

## UNDETECTED URINARY INFECTION IN PATIENTS WITH SYMPTOMS OF THE OVERACTIVE BLADDER

### Hypothesis / aims of study

The diagnosis of urinary tract infection (UTI) from culture of a mid-stream urinary specimen (MSU) has relied on the detection of  $10^5$  colony forming units per ml (cfu/ml). It has been known for some time that in symptomatic women a more appropriate threshold should be 100 cfu ml<sup>-1</sup>.<sup>(1)</sup> Few laboratories report this, so that MSU culture misses up to 50% of genuine infections<sup>(1)</sup>. A positive leucocyte esterase test has a reported sensitivity of 75 to 90 percent in detecting pyuria associated with a UTI<sup>(1)</sup> but that is against  $10^5$  cfu ml<sup>-1</sup>. However, the most reliable technique is the detection of pyuria by microscopy in fresh un-spun urine. Optimum results are achieved by counting the pus cells on a haemocytometer using the threshold of 8 wbc mm<sup>-3</sup>. This is considered to be the gold standard<sup>(2)</sup> and was used accordingly in this study. The overactive bladder involves symptoms that feature in urinary infection. If it is known that significant urinary infection may be painless<sup>(2)</sup>. Some overactive bladder symptoms could therefore reflect genuine urinary infection, undetected by traditional analysis. The study hypothesis was that by using more accurate measurement methods urinary infection would be found as a significant underlying pathology in patients presenting with overactive bladder symptoms.

### Study design, materials and methods

This was an observational cohort study of 577 patients (518 females and 59 males) presenting with overactive bladder and no dysuria. Their mean age was 54 (sd=20). They contributed a maximum of one specimen to each of three study phases. (1) 454 samples tested by dipstick including leucocyte esterase and nitrite. (2) 403 samples tested by dipstick and light microscopy of fresh un-spun specimens. (3) 263 specimens tested by dipstick, microscopy on a haemocytometer and laboratory culture.

### Results

The first phase demonstrated that 120 patients (26%) demonstrated significant pyuria on dipstick. 18 (4%) tested positive to nitrite and 72 (15%) showed haematuria.

Phase two, which included light microscopy, showed positive leucocyte esterase by dipstick in 208 specimens (51%). However microscopy showed 23 (11%) of these to be false positives. 195 specimens (48%) were leucocyte esterase negative but microscopy found 50 (25%) to be false negative. 81 specimens (20%) showed haematuria and 32 (40%) were false positive. There were only two false negatives dipstick tests for blood. 23 specimens tested positive to nitrite (6%) two of these were false positives. However 215 negative nitrite tests proved false negatives (70%) on microscopy.

Phase three used dipstick, haemocytometer examination, and MSU culture on 263 specimens. 112 (43%) of specimens showed urinary infection on examination by haemocytometer and thereby revealed 66 false negative urine cultures (35%). Only 36 urine cultures proved positive (14%) and only 4 of these (11%) had failed to demonstrate pyuria on microscopy. 91 (35%) microscopy specimens demonstrated bacteruria, without spinning down, and these were associated with 65 (35%) false negative MSUs.

The leucocyte esterase produced 91 (35%) positive tests of which 4 (4%) were false positive. Of the 167 negative leucocyte esterase tests 51 (31%) were false negatives. Nitrite was positive on 7 occasions, all true positives. There were 251 negative nitrite tests of which 129 (51%) were false negatives.

### Interpretation of results

About 50% of patients with overactive bladder symptoms without dysuria demonstrate significant pyuria on microscopy of fresh urine. Nitrite testing is extremely insensitive and the leucocyte esterase test misses 25% to 30% of infections. A MSU analysis will miss at least 35% of infections. These data mean that it is probable that many patients with overactive

bladder symptoms evince undiagnosed, significant urinary infection. These data however do not provide guidance on the significance of these infections to the symptoms.

Concluding message

The nature of the overactive bladder needs to be re-assessed with a more rigorous, scrupulous eye on coexistence of urinary infection. 50% of patients may harbour undiagnosed infections. The effect of these, on the symptoms, must be evaluated by longitudinal studies, which include interventions.

Reference List

1. Management of urinary tract infections in adults, N.Engl.J.Med., 329: pp 1328-1334. 1993
2. Diagnosis and treatment of uncomplicated urinary tract infection, Infect.Dis.Clin.North Am., 11: pp 551-581. 1997