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EDITORIAL

Urinary tract infection: a prevalent problem in pediatrics☆

Infección del tracto urinario: un problema prevalente en pediatría

Urinary tract infections (UTI) frequently occur in children. The risk of developing renal scars associated with pyelonephritis has been widely described. The approach and management of children with febrile UTI have changed in recent years in the light of new evidence.[1]

The clinical signs of UTI are non-specific. Therefore, in infants or children with an unexplained fever, adequate urine samples should be taken for urinalysis and urine culture to confirm the diagnosis. New ways to practice urine cultures in midstream urine sample had been validated in newborns using the technique based on bladder and lumbar stimulation maneuvers, which has been proved effective and less invasive than suprapubic cystostomy and bladder catheterization.[2,3] Incorporating these procedures into clinical practice with the help of parents or health personnel helps the early diagnosis.

It has been shown that the delay in antibiotic treatment for UTI increases the risk of renal scarring.[4] If there is a high suspicion of urinary infection, it is recommended to start antibiotic therapy immediately after taking the sample for urine culture. The recommendation for empirical antibiotic treatment in children with urinary infection has changed a lot in recent years due to the patterns of bacterial resistance in different countries and hospitals.

In this issue of the *Boletín Médico del Hospital Infantil de México*, Garrido et al.[5] evaluated the antimicrobial resistance of *E. coli* in pediatric patients with urinary tract infection in a hospital in Quito, Ecuador. Of 132 patients with positive urine cultures, 59 patients with urinary tract infection due to *E. coli* were analyzed. The authors found resistance to different antibiotics: to ampicillin in 88% of hospitalized patients and 92% of outpatients; to trimethoprim in 61% of hospitalized patients and 84% of outpatients; and resistance to nalidixic acid in 68% of outpatients. Based on these results, Garrido et al. concluded that these three medications were not good options for empirical therapy in Quito. Additionally, they observed 16.95% of *E. coli* with resistance to extended-spectrum beta-lactamase antibiotics.

These data are similar to those reported in a study performed in Cali, Colombia,[6] where resistance to ampicillin was found in 79.7% and to trimethoprim in 52.8% of the studied patients. The current recommendation is to know the data of bacterial resistance in a specific region to define empirical therapy with a greater possibility of success.

It has been shown that oral therapy is equally effective compared to intravenous therapy.[1] Intravenous therapy is recommended in newborns, young infants, patients with evidence of urosepsis, patients without oral intake tolerance, dehydration, failure of the oral therapy or when social conditions do not guarantee the treatment. It is essential to adjust the empirical therapy once the results of the urine culture are met.

The presence of bacteria other than *E. coli*, such as *Klebsiella*, *Pseudomonas* and *Enterococcus*, is associated with an increased risk of nephrourological malformations, such as vesicoureteral reflux and obstructive uropathy.[7,8]

There is considerable controversy regarding when imaging studies should be performed in the follow-up of children with UTI, so many follow-up guidelines have been designed in different countries. The arguments in favor of imaging studies are that they allow the detection of nephrourological malformations and the reduction of chronic kidney disease. The arguments against are the expenses, radiation and unnecessary traumas. The point of equilibrium is found, possibly, in the selection of children with higher risk of nephrourological anomalies, which are the patients with pyelonephritis. In the acute phase of UTI, it is essential to define if it is a pyelonephritis. In addition to the clinical data, such as fever, chills and general malaise, the search for biomarkers that differentiate between patients with

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pyelonephritis and those with low UTI has been proposed. The two most evaluated biomarkers are C-reactive protein (CRP) and procalcitonin. In a meta-analysis[8] of children with first urinary infection follow-up for the determination of prognostic factors in dimercaptosuccinic acid (DMSA) renal scintigraphy, CRP > 40 mg/dl in the acute phase had an OR of 3.01 (1.97-4.57 CI 95%) to develop a renal scar.

Procalcitonin in the acute phase has been shown to be a useful marker of pyelonephritis. In a study of 100 children with urinary tract infection,[9] values above 4.4 ng/ml were correlated with documented pyelonephritis with changes in renal DMSA during infection; the values < 0.4 ng/ml discarded it. Procalcitonin sensitivity was of 83% and specificity of 93% (higher than the CRP).

Despite the prenatal screening with obstetric ultrasonography, UTI continues to be a warning signal that allows detecting patients with nephrourological malformations, which are grouped currently with the acronym CAKUT (*congenital anomalies of the kidney and urinary tract*). This is important because it has been shown that it is the first cause of chronic kidney disease in children.[10]

A 50-year retrospective study of 4,476 patients with UTI at the Medellin's San Vicente Hospital[7] showed that 75% of the patients had nephrourological malformations: vesicoureteral reflux (37%), hydronephrosis (24%), posterior urethral valves (13%), hypoplastic kidney (9%), neurogenic bladder (4%), and unilateral renal agenesis (3%). Patients without nephrourological abnormalities did not develop chronic kidney disease, while the 6% of patients with these abnormalities developed chronic kidney disease during the follow-up. When there is an accurate diagnosis of UTI, at least one renal and bladder ultrasound should be performed, independently of the child's age, to detect any CAKUT[7,8] and offer an adequate follow-up.

After the antibiotic treatment, predisposing factors (anatomical or risk habits) should be corrected to decrease reinfections. Management of constipation and adequate bladder function with a complete bladder fully emptying is fundamental to decrease recurrence.

With the current evidence about the few benefits of prophylaxis compared to the risks of bacterial resistance, their use should be limited to selected patients, such as vesicoureteral reflux grade III, IV and V, obstructive uropathies and severe prenatal hydronephrosis.[1] Currently, a strict monitoring attitude is promoted for new infections and adequate urine sampling when fever or urinary symptoms to start an early treatment.

Pyelonephritis can cause kidney scars, high blood pressure and chronic kidney disease; therefore, diagnosis and proper management are very important. Regional studies allow initiating empirical therapies with the greater possibility of therapeutic success. Renal and bladder ultrasound is essential in all pediatric patients with UTI to detect CAKUT and an increased risk of chronic kidney disease. Biomarkers such as CRP and procalcitonin in the acute phase of the infection allow selecting those patients with higher risk of developing long-term scars. Empirical therapy with antibiotics should be prescribed based on epidemiological studies of the region.

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Consuelo Restrepo de Rovetto
Nefróloga pediatra, Centro Médico Imbanaco, Cali, Colombia
E-mail address: consuelo.restrepo@imbanaco.com.co

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