



What is The Duration of Treatment for Urinary Tract Infection in A Newborn Baby, Can We Give Oral Treatment?

Yenidoğan Bebekte İdrar Yolu Enfeksiyonunda Tedavi Süresi Ne Kadardır, Oral Tedavi Verebilir miyiz?

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Question: What is the duration of treatment for urinary tract infection in a newborn baby, can we give oral treatment? Some sources suggest a treatment period of 7-10 days and that oral treatment can be given. What is the appropriate approach in this manner? **Eda Çelik, MD.**

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Introduction and general information: Urinary tract infections (UTIs) are common in newborns and any type of neonatal urinary tract infection (NUTI) is considered as upper UTI [acute pyelonephritis (APN)] in principle. It has been reported that UTI is detected in approximately 10-20% of febrile young infants under three months of age (1). In NUTI, sepsis may accompany much more frequently than in other age groups or neonatal sepsis may lead to APN by via hematogenous route. Approach to APN in the newborn, evaluation and laboratory approach generally follow the principles of neonatal sepsis.

In both term and premature newborns with urinary tract infection, renal and urinary tract malformations are detected on ultrasound (US) more frequently (30-50%) compared to other age groups (1-3). The pathologies detected are frequently pelvicaliectasia and mild hydronephrosis. However, other clinically significant malformations such as major renal

or high-grade Grade III-V vesicoureteral reflux (VUR) may be detected in 5-10% (1). Renal/urinary tract US is not very reliable in the diagnosis of renal scar and VUR (especially low-grade VUR), and its sensitivity may vary between 40-90% depending on the performers (3,4,6).

In a study prospectively following 648 patients diagnosed with UTI in early infancy, radionuclide imaging performed >6 months after the first UTI showed evidence of renal parenchymal loss (scarring) and decreased renal function in 19% of the patients, and additional evidence of severely decreased renal function in 6% (4). In another prospective study (482 children, two year follow-up) conducted in children aged <6 years with first or second febrile UTI, it was found that delay in treatment for >48 hours increased the risk of renal scarring by 47%, independent of other variables (5). Renal parenchymal scars may lead to hypertension and suboptimal renal function in the future, especially in adulthood, with a possible risk of chronic kidney disease (1,4,6). The risk of development of APN-related renal scarring in the newborn is generally

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thought to be higher than the other age groups after neonatal period.

In case of suspicion of NUTI, intravenous broad-spectrum empiric antibiotic treatment should be started immediately after clinical and laboratory evaluation including cultures (blood, urine, cerebrospinal fluid, etc.). Early initiation of antibiotic treatment (<48-72 hours) may prevent renal scarring (1,3,5). The causative agents and empirical antibiotic treatment of NUTI are similar to those of neonatal sepsis (such as ampicillin+gentamicin or single cefotaxime or cefotaxime+gentamicin or ampicillin+cefotaxime at the beginning according to the additional risk group of the patient). Treatment can be adjusted according to the antibiogram and the response of the newborn. Vancomycin can be added to the treatment, if necessary, against coagulase-negative staphylococci, *Staphylococcus aureus* and *Enterococcus* species, especially in hospital-acquired APN/late sepsis developing in hospitalized infants (1,6,7).

The optimal duration of treatment is not clear, varies slightly according to authors and sources, and in recent years, there is a tendency to decrease the duration of treatment compared to the past (1,2,6-9). There are sources that consider a total treatment period of 7-10 days to be adequate in uncomplicated NUTI, and there are also sources that recommend at least 10-14 days of treatment in uncomplicated NUTI (1,7-11). In infants and children over one month of age, 7-10 days of treatment is generally recommended for cystitis (lower UTI) and 10-14 days of treatment is generally recommended for APN (upper UTI) (2,3,5,6,12). Again, in infants and children over one month of age, the entire treatment is recommended to be oral or initially parenteral followed by oral treatment to complete the total duration (2,3,6,12). When cystitis/APN differentiation is not made in febrile UTI, it is appropriate to approach the case as APN. These treatment durations are valid for uncomplicated cases. In complicated cases (e.g. slow response to treatment, presence of renal abscess or lobar nephronitis, presence of obstruction/stones in the urinary tract and kidney, presence of pathology on US, presence of recurrent UTI), treatment may be given for a longer period. In complicated cases, there may also be different antibiotic options other than routine treatment. The definition of a complicated case in APN may vary according to the guidelines in terms of imaging methods, treatment response and duration (1,2,4,5,7,10,11).

NUTI may have a more problematic prognosis due to its association with sepsis, higher rate of detection of other pathologies including VUR on US compared to other age groups, and higher risk of developing/accompanying APN compared to the post-neonatal period. For these reasons, they are po-

tentially more at risk of developing renal scarring than other age groups. Likewise, unlike in other age groups, it is recommended to perform a control urine culture in the 48-72nd hour of treatment to see that the urine is sterile. If there is growth in this control culture, the patient should be re-evaluated in terms of complications and treatment approach (1,6).

Antibiotics given in UTI are usually renally excreted antibiotics. They are highly concentrated in the urine; and therefore, the urine rapidly becomes sterile with appropriate treatment and no growth is expected in control urine culture. However, renal tissue damage/perfusion impairment/scar in APN is mainly related to tissue infection. Although absence of growth in control urine culture is a prerequisite for treatment success, optimal treatment of tissue (renal tissue) infection in APN is one of the main goals of treatment. This is especially important in NUTI where the risk of scarring is expected to be higher. Therefore, continuation of treatment for a important period of time after urinary sterilization is achieved is considered reasonable to prevent scarring and to prevent perfusion defects from turning into scars. Well-planned and prospective studies will clarify this issue. In our clinic, we give 10-14 days of treatment (parenteral or parenteral+oral) in cases of uncomplicated NUTI and in infants with good initial response to treatment. However, longer treatment may be required in complicated, high-risk cases or for fungal infections.

In conclusion, NUTI should generally be considered as neonatal-APN and may be associated with sepsis. Compared to other age groups, the risk of developing concomitant US pathologies and renal scarring is higher. There is no common and standardized recommendation for the duration of treatment in all countries, evidence-based data is still limited and the approach varies according to different sources (generally 7-14 days in non-complicated cases of NUTI). Even if some sources recommend 7-10 days of treatment, studies showing the efficacy and safety of this treatment are insufficient. In general, 10-14 days of treatment is recommended and, in our opinion, until the results of well-planned studies are available, 10-14 days of treatment is appropriate. In principle, treatment in NUTI is administered by hospitalization and parenteral administration. However, some studies suggest that in uncomplicated cases, after initial parenteral antibiotic treatment (2-14 days, usually 4-10 days), treatment can be completed with oral sequential treatment for 14 days (1,8,9,11).

In summary, our recommendation is that, depending on the patient's condition (taking into account the clinical status and risk factors), in uncomplicated cases, parenteral (10 days) or parenteral (7-10 days) followed by oral (14 days) sequential treatment may be appropriate. The patient's condition and the physician's preference may be guiding here.

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