more common as HIV disease progresses.^{3,4} Co-trimoxazole is active against most common urinary pathogens and has been widely used as prophylaxis against *Pneumocystis carinii* pneumonia (PCP) in immunocompromised individuals.⁵

This study aimed to determine the incidence of UTI in HIV positive individuals and to assess whether the incidence of UTIs varied with the stage of HIV infection, risk group or the use of co-trimoxazole as PCP prophylaxis.

Method

A retrospective case note review of 175 HIV positive patients who attended a London teaching hospital between 1 July 1988 and 31 December 1992 was performed. Minimum follow-up was six months, with a mean follow-up of 46 months. Details of the patient's sex, risk factor, stage of HIV infection, PCP prophylaxis, drug and urological history were collected.

Urinary samples were taken from mid stream specimens of urine (MSU). A UTI was defined as a pure culture of $\geq 10^5$ colony forming units (CFU)/ml in a MSU from a patient with symptoms attributable to urinary tract infection.

Patients were divided into the following groups according to eligibility for PCP prophylaxis: *Group 1*. Patients with a CD4 lymphocyte count above $0.2 \times 10^9/l$ and no AIDS defining diagnosis; *Group 2*. Patients with an AIDS defining diagnosis or CD4 lymphocyte count below $0.2 \times 10^9/l$. *Group 2* was further subdivided into; *Group 2_{co}*. Patients taking co-trimoxazole as PCP prophylaxis; *Group 2_{alt}*. Patients taking alternative or no PCP prophylaxis.

Over the follow-up period, patients changed from one group to another and so data were analysed according to the number of patient years spent in each group.

Chi square tests of significance were performed.

Results

One hundred and thirty-five (77%) of 175 patients were homosexual/bisexual men, 23 (13%) were Africans, 13 (7.4%) were intravenous drug users, and 4 (2%) had no

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Table 1 Incidence of UTI in relation to risk group

	Homosexual/ bisexual men (n = 135)	Africans (n = 23)	Intravenous drug users (n = 13)	Others (n = 4)	Women (n = 19)
No.(%) UTIs	5 (3.7%)	2 (8.7%)	1 (7.7%)	2 (50%)	4 (21%)
No. of patient years studied	592	40	26	12	43
UTIs/100 patient years	0.8	5	3.8	16	9.3

Table 2 Incidence of UTI per 100 patient years in relation to clinical status and PCP prophylaxis

RISK FACTOR					
	Homosexual/ bisexual men (n = 135)	Africans (n = 23)	Intravenous drug users (n = 13)	Women (n = 19)	Others (n = 4)
Group 1	0.2	0	4.7	3.7	13
Group 2	3.8	12	0	18.5	23
Group 2 _{cot}	3.2	0	0	0	0
Group 2 _{alt}	4.2	15	0	22	30

Group 1. Patients with a CD4 lymphocyte count above $0.2 \times 10^9/l$ and no AIDS defining diagnosis. Group 2. Patients with an AIDS defining diagnosis or CD4 lymphocyte count below $0.2 \times 10^9/l$. Group 2_{cot}. Patients taking co-trimoxazole as PCP prophylaxis. Group 2_{alt}. Patients taking alternative or no PCP prophylaxis.

identifiable risk factors. Nineteen (11%) of the patients were women, (13 African, 3 Caucasian intravenous drug users and 3 heterosexual contacts of men with HIV infection). Symptomatic UTIs occurred in 10 (5.7%) of 175 patients, 5 (3.7%) of 135 homosexual/bisexual men, 1 (7.7%) of 13 intravenous drug users, and 4 (21%) of 19 women, of whom 2 were African (table 1). Three UTIs occurred in Group 1 and seven in Group 2. A total of 670 patient years were studied, that is 540 patient years in Group 1 and 130 patient years in Group 2. Overall, 1.49 UTIs occurred per hundred patient years. In Group 1, 0.5 UTIs occurred per hundred patient years and in Group 2, there were 5.4 UTIs per hundred patient years ($p = 0.00005$).

Group 2_{cot} comprised 37 patient years on a

regime of at least 960 mg co-trimoxazole three times per week. Group 2_{alt} comprised a total of 93 patient years on alternative PCP prophylaxis, (pentamidine 300 mg monthly for 89 patient years, dapsone 50–100 mg daily for 3 patient years and pyrimethamine 25 mg plus sulphadoxine 500 mg (fansidar) weekly for 0.5 patient years) or no PCP prophylaxis (0.5 patient years). One UTI occurred in Group 2_{cot} (2.6 UTIs per 100 patient years) and 6 UTIs occurred in Group 2_{alt} (6.4 UTIs per 100 patient years) ($p = 0.39$) (table 2).

Of ten patients with UTI the causative organisms were *Escherichia coli* in nine and *Proteus spp* in one. No individual patient had a history of urological problems or recent urethral instrumentation. In no case was a urological abnormality found on investigation by intravenous urography. Six of the organisms causing UTI demonstrated antibiotic resistance at initial screening. Only one patient (No 8) had taken oral antibiotics other than co-trimoxazole in the month prior to her UTI (table 3). Two patients (one male and one female) developed UTIs with *E coli* on more than one occasion.

Discussion

Our study demonstrates that UTIs represent a considerable health problem in HIV positive patients. This was particularly so amongst symptomatic HIV positive women, who had an incidence of UTI of 18.5 per 100 patient years. This figure may be an underestimate of the true rate of infections as routine culture was not performed on all patients attending our centre. The annual incidence of UTI in women presumed to be HIV negative who attend their General Practitioners is estimated to be 6.25%.⁶ UTI in community-based populations of HIV negative men under the age of sixty-five years are uncommon, with a prevalence of less than 0.1%.⁷ This compares with the 0.9% annual incidence of UTI in HIV positive men in this study, the majority of whom were homosexual. It is currently

Table 3 Characteristics of patients and their UTIs

Patient number	Sex	Risk group	PCP prophylaxis	Organism cultured	Pyuria (WBC/hpf) *	Antibiotic resistance	Symptoms
1.	male	homosexual	pentamidine	<i>E. coli</i>	70	nitrofurantoin	dysuria recurrent UTI
2.	male	homosexual	ineligible	<i>E. coli</i>	10	trimethoprim	offensive smelling urine
3.	male	homosexual	co-trimoxazole	<i>E. coli</i>	<1	ampicillin trimethoprim	dysuria
4.	male	homosexual	pentamidine	<i>E. coli</i>	<1	none	incontinence
5.	male	homosexual	declined	<i>E. coli</i>	110	none	dysuria
6.	male	IVDU	ineligible	<i>Proteus spp.</i>	100	nitrofurantoin trimethoprim	dysuria
7.	female	African	pentamidine	<i>E. coli</i>	<1	trimethoprim nitrofurantoin	fever
8.	female	African	pentamidine	<i>E. coli</i>	80	trimethoprim nitrofurantoin ampicillin cephalixin	fever
9.	female	heterosexual	ineligible	<i>E. coli</i>	<1	none	dysuria
10.	female	heterosexual	pentamidine	<i>E. coli</i>	70	none	dysuria recurrent UTI

*White blood cell count per high powered field.

unclear whether sexual orientation influences the incidence of UTI. One study of sexually active men with acute urinary symptoms,⁸ for example, suggested an increased incidence of UTI amongst homosexual/bisexual men. However, another report of men attending a genitourinary medicine clinic who were routinely screened for UTIs failed to demonstrate any difference between homosexual/bisexual and heterosexual men.⁹

Our data demonstrate that UTI is more common in patients with more advanced HIV disease. Abnormalities of B cell activation and immunoregulation are profound in patients with AIDS, although the mechanisms by which HIV infection affects the development of UTI is not yet clear.¹⁰ In immunocompetent individuals, pyuria is present in 87% of UTIs.¹¹ However, in our study pyuria was present in only six of 10 cases of UTI (one patient in whom UTI was present without pyuria was neutropenic). Furthermore, the spectrum of organisms causing UTI in our study is similar to community acquired infections in the HIV negative population, where nearly 90% of UTIs are due to *E coli*, and where resistance to amoxycillin occurs.¹¹

The morbidity, mortality and costs associated with PCP may be substantially reduced by appropriate use of prophylaxis in subgroups of HIV-infected patients known to be at high risk.⁵ The use of co-trimoxazole in the HIV positive population may also reduce the risk of toxoplasmic encephalitis.^{12,13} The data presented have failed to show that co-trimoxazole used as PCP prophylaxis reduced the incidence of UTI in HIV positive individuals, but a trend was demonstrated. Prospective

studies are needed to clarify whether co-trimoxazole confers some benefit in protecting HIV seropositive individuals against UTI.

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