Brief Original Article

Antibiotic screening of urine culture as a useful quality audit

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Abstract
Introduction: The diagnosis of urinary tract infections includes microbiologic culture of urine to determine the etiology of the infection. However, interpretation of the results can be confounded by various factors including the accuracy of a patient's history of current antibiotic usage.
Methodology: In this report, we tested urine specimens for the presence of antibiotics and compared our results to the accuracy of antibiotic data entry on the accompanying request forms. In addition, the consequences of culturing urine specimens with incomplete antibiotic history received in the laboratory were investigated.
Results: During the study period, 14,680 urines were obtained and tested with a modified urine antibacterial substance assay (UABA). There were (97.32%) true-negative, 6 (0.04%) false-negative, 222 (1.51%) true-positive and 166 (1.13%) false-positive results. The sensitivity and specificity of this test was 97.37% and 98.85% respectively.
Conclusion: This internal audit practice demonstrates the importance of accurately completed request forms and how this information impacts the clinical interpretation of urine culture results.

Introduction

Urinary tract infections (UTIs) are usually diagnosed on the basis of history, physical examination, urinalysis and urine culture. Collection of urine specimens for quantitative culture before initiation of antimicrobial therapy is considered the gold standard for the diagnosis of bacterial UTIs [1] A number of confounding factors affect the interpretation of results from routine urine cultures received in the clinical microbiology laboratory. Antibiotic history is often not included by physicians on the laboratory request forms or patients do not admit to taking antibiotics prior to urine culture collection. This information is important when correlating culture results with other laboratory findings. This study focused on the incidence of unreported antibiotic consumption prior to culture and the clinical consequences. We describe a simple technique which helped improve quality auditing of urine culture requests at our hospital.

Methodology

Detection of antibacterial activity in the urine

We modified the urine antibacterial substance assay (UABA), a technique described by Sombrero *et al*. [2] and others [3,4] by using two Mueller-Hinton agar plates each inoculated with a lawn of *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923. The ATCC strains were suspended in 0.85% sterile saline and adjusted to a 0.5 McFarland standard using a nephelometer. The plates were then inoculated by rotary plating with a sterile cotton swab dipped into the standardized suspension and excess fluid removed by rotation of the swab against the side of the tube. Autoclaved sterile discs of 6 mm diameter were prepared from Whatman Grade 1 filter paper (Whatman International, Ltd., Maidstone, England). After the inoculum dried, the discs were placed aseptically on the inoculated plates at a distance of 10-12 mm apart.

Quality control (QC) was ensured by placing one set as a negative control, *i.e.*, discs without

antibiotics, and another set inoculated with standard antibiotic impregnated discs. QC passed when the negative control showed no zone of inhibition around the disc and the positive control had a zone of inhibition of any size around the disc.

Urine cultures

All urine cultures received in the laboratory from 1 July 2008 to 30 June 2009 were processed using standard methods for urine culture [5], including microscopy, at the Hamad Medical Corporation-Al Khor Microbiology laboratory, which services both the Al Khor Hospital and Community Health Centers at Qatar. Specimens were inoculated onto Cystine Lactose Electrolyte Deficient (CLED) culture medium within two hours of collection and incubated overnight at 35-37°C. Any growth on the media was considered a positive urine culture.

Urine Antibacterial Substance Assay (UABA)

Simultaneously each urine sample was inoculated onto an individual disc on each Mueller-Hinton plate (one with *Escherichia coli* ATCC 25922 and the other *Staphylococcus aureus* ATCC 25923 using a 1 µL loop. Each disc on both plates was labeled with the corresponding urine sample number and incubated overnight at 35-37°C along with the routine culture plates. Any zone of inhibition around the disc was considered positive for antibacterial activity and these samples were recorded and analyzed.

Results

From a total of 14,680 consecutive urine specimens submitted for culture and susceptibility, 2,494 (16.99%) samples yielded positive cultures and 388 (2.64%) were UABA positive. Of 388 UABA positive samples, no growth was detected in 345 (88.92%) samples, while 32 (8.25%) showed insignificant growth and 11 (2.84%) showed mixed growth. The data obtained from the 14,680 urines showed 14,286 (97.32%) true-negative, 6 (0.04%) false-negative, 222 (1.51%) true-positive and 166 (1.13%) false-positive results. The sensitivity and specificity of this test was 97.37% and 98.85% respectively. The positive and negative predictive values were 57.22% and 99.96% respectively.

Of the 388 UABA positive samples, 115 (29.6%) had leukocyte counts $\geq$ 10/High power field (HPF), 165 (42.53%) of which were received from out-patients and 223 (57.47%) from in-patients. Of these 223 UABA positive samples from in-patients, 208

(93.69%) reported no growth. Compliance in obtaining antibiotic histories for in-patients (183; 82.06%) was higher than that reported in out-patient community health centers (39; 23.64%). The UABA had a positive diagnostic likelihood ratio of 84.77.

Discussion

Failure to either perform urine cultures or to correctly interpret their results may lead to therapeutic failures. UTI diagnosis can be further complicated by the presence of antibiotics in urine specimens submitted for culture, particularly from areas where they are readily purchased over the counter, without prescriptions [2,3,6,7]. This situation can compromise the recovery of bacterial pathogens and their accurate colony count, resulting in false-negative results and diagnostic dilemmas, especially in symptomatic patients. Bacterial counts per ml urine can be temporarily reduced by antibiotics, causing a transient remission of clinical symptoms, thus confounding the efficacy of treatment in chronic or recurrent asymptomatic infections [8].

The true-positive UABA results correlated well with transcribed history provided on the laboratory request forms and the false-negatives could indicate inert drug compounds, counterfeit anti-infective drugs, and/or patient's ignorance of content of medicine consumed. The false-negative UABA could also indicate the empiric antibiotic to be used by the physician in the treatment of the suspected UTI. In this study, 88.92% of positive UABAs showed no growth, reemphasizing the fact that samples sent to the microbiology laboratory during a course of antibiotic treatment may not yield clinically significant results [6,9]. Efficacy on the selection of antimicrobial agents using cultures repeated two to three days after beginning therapy as suggested by Barsanti *et al.* [8] cannot be recommended as evidenced from our study. Cultures, however, can be used to monitor the efficacy of treatment in chronic and recurrent infections and can be repeated three to five days after termination of antimicrobial therapy to ensure elimination of infection [8].

In this study, a total of 166 (1.13%) false-positive results were detected by UABA test, indicating the use of antibiotics prior to the culture and/or other substances present in the urine. This scenario indicates that (a) the history was not taken properly; (b) the patient either could not or was unwilling to give history due to ignorance of content of medicine [2], poor recall, or intentional false denial due to self-

perceived misuse of drugs; or (c) the antibiotic treatment of a patient with infection other than urinary tract infection. Beers *et al.* found that medication histories were frequently inaccurate due to failure to obtain or document the antibiotic taken or patient denial of usage [10]. Inaccurate interpretation of culture reports and promoting the emergence of drug resistance can result from this practice [11]. Leading questions regarding drug history by using the brand names of antibiotics can reduce the recall errors [2].

The absence of pyuria provides strong evidence against the presence of urinary tract infection [9, 11, 14]; however, sterile pyuria should induce a high suspicion of antibiotic usage [3] and if urinary tract infection is further suspected as in our study, *i.e.*, when pus cells $\geq$ 10/HPF (29.64%), alternative systems using non culture based systems may be effective in diagnosing such infectious agents.

Obtaining antibiotic history on a patient is often neglected and this diagnostic information can influence interpretation of culture results. Limited sensitivity of urine cultures due to prior antibiotic consumption enforces the need to take proper history and avoid sending such samples for culture to the microbiology lab. Non culture based diagnostics may help in detection of those pathogens which are expected to be isolated as etiological agents. Simple adjustments in history taking, especially samples from the community, and such periodic laboratory audits could significantly improve patient care, limit misuse of antibiotics, and have a lasting impact on the quality of the laboratory report.

Conclusions

A periodic internal audit using the UABA described here to measure the presence of antibiotics in urine cultures can provide a quality assurance measure to determine the impact on urine culture interpretation. This raises awareness of the importance involved in obtaining patient history of antibiotic consumption using an evidence-based protocol. An internal quality improvement program can include UABA monitoring, upgrading the current benchmark, to trigger a change in physicians' practices. This practice can lead to overall quality improvement in the management of urinary tract infections.

Disclosure

This work is accepted and will be presented as a poster at the 20th European Congress of Clinical Microbiology and Infectious Disease in Vienna, Austria on the 10nth of April 2010.

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