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Evaluation of the Nitrite Test in Screening for Urinary Tract Infection in Febrile Children with Sickle Cell Anaemia

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Summary

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Background: Urinary tract infection (UTI) is a significant cause of morbidity in children and individuals with sickle cell anaemia (SCA) have been reported to be at increased risk. It will be useful to have a simple means of screening such children for UTI with a view to instituting prompt treatment.

Objectives: The objective of the study was to evaluate the usefulness of the nitrite test in detecting UTI in febrile SCA children.

Methods: This prospective study was carried out in the department of Paediatrics, University College Hospital, Ibadan. The study group consisted of 171 children aged one to 15 years with SCA presenting with fever (temperature e" 37.5°C). Midstream urine specimen was collected from each patient and subjected to nitrite test, microscopy, culture and sensitivity.

Results: There was significant bacteriuria in 37 (21.6 percent) children. A positive test for nitrite was obtained in the urine of eight patients, seven of whom had bacteriuria. The nitrite test in detecting bacteriuria had a specificity of 99.2 percent, a sensitivity of 18.9 percent, a positive predictive value of 87.5 percent and a negative predictive value of 81.6 percent. A positive nitrite test was significantly associated with bacteriuria, while a negative test was also significantly associated with an absence of bacteriuria.

Conclusion: The nitrite test is useful as a screening test for UTI in SCA children. However, in sick children, urine microscopy and culture should still be done in spite of a negative test.

Introduction

URINARY tract infection (UTI) is a significant cause of morbidity in children[1] and individuals with sickle cell disease have been reported to be at increased risk.[2,3] The diagnosis of UTI in children is often missed due to the fact that the clinical features are seldom overt and in many cases, not referable to the urinary tract.[1] This problem may be compounded in children with sickle cell anaemia (SCA) in whom it may be difficult to differentiate UTI from abdominal painful crises. It would therefore be useful to have a simple means of screening such children for UTI with a view to instituting prompt treatment. This study was designed to evaluate the usefulness of the nitrite test in detecting UTI in febrile SCA children.

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Subjects and Methods

This prospective study was carried out in the Department of Paediatrics, University College Hospital Ibadan, from March 1999 to February 2000. The study group consisted of 171 children aged one to 15 years with sickle cell anaemia (homozygous haemoglobin S) presenting with fever (temperature $\geq 37.5^{0}$C).[4] Haemoglobin electrophoresis was carried out on all the patients using cellulose acetate strips at pH of 8.9 in the haematology laboratory of the hospital.[5] Children with a history of recent or current antibiotic or urinary antiseptic usage were excluded from the study. Ethical clearance was obtained from the Joint University of Ibadan and University College Hospital Ethical

Committee. Informed verbal consent was obtained from the parents or guardians of the children studied.

Midstream urine specimen was carefully collected at the time of presentation into two sterile universal containers for each patient and one sample immediately used for dipstick urinalysis using *Multistix 10SG (Bayer Corporation USA)* and the nitrite test performed according to the manufacturer's instruction. The other sample was received into a container with boric acid crystals such that when urine was added, there was a final concentration of 1.8 percent boric acid;[6] this was also processed immediately for microscopy and culture. Ten millilitres of urine was centrifuged at 2000 rpm for five minutes and a wet preparation made from the sediment and examined under the 40x objective of a microscope.[7,8] Greater than five pus cells per high power field (HPF) was regarded as significant pyuria.[9] Each urine specimen was well mixed, and inoculated into blood and MacConkey agar plates (using standard wire loop) and incubated aerobically at 37°C.[10] A pure colony count of e"10^5 organisms/ml of urine was considered a significant growth.[11] In cases of significant bacteriuria, systematic bacteriology and biochemical tests using standard techniques were carried out to identify the organism.[7]

All data were entered into Epi Info version 6 and analyzed. The sensitivity, specificity and predictive values of the nitrite test and pyuria in detecting bacteriuria were calculated.[12] Associations were tested using the Fisher exact test, while statistical significance was set at $p < 0.05$.

Results

There were 92 males and 79 females with a mean age (standard deviation) of 7.2 (3.7) years. Their temperatures ranged from 37.5 – 40.6°C with a mean (standard deviation) of 38.1(0.6) °C. There was significant bacteriuria in 37 (21.6 percent) specimens. Of these positive cultures, 24 grew *Escherichia coli*, seven grew *Klebsiella species*, two grew *Pseudomonas species* and the remaining four grew *Staphylococcus aureus, Salmonella, non-haemolytic Streptococcus* and *â-haemolytic Streptococcus,* respectively.

The urine white blood cell (WBC) counts ranged from 1 to 100 cells per high power field (HPF) with a median of 3.0. Pyuria was significant in 21 children and insignificant in the remaining 150 children. Among the children with significant pyuria, nine (42.9 percent) had significant bacteriuria whereas among those without significant pyuria only 28 (18.7 percent) had significant bacteriuria (Table I). Thus, pyuria was associated with increased risk of bacteriuria with an odds ratio of 3.27, (1.09<OR<9.35, Fisher exact 2-tailed p value 0.021). The sensitivity of pyuria in detecting bacteriuria among the patients was 24.3 percent, the specificity was 91.0 percent, the positive predictive value was 42.9 percent and the negative predictive value was 81.3 percent.

Table I

Significant Pyuria compared with Culture Results

Pyuria	*No. with Bacteriuria (%)*	*No. without Bacteriuria (%)*
Positive (n=21)	9 (42.9)	12 (57.1)
Negative (n=150)	28 (18.7)	122 (81.3)

A positive test for nitrite was obtained in urine specimens of eight (4.7 percent) children out of whom seven had bacteriuria (Table II). Thus, the nitrite test in detecting bacteriuria had a specificity of 99.2 percent, a sensitivity of 18.9 percent, a positive predictive value of 87.5 percent and a negative predictive value of 81.6 percent. A positive nitrite test was significantly associated with bacteriuria and a negative test also significantly associated with an absence of bacteriuria (Fisher exact 2-tailed p-value <0.001).

Table II

Nitrite Test compared with Culture Results

Nitrite test	*Positive Culture (%)*	*Negative Culture (%)*
Positive (n=8)	7 (87.5)	1 (12.5)
Negative (n=163)	30 (18.4)	133 (81.6)

Discussion

The nitrite test is based on the ability of most urinary pathogens to reduce nitrate to nitrite. The reduction is time dependent and a positive test requires a long bladder time, preferably > 4 hours, or significant residual urine.[13] The 18.9 percent sensitivity of the nitrite test in this study is lower than that reported by some workers. While Wammanda *et al* [14] reported a sensitivity of 28.9 percent and Goldsmith and Campos[15] a sensitivity of 29 percent, others have reported values of up to 60 percent.[16] The low value observed in the present study might be due to the fact that many of the specimens were collected at random in the clinic. Many of the children had most probably received increased fluid started by their parents at home because of its usefulness in managing painful crises of sickle cell disease. This is the usual practice of mothers whose children attend the clinic at the onset of each episode of crisis or acute illness before bringing their

children to the clinic. This increase in fluid intake may result in diuresis and a relative urinary frequency and therefore shortening of urine bladder time. This has the potential of producing false negative results and so reduce the sensitivity of the test.

The high specificity of the test observed in the present study is in keeping with findings by other workers. Cannon *et al*[7] reported a specificity of 99 percent while that in the report by Munyin *et al*[16] was 97.7 percent. The high negative predictive value observed in this study is also in keeping with the observation by workers such as Wammanda *et al*[14] who reported a negative predictive value of 80.8 percent. The high specificity and negative predictive value of the nitrite test are of great value as a screening test for UTI. The high positive predictive value of the nitrite test (87.5 percent) in detecting bacteriuria observed in this study is also in keeping with findings by others.[14, 16]

In the present study, pyuria had a higher sensitivity than the nitrite test in detecting bacteriuria. This corroborates findings by other workers who used e"5 WBC/HPF as their definition of significant pyuria. Munyin *et al*[16] reported 80 percent sensitivity for pyuria and 60 percent for the nitrite test while the corresponding values reported by Goldsmith and Campos[15] were 82 percent and 29 percent, respectively. However, in support of the findings of Munyin *et al*,[16] the positive predictive value of the nitrite test in detecting bacteriuria in the present study was higher than that of pyuria.

The high positive predictive value, negative predictive value and specificity in the present study support the usefulness of the nitrite test as a screening test for UTI even when random urine specimens are used. Many health centres where children with SCA are seen do not have facilities for urinalysis and culture. However, the dipstick is easily performed with accurate results recorded by personnel after minimal training. The cost of the single test strip is also a fraction of the cost of urinalysis and culture. Widespread use of the test may therefore, help to identify more febrile children with UTI who should then be appropriately managed. We recommend that patients who test positive should be commenced on empiric antibiotic therapy after urine specimen has been sent for microscopy, culture and sensitivity. The low sensitivity of the test in the present study and that in a previous Nigerian-based study[14] suggest that many cases of UTI may be missed in children if the examination of the urine is limited by the outcome of the nitrite test. Therefore in sick children, urine microscopy, culture and sensitivity should still be done despite a negative nitrite test. The decision whether or not to commence empiric antibiotic should be based on a careful review of the overall clinical condition of the patient.

In spite of the shortcoming already mentioned, this test still has some merit if used as a screening tool in children with SCA. A positive test not only strengthens the need for immediate commencement of antibiotics, it also guides the clinician to prescribe an antimicrobial to which the common urinary pathogens in the environment are known to be sensitive. In addition, the rate of indiscriminate prescription of broad-spectrum antibiotics will be reduced. Furthermore, it might help in differentiating a UTI from an abdominal painful crisis in these children and thereby, facilitate early commencement of therapy.

Since early detection of UTI and prompt institution of appropriate therapy is important in reducing the risk of sequelae of UTI such as renal scars and hypertension, we recommend the use of the nitrite test as a screening tool during febrile illnesses in children with SCA. Collection of urine specimen after a longer bladder time when feasible, may increase the sensitivity of the test in children who are able to co-operate.

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