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Original Article

Urine dipstick test for diagnosing urinary tract infection

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Abstract

Background Urinary tract infection (UTI) is a common disease in children. Approximately 3-5% of girls and 1% of boys develop a UTI. In children, prompt treatment is essential because UTI may be a risk factor for developing renal insufficiency or end stage renal disease. However, prompt treatment depends on having a rapid diagnosis. Urine dipstick test is a useful and commonly used because it is low cost and gives rapid results, compared to urine cultures for diagnosing UTIs. However, the diagnostic accuracy of the urine dipstick test is debatable.

Objective To compare urine dipstick test (leukocyte esterase, nitrite, and combined leukocyte esterase and nitrite) to urine culture for diagnosing UTIs.

Methods A diagnostic study was held in H. Adam Malik Hospital from May to June 2010. There were 70 children aged 2 to 14 years and recruited by consecutive sampling. Two midstream urine specimens were collected from subjects after cleaning the external urethral orifice. The first specimen was used for urine dipstick testing for leukocyte esterase and nitrite. The second urine specimen was cultured in the laboratory. Urinalysis for leukocyte esterase and nitrite studies were performed with fresh and uncentrifuged urine. Leukocyte esterase and nitrite caused a change in dipstick color apparent within 2 minutes. Urinalyses were considered to be positive for UTI if either leukocyte esterase or nitrite were positive. The results of urine culture were used as the golden standard.

Results The sensitivities of leukocyte esterase and nitrate tests were 90.5% and 73.8%, respectively. However, the sensitivity for combined leukocyte esterase and nitrite test was 96.4%. Nitrite test was more specific (60.7%) than the leukocyte esterase test (39.3%). The specificity of both tests taken together was 64.3%. For leukocyte esterase alone, nitrate alone, and the two combined the positive predictive values (PPV) were 69.1%, 73.8%, and 64.3.%, respectively, and the negative predictive values (NPV) were 73.3%, 60.7%, and 96.4%, respectively.

Conclusion Urine dipstick test for leukocyte esterase and nitrite combined may be a good alternative diagnostic test for UTIs in children than leukocyte esterase or nitrite by themselves in areas with limited resources. **[Paediatr Indones. 2013;53:315-9.]**

Keywords: *dipstick urine, urine culture, urinary tract infection*

Urinary tract infection (UTI) is a non-specific term referring to bacterial invasion into the urologic system. Urinary tract infections may be classified into two anatomically distinct categories: lower tract infection, including urethritis and cystitis, and upper tract infection, such as ureteritis, pyelitis (upper collecting system), and pyelonephritis (renal parenchyma).[1] Based on multiple investigations, it is estimated that three-quarters of children with a febrile UTI have

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pyelonephritis by renal scan. Therefore, children with fever and signs of a UTI are presumed to have pyelonephritis.[2] Three principles should be followed for correctly identifying patients with UTIs: suspect UTI and screen patients at risk (based on prevalence data and clinical factors), understand the limitations of screening tests, and rely on appropriate urine cultures.[3]

Classic symptoms, including frequency, dysuria, urgency, incontinence, and vomiting, as well as signs, including fever, suprapubic tenderness, and flank tenderness are often present in older children, but these features are often absent in infants, toddlers, and pre-schoolers.[4] In neonates, UTIs may be the etiology for unexplained hyperbilirubinemia or failure to thrive.[5] The Kass criteria are still used for midstream voided specimens: the cut-off level for urine culture growth is 100,000 cfu/mL.[3,6,7]

Dipstick urine screening has been augmented with leukocyte esterase and nitrite tests available as part of a nine-test dipstick. Leukocytes can be detected by the action of esterase present in granulocytes and histiocytes, enabling the detection of even lysed leukocytes that may not be recognized on sediment microscopy. The leukocyte esterase strip test is able to detect 10 white blood cells (WBC)/μl by chamber counting, denoting sensitivity of 87.9% and 95.3%, respectively. Nitrite test is based on the ability of enteric Gram-negative bacteria to reduce dietary-derived nitrates to nitrites.[8] In a meta-analysis, the sensitivity of the urine dipstick test for leukocyte esterase was, in general, slightly higher than that of the dipstick test for nitrite (48% and 86%), respectively, while the specificity was slightly lower (17% and 93%), respectively. Sensitivity of the urine dipstick test for nitrite was low (45% and 60% in most situations) with higher levels of specificity (85% and 98%). The typically low pretest probabilities resulted in high predictive values of negative test results.[9] In addition, the finding of any bacteria on a urine dipstick specimen has a very high sensitivity and specificity for predicting a positive urine culture.[10] Urine dipstick test is a simple, effective method not requiring a laboratory centrifuge or culture media. As such, it is an ideal test for peripheral laboratories lacking in resources and facilities to deal with one of the most commonly received specimens.[11]

The aim of our study was to compare urine dipstick tests to urine culture tests for diagnosing UTIs.

Methods

We conducted a cross-sectional study to compare urine dipstick test to urine culture result as a diagnostic tool for UTIs. The study was conducted from May to June 2010 in H. Adam Malik Hospital, North Sumatera Province, in both outpatient and inpatient clinics.

We included 70 children aged 2 to 14 years who were suspected of having UTIs, with or without other diseases. We excluded patients who had received corticosteroids for at least three months prior to the study, took antibiotics less than 48 hours before urine collection, or incorrectly collected their urine specimen. All study procedures were explained to the subjects and their parents or guardians prior to the study. All subjects' parents/guardians provided informed consent. We collected data on subject characteristics and physical examination status, and we prepared two test tubes of urine with the participant's identity for each subject.

All participants underwent urine dipstick and urine culture tests. All urine specimens were midstream and collected without catheter. Midstream urine was collected into two test tubes after cleaning the perineum with soapy water or with an antibacterial skin cleansing agent. After collection, urine was sent to the lab for urine culture and urine dipstick tests. The specimens were transported to be examined as early as possible.

An aliquot of uncentrifuged urine was tested for the presence of leukocyte esterase and reducing nitrate with *Verify*® urinalysis reagent strips (Taiwan). Test results were considered to be positive if the dipstick turned purple (from trace to +2) for leukocyte esterase or pink or red for nitrites, within 2 minutes of the dipstick being in contact with the urine. *Verify*® urinalysis reagent strips contain reagent tests for determining pH, protein, glucose, ketones, blood, leukocyte esterase, nitrite, bilirubin, urobilinogen, and specific gravity. We evaluated only two parameters of the strips, namely, leukocyte esterase and nitrite. All urine dipstick tests were performed by the principal investigator. Urine culture procedures were done in the clinical pathology laboratory of H. Adam Malik

Hospital. MacConkey agar and blood agar were used for urine cultures.

This study was approved by the Research Ethics Committee of the University of Sumatera Utara, Indonesia, and appropriate follow-up was provided for all children with confirmed diagnoses.

Statistical analysis was performed using SPSS version 14.0. An association between urine dipstick and urine culture was investigated, with urine culture considered to be the gold standard. We calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of urine dipstick compared to urine culture tests.

Results

The 70 subjects were comprised of 30 boys and 40 girls, with a mean age of 6.5 (SD 3.95) years. Compared to nitrite, the sensitivity of leucocyte esterase was higher mean while the specificity was lower (**Table 2**). The number of positive cultures was 42, dominated by *E. coli* which account up to 57,1% (**Table 3**).

Table 1. Subjects' characteristics

Characteristics	n = 70
Gender, n (%)	
Male	30 (42.9)
Female	40 (57.1)
Mean age (SD), years	6.5 (3.95)

Discussion

In this study, more girls than boys were suspected of having UTIs. Our subjects' mean age was 6.5 (SD 3.95) years. The best epidemiologic studies, performed in Scandanavia, estimated a 1.7% cumulative risk of UTI for boys and 7.8% for girls prior to the age of 7 years, with the greatest risk during the first year of life for both boys and girls.[12-13] A study in New Delhi showed that all of 945 infants less than 1 year of age presenting with a temperature ≥ 38.5°C.[14] Another study found the risk of developing a symptomatic UTI before the age of 14 years to be 1-2% in boys and 3-8% in girls.[15]

Bacterial pathogens found in urine cultures in our study were Gram negative, including *Escherichia coli* (57.1%), followed by *Enterobacter aerogenes* (9.5%), *Enterobacter gerogates* (9.5%), *Klebsiella pneumonia* (7.1%), *Enterobacter* sp (4.8%) and *Pseudomonas* sp (4.8%). The Gram-positive bacteria *Staphylococcus aureus* and *Staphylococcus epidermidis* were also cultured from our subjects. *Escherichia coli* was the predominant pathogen of bacteremic Gram-negative UTIs, followed by *Klebsiella pneumoniae* and *P. mirabilis*. Similar results were found in a previous, population-based study of UTIs in North America.[16]

We used fresh, uncentrifuged urine as specimens. Dipsticks test may be used to test for a number of urinary constituents, two of which are helpful in the diagnosis of UTIs. The first is leukocyte esterase, produced by white blood cells. Its presence in the urine raises the suspicion of a UTI, but the test is often positive in the absence of a UTI. However, if it is negative, the chance is low of the patient having a UTI. The other useful test detects the presence of nitrites in the urine. Many urinary pathogens will convert nitrates in the urine to nitrites. As such, the presence of nitrites in the urine is highly suggestive

Table 2. Sensitivity and specificity of urine dipstick tests (leukocyte esterase, nitrite, combined leukocyte esterase and nitrite)

	Sensitivity (%)	Specificity (%)	PPV	NPV
Leukocyte esterase	90.5	39.3	69.1	73.3
Nitrite	73.8	60.7	73.8	60.7
Combined leukocyte esterase and nitrite	96.4	64.3	64.3	96.4

Table 3. Bacteria isolated from urine cultures

Bacteria isolated from urine cultures	n (%)
Enterobacter aerogenes	4 (9.5)
Enterobacter gerogates	4 (9.5)
Enterobacter sp	2 (4.8)
Escherichia coli	24 (57.1)
Klebsiella pneumoniae	3 (7.1)
Pseudomonas sp	2 (4.8)
Staphylococcus aureus	2 (4.8)
Staphylococcus epidermidis	1 (2.4)
Total	42 (100)

of infection (false positive rate of only 2%). However, some pathogens do not induce this reaction. Also, the urine needs to have been in the bladder for a few hours for the reaction to be complete.[17]

The urine specimens in our study were from toilet-trained children and were collected midstream, after we cleaned their genitalia. A randomized trial study found that urine contamination rates were higher in midstream urine collected from toilet-trained children who did not clean the perineal/genital area. Cleaning may reduce the need to return for repeat cultures, or for receiving unnecessary antibiotic treatment and lab tests.[18]

We found that the sensitivity of leukocyte esterase test was 90.5% while that of nitrite was 73.8% for positive cultures. However, the sensitivity for combined leukocyte esterase and nitrite tests was 96.4%. Nitrite test was more specific at 60.7% than the leukocyte esterase test at 39.3%. Both tests taken together had a specificity of 64.3%. The PPVs were 69.1% for leukocyte esterase, 73.8% for nitrite, and 64.3% for the combined tests. The NPVs were 73.3% for leukocyte esterase, 60.7% for nitrite, and, 96.4% for the combined tests. A previous cross-sectional study concluded that the urine dipstick had the highest sensitivity, specificity, PPV, and NPV, and recommended it as a rapid tool to rule out a UTI diagnosis in both clinical and laboratory settings.[19]

A Turkish study of 100 children reported the sensitivity and specificity of overall urinalysis (leukocyte esterase and nitrite) to be 74% and 3.5%, respectively.[20] A review in 2000 showed that the sensitivity and specificity of the dipstick test (leukocyte esterase and nitrite) were 88% and 93%, respectively, but those of leukocyte esterase only were 83% and 84%, respectively, and those of nitrite only were 50% and 98%, respectively.[21]

Another study of 92 children in Japan showed that the combined tests (leukocyte esterase and nitrite) had a sensitivity and NPV of 100%.[22] The leukocyte esterase test, however, showed lower specificity. Sensitivity of the combined leukocyte esterase and nitrite test when either of them were positive, was consistent with the results of studies conducted in Wilmington and Pennsylvania, but their results showed comparatively lower specificity. The PPVs of the leukocyte esterase test and nitrite test were high either alone or combined.[23-24] An Amsterdam study reported that 100% PPV for the combined positive results tested in children with acute abdominal pain.[25] A study in Boston also showed a high PPV (87.2%) for the combined test in febrile newborn babies and infants.[26]

A limitation of our study was that we do not know if the lab tests were conducted in a prompt manner in the laboratory, after the specimens arrived. Lab tests should not be delayed in order to avoid contamination.

In conclusion, urine dipstick test using a combination of leukocyte esterase and nitrite tests is a good alternative to urine cultures as a diagnostic tool for UTIs in children in areas with limited resources. Also, the combination of the two tests shows better sensitivity and specificity than either test alone.

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