Accuracy of a new clean-catch technique for diagnosis of urinary tract infection in infants younger than 90 days of age

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OBJECTIVE: To evaluate the accuracy of diagnosing urinary tract infections using a new, recently described, standardized clean-catch collection technique.
METHODS: Cross-sectional study of infants <90 days old admitted due to fever without a source, with two matched samples of urine obtained using two different methods: clean-catch standardized stimulation technique and bladder catheterization.
RESULTS: Sixty paired urine cultures were obtained. The median age was 44-days-old. Seventeen percent were male infants. Clean-catch technique sensitivity was 97% (95% CI 82% to 100%) and specificity was 89% (95% CI 65% to 98%). The contamination rate of clean-catch samples was lower (5%) than the contamination rate of catheter specimens (8%).
CONCLUSIONS: The sensitivity and specificity of urine cultures obtained using the clean-catch method through the new technique were accurate and the contamination rate was low. These results suggest that this technique is a valuable, alternative method for urinary tract infection diagnosis.

Key Words: *Bladder stimulation; Catheterization; Clean-catch; Urine sample; Urinary tract infections*

La précision d'une nouvelle technique de prélèvement d'urine propre pour diagnostiquer les infections urinaires chez des nourrissons de moins de 90 jours

OBJECTIF : Évaluer l'exactitude des diagnostics d'infection urinaire au moyen d'une technique de prélèvement d'urine propre standardisée décrite récemment.
MÉTHODOLOGIE : Étude transversale de nourrissons de moins de 90 jours hospitalisés à cause d'une fièvre sans source connue disposant de deux prélèvements d'urine appariés obtenus par deux méthodes différentes : la technique de prélèvement d'urine propre par stimulation standardisée et le cathétérisme vésical.
RÉSULTATS : Les chercheurs ont obtenu 60 prélèvements d'urine appariés. Les nourrissons avaient un âge médian de 44 jours, et 17 % étaient de sexe masculin. La sensibilité de la technique par prélèvement d'urine propre s'élevait à 97 % (95 % IC 82 % à 100 %) et sa spécificité, à 89 % (95 % IC 65 % à 98 %). Le taux de contamination des prélèvements d'urine propre était plus faible (5 %) que celui des prélèvements par cathétérisme (8 %).
CONCLUSIONS : La sensibilité et la spécificité des cultures d'urine prélevées au moyen de la nouvelle technique de prélèvement d'urine propre étaient précises, et le taux de contamination, faible. Selon ces résultats, cette technique est une solution précieuse pour diagnostiquer les infections urinaires.

Urinary tract infections (UTIs) are the most common cause of serious bacterial infections in febrile infants <90 days old (1). Diagnosis of a UTI requires the collection of urine. This is generally accomplished using one of four methods: urethral catheterization, supra-pubic aspiration, a urine bag or clean-catch technique (2). Both catheterization and suprapubic aspiration are believed to be the most reliable methods because they minimize false-positive results; however, these methods are invasive and uncomfortable for children. The urine bag is noninvasive and is an easy alternative but has been criticized because of high false-positive rates, prompting the American Academy of Paediatrics to discourage its use for urine cultures in infants (3).

Obtaining a clean-catch urine sample is the recommended method for urine collection in toilet-trained children. However, in children lacking sphincter control, urine catch is difficult and time-consuming. Therefore, invasive methods are commonly used (4,5).

The use of standardized stimulation techniques as described elsewhere by our group (6) can facilitate and shorten the time for sample collection. Data comparing the yield of cultures obtained using catheterization and clean-catch are limited (7). There is wide variability in false-positive and false-negative rates.

The aim of the present study was to compare the accuracy of clean-catch collection in infants using a standardized technique, with urine collected using catheterization used for UTI diagnosis.

METHODS

A cross-sectional study was designed to determine the validity of the urine culture collected using a safe new standardized clean-catch technique in infants with a suspected UTI. The technique consists of three steps: encouraging oral intake based on the age and weight of the patient, a genital cleaning protocol specific for children and stimulation of voiding (suprapubic and lumbosacral percussion) (6).

The present study was approved by the Ethics Board at La Paz University Hospital (Madrid, Spain) and the Research Committee at the Infanta Sofia University Hospital (Madrid, Spain). Data were collected from infants presenting to the emergency room from January 2011 to January 2013. Inclusion criteria were infants <90 days old admitted because of fever without a source, not fulfilling Rochester low-risk criteria (8). Fever was defined as an axillary temperature ≥38°C. Infants with matched urine cultures obtained using both methods (clean-catch with standardized-stimulation technique and catheterization collection) were recruited. The second sample was obtained using catheterization within 1 h. Criteria for exclusion were: informed consent not obtained, inability to obtain both samples of urine, poor feeding, hemodynamic instability, external genitalia or bladder malformation, and previous antibiotic treatment. Patients who fulfilled the inclusion criteria but did not complete the study were considered lost to follow-up.

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TABLE 1
Results of cultures obtained from both clean-catch and catheterization

		Culture result – catheterization		
		Positive	Negative	Total
Culture result – clean-catch	Positive	32	2	**34**
	Negative	1	17	**18**
Total		**33**	**19**	**52**

The urine was immediately sent to the laboratory in Vacuette and Vacuette urine culture (boric acid) tubes (Greiner Bio-One International, Austria). An initial analysis of all samples using Multistix colorimetric test strips (Siemens, Germany) for determination of nitrite and leukocyte esterase was performed. The dipstick test strip was considered positive if leukocyte esterase and/or nitrites were positive.

The urine was inoculated with 10 µL calibrated loop in parallel in myeloperoxidase chromogenic medium and cysteine lactose electrolyte-deficient medium (Becton, Dickinson and Company, USA). Samples were then incubated at an ambient air temperature of 37°C. Urine culture results were evaluated after 24 h. Samples without any growth or less than minimum colony counts were considered to be negative. The identification of bacteria growing in positive culture was based on biochemical reactions that were included in the database of the MicroScan WalkAway 96 commercial system (Siemens, Germany). The susceptibility pattern was performed using the same commercial system according to Clinical and Laboratory Standards Institute recommendations. When evaluation after 24 h of incubation was not clear, plates were checked again after 48 h.

Interpretation of culture results was undertaken independently and in a blinded fashion by a pool of technicians. Urine culture was considered to be positive if the presence of a pure growth was >10,000 colony forming units per mL (CFU/mL) in specimens obtained using catheterization, and >100,000 CFU/mL if the specimen was obtained using the clean-catch technique. Urine culture was considered to be negative if <1000 CFU/mL were obtained in a sample using catheterization or if <10,000 CFU/mL were obtained using the clean-catch technique (9,10). Intermediate counts with nitrite and/or leukocyte esterase in the urine were considered to be positive and those with neither were considered to be negative.

Urine culture was considered to be contaminated if it had mixed bacteria growth or growth of one or more nonpathogenic bacteria (organisms such as *Lactobacillus* species, coagulasa negative *Staphylococci* and *Corynebacterium* species), irrespective of the colony count. Subsequent patient management was performed according to current protocol at Infanta Sofía University Hospital.

SPSS version 18.0 (IBM Corporation, USA) was used to perform the data analysis. Catheterization was considered to be the gold standard for urine culture-collection techniques. Sensitivity, specificity, false positive, false negative and odds pretest values of clean-catch urine were calculated compared with the gold standard. Contaminated urine cultures were excluded for diagnostic accuracy but the percentage obtained using each method was reported.

RESULTS

There were 150 patients considered for the study, of whom 19 were excluded because parents did not provide consent. Sixty-three others were excluded because there was only one urine sample (35 underwent direct voiding only and 28 underwent catheterization only). Five patients were excluded for being on antibiotic treatment and three because of hemodynamic instability.

TABLE 2
Results of urinalysis

Collection technique; culture result	Leukocyte esterase positive	Nitrite positive
Catheter; positive (n=34)	30	8
Catheter; negative (n=21)	0	1
Clean-catch; positive (n=37)	32	9
Clean-catch; negative (n=20)	4	0

Data presented as n

One hundred twenty matched samples were obtained from the remaining 60 patients. Mean age was 44 days old and median age was 40 days old (range two to 90 days). Forty-two (70%) were male (all were uncircumcised).

The culture results from clean-catch samples included 37 positive (62%), 20 negative (33%) and three contaminated (5%). The results from catheterization samples included 34 positive (57%), 21 negative (35%) and five contaminated (8%). No intermediate counts were obtained in any of the samples. The clean-catch technique resulted in two false-positive (10%) and one false-negative (7%) culture corresponding to a sensitivity of 97% (95% CI 82% to 100%); specificity was 89% (95% CI 65% to 98%). The prevalence of UTIs in this population was 63% (95% CI 49% to 76%). Positive likelihood ratio was 9.21 (95% CI 2.48 to 34.22) if the clean-catch urine culture was positive. Negative likelihood ratio was 0.03 (95% CI 0.00 to 0.23). The post-test probability of having a UTI was 94% (95% CI 81% to 98%) if the clean-catch urine culture was positive. The results of both the clean-catch and catheterization cultures are summarized in Table 1. Table 2 shows the results of urinalysis excluding contaminated samples.

Clean-catch and catheterization yielded the same bacteria in 32 patients: *Escherichia coli* were isolated in 27 cultures, *Enterobacter cloacae* in two, *Enterococcus faecalis* in one, *Klebsiella pneumoniae* in one and *Serratia marcescens* in one. There were two positive cultures obtained using the clean-catch technique for *E coli* that were negative when obtained using catheterization. One positive culture for *E coli* using direct catheterization was negative for the clean-catch culture.

DISCUSSION

Fast and accurate diagnosis of UTIs is relevant in febrile infants (11). However, improperly collected specimens or incorrect interpretation of test results may contribute to under or overdiagnosis of UTI (12,13).

The present study analyzed the validity of urine cultures from samples obtained using the clean-catch method through a new, standardized, sequential technique in infants <90 days old. In our setting, catheterization collection is routinely used as the gold standard, with some concerns about the invasiveness of sample collection.

Few studies compare the clean-catch technique with other techniques. There are no published studies examining the accuracy of specimens obtained using standardized stimulation techniques to obtain clean-catch specimens.

In a small sample, Braude et al (7) compared samples collected using direct urination and bladder catheterization, without establishing a clear cut-off for positivity of urine culture, and reported 81% sensitivity and 86.7% specificity in children <5 years of age. Ramage et al (14) compared clean-catch technique and suprapubic tap in infants <24-months-old, using the same colony counts in the urine clean-catch collection that were used in the current study and obtained an 88.9% sensitivity and 95% specificity. A systematic review assessed the validity of urine obtained using clean voided

midstream urine compared with suprapubic aspiration in children <5 years of age, showing sensitivity between 71.4% and 100%, and specificity between 57% and 100% (5). Studies are highly heterogeneous because they include a wide spectrum of patients and little standardization in sample collection.

The present study adds a comparison of a new, easy technique for clean-catch samples, in a subset of patients not usually able to provide clean-voided, midstream urine with traditional bladder catheterization. The sample was very homogeneous. The results of the present study suggest that this technique has high sensitivity and specificity, confirmed by the concordance of bacterial isolates.

Some studies report a false-positive rate of 4% to 53% comparing clean-catch with invasive techniques (bladder catheterization or suprapubic aspiration) (12,15,16). Our data yielded two false positives (6%), using catheter-collected urine as the reference standard. One of these cases was a two-month-old infant who had irritability and hematuria. Urinalysis from directly voided urine showed pyuria and positive nitrites. The urine culture was positive with 100,000 CFU/mL of *E coli*. The catheter urine was negative on dipstick and in the culture. This entire clinical picture suggested that catheterization yielded a false-negative result, rather than that the clean-catch urine yielded a false-positive result.

In our study, there was only one (5%) false-negative culture . This is a smaller percentage than those reported by other authors (14).

Contamination may lead to unnecessary intervention or delay in diagnosis and treatment. In our study, the contamination rate in samples obtained using the clean-catch technique (5%) was lower than those obtained using catheterization (8%). Avoiding handling the urethra and the rapidity of obtaining the sample may favourably affect results. The contamination rate using the clean-catch technique appeared to be lower than those reported in medical literature, albeit the number of cases in the present study was limited. Karacan et al (17) analyzed the validity of four different methods for collecting urine (urethral catheterization, suprapubic aspiration, urine bag collection and clean-catch) in a sample of 1067 children zero to 16 years of age. The clean-catch and urethral catheterization specimens showed the same contamination rate (14.3%). In 2012, Tosif et al (18) reported 26% contamination with clean-catch urine. Altuntas et al (19), applying stimulation technique described by Herreros et al (6), obtained acontamination rate of 27.2%. The difference found in our results may be due to the inclusion of intermediate counts of contaminants in their study, while there were none in our study.

The present study had several limitations. The sample size was small, with more males than females. Ideally, clean-catch urine would have been compared with urine obtained using a suprapubic tap. Another limitation is that we only included children with a high index of suspicion for UTI. Further studies with paired analysis of urine samples in a large group of children <3 months of age with risk for UTIs may be able to address these limitations.

In conclusion, sensitivity and specificity of cultures from urine obtained using the clean-catch method through the new sequential technique were accurate and yielded low contamination rates. These results suggest that this noninvasive technique is a safe, valuable alternative method for the diagnosis of UTIs in infants <90 days old.

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