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1. *UCL*

ROUTINE MSU CULTURE IN PATIENTS WITH SYMPTOMS OF OAB MAY BE MISSING MANY GENUINE INFECTIONS

Hypothesis / aims of study

The diagnosis of urinary tract infection (UTI) from culture of a mid-stream urinary specimen (MSU) has relied on a threshold of 10^5 colony forming units (cfu) ml^{-1} of a known urinary pathogen. This is based on seminal experiments conducted in the 1950s on asymptomatic women [1]. The author did not define a threshold applicable to symptomatic UTI. Nevertheless, 10^5 cfu ml^{-1} has been widely adopted in clinical practice. In more recent studies, conducted on urine from women with the classical symptoms of acute cystitis; frequency and urethral pain, a culture result of only 10^2 cfu ml^{-1} was deemed the appropriate diagnostic threshold. This has been validated in several ensuing studies. Furthermore, there are no data on a threshold applicable to patients with urgency ± incontinence, frequency or nocturia. Additionally, the transport and processing delays that affect clinical urine samples have not been addressed. The diagnosis of the overactive bladder (OAB) presupposes the exclusion of urinary infection. It is logical to deduce, therefore, a significant number of patients labelled with OAB may in fact be harbouring UTI.Despite using MSU in clinical practice, we adopted CSU for initial experimentation. Bacteria isolated from CSU have such a high probability of urinary tract origin that it has been established that a 10^2 cfu ml^{-1} threshold can be applied to all CSUs. It is also advisable to avoid *a priori* restrictions on sampling, so a study should be powered to include patients on or off antibiotics.This study tested the hypothesis that more meticulous culture methods and a diagnostic threshold of 10^2 cfu ml^{-1} would demonstrate more infections than routine clinical laboratory methods applying the 10^5 cfu ml^{-1} criterion. If a difference were evident from this experiment, further comparison with MSU would be merited

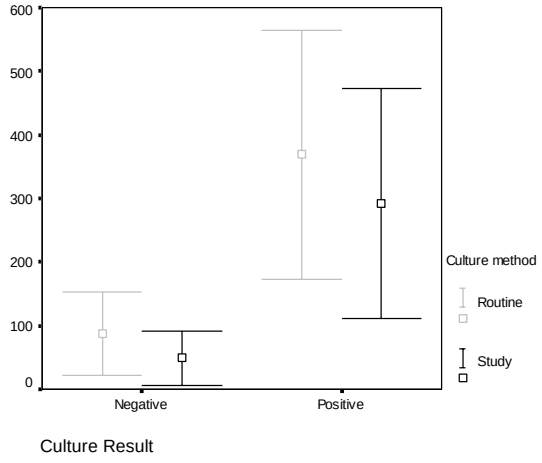
Study design, materials and methods

Because we wished to include patients taking antibiotics, we estimated a clinically significant difference as a diagnostic bacterial culture in 10% of routinely processed samples and 20% of those using the study method. It was calculated that a sample size giving 400 pairs would have a power of 97.8% to yield a statistically significant result. Female patients with symptoms of OAB, gave their consent to participate. Their symptoms were recorded using a validated questionnaire and their antibiotic consumption noted. A CSU was obtained by inserting a Lofric 12 Fr catheter into the urinary bladder under aseptic conditions. The urine was collected into a sterile container and processed immediately. One pre dried ChromID CPS (Biomerieux) culture plate and two pre dried blood agar culture plates (horse) were inoculated with 200 µL of fresh unspun urine and incubated. The Chrome plates were incubated aerobically for 24 hours at 35-37oC and the blood plates were incubated anaerobically at 35-37oC for five days. The lower threshold of 102 cfu ml-1 was used to identify a positive culture. An aliquot of each CSU also underwent routine analysis at the threshold of 105 cfu ml-1. An aliquot of urine was also taken for enumeration of white blood cells using a light microscope and haemocytometer.

Results

194 women with OAB symptoms were recruited with a mean age of 57 (sd=18). They yielded 378 urine samples collected by CSU. The routine laboratory cultures reported positive results in 46 (12%) samples whereas the study culture methods isolated bacteria in 114 (30%) samples (X^2=100, df=1, p<0.001, 95% CI of difference 17% to 26%). Figure 1 describes the pyuria counts according to culture result for the two methods. The study method identified bacteria in 43 (94%) samples positive on routine culture. More Significantly, 71 (21%) of those positive with special culture did not grow bacteria with the established laboratory method. The concomitant consumption of antibiotics had no effect on these differences.

Figure 1 The mean white cell count and 95% CI according to culture method and culture result



Interpretation of results

Our data demonstrate more than doubling of the bacterial isolation rate when a more meticulous culture method is deployed. By using CSU sample, we are confident that the isolates originate from the bladder. Figure 1 illustrates the fact that the differences between the methods occurs over the whole spectrum of the inflammatory response and is not limited to the most symptomatic. These data imply that the misgivings about the validity of routine culture methods apply to patients with symptoms of OAB. They indicate that genuine bacterial infection may be frequently missed during the usual assessment of a patient with OAB symptoms

Concluding message

The routine methods for culturing urine to detect ≥10^5 cfu ml^{-1}, when applied to patients with symptoms of OAB, may be failing to identify a significant proportion of patients with genuine urine infection. We feel that the laboratory diagnosis of UTI should be fundamentally reviewed especially in the context of patients with OAB symptoms.

References

1. Arch.Intern.Med. 100, 709-714. 1957

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Was this study approved by an ethics committee?	**Yes**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**