Original Article

Efficacy of Antimicrobial Agent to Treat Acute Uncomplicated Cystitis through Estimation of Causative Bacterial Group from Bacterial Scattergrams by Using Fully Automated Urine Particle Analyzer UF-1000*i*

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Objectives: Currently, physicians can identify bacterial group causing infection, only when the results of urine culture become available, a few days after initial consultation. In the present study, patients with acute uncomplicated cystitis were prescribed antimicrobial agents according to a developed bacteria morphology information (BACT- Info.) program by analyzing the bacterial scattergram on the UF-1000i (UF-1000i; Sysmex Corporation, Kobe, Japan.) This parameter is research use only and cannot be used for diagnosis.

Methods: Urine samples from a total of 40 females with cystitis were examined separately by BACT-Info., bacterial culture and Gram staining. When BACT-Info., flagged the sample with the IP Message "Rods?", the patients were treated with cefdinir. For the patients whose sample flagged with the IP Message "Cocci/mix?," levofloxacin was administered.

Results: The sensitivity of BACT-Info. for "Rods?" was high, as 95.8% cases of bacillus were identified. When BACT-Info. demonstrated "Rods?", bacilli were suspected as causative bacteria, and the patients were treated by cefdinir with 91.7% efficacy. On the other hand, when BACT-Info. reported "Cocci/mix?", cocci and/or mixed bacterial infection was suspected, and levofloxacin with 57.1% efficacy (less effective than "Rods?" [p = 0.008]) was administered. The BACT-Info. results indicate that this Scattergram Software may be easier/faster in obtaining data compared to urine bacterial culture, as urine culture may grow different types of contaminated bacteria in some cases.

Conclusions: When the BACT-Info. IP Message displayed "Rods?", cystitis with bacillus was suspected and the patient could be fully treated by short term oral administration of antimicrobial agents. When the program demonstrated "Cocci/mix?", some patients could not be fully treated with ordinary antimicrobial agents as there are resistant bacteria in Cocci/mix. The Sysmex BACT-Info IP Messaging Software can be used as a guide to select appropriate antimicrobial agents for treating patients on the day of first visit.

Key Words

Antimicrobial Agent, Bacterial Class Estimation, Bacterial Culture, Urinary Tract Infection, Urine Particle Analyzer

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INTRODUCTION

When a clinician suspects a patient suffers from a urinary tract infection (UTI), the urine is examined at the time of the initial outpatient visit. Urine bacterial culture and antimicrobial susceptibility tests are ordered while diagnosing a UTI¹). As it takes a few days to get the results, resorting to empiric treatment with antimicrobial agent right after the patient's first visit is unavoidable²). If the patient's urine contains cocci or mixed bacteria, such initial empiric antibiotic therapy is often ineffective³). However currently, physicians can only identify the causative bacteria

Notes: This article is based on the rules of author's facility in Japan. (as of Oct. 2018) The specifications, performances and functions described here may be different depe

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when the results of urine culture become available, a few days after initial consultation $^{4)}\!.$

We reported that bacterial scattergrams generated by the UF-1000*i* (UF-1000*i*; Sysmex Corporation, Kobe, Japan.) could predict whether the causative bacteria were bacilli or $\operatorname{cocci}^{5,6}$. The UF-1000*i* is a urine particle analyzer, which can quantitatively measure RBC, WBC, epithelial cells, casts, and bacteria in non-centrifuged urine for 72 seconds, using urine flow cytometry ⁷). In this analyzer, fluorescent polymethine dye specifically stains the nucleic acids of bacteria and carries out highly accurate quantitative analysis using the dedicated bacteria channel (BACT channel). After that, results of analysis can be graphically displayed as bacterial scattergrams. The bacterial group can be roughly predicted from the distribution angle of dots with respect to the x-axis in the scattergrams. Gram-negative bacillus were detected more often with a distribution angle less than (<)30 degrees, and gram-positive cocci were detected more often when the angle was greater than (>) 30 degrees ⁵⁾.

Sysmex Corporation (Sysmex; Kobe, Japan) has developed an automated urinalysis software program named the bacteria morphology information (BACT- Info) program which employs an algorithm to identify bacteria morphology. When BACT-Info identifies the bacterial scattergram dots distribution angle of less than 30 degrees, it then flags the cell events as "Rods?", and for any other angles the program flags as "Cocci/mix?". In the present study, patients with uncomplicated cystitis were prescribed antimicrobial agents according to the flagging results from the BACT-Info program. It was tested whether the software can be useful for first visit outpatients in the selection of antimicrobial agents for treating uncomplicated cystitis.

MATERIALS AND METHODS

This study is aimed to demonstrate the clinical usability of the developed diagnostic technique (BACT-Info.) for acute uncomplicated cystitis through comparative analysis between BACT-Info. and bacterial culture. In order to ensure the reliability of the data and consistency in observation, the same examiner performed both the bacterial culture and Gram stain for all the species. It should be noted that the tests were carried out at single institution.

Urine samples from a total of 40 subjects with acute uncomplicated cystitis (40 females with ages ranging from 20 to 87 years-old with a mean age of 64.3 years) were selected from the patients examined in the Department of Urology, Kawasaki Medical School General Medical Center during a period from February 2013 to September 2013. All study procedures were approved by the institutional review board of the Kawasaki Medical School (Permission No.1376). Although the ideal urine specimen for determining the microbial cause of infection would be collected by suprapubic aspiration or transurethral catheter, neither type of specimen is routinely obtained because of inconvenience, discomfort, and the potential for adverse events. The customary urine specimen collected for culture is the midstream portion of voided urine⁸. The urine sample was analyzed by UF-1000*i* and bacterial species were identified by urine bacterial culture. Subjects, whose white blood cell count was more than $10/\mu$ L and bacterial count was more than $100/\mu$ L according to the results of UF-1000*i*, were considered for analysis with prior written consent. Results of BACT-Info., bacterial culture and Gram staining were compared and the effectiveness of antimicrobials corresponding to the BACT-Info results were evaluated.

UF-1000*i*

The standard urinalysis is done by UF-1000i. The UF series urine particle analyzer (Sysmex Corporation; Kobe, Japan) is equipped with systems that can quantitatively measure RBC, WBC, epithelial cells, casts, and bacteria in non-centrifuged urine within 72 seconds, using flow cytometry⁹ (**Fig. 1**). The fully automated urine particle analyzer UF-1000*i* uses a red semiconductor laser (wave length λ =635nm), and the device is smaller and consumes less power than earlier models. In this analyzer, fluorescent polymethine dye specifically stains the nucleic acids of bacteria, and carries out highly accurate quantitative analysis using the dedicated bacterial channel (BACT channel). At the same time, the results of analysis can be graphically displayed as scattergrams ⁵ (*Fig. 2*). Particle/ µL could be transformed to the traditional number per high power field (HPF) by multiplying with a specific factor.

Bacteria morphology information (BACT-Info.)

A study by Muratani et al. reports that bacilli can be broadly differentiated from cocci in actual clinical samples within a minute by measuring the angle of distribution of dots in the bacterial scattergram ⁵). The causative organisms can be rapidly differentiated without any additional processing (*Fig. 3*). However, it is sometimes difficult to determine whether the angle of distribution of dots in bacterial scattergram is grater/less than 30 degrees. Therefore to solve this issue, "BACT-Info." program has been developed by Sysmex.

The BACT-Info Software uses an algorithm adopted by the UF-1000*i* to identify the probable bacterial morphology from info in the bacterial scattergram. Here two parameters of interest in bacterial scattergrams were θp and α (**Fig. 3**). In the bacterial scattergram the angle between each dot and x-axis was represented by θ . From the histogram of θ , the angle corresponding to maximum frequency was identified and denoted by θp . Whereas α represents distribution percentage within 18 degrees. In the BACT-Info., when θp is less than 18 degrees and α is larger than 80%, the program defined to report "Rods?". Otherwise, the program reports "Cocci/mix?" (**Fig. 3**).

Urine culture

A standard quantitative urine culture was performed with a 10µL inoculation platinum wire loop onto commercial chromogenic agar medium (Kyokuto Pharmaceutical Industrial Company. Tokyo). Culture plates were incubated aerobically at 35°C for 18-24 hours. Quantification (CFU/mL)

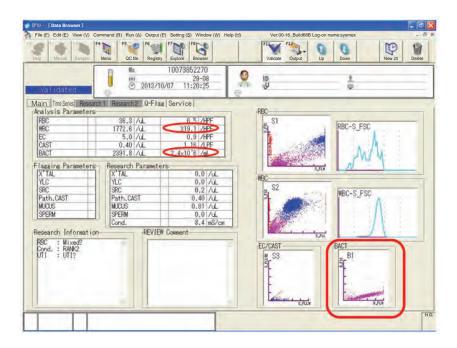


Fig. 1 UF-1000i analysis screen (A case of acute uncomplicated cystitis) The bottom right figure indicates the bacterial scattergram (BACT channel). The purple dots representing bacterial clusters are distributed in a zone of a less than 30 degree angle from the x-axis "Rods?".

S1: Sediment channel 1, S2: Sediment channel 2, S3: Sediment channel 3, B1: Bacteria channel 1 RBC-S_FSC: Forward scattered light intensity in the red blood cells of sediment channel WBC-S_FSC: Forward scattered light intensity in the white blood cells of sediment channel B_FLH: Fluorescent light intensity of bacterial channel (high) (depth of staining) B_FSC: Forward scattered light intensity of bacterial channel (size)
(1) The white blood cell(WBC) count in the urine was elevated at 319.1/HPF.
(2) Enhanced image of WBC distribution in the sediment channel shows a large number of blue dots.

(3) The bacterial count in the urine was elevated at $BACT = 2.4 \times 10^{\circ}/ml$.

(4) BACT channel.

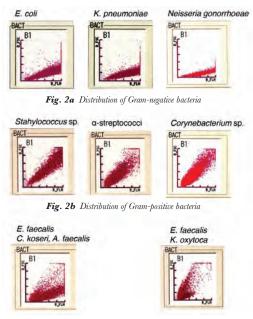


Fig. 2c Distribution of Gram-positive and gram-negative bacteria

Fig. 2 Scattergrams represented as the BACT channel by UF-1000i Bacterial group can be roughly estimated from the distribution angle of dots in the bacterial scattergram. (Reprinted with permission from Muratani T. et al.⁵)

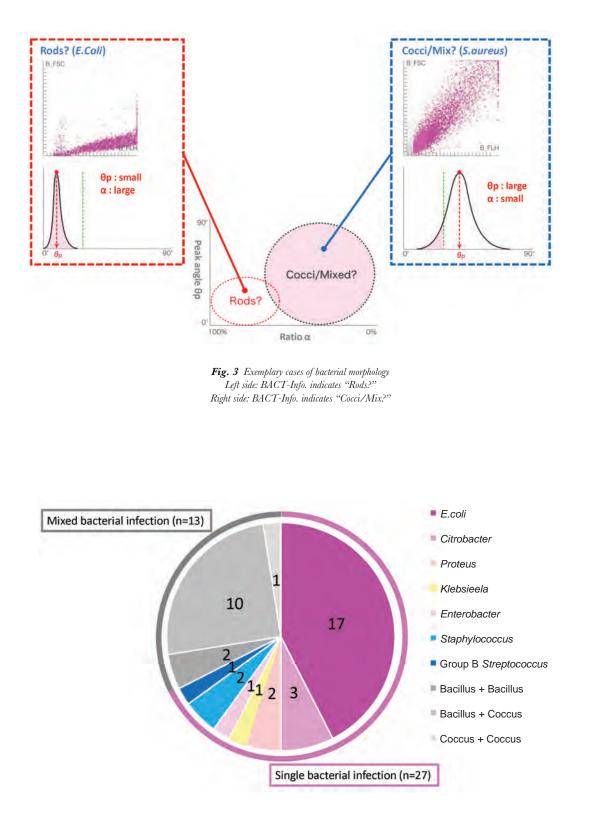


Fig. 4 Types of bacteria and bacterial infection detected by urine culture Single bacterial infection detected by bacterial culture was observed in 27 cases (67.6%). Bacilli were in the majority identified in 24 (88.9%) out of 27 cases of single bacterial infection. Escherichia coli was the most frequently observed species. Mixed bacterial infection was observed in 13 cases, which was described in detail in **Table 2**. The cases categorized as "bacilli and cocci" were mostly found to be mixed bacterial infection cases. was obtained by multiplying the number of colonies on an agar plate by the dilution factor. Positive cultures were defined as bacterial growth $>10^5$ CFU/mL. Mixed growth was defined as the growth of two or more bacterial species. Species identification was performed for the category of mixed growth.

Gram staining

Classic Gram staining technique involves the following steps ¹⁰. A primary stain (crystal violet) is applied to a heat fixed smear of bacterial culture. Iodide is added for binding and trapping of crystal violet into the cell. The slide is flooded with decolorizing agent (Acetone-alcohol decolorizer), and counter-stained with Pfeiffer solution. The results of the staining procedure were observed under oil immersion (100x) through a bright field microscope. After decolorization, the gram-positive cells remain purple and the gram-negative cells lose the purple color. Counterstain, which is usually positively charged safranin, is applied last to give decolorized gram-negative bacteria a pink or red color.

Antimicrobial selection

The urine sample with "Rods?" as detected by BACT-Info. is suspected to have infection with bacillus, which is susceptible with any anti-microbial agents. In this study, when the program demonstrated "Rods?", the patients were treated with cefdinir for seven days. When the program displayed "Cocci/mix?", the urine sample was suspected of having a poly-microbial infection involving both bacilli and cocci. Therefore, the "Cocci/mix?" group could not be fully treated with ordinary antimicrobial agents as there are resistant bacteria in Cocci/mix. For the patients belonging to the "Cocci/mix?" group, levofloxacin was administered for seven days. Both cefdinir and levofloxacin are recommended antimicrobials for the first and second line treatment of acute uncomplicated cystitis according to JAIDS/JCS Guideline 2015¹¹. After seven days of antimicrobial treatment, a urinalysis was performed using the UF-1000*i*. When the WBC count was less than $10/\mu$ L, the treatment could be considered effective. Higher WBC counts indicated that the antimicrobial agent was ineffective.

Statistical analysis

StatMate III (Atoms Company, Japan) was used for testing statistical significance. Wilcoxon test, Mann-Whitney U test and chi-square test were used for testing the differences between groups. In all these tests, p < 0.05 was chosen as a significant difference.

RESULTS

Bacterial urine culture results were summarized as a pie chart in **Fig. 4**. Bacterial infection caused by bacillus alone was observed in 24 cases (60.0%) out of 40 cases, whereas infection by cocci alone was detected in only 3 cases (7.5%). Mixed infections were categorized as "bacillus and cocci" (25.0%), "bacillus and bacillus" (5.0%) and "cocci and cocci" (2.5%).

Fig. 5 shows the age distribution of patients separated according to the results of the BACT-Info scattergrams. The "Cocci/mix?" group also distributed widely among young women aged 20-39 years-old and post-menopausal women aged 60-89 years old.

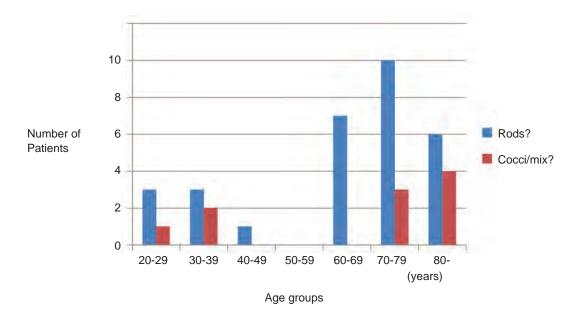


Fig. 5 Age distribution of patients

Table 1 shows comparison of results between the BACT-Info scattergram results and bacterial culture. The sensitivity of BACT-Info. for "Rods?" was relatively high, as 95.8% cases of rods were identified. However, the sensitivity for the "Cocci/mix?" IP Message was not as high (50.0%). This was because 8 cases of mixed infection identified by urine culture were flagged as "Rods?" instead of "Cocci/mix?". When the BACT-Info. demonstrated "Rods?", Gramnegative bacillus were suspected as the causative bacteria, and the patients were treated by cefdinir with a 91.7% efficacy. On the other hand, when the BAC-Info. flagged as "Cocci/mix?," gram positive cocci and/or contaminated infection was suspected, and levofloxacin with 57.1%, less efficacy than "Rods" group (p < 0.01: p = 0.008), was administered.

The cases of mixed infection identified by urine culture were summarized in **Table 2**. Eight mixed cases identified as "Rods?" by BACT-Info. were infected with the largest number of bacillus among the detected species. They were effectively treated by cefdinir, similar to the cases of "Rods?" (17 cases) infected by bacillus alone. The remaining 5 mixed

cases identified as "Cocci/mix?" were infected with a large variety of bacteria species, among which staphylococci or *Enterococci* was frequently observed. These cases were treated by levofloxacin with less efficacy. *Enterococci* with resistance against quinolone derivatives are often detected by susceptibility testing accompanied with bacterial culture. Gram staining results were presented on the fifth to seventh column of **Table 2**. Most of the mixed infection cases (11 out of 13 cases) showed gram negative bacillus for Gram staining. Only two cases demonstrated gram positive cocci, whereas gram positive bacillus was found in four cases during the Gram staining, the Gram staining results agreed with bacterial culture results only to some extent.

In **Table 2** the bacteria detected in mixed infection cases were separated in two different groups. One group (upper 8 cases) was susceptible to normal skin flora contamination. These cases were demonstrated as "Rods?" by BACT-Info. and the treatment by the antimicrobial agent was effective. The other group (lower 5 cases) was identified as "Cocci/ mix?" and might be difficult to treat by ordinary antibiotics. These cases often contained staphylococci or *Enterococci*

 Table 1
 BACT-Info. results compared with bacterial culture

 Sensitivity of the "Rods?" IP Message while using the BACT-Info software was as high as 95.8%.
 On the other hand, the sensitivity of the "Cocci/mix?" IP Message was as low as 50%.

 The agreement between the bacterial culture and BACT-Info results was 77.5%.
 Content of the sensitivity of the "Cocci/mix?" IP Message was as low as 50%.

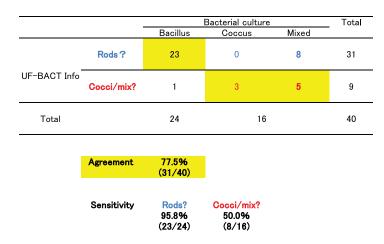


 Table 2
 The bacterial species in the cases of mixed infection detected by urine culture, listed in descending order of bacterial counts from left to right.

 The Gram staining, BACT-Info. and treatment results also appear in the table.

GNR: Gram-negative rods. GPC: Gram-positive cocci. GPR: Gram-positive rods. CNS: Coagulase negative staphylococci

Age-gender_	Bacterial culture			Gram Staininng			UF-BACT Info	Treatmenat
	Species 1	Species 2	Species 3	GNR	GPC	GPR		
24-F	Escherichia coli	Streptococcus oralis	Staphylococcus (CNS)	4+	0	0	Rods?	Effective
30-F	Escherichia coli	Group B Streptococcus		±	±	\pm	Rods?	Effective
39-F	Escherichia coli	Sterptococcus epidermidis		2+	0	3+	Rods?	Effective
63-F	Escherichia coli	Streptococcus bovis		0	0	0	Rods?	Effective
74-F	Escherichia coli	Staphylococcus (CNS)		2+	0	0	Rods?	Effective
78-F	Citrobacter freundii	Escherichia coli		4+	0	0	Rods?	Effective
82-F	Escherichia coli	Staphylococcus (CNS)	Streptococcus spp.	3+	0	0	Rods?	Effective
82-F	Escherichia coli	Corynebacterium spp.		2+	0	0	Rods?	Effective
24-F	Lactobacillus spp.	Staphylococcus (CNS)	Acinetobacter baumannii	3+	0	3+	Cocci/mix?	Ineffective
36-F	Enterococcus faecalis	Staphylococcus (CNS)	Streptococcus spp.	0	0	2+	Cocci/mix?	Effective
77-F	Group B Streptococcus	Staphylococcus aureus	Escherichia coli	2+	0	0	Cocci/mix?	Effective
77-F	Enterococcus faecalis	Enterobacter aerogenes	<i>Staphylococcus</i> (CNS)	2+	±	0	Cocci/mix?	Effective
87-F	Klebsiella pneumoniae	Enterococcus faecalis		±	0	0	Cocci/mix?	Ineffective

which can easily become multi-drug resistant. Treatment with antimicrobial agent like levofloxacin was found to be ineffective in some cases. The BACT-Info results indicate that it is more prompt and reliable compared to urine bacterial culture, as urine culture may grow different isolates of contaminated bacteria in some cases which may each need to be identified.

DISCUSSION

UTI patients are diagnosed by examining a urine sample during the initial visit to the outpatient clinic. Appropriate antimicrobial agents could be selected if it can be judged quickly at an earlier stage whether it is an infection caused by cocci or by bacillus in a complicated UTI. Moreover, patients infected with bacillus can be treated by short-term administration of a suitable antibiotic agent. In quantitative bacterial culture, a certain amount of urine was collected with a platinum loop, then placed onto the agar plate for colony development, and results were obtained after 24 plus hours of culture ¹²). Thus the results of the culture test are not available at first visit, and in current practice a few days are required to arrive at a definitive diagnosis. In this respect, gram-negative/positive differentiation of the bacteria by Gram staining has proven to be a useful and cost-effective method. However, there is a possibility of the result being affected by the level of expertise of the technologist as sometimes the bacterial cells may be missed altogether¹³. Contrary to such subjective testing, the UF-1000i can display the RBC count, WBC count, and bacterial count in a urine sample through its basic cell analysis function in a very short time and thus can contribute to diagnosing a UTI¹⁴. Furthermore, it can output a bacterial scattergram in around one minute without any additional treatment of the urine sample. Muratani et al. measured the distribution angle of dots from the x-axis in the UF-1000i bacterial scattergrams of known bacterial suspensions. They reported that gram-positive cocci showed a distribution angle of about 40 degrees, gram-negative bacilli had about 20 degrees, Corynebacterium (gram-positive bacillus) had 43 degrees, and Neisseria gonorrhoeae (gram-negative cocci) had 11 degrees. By measuring the angle of the distribution of dots in the bacterial scattergram, cocci can be broadly differentiated from bacilli in actual samples rapidly ^{5,6}). These results suggest that in flow cytometric analysis with UF-1000i, not all of the individual dots in the scattergrams represent individual bacterial cells. Some represent certain clusters of bacteria, without differentiating between cocci and bacilli. For example, gram-positive cocci and the genus Corvnebacterium (gram-positive bacillus) both multiply by dividing in 2 or 3 dimensions to form grape-like irregular clusters. Therefore, they can appear on the scattergram as relatively large dots with strong staining intensity. On the other hand, gram-negative bacilli and bacteria of Neisseria gonorrheae, gram-negative cocci, divide after reaching a certain size. In these isolates, the depth of staining is almost consistent for the all the bacterial cells. In flow cytometry, bacterial cells appear as small dots with weaker stained bacterial nuclei when compared to clusters of bacterial nuclei/gram positive cocci. Also, the distribution is more convergent¹⁵. These facts clearly indicate that the difference

in the distribution angle of the dots in the scattergram is a result of the variation in the two-dimensional pattern of bacterial cell multiplication. This demonstrates the possibility of predicting the bacterial group from the scattergram.

It is important to apply scattergram-based diagnosis and treatment of uncomplicated cystitis. Therefore, Sysmex has developed the "BACT-Info" program which can generate a bacterial scattergram. It use the urine samples as diagnostic materials and classifies "Rods?" or "Cocci/ mix?" within 72 seconds. When the program indicated "Rods?", the patients were treated with cefdinir with a 91.7% effectiveness rate, whereas for the "Cocci/mix?" group levofloxacin was administered with a 57.1% efficacy. The efficacy of antimicrobial administration for the "Rods?" group was high on the other hand, that for the "Cocci/ mix?" group was low. These results demonstrated that the cases which flagged with the "Rods?" IP Message could be treated by ordinary antimicrobial agent. When the Software flags the cases as "Cocci/mix?" either peroral faropenem or intravenous application of carbapenem derivative should be chosen, which is quite effective against many Gram-positive and negative aerobes and resistant to hydrolysis by nearly all beta-lactamases ^{16,17}). Therefore, BACT-Info. can be used to detect the high-risk UTI cases at the first visit. With the currently available techniques, the "Cocci/mix?" cases cannot be distinguished from the "Rods?" cases and both instances are treated with empiric ordinary antimicrobial agents at the time of first visit. As a consequence, bacteria become resistant to multiple classes of antimicrobial agents. Using BACT-Info, the "Cocci/mix" cases could be identified at the time of first visit and consequently be treated with a sensitive antimicrobial agent. Therefore, the use of BACT- Info. in treating uncomplicated cystitis can prevent the increase of multi-drug resistant bacteria. The Gram stain might also help identify bacillus isolates, which are very susceptible to many antimicrobials. This was used to differentiate bacterial species into two groups (Gram-positive and Gram-negative)¹⁰⁾. The results can be obtained at the day of first visit. The gram positive cell wall contains a thick layer of peptidoglycan with numerous teichoic acid cross linking which resists the decolorization.

The Gram-positive bacteria include many well-known cocci genera such as staphylococci, *Group B Streptococci*, and *Enterococci*. Gram negative bacteria contain most of the bacilli genera like *Escherichia*, *Klebsiella*, *Citrobacter* and *Proteus*. *Neisseria gonorrhoeae*, which is rare to find in acute uncomplicated cystitis, belongs to Gram negative bacteria. In our study, to some extent, Gram-staining results did not agree with bacterial culture results. Therefore, it was confirmed that the Gram staining was not an infallible tool for identification of bacteria causing cystitis, when compared to BACT-Info.

At present, a urine culture is the only useful test when the initial empiric antibiotic therapy is not effective. However, results of the urine culture are often interpreted in conjunction with the urinalysis results and sample handling considerations. Since some urine samples have the potential to be contaminated with normal skin flora, care must be taken when interpreting some culture results ¹⁸. In our study, mixed bacteria results obtained from urine culture were analyzed in detail.

Collection of urine specimen by suprapubic aspiration or transurethral catheter is standard reference for determining the microbial cause of infection. In this study, a midstream portion of voided urine was collected for culture as it is customary to do. This explains the reason for the higher percentage of mixed bacterial infections. We intended to check not only the bacteria present solely in the urine that caused the infection, but also the contaminated bacteria from external genital skin using bacterial culture. In our study, BACT-Info. helps us to determine whether the symptom is contaminated by bacteria by providing the results within 72 seconds. Eight samples with "Rods?" flagging consisted of both causative bacilli and contaminated bacteria normally found on the skin. On the other hand, 5 samples with "Cocci/mix?" flagging contained staphylococci or *Enterococci*, which can easily become drug resistant. Therefore, BACT-Info. provides prompt, more accurate and simple results.

Excessive reliance on antibiotics leads to the emergence/ spread of resistant bacteria, which is an incidental damage in healthcare today. Inconsiderate mass medication of drugs results in drug resistance, which is a big threat not only for the patient treated now, but also for patients in the future. Therefore, medication management to keep currently available drugs effective for all patients and for a long period is a critical issue. A bacterial analysis functional program like BACT-Info. on the UF-1000*i* may assist in the optimum drug selection for UTI. It will contribute to control collateral damage associated with UTI treatment.

Patients with acute uncomplicated cystitis were treated by different antimicrobial agents based on the results of the BACT-Info Software. When the program demonstrated the "Rod?" IP Message, the patients were treated with cefdinir showing a 91.8% efficacy. An uncomplicated cystitis with bacillus was suspected and the patient may be fully treated by short term wide spectrum anti-microbial agents. On the other hand, when the program demonstrated the "Cocci/mix?" IP Message, levofloxacin with a 57.4% efficacy was administered. Lower curable rates were observed with ordinary anti-microbial agents. Therefore, we think that this scattergram software can be used as a guide to select appropriate antimicrobial agents for treating UTI patients.

The clinical data presented in this article was collected on the UF-1000i about five years ago. Since then, the development of new clinical technology has been remarkably quick and the successor model of the UF-1000*i*, the UF-5000, is now being sold. The UF-5000 boasts a novel blue LED light source (replacing the red LED of the UF-1000*i*) and includes enhanced analytical capabilities beyond what is discussed in this current urine particle study.

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