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Evaluation of the accuracy of leukocyte esterase testing to detect pyuria in young febrile children: prospective study

白血球脂酶測試對發現發燒病童膿尿的精度評價：預期研究

Objective. To study the accuracy and clinical application of the dipstick leukocyte esterase test in the detection of pyuria in young febrile children suspected to have urinary tract infection.

Design. Prospective study.

Setting. Regional hospital, Hong Kong.

Patients. Urine samples were taken from 215 children younger than 2 years who were suspected to have urinary tract infection (fever without an obvious focus of infection).

Main outcome measures. The accuracy of the dipstick leukocyte esterase test in detecting significant pyuria defined as a leukocyte count $\geq 10 \text{ mm}^3$ ($\geq 0.01 \times 10^9 / \text{L}$).

Results. Two hundred and fifty-four urine samples collected by bag, mid-stream clean-catch, suprapubic bladder aspiration, or urethral catheterization were examined. Using urine microscopy results as a reference, the sensitivity and specificity of the leukocyte esterase test in detecting significant pyuria were found to be 72.0% and 85.8%, respectively; the positive and negative predictive values were 55.4% and 92.6%, respectively; and the positive and negative likelihood ratios were 5.1 and 0.3, respectively.

Conclusions. The dipstick leukocyte esterase test cannot accurately detect pyuria in young febrile children. It is also not appropriate as a screening test to exclude pyuria, reduce the need for the microscopic examination of urine, or indicate when a hospital admission for probable urinary tract infection is needed.

目的：研究檢驗片白血球脂酶測試對發現被懷疑患有尿道感染的發燒病童的膿尿的精度和臨床應用。

設計：預期研究。

安排：香港；地區醫院。

患者：尿液樣本取自215名年齡小於2歲，被懷疑患有尿道感染的病童(無明顯感染病灶的發燒)。

主要結果測量：檢驗片白血球脂酶測試在發現以白血球數 $\geq 10 \text{ mm}^3$ ($\geq 0.01 \times 10^9 / \text{L}$) 定義之顯著膿尿的精度。

結果：檢查了由袋收集，取中流清白部份，恥骨弓上的囊抽吸，或導管插入尿道獲取的254個尿液樣本。使用尿顯微鏡結果作參考，檢驗片白血球脂酶測試在發現顯著膿尿的靈敏度和專一性分別為72.0%和85.8%，陽性和陰性預測分別為55.4%和92.6%，陽性和陰性可能性比分別為5.1和0.3。

結論：檢驗片白血球脂酶測試不能精確地發現發燒病童中的膿尿，它也不適合作為普查檢測以排除膿尿、減少顯微鏡查尿的需要，也不能作為疑有尿道感染而需入院治療的依據。

Key words:

Child;
Pyuria/diagnosis;
Reagent strips;
Sensitivity and specificity;
Urinalysis;
Urinary tract infections

關鍵詞：

兒童；
膿尿／診斷；
試劑條；
靈敏度和專一性；
尿分析；
尿道感染

HKMJ 2001;7:5-8

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Introduction

Urinary tract infection (UTI) is the most common serious bacterial infection found in febrile young children, with a reported prevalence of 4.1% to 7.5%.¹⁻⁴ A presumptive diagnosis of UTI is often made on the basis of the clinical presentation and the presence of pyuria. To diagnose UTI in young children, a quantitative urine culture of a sample obtained by suprapubic tap or catheterization should be completed.⁵ The detection of pyuria can assist in selecting appropriate patients for proper urine culture, thus reducing unnecessary invasive procedures.

Microscopic examination of urine is the standard method used to detect pyuria. However, the dipstick test to measure urinary leukocyte esterase (LE) activity is quick, inexpensive, and does not require technical expertise. This test is commonly used to identify pyuria in accident and emergency departments and in out-patient clinics in which a urine microscopy service is not available. Studies have investigated the efficacy of the dipstick LE test in detecting pyuria in adults.⁶⁻¹⁰ The sensitivity of the test ranges from 78.0% to 99.3% whereas the specificity of the test ranges from 69.0% to 99.3%.¹¹ Studies of children have suggested that dipstick tests (the LE test with or without the nitrite test) are as accurate as microscopic examination in predicting bacteriuria.¹²⁻¹⁵ The accuracy of using the dipstick LE test to detect pyuria in children, however, remains uncertain.

The dipstick LE test is seldom used in the Department of Paediatrics at the Pamela Youde Nethersole Eastern Hospital. Referrals of children with suspected UTI are often received from accident and emergency departments based on a positive result from the dipstick LE test alone. Pyuria or UTI is subsequently diagnosed in only a few such patients. This prospective study aimed to determine the accuracy of the dipstick LE test and its usefulness as a screening test for pyuria. The study was confined to children younger than 2 years—the age-group at the greatest risk of renal scarring resulting from UTI.

Methods

Specimen collection

Urine specimens were obtained from children younger than 2 years who presented to the paediatric department of the Pamela Youde Nethersole Eastern Hospital from July 1998 through October 1998 for in-patient care because of suspected UTI (fever without an obvious focus of infection). The method of urine collection was decided by the paediatrician managing the patient's

care: by bag collection, midstream clean-catch, suprapubic bladder aspiration, or urethral catheterization. For most patients, urine was first collected non-invasively. Urine cultures obtained by suprapubic aspiration or catheterization were performed for those patients with a higher likelihood of having a UTI (positive for pyuria by microscopic examination of urine) or for those undergoing a full work-up.

Examination of urine

Urine specimens were examined within 1 hour of collection by dipstick LE testing and by light microscopy.

Dipstick analysis

Dipstick analysis is a semi-quantitative test that detects neutrophil-specific esterase activity by the conversion of indoxyl carboxylic acid ester in the reagent strip into an indoxyl moiety, which then reacts with a diazonium salt to produce a violet pigment. The Ecur-Test reagent strip (Boehringer Mannheim, UK Limited) was used in this study.⁴ Nurses performed the test according to the manufacturer's instructions, without knowing the result of the microscopic examination. A leukocyte count of 10-25 mm³ (0.01 to 0.025 x 10⁹ /L) or higher was considered a positive result.

Microscopic examination

Using the Fuchs-Rosenthal cell counting chamber, uncentrifuged urine from the same urine sample was examined under the light microscope by the doctor on call, who was not aware of the dipstick LE test result. A leukocyte count of ≥ 10 mm³ ($\geq 0.01 \times 10^9$ /L) was taken to be a positive result.

Statistical analysis

Using results from the microscopic examination as a reference, the sensitivity and specificity of the dipstick LE test, positive and negative predictive values, and likelihood ratios were calculated.

Results

During the study period, 296 urine specimens were examined microscopically. All but 42 specimens were tested with the dipstick LE test. The results of microscopic examination and the dipstick LE test were compared in 254 urine specimens from 215 patients. The urine collection methods were as follows: 204 were obtained by bag collection, 12 by midstream clean-catch, 17 by suprapubic bladder aspiration, and 21 by urethral catheterization.

The dipstick LE test and microscopic examination results are shown in the Table. The dipstick LE test

Table. Urine test results*

Leukocyte esterase test	Microscopic examination		Total
	Positive	Negative	
Positive	36	29	65
Negative	14	175	189
Total	50	204	254

* Sensitivity = 36/50 (72.0%), specificity = 175/204 (85.8%); positive predictive value = 36/65 (55.4%); negative predictive value = 175/189 (92.6%); positive likelihood ratio = 36/50:29/204 (5.1); negative likelihood ratio = 14/50:175/204 (0.3)

had a sensitivity and specificity of detecting clinically significant pyuria of 72.0% and 85.8%, respectively. The positive and negative predictive values were 55.4% and 92.6%, respectively, and the positive and negative likelihood ratios were 5.1 and 0.3, respectively.

Twenty-six patients were subsequently shown to have a UTI based on a positive culture of urine that had been sampled by suprapubic tap or catheterization. Six (23%) of the 26 patients tested had negative results according to the dipstick LE test.

Discussion

The risk of renal damage from UTI is greatest in children younger than 2 years; thus, early diagnosis and prompt treatment are important. Studies of the dipstick LE test in adults⁶⁻¹⁰ have shown that the test is both sensitive and specific in detecting pyuria microscopically.¹¹ Only a limited number of studies in children have so far been reported.¹⁶⁻¹⁸ Hoberman and Wald¹⁸ have demonstrated that the dipstick LE test has a low sensitivity (52.9%) in detecting pyuria (as defined by a leukocyte count of $\geq 10 \text{ mm}^3$ [$\geq 1.0 \times 10^7$ /L]) in febrile children younger than 2 years. The difference between studies of adults and children might relate to the degree of pyuria, the enzyme content of immature leukocytes, or both. Hoberman and Wald¹⁸ calculated a positive predictive value for the dipstick LE test of 82.1%, but the specificity was not reported in their study.

In this study, the dipstick LE test was found to have a sensitivity of 72.0% and a specificity of 85.8% (Table). The positive and negative predictive values (55.4% and 92.6%, respectively) imply that using the dipstick LE test alone to detect pyuria would result in a large number of false-positive and some false-negative results. More invasive urine sampling procedures would consequently be performed unnecessarily, whereas some patients with pyuria and possible UTI would be overlooked. A further question that arises is whether the dipstick LE test could act as a screening test for

selecting urine samples for microscopy. The high negative predictive value (92.6%) appears favourable in this regard. Nevertheless, six (23%) of the 26 confirmed cases of UTI tested negative according to the dipstick LE test. If microscopic examination had not been performed, these six patients would not have been confirmed to have UTI. Hence, the dipstick LE test cannot be used reliably as a screening test in selecting urine samples for microscopic examination or bacterial culture.

Although this study was performed in children younger than 2 years who were admitted to hospital, it is reasonable to believe that findings will be similar for paediatric patients in emergency or out-patient settings. If the dipstick LE test is used widely in febrile children and a positive test is taken to indicate pyuria and probable UTI, many children would be admitted to hospital unnecessarily.

Conclusion

The dipstick LE test is not an accurate method of detecting pyuria in young febrile children. Furthermore, it cannot be used as a screening test to exclude pyuria because, although it would reduce the number of microscopic examinations needed, this reduction would be at the expense of failing to diagnose UTI in some patients. The widespread use of dipstick LE testing for the screening or diagnosis of suspected UTI in young children is not supported by the findings of this study. Using a positive dipstick LE test result as an indication of pyuria and probable UTI in accident and emergency departments appears to result in unnecessary hospital admissions.

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