

BACTERIAL CYSTITIS IN REFRACTORY IDIOPATHIC DETRUSOR OVERACTIVITY – AN UNEXPECTED FINDING

Hypothesis / aims of study

For the past 50 years, the standard microbiological definition of bacterial cystitis has been $>10^8$ CFU/L with associated pyuria >10 WBC/ \square L. This was originally defined by a renal physician to distinguish infection from contamination in asymptomatic women at risk of pyelonephritis (1). Subsequent studies have suggested that, in acutely dysuric women, a lower threshold of $>10^5$ CFU/L may be more appropriate (2). Furthermore, the policy of adhering to this definition ($>10^8$ CFU/L) in women with lower urinary tract symptoms (LUTS) such as overactive bladder (OAB) symptoms, has recently been questioned (3). To date, the role of “low grade” bacterial cystitis in the aetiology of refractory idiopathic detrusor overactivity (IDO) has not been examined.

Our unit sees 5,200 patient visits annually and, over the past 5 years, we have noted anecdotally that women with refractory IDO, who experience an acute exacerbation of OAB symptoms without dysuria or foul smelling urine, may often be found to have microbiological evidence of cystitis. We aimed to systematically document the relative proportions of “classical” bacterial cystitis ($>10^8$ CFU/L) and “low grade” bacterial cystitis ($>10^5$ CFU/L) in patients with refractory IDO.

Study design, materials and methods

A prospective pilot study was undertaken, which involved more extensive microbiological testing in women who had refractory IDO and an unexplained exacerbation of symptoms. Refractory IDO was defined in women with urodynamically-proven DO who failed to respond to ≥ 2 anti-cholinergic drugs, with persistent disabling symptoms for >12 months. All women presenting to our unit over an 18-month period with refractory IDO were recruited and asked to submit a midstream urine culture whenever their DO symptoms were exacerbated. All post-menopausal women were treated with vaginal oestrogen cream according to unit policy.

Only women with urodynamically-proven detrusor overactivity (DO) were included. Women with high (>100 ml) post-void residual bladder volumes secondary to voiding dysfunction are known to be at increased risk for bacterial cystitis and were excluded. If the patient had undergone anti-incontinence surgery, she was excluded if the DO occurred post-operatively (“de novo”) but included if there was evidence of DO on pre-operative urodynamic testing.

The Microbiology Department collaborated by reporting all organisms $>10^5$ CFU/L in study patients, rather than the traditional $>10^8$ CFU/L threshold. The definition of pyuria was unchanged (>10 WBC/ \square L). Patients with any proven bacteriuria were treated with appropriate antimicrobial therapy and the response noted subjectively and on frequency volume charts (FVC).

Results

Between November 2007 and April 2009, 42 consecutive patients with refractory IDO were recruited, who provided 118 mid-stream urine specimens at the time of symptomatic exacerbation. The median age was 60 years (range 42-84). In total, 57% (24/42) had evidence of bacteriuria $>10^5$ CFU/L, +/- pyuria (Table 1). 21% of women (9/42) had low-grade bacteriuria ($>10^5$ CFU/L) only. An additional 5 women (12%) had evidence of both classical and low-grade cystitis on separate specimens.

Amongst women with low-grade bacteriuria, the organisms isolated were *E. coli* (n=4), *Streptococcus agalactiae* (n=4) and *Klebsiella* (n=1). No difference was found in the ages of women with bacteriuria versus no bacteriuria (median age 59.5 v 60 respectively; $p=0.8062$). Subjectively, the majority of women had improved symptoms after treatment and analysis of the FVC data continues.

Interpretation of results

Twenty years ago, Stamm pointed out that the diagnostic cut-off of $>10^8$ CFU/L failed to detect 50% of bacteriuria with pyuria in women with dysuria (2). This issue does not appear to have been pursued in women with OAB symptoms without dysuria. To our knowledge, this is the first report of the incidence of either classical ($>10^8$ CFU/L) or low-grade ($>10^5$ CFU/L) bacteriuria +/- pyuria in patients with treatment-refractory IDO and an exacerbation of symptoms.

Importantly, a significant proportion of women (21%) had low-grade bacteriuria only, which would have been missed using traditional microbiological criteria. These data indicate that a prospective, randomized controlled multi-center trial to determine the appropriate management of low-grade bacteriuria in women with refractory IDO is definitely warranted.

Concluding message

Women with refractory IDO who suffer an acute exacerbation of symptoms should have a urine specimen cultured to exclude bacterial cystitis. The bacteriological threshold for diagnosing bacterial cystitis in women with LUTS needs thorough re-evaluation.

Culture Results	Total (%)	Pyuria (>10 WBC/ \square L)
Bacterial cystitis	24 (57)	17
$>10^8$ CFU/L only	10 (24)	10
$>10^8$ CFU/L and $>10^5$ CFU/L on separate occasions	5 (12)	4
$>10^5$ CFU/L only	9 (21)	3
No bacterial cystitis	18 (43)	0

Table 1

References

1. AMA Arch Intern Med. 1957 Nov;100(5):709-14
2. Urology. 1988 Aug;32(2 Suppl):6-12
3. ICS Proceedings 2007, abstract 42

Specify source of funding or grant	None
Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	No
This study did not require ethics committee approval because	This study was discussed with the Chairman of the Hospital Ethics Committee. Given that it is a pilot study of routine Unit policy, it was deemed exempt from formal ethical approval.
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	No