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ORIGINAL ARTICLE

Evaluation of The Nitrite Test in Screening for Urinary Tract Infection in Febrile Children with Sickle Cell Anaemia in Maiduguri- Nigeria

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ABSTRACT

Background: Urinary tract infection is a significant cause of morbidity in children with sickle cell anaemia (SCA). Individuals with SCA have increased risk of urinary tract infection (UTI). Facilities for urine culture may not be available in most rural and even some urban areas in most developing countries like Nigeria. It will therefore be useful to have a simple means of screening such children for UTI with the intent of prompt treatment. **Materials and Methods:** The study will evaluate the usefulness of the nitrite test in detecting UTI in febrile SCA children. This study was carried out in the Department of Paediatrics University of Maiduguri Teaching Hospital and State Specialist Hospital Maiduguri. **Results:** The study consisted of 250 children aged 6 months to 15 years with SCA presenting with fever (temperature ≥37. 5°C). Midstream urine specimen was collected from older children and suprapubic bladder aspiration of urine specimen was collected from infants. Samples were subjected to nitrite test, culture and sensitivity.

There was significant bacteriuria in 65 (26%) children with SCA. A positive test for nitrite was obtained in 43 of the 65 (66.2%) children. The nitrite test has a specificity of 93.5% in detecting bacteriuria, a sensitivity of 66.2%, a positive predictive value of 78.2% and a negative predictive value of 93.5%. A positive nitrite test was significantly associated with bacteriuria, while a negative test was also significantly associated with an absence of bacteriuria. **Conclusions:** From this study, the nitrite test is useful as a screening test for UTI in SCA children. However in sick children with SCA, microscopy, culture and sensitivity should still be done in spite of a negative nitrite test.

Key words: Nitrite, Screening,Urinary tract infection.

INTRODUCTION

Urinary tract infection (UTI) is a significant cause of morbidity in children[1] and children with sickle cell disease have been reported to be at increased risk.[2, 3] The diagnosis of UTI is often missed due to the fact that the clinical features usually are not overt and in many presentation symptoms and or signs are 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 of use to have a simple means of screening such children for UTI with a view to instituting prompt treatment. This study was therefore designed to evaluate, the usefulness of nitrite test in detecting UTI in febrile children with SCA.

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SUBJECTS AND METHODS

This prospective study was carried out in the Department of Paediatrics University Teaching Hospital Maiduguri (UMTH) and State Specialist Hospital (SSH) Maiduguri, from Oct. 2005 to Jan 2008. The study group constituted of 250 children aged 6 months to 15 years with SCA (HbSS) with fever (temperature ≥37. 5°C) [4]. Haemoglobin electrophoresis was done in all the patients using cellulose acetate electrophoresis at pH 8.9, in the haematology laboratory of the teaching hospital. Children with history of antibiotic use less than 7 days before presentation and children with conditions

associated with increased risk of UTI, [5, 6] were excluded. Also excluded were children with non infective cause of fever such as children with tetanus and dehydrated children. Ethical clearance was obtained from the Ethics Committee of (UMTH). Informed consent was obtained from parents or guardians of all children recruited in study.

The subjects were recruited from the out patient consultant clinics of UMTH and SCA clinic at the State Specialist Hospital or on admission in the emergency paediatric unit of both hospitals. Midstream urine specimen was carefully collected at the time of presentation into two sterile universal bottles for each patient and one sample immediately used for dipstick urinalysis using the multistix 10 SG (Bayer corporation USA) and the nitrite test performed according to the manufacturer's instruction. The other sample was send immediately to microbiology department of the UMTH. The specimen taken at the state specialist hospital was kept in a refrigerator at 4°C for period of the clinic (2- 3 hours) before being taken to UMTH, which is about 10 – 20 minutes drive, where it was processed immediately for microcopy and culture. Each urine specimen was mixed, inoculated onto blood and MacConkey agar plates and incubated aerobically at 37°C.[7] A pure colony count of 10^5 organisms / ml of urine was considered a significant growth.[8] In case of significant bacteriuria; systematic bacteriology and biochemical tests using standard techniques were carried out to identify the organism .[7]

All data were entered onto IBM /PC/AT computer using SPSS version 13 software and analyzed. Indices to determine the diagnostic usefulness of nitrite test in detecting significant bacteriuria were calculated separately using the methods of Galen and Gambino [9]. Statistical difference at the 5% level (i.e $P < 0.05$) was regarded as significant.

RESULTS

A total of 250 febrile children were studied. The mean age was 5.6 ± 4.4 years with age ranged from 6 months to 15 years. There were 145 boys and 105 girls giving a male: female ratio of 1.4:1. All subjects had fever ranging from 37.8°C to 42°C. The mean, median and mode of axillary temperature of the studied population were 38.6°C, 38°C and 38°C respectively.

Table1: Shows the bacterial isolates from the urine culture of febrile children with SCA. The most frequently isolated organism was *Escherichia coli* 18 (27.7%); *Klebsiella spp* was second commonest 16 (24.6%). The least were *Coliform* (13.8%) and *Salmonella spp* (3.1%).

Table 2: Shows the age and sex distribution of the febrile SCA children is shown, 28 (19.3%) boys with SCA had bacteriuria, whereas 37 (35.2%) girls with SCA had bacteriuria. Bacteriuria was more common among female with SCA in all age groups as seen in the table below. The overall differences between female and male with significant bacteriuria were statistically significant with $\chi^2 = 7.957$, p-value 0.005.

Table 1: Bacterial isolates from urine of febrile SCA children

Organism	n (%)
E.coli	18 (27.7)
Klebsiella	16 (24.7)
Proteus	11 (17.0)
Staphylococcus aureus	9 (13.8)
Coliforms	9 (13. 8)
Salmonella	2 (3.1)
Total	**65 (100)**

Table 2: Age and sex distribution of 65 SCA children with bacteriuria.

Age range (years)	*Male n (%)*	*Female n (%)*	χ^2	p-value
0.5 - 5	16 (11.1)	19 (18.1)	3.011	0.083
6 – 10	6 (4.1)	9 (8.6)	2.888	0.089
11 - 15	6 (4.1)	9 (8.6)	2.223	0.136
Total	**28 (19.3)**	**37 (35.2)**	**7.957**	**0.005**

Note; The denominator for these % are total numbers of SCA studied (250). The denominator for males is therefore the total numbers of males (145) and for females (105).

Table 3: Comparison of results of nitrite test and urine culture in SCA.

Nitrite test	*Significant bacteriuria n (%)*	*No significant bacteriuria n (%)*	Total n (%)
Positive	43 (66.2)	12 (6.5)	55 (22.0)
Negative	22 (33.8)	173 (93.5)	195 (78.0)
Total	**65 (100)**	**185(100)**	**250 (100)**

Sensitivity of nitrite test in detecting bacteriuria = 66.2%
Specificity = 93.5% Positive predictive value (PPV) = 78.2%
Negative predictive value (NPV) = 88.7% Efficiency of the test = 86.4%

Table 3: Shows nitrite test was positive in 66.2% (43 of the 65) of study group who had significant bacteriuria and negative in 93.5% without bacteriuria. The nitrite test has sensitivity of 66.2% and specificity of 93.5% in detecting significant bacteriuria. The positive predictive value of nitrite test in detecting bacteriuria was 78.2% and the negative predictive value was 88.7% and the efficiency of the test was 86.4%.

DISCUSSION

The nitrite test is based on the ability of the urinary pathogens to reduce nitrate to nitrite. The reduction is time dependent and a positive test requires a prolonged bladder incubation time preferably > 4 hours, of significant residual urine[10]. The sensitivity of 66.2% found in this study is higher than that reported by some workers; While Wammanda et al[11] reported a sensitivity of 28.9% and Brown et al[12] reported 18.9% sensitivity of nitrite test. Goldsmith and Campos[13] reported a sensitivity of 29%. Others have reported values as in the current study, up to 60%.The high sensitivity of the test may be explained by the fact that Gram negatives which predominates compare to Gram positive, are actually the ones that can reduce nitrate to nitrite; therefore the findings of significant *E. coli* and *klebsiella spp* in the current study might have increased the sensitivity of the test. Non of the patient in this study was given water to encourage urine production, because such has lead to low sensitivity of the nitrite test because the Gram negative organisms needed at least 4 hours in the bladder for them to be able to reduces dietary nitrate to nitrite. Giving water induces diuresis and relatively increases the urinary frequency and therefore shortening, the urine bladder time.

The high specificity 93.5% of nitrite test in the present study is in keeping with findings by other workers. Connon et al[14] reported a specificity of 99%, while Munyin et al [15] reported 97.7%. The high positive pedictive value of 78.2% observed in this study is also in keeping with the observation by workers such as Wammanda et al [11] who reported value of 80.8%. The high specificity and predictive value of nitrite test are of great value as a screening test for UTI.

The high sensitivity, positive predictive value and high specificity in the present study support the usefulness of the nitrite test as a screening tool for UTI even when random urine specimen are used. Many health centres where children with SCA are seen may not have facilities for urinalysis and cultures. However the dipstick is easily performed with accurate result and the personnel needed only minimal training. The cost of a single test strip is also a fraction of the cost of 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 patient who test positive with nitrite test should be commenced on empirical antibiotic after urine specimen has been sent for microscopy, culture and sensitivity. Urinary tract infection may be missed in some children if the examination is limited to this simple test alone. Therefore in sick children, urine microscopy culture and sensitivity should still be done if facilities are available despite a negative nitrite test. The decision whether or not to commence empirical antibiotic should in this case be based on review of history and condition of the patient. Since children with SCA do frequently have abdominal pain crises this test might help in differentiating a UTI from abdominal painful crisis, thereby facilitating early commencement of therapy.

Early detection of UTI and prompt appropriate treatment is very important in reducing the risk and sequel of UTI we recommend the use of nitrite test as a screening tool during febrile illnesses in children with SCA. Also collection of urine after prolong bladder incubation time when feasible will increase the sensitivity of the test in children who can cooperate.

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