

REFRACTORY IDIOPATHIC DETRUSOR OVERACTIVITY: INCIDENCE OF “LOW-COUNT” BACTERIURIA DURING ACUTE SYMPTOMATIC EXACERBATION.

Hypothesis / aims of study

Women with idiopathic detrusor overactivity (IDO) who do not respond to bladder training and anti-cholinergic medication are often labelled “refractory”. Contemporary 2nd line management of these patients includes intravesical botulinum toxin and neuromodulation. It is imperative that bacterial urine infection is excluded in such women before such invasive treatment modalities are considered. Indeed, the widely accepted definition of overactive bladder (OAB) syndrome requires that infection be excluded (1). The traditional microbiological threshold for “significant” bacteriuria ($\geq 10^5$ CFU/ml) fails to detect up to 50% of infections in acutely dysuric women. Thus, recent expert guidelines from the European Association of Urology support the inclusion of “low-count” bacteriuria ($10^3 - 10^5$ CFU/ml) in the diagnostic assessment of dysuric women, to minimise false-negative cultures (2). We aimed to document the incidence of “low-count” bacteriuria in women with refractory IDO who experienced an acute exacerbation of their overactive bladder (OAB) symptoms without dysuria.

Study design, materials and methods

A 2-year, prospective study of women with “refractory” IDO was conducted. “Refractory” was strictly defined as “failure to respond to ≥ 2 anti-cholinergic agents with out-patient bladder training for ≥ 1 year, with persistent disabling symptoms on frequency-volume chart” (3). Such women would usually be offered intravesical botulinum toxin in our unit. Women with known voiding dysfunction ($Q_{max} < 15$ ml/s and post-void residual ≥ 100 ml), suspected neurogenic DO and those with recent (≤ 2 weeks) urethral instrumentation were excluded. Women with previous stress incontinence surgery were included only if DO was evident on the pre-operative urodynamic testing. Eligible women were recruited and asked to submit a standard mid-stream urine specimen (MSU) whenever their OAB symptoms worsened. This specimen was immediately refrigerated at 4°C and transported to the laboratory in a refrigerated container within 1-2 hours. In collaboration with a senior microbiologist, MSUs were cultured at the 10^3 CFU/ml threshold, rather than the traditional 10^5 CFU/ml cut-off. Pyuria was determined using haemocytometer counts on uncentrifuged urine specimens, with counts of >10 white blood cells (WBC)/mm³ considered significant. Any bacteriuria $\geq 10^3$ CFU/ml was treated with appropriate antibiotic therapy. Categorical data were analysed using Fisher’s exact test. Median values were compared using the Mann-Whitney U test. Two-tailed p-values were used throughout and the 5% level was considered significant.

Results

Between November 2007 and November 2009, 50 consecutive eligible women were included. The median duration of OAB symptoms for study participants was 10 (inter-quartile range [IQR] 5-20) years. Women had trialled a median number of 3 anti-cholinergic medications (IQR 2-4). 88% (44/50) of women were multiparous. In total, 164 MSU specimens were analysed, with study participants providing a median of 3 MSU specimens over the 2 years (IQR 1-5). Bacteriuria $\geq 10^3$ CFU/ml was present in 37% (61/164) of total samples, of which 20/61 was low-count bacteriuria (10^3 - 10^5 CFU/ml) only. In total, 34% of women (17/50) provided specimens which were positive for “low-count” bacteriuria. *Escherichia coli* was the predominant microbiological organism cultured for both groups (Figure 1). There was a higher prevalence of Group B streptococci among the specimens positive for low-count bacteriuria only ($p=0.004$). Pyuria was more common in cultures positive for traditional ($>10^5$ CFU/ml) bacteriuria compared to specimens positive for low-count bacteriuria only (88% v25%, $p<0.0001$).

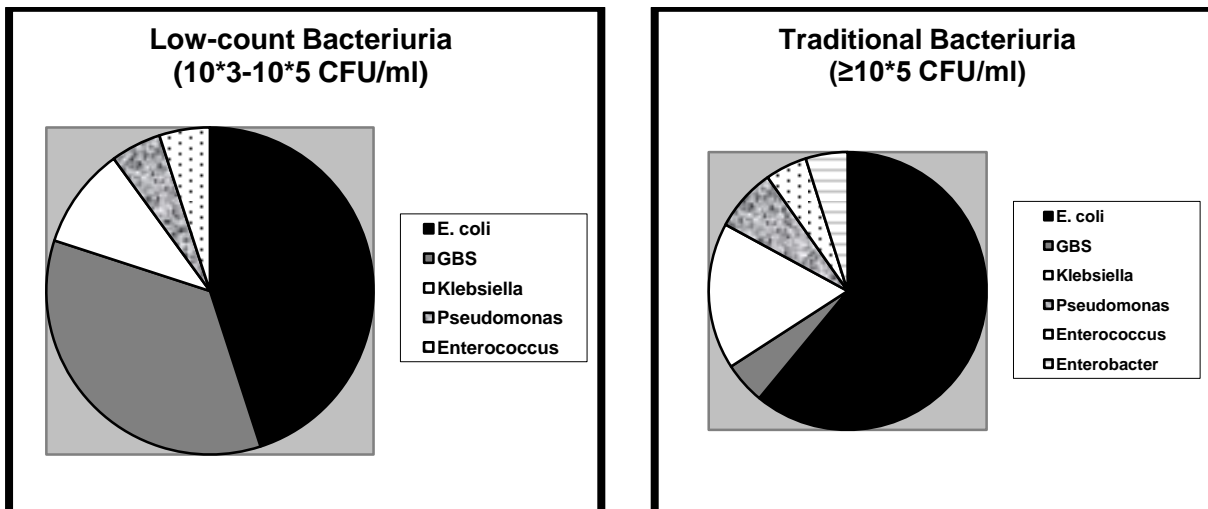


Figure 1: Bacterial organisms in MSU cultures positive for “low-count” and “traditional” bacteriuria

MSU specimens from women with previous continence surgery were significantly more likely to culture positive for traditional bacteriuria, but not low-count bacteriuria, despite PVR<100ml in all cases (p<0.0001). Study participants had a median age of 64.5 years (IQR 53-72 years). Overall, specimens from women ≥ 65 years were significantly more likely to culture both low-count (p=0.0467) and traditional bacteriuria (p=0.0163). However, among positive cultures, women whose MSUs cultured positive for low-count bacteriuria (median age 47) were significantly younger than those with specimens positive for traditional bacteriuria (median age 72; median difference =18 years, 95% confidence interval for median difference = 8-27; p=0.0013).

Interpretation of results

This study features a highly selected group of women with refractory IDO, who can be very difficult to manage. One-third (34%) of such women provided urine cultures during an acute exacerbation of OAB symptoms which were positive for “low-count” bacteriuria. The present study suggests that the aetiology of IDO may include an “infective” subset, alongside the different “congenital” subset that has often been proposed.

Concluding message

To our knowledge, this is the first study of urine microbiology in women with urodynamically-proven IDO who are refractory to therapy by a strict definition. We were surprised to find evidence of “low-count” bacteriuria in one-third of such women at a time of acute symptomatic exacerbation, despite them having no dysuria. We conclude that precise microbiological thresholds should be used to detect bacteriuria in women with refractory IDO, particularly if invasive treatment modalities are being considered. Low bacterial counts should be incorporated into the routine assessment of women with IDO.

References

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2. Grabe M, Bishop MC, Bjerklund-Johansen TE et al. Guidelines on urological infections. *European Association of Urology.* 2009.
3. Moore KH, Simons A, Mukerjee C, Lynch W. The relative incidence of detrusor instability and bacterial cystitis detected on the urodynamic-test day. *BJU Int* 2000;85:786-92.

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<i>Is this a clinical trial?</i>	Yes
<i>Is this study registered in a public clinical trials registry?</i>	No
<i>Is this a Randomised Controlled Trial (RCT)?</i>	No
<i>What were the subjects in the study?</i>	HUMAN
<i>Was this study approved by an ethics committee?</i>	Yes
<i>Specify Name of Ethics Committee</i>	Human Research and Ethics Committee (HREC), Central Network, Sydney, Australia.
<i>Was the Declaration of Helsinki followed?</i>	Yes
<i>Was informed consent obtained from the patients?</i>	No