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Diagnostic sensitivity of microscopic and chemical analysis of the urine in diagnosis of urinary tract infections

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ABSTRACT

Leukocyte in the microscopic examination of the urine, and leukocyte esterase (LE) and nitrite positivity in chemical urine analysis all indicates urinary tract infection (UTI). We aimed to demonstrate the diagnostic sensitivity of urine strips as well as the microscopic analysis of urine and to determine the effect of isolated pathogens in the urine culture as well as the number of colonies of pathogens and pathogen species on these parameters. We retrospectively analyzed the results of patients with a prediagnosis of UTI between August 2014 and January 2015. According to the amount and variety of pathogens isolated in urine cultures, patients were divided into two groups of patients. Group1 consisted of patients with more than 10^5 cfu/ml and group 2 consisted of patients with 10^3-10^5 cfu/ml in urine culture. Group 3 was consisted of patients with *Escherichia Coli (E. Coli)* in urine culture and group 4 was consisted of patients with pathogens other than *E. Coli* in urine culture. Diagnostic sensitivity of LE, nitrite and leukocyturia were 46%, 18% and 57%, respectively. Diagnostic sensitivity was 48% when at least one positive result of LE and nitrite. Sensitivity reached 59% when at least one positive result of LE, nitrite and leukocyturia. LE, nitrite and leukocyturia test results were significantly different in group 1 compared to those in group 2(all $p<0.001$). LE and nitrite results were significantly different in group 3 compared to group 4($p=0.004$ and $p=0.036$ respectively). According to the results of this study; highest diagnostic sensitivity has been reached at least one positive result of LE, nitrite test or with leucocyturia found however, even in this condition, all patients have not been diagnosed with these tests. The breeding pathogen species and number of the colonies isolated in urine culture have been found to be effective factor on diagnostic sensitivity.

1. Introduction

Urinary tract infections (UTI) are the most common community-acquired infections (Patel et al., 2005). In particular, the risk of having a UTI at least once during the women's lives has been reported as high as 60% (Warren et al., 1999; Foxman, 2002; Hooton et al., 2004). UTI can be cured largely uncomplicated with early diagnosis and treatment. The gold standard for clinical diagnosis of UTI is detection of causative pathogen by urine culture in the presence of clinical symptoms (Schmiemann et al., 2010). However results of the urine culture need at least 24 hours, therefore the diagnosis and treatment may delay. Microscopic and chemical analysis of urine for the diagnosis of UTI give quick results and are preferred test because it is cheaper. Leukocytes in the microscopic examination of the urine; and detection of leukocyte esterase (LE) and nitrite in chemical analysis are positive signs pointing UTI (Nys et al., 2006).

Diagnostic sensitivity of the test is of utmost importance

as the diseases like UTI which can be treated with early diagnosis without causing any complications (Deville et al., 2004). Urinary strips are used in chemical analysis of urine. Two of the guiding test in the diagnosis of UTI, nitrite and LE can be measured by dipstick tests. Different diagnostic values of nitrite and LE has been reported in literature (Hurlbut and Littenberg, 1991; Deville et al., 2004). We conducted this study because of this heterogeneity in the literature and we aimed to demonstrate the diagnostic sensitivity of urine strips we use in our own laboratories and the microscopic analysis of urine to determine the contribution to the diagnosis. We also aimed to determine the effect of reproduced pathogens in the urine culture as well as the number of colonies of pathogens and pathogen species on these parameters.

2. Material and methods

We retrospectively analyzed the results of urine strip analysis and microscopic analysis of patients with a prediagnosis of UTI between August 2014 and January 2015. The study was set up according to the Helsinki declaration. Patients enrolled in the study if urine culture revealed 10^3 colony forming units cfu/ml. Thirty seven of 108 patients in study were men and others were women. In order to exclude possible errors patients were included when urine dipstick analysis and microscopic analysis were simultaneously. The patients without simultaneous examination, or absence of one of the dipstick urine analysis or microscopy results were excluded from the study. Patients with positive urine glucose or protein analysis were also excluded in order to prevent the interaction with strip tests.

Clean-catch midstream urine is used for all urine analysis in our laboratory. Microscopic analysis of urine was carried out in a fully automated urine analyzer (LabUMat&UriSed, 77 Elektronika, Budapest, Hungary). This device is performed using image processing software microscopic analysis of urine. The cells can be detected by means of digital imaging, and results are obtained full-field image. The obtained results are standardized with manual urine microscopy. The dipstick analysis was carried out with the same device.

0.001 ml of extract used for urine culture and cultured into 5% blood agar (Merck, Germany) and Eosin-Methylene Blue (EMB) agar (Merck, Germany). Samples incubated at 37^0C for 18-24 hours. Bacterial growth was expressed as units forming colonies per milliliter (cfu/ml). Reproducing bacteria have been identified by conventional methods (gram staining and biochemical tests). Phoenix identification cards (Becton Dickinson Diagnostic Systems, Sparks, MD, ABD) used for identification of unidentified bacteria by conventional methods.

According to the amount and variety of pathogens isolated in urine cultures, patients were divided into four groups of patients. Group 1 consisted of patients with more than 10^5 cfu/ml and group 2 consisted of patients with 10^3-10^5 cfu/ml in urine culture. Group 3 was consisted of patients with *Escherichia Coli (E.Coli)* in urine culture and group 4 was consisted of patients with pathogens other than *E.Coli* in urine culture.

Statistical analyses were performed with SPSS 15 software (SPSS; Chicago, IL, USA). Variations between study groups about test results were analysed with chi-square test. A p value <0.05 considered as statistically significant.

3. Results

Sixty five percent of pathogens isolated were *E. Coli*. Diagnostic sensitivity of LE and nitrite were 46% and 18% respectively. Leucocyturia is defined more than 2 WBC in each field in men and more than 5 in women in microscopic analyze (Little et al., 2009). According to these cut off values, diagnostic sensitivity of leucocyturia was 57%. To investigate the diagnostic sensitivity of the combination of tests; for nitrite and LE combination of at least one test was positive in 48%, case the diagnostic sensitivity is determined at least one of positivity nitrite, LE and leucocyturia was found to be 59%.

The groups were compared for LE, nitrite and leucocyturia. There was significant difference between group 1 and 2 according to LE and nitrite results (p<0.001) (Table 1). LE and nitrite results were also different between group 3 and 4 (Respectively p=0.004 and p=0.036). Leucocyturia was not significantly different between groups 3 and 4 (p=0.051).

Diagnostic sensitivity of the tests studied after grouping again (Table 2). Sensitivity of LE and nitrite and leucocyturia has been found to be greater in group 1 compared to group 2 and all other patients. In addition, diagnostic sensitivity was greater in group 3 than group 4 and all other patients.

Table 1. Comparison of leukocyte esterase, nitrite and leucocyturia for detecting urinary tract infection in study groups.

	Group 1 (n=49)	Group 2 (n=59)	Group 3 (n=62)	Group 4 (n= 46)
LE (+/-)	35/14 *	15/44 *	36/26 †	14/32 †
Nitrite (+/-)	17/32 *	2/57 *	15/47 ‡	4/42 ‡
Leucocyturia (+/-)	41/8 *	20/39 *	40/22 §	21/25 §

Group 1: Over 10^5 cfu/ml growth in urine culture.
Group 2: Over 10^3 cfu/ml growth in urine culture.
Group 3: *E. Coli* growth in urine culture.
Group 4: Other than *E. Coli* growth in urine culture.
TD: Diagnostic sensitivity; **LE:** Leukocyte esterase; ***E.coli:*** *Escherichia Coli*
Chi-Square test, group 1 vs group 2 *p<0.001 (for every three parameters)
Chi-Square test, group 3 vs group 4 † p=0.004, ‡ p=0.036, § p=0.051

4. Discussion

According to the results of this study; highest diagnostic sensitivity has been reached at least one positive result of LE, nitrite test or with leucocyturia found however, even in this condition, all patients have not been diagnosed with these tests. The number of colonies isolated in the urine culture and breeding of this species pathogen have been found to be effective factor on diagnostic sensitivity values. Diagnostic sensitivity reduced by isolated pathogen other than *E. Coli* and the low number of pathogens isolated in urine cultures.

LE enzyme is only secreted from leukocytes (European Confederation of Laboratory, 2000). Thus, consistence of leukocytes in the urine is indirectly assessed by this test. Different values reported in the literature on diagnostic sensitivity of LE. Factors that may cause false negative results are the presence of reducing substances in urine, high glucose concentration, and high protein concentration (Woolhandler et al., 1989; Beer et al., 1996).

Nitrate occurs naturally in the human diet and are excreted in urine (European Confederation of Laboratory, 2000). In the presence of bacteria reduces nitrate to nitrite it should be detected in urine. Therefore, positive nitrite is an indirect indication of the presence of bacteria in the urine. However,

Table 2. Diagnostic sensitivity to detect UTI for LE, nitrite and leucocyturia in study groups

	Group 1 (n=49)	Group 2 (n=59)	Group 3 (n=62)	Group 4 (n= 46)	All patients (n=108)
LE	%71	%25	%58	%30	%46
Nitrite	%35	%3	%24	%8	%18
Leucocyturia	%84	%34	%64	%46	%57

UTI: Urinary tract infections; **LE:** Leukocyte esterase

except for the presence of bacteria in the urine certain factors are needed to give a positive nitrite test result (Arinzon et al., 2009). First, the diet should include enough nitrate. Second, to have urine at least 4 hours in the bladder are required to reduce nitrate to nitrite. In addition, dilute urine test can give false negative results for nitrite. Therefore, sensitivity of nitrite test in the diagnosis of UTI is low.

The classical approach to the evaluation of urine culture is reproduction of 10^5 cfu/ml considered as positive result. Recently, 10^3 cfu/ml is considered as positive result in order to improve the diagnostic sensitivity of urine culture (Rubin et al., 1992). Therefore, we use this limit in present study. However, diagnostic sensitivity of the chemical and microscopic examination of urine was low according to these limit values in the diagnosis of UTI.

A meta analyses by Williams et al evaluated the data of 95 studies and reported that diagnostic sensitivity was 47-95% for LE, 8-95% for nitrite, which ranged from 0-100% for leukocyte counts in urine microscopy (Williams et al., 2010). Evaluation of 70 study by Deville et al revealed that diagnostic sensitivity was 48-86% for LE and 45-60% for nitrite (Deville et al., 2004). All these results indicate that diagnostic sensitivity of the tests was quite variable. Therefore, each laboratory should absolutely aware of the level of diagnostic sensitivity for these tests in their laboratory own.

Today, some guidelines suggest that UTI should be ruled out when LE and nitrite tests were negative (Wiersma and Timmermans, 2001). However, it does not seem possible according to our results. Even when both LE, nitrite and leukocytes in urine microscopic examination were all positive, it was not sensitive enough to detect all of the patients.

Pathogens growth in cultures were similar to those in literature (Gupta et al., 2001; Arredondo-Garcia et al., 2004). Sensitivity of LE and nitrite were higher in *E. Coli* group compared to other pathogens. Enterobacteriaceae, like *E. Coli* reduce nitrate to nitrite (Beer et al., 1996). That may describe to increase in diagnostic sensitivity in *E. Coli* group. However, it is not clear why the diagnostic sensitivity of LE was higher in this group. Literature is lack of data to explain such increase. Therefore further studies are needed in this topic.

Limited study population, single center design are limitations of present study. In addition, we did not calculate the specifity of LE, nitrite, and leucocyturia.

As a result of our study, negative urinalysis for LE, nitrite, and leucocyturia can not exclude the presence of UTI. Because all of these tests were negative in 41% of patients in our study. Especially diagnostic sensitivity was lower in patient's urine culture with 10^3-10^5 cfu/ml, breeding of pathogens other than *E. Coli*. Therefore, in patients investigated for UTI number of colonies isolated may be lower especially the symptoms have started recently. In addition, if it is probable to growth in urine pathogens other than *E. Coli*, it must be kept in mind that these tests gave negative results.

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