Management of Febrile Neonate

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ABSTRACT:

Management of febrile neonate

The recommended management of febrile neonates, in first 28 days of life is controversial. Given that the overall prevalence of serious bacterial infection is higher in the neonate, most experts would advocate for a full sepsis evaluation, and hospitalization for giving antibiotics. In recent years, opinions have been raised regarding the follow-up without hospitalization and antibiotics or follow-up even without hospitalization in febrile newborn infants. In our review the evidence for diagnostic accuracy of screening methods for identification of serious bacterial infection in febrile neonates will be evaluated.

Keywords: Fever, management, newborn, serious bacterial infection

ÖZET:

Ateşli yenidoğan bebeklerin yönetimi

Yaşamın ilk 28 günü içerisindeki ateşli yenidoğan bebeklerin önerilen yönetimi tartışmalıdır. Yenidoğan döneminde yüksek oranda ciddi bakteriyel enfeksiyon görülmesi nedeniyle bir çok uzman, bebeklerin sepsis yönünden değerlendirilmesini ve yatırılarak antibiyotik başlanmasını savunmaktadır. Son yıllarda ateşli yenidoğan bebeklerin antibiyotiksiz yatarak izlemi veya yatırılmadan izlemi ile ilgili görüşler ortaya atılmaktadır. Derlememiz; ateşli yenidoğan bebeklerde, ciddi bakteriyel enfeksiyonu tanımlamada kullanılan yöntemlerin güvenilirliği hakkındaki bulguları değerlendirilecektir.

Anahtar kelimeler: Ateş, yönetim, yenidoğan, ciddi bakteriyel enfeksiyon

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INTRODUCTION

Currently, there is no accepted diagnosis and treatment model for follow-up and treatment management of newborn infants brought to outpatient clinic with fever complaints. The standard treatment of febrile neonates today is to examine sepsis screening tests, followed by the hospitalization of the infants and treatment with antibiotics until the culture results are obtained. The main reason for this approach seems to be the concern caused by the high mortality and morbidity rate in cases of severe bacterial infection (SBI) in the absence of early diagnosis and treatment in neonatal period, compared to other age groups. For this reason, after the laboratory studies have been done, the babies are mostly hospitalized and followed up (1,2). However, it has been reported that the application of antibiotic treatment to all febrile newborn infants leads to unnecessary serious emotional stresses in infants' families, development of iatrogenic complications related to hospitalization, , serious labor loss due to unnecessary hospitalization and costly increase as a result of antibiotic usage (1). In studies performed in the light of these data, various protocols are known to be developed in the detection of severe bacterial infections (SBIs), the identification of various low risk criteria, and the monitoring of the infants who meet these criteria, whether in the hospital without antibiotics or without hospitalization (3,4). It is observed that the developed protocols are between the years 1980 and 1990, including particularly the first three months of life, and no protocol could be applied only for the new-born period. During early childhood, three main protocols are widely accepted, including low risk factors for determining SBI in

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infants with fever (3,5,6). The protocols of Philadelphia, Boston and Rochester are used for babies whose age is less than 90 calendar days (5,7,8). However, the number of neonates is very low in these studies conducted with these three protocols.

It seems that quite different applications have been made regarding the evaluation of febrile babies during the neonatal period. In this regard, the absence of international and national protocol recommendations is considered to be the main difference in practice (9). In the literature, it is emphasized that the approach models for febrile infants are modified by adding C-Reactive Protein (CRP) and erythrocyte sedimentation rate (ESR) values, and according to these new models, neonates with low risk factors can be hospitalized without antibiotic administration (10).

We will review the management of the diagnosis and treatment of infants who are brought up with complaints of fever during neonatal period in accordance with literature information.

A-Definitions

Fever: The rectal temperature measured during newborn period to be ≥38°C.

Clinical evaluation: It is accepted as a physical examination in which the general condition of the newborn infant and systemic findings (cutis marmoratus, tonus, turgor, heart rate and blood pressure) are evaluated. In the clinical evaluation, infants are included in the risk group within the presence of symptoms in terms of infection. In clinical evaluation, cases where bacterial infections such as cellulitis, mastitis or otitis are considered as infection agents are recorded. Clinical evaluation is recommended to be performed by a physician experienced in neonates (pediatrician or pediatry resident, neonate specialist or resident of neonatal care).

Laboratory evaluation: Laboratory analyses to identify severe bacterial infection are listed below.

Blood analysis: Complete blood count (leukocyte count), erythrocyte sedimentation rate, CRP, procalcitonin, absolute neutrophil count (ANC), absolute band count (ABC), blood culture.

Urine analysis: Urine assessment by bladder catheterization or suprapubic aspiration. Complete urine analysis and urine culture examination.

CSF (Cerebrospinal fluid): Protein, sugar, cell count, gram staining and culture analysis.

Imaging: Chest x-ray is taken in the presence of findings of respiratory tract disease in the baby (tachypnea, coughing, presence of pathology in the respiratory sounds in the examination findings).

Stool tests: Cell count and faecal culture in stool if there is a history of diarrhea in the baby.

Other tests: Local fluid cell count, gram staining and fluid culture in the presence of local infective focus (such as cellulitis, otitis, arthritis) in the baby.

Viral evaluation: Viral culture cannot be routinely performed due to difficulties in administration. However, RSV and influenza nasal swab kits that results according to the antigen structure of viruses are used during infancy. There is no sufficient knowledge about the routine use during the newborn period.

B- Severe Bacterial Infection Criteria

The definition of severe bacterial infection (SBI) is divided into two main categories.

A- Production of pathogenic bacteria in one or more cultures.
B- Infections usually detected with bacterial agents (such as pneumonia, acute otitis media, mastitis, and omphalitis). Soft tissue infections can be diagnosed by physical examination findings regardless of bacterial pathogen production. Pneumonia is defined by the presence of new infiltrates in chest X-rays and evaluation of findings by a radiologist in infants with typical clinical findings.

C- Severe Bacterial Infection Prevalence

Severe bacterial infection prevalence is reported as 7.1% -19.7% in infants younger than 3-month-old with fever. The prevalence of SBIs in the neonatal period (0-28 days) was reported as 9-28% in the subgroup distribution of febrile infants, while it was 7.1% in infants 2-3 months old (1,11-17). In a study of febrile newborn infants, SBIs were reported in 31.9% of newborn infants 7-14 days old, 33.3% of newborn infants 15-21 days old, and 18.3% of infants older than 21 days (15). Studies have shown that the incidence of severe bacterial infections in febrile newborn infants is higher than the incidence in febrile infants at early infancy.

D- Etiological and Factor Distribution of Severe Bacterial Infection

Many studies on febrile neonates and febrile infants did not reveal a bacterial effect of fever etiology and it is seen that this condition was named as a diagnosis of viral syndrome. Studies conducted by Baker and Marom separately reported viral syndrome with a frequency of 60-72% (1,8). Both studies did not have viral culture or rapid viral antigen testing. It is known that the reliability of rapid viral antigen tests is high during infancy but there is not enough information about the reliable application of the tests in the newborn period (18). In infants with viral upper respiratory tract symptoms, performing rapid viral antigen tests will be helpful in differential diagnosis. In recent years, it is suggested that RSV and Influenza A/B virus scanning with rapid immunoassay in infants with respiratory tract infection, especially with bronchiolitis, and virus detection with PCR in infants with enterovirus pre-diagnosis are recommended.

The most common localization for serious bacterial infection is the urinary tract. Urinary tract infection (UTI) is diagnosed by producing a single pathogenic agent in suprapubic aspiration (>1000 colonies/ml) or in catheterized urine (>10 000 colonies/ml) (19). Studies have reported that UTI frequency is seen in 3-14% of all febrile infants (1,9,18). When the distribution of UTI in SBI factors is analyzed, it is known that UTI has a 15-90% frequency in whole SBIs.

Bacterial meningitis and/or aseptic meningitis prevalence is reported to be in the range of 0.2-14% in babies younger than 90 days of chronological age (8). In studies involving newborn infants only, the frequency of bacterial meningitis is reported as 0.5-4.4% (6,9,20).

The need to perform lumbar puncture in febrile babies is still an important controversial issue. In the studies described above for febrile babies, there is no indication of lumbar puncture application criteria, routine application descriptions, or rates of lumbar puncture performed. However, it has been reported that meningitis diagnosis is missed in febrile newborn infants who have low risk and not performed lumbar puncture in a small number of studies (21,22). Today, there is no clear consensus about routine lumbar puncture for infants brought with a complaint of fever.

When all SBIs are evaluated, it is reported that Escherichia coli bacteria are most frequently isolated in growing in culture and its frequency is around 60% (18). Escherichia coli bacteria have been reported to be the causative agent in 68% (range 37.5-100%) of urinary tract infections, in 24.3% (range 0-55%) in bacteraemia, and in 8% (range 0-40%) in bacterial meningitis (18). Group B Streptococcus and Streptococcus pneumoniae are the main causes of bacteremia and pneumonia, while Staphylococcus aureus is the main causative agent of local infections (1,7,8,23).

E- Comparison of laboratory analyses

In defining SBI, it has been reported that the accuracy rates of ABC and ANC are higher than those of leukocyte count (18,24). In different studies related to the subject, CRP value is reported to have a higher accuracy level than leukocyte count, ANC, and procalcitonin levels (25,26). Recently, in a study by Nosrati et al. in febrile infants in the first 3 months of life, it was reported that the CRP value was the only significant parameter for defining SBI when the cut-off value

of 2 mg/dl was taken (27). There are no CRP studies involving only febrile neonates in defining severe bacterial infection.

Standard urine analysis and urine gram staining are reported to have low sensitivity and specificity in detecting urinary tract infections during neonatal and early infancy and found to have a reliability of 48-65% (22,23,28). In studies that determine risk factors for SBI; it is reported that the most frequent missed bacterial infection in infants with low risk factors is UTI (6,23). It has been reported that improved urine analysis (when urine analysis is performed with a hemocytometer) is more sensitive and specific in determining urinary tract infection (23). For this reason, it is recommended to perform an improved urine analysis instead of standard urine analysis in determining the urinary tract infection during neonatal period.

F- Evaluation of effectiveness of protocols for fever

In practice, the most commonly used protocol for identifying bacterial infections in febrile infants is Rochester criteria (29). Boston and Philadelphia criteria are used as an alternative (5,27). The criteria and different aspects of each of the three protocols are presented in Table 1. The age distribution of the protocols was reported as Philadelphia: 29-60 days, Rochester <60 days and Boston 28-89 days. These three protocols are known to have similar accuracy rates (Sensitivity: 84.4% to 100.0%, Specificity: 26.6% to 69.0%, Negative Predictive Value: 93.7% to 100.0%, and Positive Predictive Value: 3.3% to 48.6%) (18). In the literature, there are studies about the feasibility of these protocols in babies under 1 month old. However, the higher incidence of severe bacterial infections during the neonatal period

Table-1: The characteristics and differences of Boston, Philadelphia and Rochester criteria that can be applied in the evaluation of febrile infants.

	BOSTON	PHILADELPHIA	ROCHESTER
Study plan	Prospective	Prospective	Prospective
Study period	3 years (1987-1990)	5 years (1987-1992)	8 years (1984-1992)
Patient age group	28-89. days	29-60. days	≤60. days
CRITERIA			
Fever, rectal temperature, ºC	≥38.0	≥38.2	≥38.0
Anamnesis	No vaccination in the last 48 hours, No antimicrobial use in the last 48 hours	Unidentified	No perinatal antibiotic use No underlying disease No history of further hospitalization than the mother
Clinical appearance is good, there is no local infection center on physical examination	Yes	Yes	Yes
Pregnancy period	Unidentified	Unidentified	≥37 weeks
All healthy before	Yes	Unidentified	Yes
No dehidratation	Yes	Unidentified	Unidentified
Leukocyte count, mm³	<20 000	<15 000	5 000-15 000
Band/neutrophil ratio (I/T)	Unidentified	<0.2	Unidentified
Urine analysis, leukocyte count	<10	<10	≤10
CSF, leukocyte, mm³	<10	<8	Unidentified
Chest x-ray	No infiltration (if x-ray was obtained)	No infiltration	No focal infiltration (in the presence of clinical indication)
Stool analysis	Unidentified	No blood or leukocytes (if necessary)	≤5 leukocytes (if necessary)

CSF: Brain spinal fluid. [Babies brought with a complaint of fever are considered low risk for bacterial infection if all the criteria of the protocols are provided.]

affects protocol outcomes. In the different studies in which the protocols were applied on babies younger and older than 28 days, Boston and Philadelphia protocols showed a higher sensitivity rate in babies older than 28 days, and a lower rate of specificity (11,21). Rochester criteria for determining bacterial infection in febrile infants during the newborn period give more accurate results (higher sensitivity, specificity and positive predictive value). In all studies, in identifying SBI; it is reported that the false positivity rate is significantly higher in infants in the newborn period (range 1-6.2%) than in the older infants (range 0-5.4%) (21). In the evaluation of febrile neonates, it is seen that the protocols for approaching febrile infants are not valid and new studies involving only newborn babies are needed.

In conclusion, the rate of SBIs is quiet high in febrile neonates. The most common bacterial infection location is urinary tract infection. The most frequent pathogenic agent is Escherichia coli bacteria. There is no approved protocol for the evaluation, screening and treatment of febrile neonates. Low risk criteria in the Rochester, Philadelphia, and Boston protocols are not sufficient to rule out severe bacterial infection in febrile neonates. Applicable and reliable tests are needed in determining the viral factors in the newborn period.

Today, all febrile neonates should be hospitalized and evaluated with all laboratory examinations in terms of infection and given antibiotic treatment according to the results of the evaluation, until the development of a new acceptable protocol.

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