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Research Article

Compatibility of the Results of an Automated Urine Analyzer with Urine Culture

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Abstract

Objectives: We aimed to evaluate incidence of leukocyte esterase (LE) and nitrite positivity, leukocyte and bacterial counts in urine, and Gram positive and negative bacterial results interpreted by an automated urine analyzer for compliance with culture results.

Materials and Methods: 3194 urinalysis results were examined retrospectively. Measurements were made on Sysmex UF-5000 automated urine analyzer. Gram positive and negative bacterial interpretations were compared with results of culture.

Results: Out of 889 patients with bacterial interpretation, 577 were Gram positive and 312 were Gram negative. There were 6 positive culture results in Gram positive group (2 E. faecalis, 4 S. Agalactia) and 61 positive culture results in Gram negative group (52 E. coli, 4 K. pneumoniae, 5 P. Aeuroginosa). As incompatible with results of culture, incorrect gram-stain interpretations were made by the analyzer in 3 samples (1 K. Pneumoniae, 2 Candida spp) in Gram positive group and in 3 samples (2 E. faecalis, 1 S. Agalactia) in Gram negative group. Rates of LE, nitrite positivity, leukocyte and bacterial counts were higher in Gram negative group.

Conclusions: Especially Gram negative bacterial interpretation obtained from automated urine analyzers may be beneficial for rapid typing of bacteria and early treatment in urinary tract infections.

Keywords: Urinary Tract İnfections; Automated Urine Analyzer; Urinalysis; Urine Culture

Introduction

Urinary tract infections (UTIs) are the most common bacterial and hospital-acquired infections in adults and especially in women. In the diagnosis of UTI, clinicians often ask for urine analysis and urine culture tests, which are the gold standard. Today, fully automated urine analyzers in laboratories take the time-consuming gold standard manual microscopic analysis' place because of the excess of workload in routine urine analysis. In general, the detection of leukocyte esterase activity due to pyuria in chemical analysis with fully automated urine analyzers and the increase in the number of leukocytes and bacteria in the microscopic analysis are interpreted in favor of UTI [1-3]. In recent years, rapid assessment of bacteria can be performed based on differences in cell wall composition of Gram positive and negative bacteria in fully automated urine analyzers [4,5]. Rapid typing of bacteria in the urinary tract infections by using this feature may be beneficial for early treatment.

We aimed to evaluate the percentage of leukocyte esterase (LE) and nitrite positivity, leukocyte and bacterial counts in our study and the results of Gram positive and negative bacteria interpreted in an automated urine analyzer with urine culture results.

Materials and Methods

The results of the urine analysis of a total of 3194 patients who applied to the Urine Laboratory of Medical Biochemistry Department between July 24 and August 4, 2017 were examined. All the patients enrolled in the study were outpatients, and there were no patient with urolithiasis or catheter use.

Measurements were made with a fluorescence flow cytometry technique in a UF-5000 fully automated urine analyzer, a third generation automated urine particle analyzer developed by Sysmex (Japan).

In fluorescent flow cytometry technique; cells can be identified, counted, and classified by analyzing forward scattered light (FSC), sideways scattered light (SSL), side fluorescent light (SFL), and depolarized side scattered light (DSS). DSS is intended to improve the sensitivity of crystals, to better distinguish erythrocytes and crystals. The UF-5000 can provide valuable information on early treatment of a UTI patient with BACT-info, which can be very useful in the screening and identification of UTI. Here, after dilution of the non-centrifuged urine samples, bacterial staining is carried out with fluorescent dyes bound to the cytoplasm and membrane or to nucleic acid in bacterial cell nucleus. After painting, the urine particles are transferred to a flow cell and passed through a laser beam. The device displays the Gram stain information of the bacteria on the distribution graph. The Gram positive and negative properties are evaluated based on the forward scatter light and side fluorescence signal intensities according to differences in the cell wall composition of the bacteria.

In our study, LE and nitrite positivity, leukocyte and bacterial counts, and Gram positive and negative bacterial evaluations were retrospectively examined in urine samples obtained from complete urine analysis and were compared with the results of the patients whose urine culture was requested.

Results

Tables 1 and 2 show age, gender and information of the outpatient clinics where the urine analysis was requested. 577 Gram positive (64.9%) and 312 Gram negative (35.1%) bacterial interpretation were detected in 889 patients.

Patients	n (%)	Age (mean ± SD)
Male	1009 (31.6)	41.8 ± 21.4
Female	2185 (68.4)	41.5 ± 21.9
Total	3194 (100)	41.6 ± 21.7

Table 1: Demographic information of the working groups.

Departments (outpatient clinics)	Number (%)
Internal Medicine	807 (25.3)
Pediatry	505 (15.8)
Gynecology and Obstetrics	462 (14.5)
Urology	380 (11.9)
Nephrology (o	195 (6.1)
Family Medicine	175 (5.5)
Endocrinology	123 (3.9)
Rheumatology	101 (3.1)
Others	446 (13.9)

Table 2: Number and % values of patient groups according to the departments.

Gram positive interpretation was found in the culture of 122 (21.1%) specimens. There were 9 positive culture results in Gram positive group (2 *E. faecalis* and 4 *S. Agalactia*) bacteria breeding was found in culture and in 3 of 9 samples (1 *K. pneumoniae*, 2 *Candida spp)* as incompatible with the result of culture, incorrect gram-stain interpretation was made by the analyzer. Also, 62 contamination and 51 non-breeding specimens in culture.

Gram negative interpretation was found in the culture of 95 (30.4%) specimens. There were 64 positive culture results in Gram negative group (52 *E. coli*, 4 *K. pneumoniae*, 5 *P. Aeuroginosa*) bacteria breeding was found in culture and in 3 of 64 samples (2 *E. faecalis* and 1 *S. Agalactia*) as incompatible with the result of culture, incorrect gram-stain interpretation was made by the analyzer. Also, 18 contamination and 13 non-breeding specimens in culture.

The percentage values of the automated urine analysis parameters (LE, nitrite, leukocyte and bacteria counts) of groups with Gram positive and negative breeding are shown in Tables 3. The percentage values of the automated urine analysis parameters (LE, nitrite, leukocyte and bacteria counts) of groups with Gram positive and negative contamination and non-breeding are shown in Tables 4. In addition, asymptomatic bacteriuria was detected in 12 (63.2%) of 19 patients with negative LE/nitrite and non-breeding culture results, and in 11 (61.1%) of 18 patients with negative LE/nitrite and contamination culture results.

Parameters	The Culture Group with Gram positive Breeding % (n: 9)	The Culture Group with Gram negative Breeding % (n: 64)
Leukocyte Esterase (positive)	88.8 (n: 8)	95.3 (n: 60)
Nitrite (positive)	33.3 (n: 3)	71.9 (n: 46)
Leukocyte > 20/µL	88.8 (n: 8)	95.3 (n: 60)
Bacteria > 300/µL	66.7 (n: 6)	76.5 (n: 49)

Table 3: Percentage values of automated urine analysis parameters (LE, nitrite, leukocyte and bacteria) of groups with Gram positive and negative breeding.

Parameters	The Culture Group with Gram positive Contamination % (n: 62)	The Culture Group with Gram positive Non-Breeding % (n: 51)	The Culture Group with Gram negative Contamination % (n: 18)	The Culture Group with Gram negative Non-Breeding % (n: 13)
Leukocyte Esterase (positive)	74.2 (n: 46)	72.5 (n: 37)	33.3 (n: 6)	46.2 (n: 6)
Nitrite (positive)	16.1 (n: 10)	17.6 (n: 9)	27.7 (n: 5)	7.7 (n: 1)
Leukocyte >20/µL	74.2 (n: 46)	72.5 (n: 37)	33.3 (n: 6)	46.2 (n: 6)
Bacteria > 300/µL	24.2 (n: 15)	23.5 (n: 12)	27.7 (n: 5)	23.1 (n: 3)

Table 4: Percentage values of Gram positive and negative contamination and non-breeding groups in automated urine analysis parameters (LE, nitrite, leukocyte and bacteria).

Discussion

A urine analysis test in clinical laboratories is important because it is easier to obtain the sample than the blood sample and it is useful in diagnosis and treatment of urinary tract diseases. Urine analysis is the most frequently requested tests in routine studies and causes labor and time loss in laboratories where manual urine analysis is performed. Because of this, automated urine analysis systems are more suitable for reducing the technologist's burden in workload intensive laboratories. Simultaneous urine culture testing with urine analysis is also requested by the physician for the patient with complaints. It is stated that despite the gold standart urine culture in UTI, interpretations about reducing the need for urinary cultures can be obtained by using the parameters measured in the automated urine analyzers [3-9].

Urine analysis by flow cytometry technique on a Sysmex UF-5000 automated urine analyzer evaluates Gram positive and negative bacterial cells in UTI based on differences in cell wall layer such as peptidoglycan layer. Gram positive bacteria with a thick peptidoglycan layer generally exhibit a diffuse light signal intensity at higher intensity than Gram negative bacteria. Side fluorescence signal intensity indicates the amount of fluorescence that is affected by differences in cell wall structure and penetrates into the bacterial cell. The intensity of the side fluorescence signal is lower because the peptidoglycan layer of the Gram positive bacterial cells is thicker and the fluorescence penetrating into the nucleic acid layer is less. In Gram negative bacteria, the peptidoglycan layer is thin and has a high side fluorescence signal intensity, which is the amount of fluorescence penetrating the bacterial nucleic acid structure. In our study, it was observed that the results of LE and nitrite positivity, leukocyte and bacterial counts in the urine and Gram positive and negative bacterial interpretation in the automated urine analysis were consistent with the urine culture results.

Previtali et al., in their studies of the UF-5000 fully automated urine particle analyzer to validate it's performance in the clinical laboratory environment, found that the AUC value of the ROC curve ranged from 0.86 to 0.99, sensitivity was> 0.90 for all elements and specificity was 0.74-0.89 for epithelial/squamous/renal tubular cells, crystals and RBC. Non-centrifuged normal and abnormal urine specimens were assessed using the Fuchs-Rosenthal chamber by the two pathologists, and the comparison was very good for all parameters and that the UF-5000 was performing well for the detection of urine particles related to the pathological processes of the urinary tracts [10].

The diagnosis of urinary tract infections (UTIs) with urine culture is time-consuming and costly. The use of a screening method to identify negative samples positively affects the time to diagnosis and the laboratory cost. Urine flow cytometers can identify particles in the urine. The number of cultures can be reduced by introducing a cut-off value that determines whether a urine sample can be cultured later. Geerts et al., evaluated the update of the additional software developed for the Sysmex UF1000i urine flow cytometers. The Sysmex UF1000i separates the bacteria into two categories: rod and spherical. They found that the probability of correctly classifying rod-shaped bacteria was 91%, and that of spherical bacteria was 29%, which was significantly lower. They pointed out that with the use of urine flow cytometry, UTI would be able to be detected, but with this software, bacteria could not be classified well to be clinically usable according to their morphology [11].

Erdman et al., compared leukocyte esterase and nitrite results in stripe with urine cultures and Sysmex UF-1000i results in the UTI in hospitalized patients. Using Sysmex UF-1000i with cut-off values defined for leukocyte count and bacteria, it is possible that the negative predictive value may be 100% and false negatives may be 0%, resulting in a decrease in unnecessary antibiotic use. This method will increase the quality with high sensitivity and specificity and reduce the costs with less urine culture tests and fewer technologists [12].

Herráez et al., found that UF-1000i could identify 95% urinary tract infections with high negative predictive value, avoid culturing approximately 38% of urine samples, reduce time to diagnosis of UTI and unnecessary antibiotic treatments, and improve cost-effectiveness [13].

Kawamura et al., compared an automated urine analyzer with improved bacterial identification function to Gram stain and urine culture and evaluated the performance of the Sysmex UF-5000, an automated urine particle analyzer with an advanced function to identify bacterial Gram stain (BACT-info). Gram stain consistency was 85.1% with culture results and 83.2% with UF-5000 results, while culture results' consistency was 81.0% with UF-5000 results. Because of the high positive predictive value (93.3%) between the Gram negative results obtained with UF-5000 and both Gram stain and culture results, the Sysmex UF-5000, which uses bacterial Gram stain (BACT-info), has a great promise in screening the UTI pathogens [14].

In our study, LE and nitrite positivity rates were 88.8% and 33.3% and positive rates of > 20/μL leukocyte and > 300/μL bacteria were 88.8% and 66.7%, respectively in 9 patients (5 female, 4 male) who had Gram positive bacterial interpretation in the automated urine analyzer and positive culture breeding results. LE and nitrite positivity rates were 95.3% and 71.9% and positive rates of > 20/μL leukocyte and > 300/μL bacteria were 95.3% and 76.5% respectively. in 64 patients (60 females, 4 males) with Gram negative bacterial interpretation in the automated urine analyzer and positive culture results. Especially the breeding results of *E. coli* (81.3%) and high percentage of LE, nitrite, leukocyte and bacterial counts in culture with Gram negative bacterial interpretation indicate that this information in the urine report has a diagnostic value in terms of UTI and matches with other results.

Conclusion

UF-5000 appears to be a device that can be useful in screening and identifying UTI by providing a faster and easier route than classical Gram stain and urine culture. In addition, with the new BACT-info definition, it may give valuable information about early treatment to a patient with UTI. Especially in Gram negative bacterial interpretation, this approach will improve the appropriate test requesting and utilization by clinicians. With more comprehensive studies, it is possible to obtain information about the etiological agent within a few minutes and to guide in early treatment initiation by monitoring the UTI with automated urine analysis.

Acknowledgement

None.

Conflict of Interest

None.

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