



Fever in infants: the tools currently available for classic diagnostic uncertainties

A high temperature is the most common reason people come to the paediatric emergency department, especially when a child under the age of 2 is affected¹. Although the vast majority of cases involve self-limited viral infections, occasionally a febrile infant who appears healthy may be suffering from a serious bacterial infection (SBI). The most common SBI found in this group of patients is urinary tract infection (UTI) and therefore it is worth testing the patient's urine at the GP's surgery to rule out this possibility.

It is less common for a patient with these symptoms to have occult bacteraemia (OB). Before heptavalent pneumococcal conjugate vaccines were available, pneumococcal OB incidence ranged between 1.5% and 2% in healthy-looking infants with non-focal fever above 39°C. This figure has now decreased significantly with the introduction of the heptavalent pneumococcal conjugate vaccine^{2,3}. Nowadays, the incidence of pneumococcal OB in children who have been vaccinated against pneumococcus is below 1%⁴, even though it is of note that there has recently been an increase in pneumococcal OB affecting high risk patients⁵. However, this trend has not spread to affect the general population. The risk of pneumococcal OB increases for infants with leukocyte counts over 15,000/mm³ and an absolute neutrophil count over 10,000/mm³, even though this is rarely tested⁶. Nevertheless, if we take into consideration the fact that between 4% and 10% of febrile infants with pneumococcal OB develop meningitis within days, it is easy to understand why most medical guidelines and expert recommendations suggest that blood tests and blood culture should be carried out.

Emergency physicians who follow the different protocol regarding the management of febrile infants often do so inconsistently^{7,8} because of the low incidence of OB and in many cases it is resolved quickly, the fact that traditional tests are rarely useful and finally because the main cause of fever is a viral condition. The development of these infections in infants is relatively atypical and therefore it is often very difficult for doctors to determine whether a healthy-looking febrile infant has a self-limited virus or a SBI just by carrying out a physical examination⁹. Infection caused by the

influenza virus and more unusually, by respiratory syncytial virus may develop, with a fever being the only symptom in infants under 2 years old. Before rapid diagnostic tests were available for respiratory viruses, these children had to undergo different additional tests, they also received inadequate treatment and in some cases were inefficiently hospitalised. This was especially the case when dealing with infants under 3 months old. The key to obtaining effective results from these tests in the emergency department is to choose the best moment to carry them out (flu epidemic or respiratory syncytial virus) and the best type of patient (an infant with non-focal fever is the ideal patient in an emergency setting). These tests have already been carried out in infants aged between 3 and 24 months old by different groups and their effective use in the emergency department is linked to a significant reduction in additional tests being carried out, treatments, use of antibiotics and the unnecessary hospital admission⁹⁻¹². Most importantly for the emergency physician, these tests identify the infants who have the lowest risk of suffering from an SBI. The risk of an infant with non-focal fever with a SBI who tests positive for influenza following a rapid diagnostic test is significantly lower than that of a febrile infant with a negative test result¹³. Traditional management programmes are valid in the latter case whereas in the former the approach by emergency physicians to managing the patient can be more conservative.

In the emergency department, these tests are carried out in special circumstances given that febrile infants are often brought to the emergency department quickly and an increased number have limited accompanying symptoms irrespective of the cause¹⁴. Furthermore, it is worth bearing in mind that these tests can be carried out at a GP's surgery and the results can be obtained in an hour.

The study carried out by Gargallo et al. which has been published in this edition of EMERGENCIAS¹⁵ describes the experiences with these tests after they were carried out on a differentiated group of febrile infants under 3 months old in the paediatric emergency department. This study shows how the positive result of a rapid diagnostic test for respiratory viruses carried out in an epidemic period significantly redu-

ces the chances of the infant with a SBI. Despite the fact the authors themselves acknowledge that the size of the sample made it is difficult to draw conclusions, it seems obvious that these rapid diagnostic tests for respiratory viruses should be included in the management programme for infants under three months old with non-focal fever.

Similarly, polymerase chain reaction (PCR) for detecting enterovirus is an incredibly useful tool for managing infants with suspected viral meningitis^{16,17}. Meningitis caused by enterovirus affecting children has a good prognosis and different groups have advocated its use in outpatient clinics following a few hours in hospital under observation^{18,19}. Differential diagnosis with bacterial meningitis does not normally, pose any problems in older children but it may be more complicated when dealing with infants with a less developed condition. In fact, the management of children with suspected viral meningitis may be adapted because of age^{18,19}. PCR for enterovirus is not only more effective compared to the classic CSF culture but the results are also available only a few hours after the CSF is extracted^{16,17}. It is easy to understand the impact of PCR for detecting enterovirus in the management of children with suspected viral meningitis, in terms of cutting down the number of additional tests, bypassing treatment with antibiotics and reducing ineffective hospitalisation.

The emergence of these different rapid diagnostic tests has changed the management of febrile infants in emergency departments. These tests are becoming extremely useful tools for providing the most appropriate care for the patients that have been specially selected for their implementation including infants with non-focal fever in a flu or respiratory syncytial virus epidemic, or children with suspected meningitis caused by enterovirus.

REFERENCES

- 1- Mintegi S, Benito J, García S, Corrales A, Bartolomé MJ, Trebolazabala N. Demanda y asistencia en un servicio de urgencias hospitalario. *An Pediatr (Barc)* 2004;61:156-61.
- 2- Kaplan SL, Mason EO Jr, Wald ER, Schutze GE, Bradley JS, Tan TQ, et al. Decrease of invasive pneumococcal infections in children among 8 children's hospitals in the United States after the introduction of the 7-valent pneumococcal conjugate vaccine. *Pediatrics* 2004;113:443-9.
- 3- Herz AM, Greenhow TL, Alcantara J, Hansen J, Baxter RP, Black SB, et al. Changing Epidemiology of Outpatient Bacteremia in 3- to 36-Month-Old Children After the Introduction of the Heptavalent-Conjugated Pneumococcal Vaccine. *Pediatr Infect Dis J* 2006;25:293-300.
- 4- Stoll ML, Rubin LG. Incidence of occult bacteremia among highly febrile young children in the era of the pneumococcal conjugate vaccine: a study from a Children's Hospital Emergency Department and Urgent Care Center. *Arch Pediatr Adolesc Med* 2004;158:671-5.
- 5- Singleton RJ, Hennessy TW, Bulkow LR, Hammit LL, Zulz T, Hurlburt DA, et al. Invasive pneumococcal disease caused by nonvaccine serotypes among Alaska native children with high levels of 7-valent pneumococcal conjugate vaccine coverage. *JAMA* 2007; 297:1784-92.
- 6- Lee GM, Harper MB. Risk of Bacteremia for Febrile Young Children in the Post-*Haemophilus influenzae* Type b Era. *Arch Pediatr Adolesc Med* 1998;152:624-8.
- 7- Isaacman DJ, Kaminer K, Veligeti H, Jones M, Davis P, Mason JD. Comparative practice patterns of emergency medicine physicians and pediatric emergency medicine physicians managing fever in young children. *Pediatrics* 2001;108:354-8.
- 8- Belfer RA, Gittelman MA, Muniz AE. Management of febrile infants and children by pediatric emergency medicine and emergency medicine: comparison with practice guidelines. *Pediatr Emerg Care* 2001;17:83-7.
- 9- Segura S, García JJ, Corrales E, Lasuen N, Palacín E, Juncosa T, et al. Influencia de la prueba de detección rápida del virus de la gripe en el manejo del niño febril en urgencias pediátricas. *Emergencias* 2005;17:115-20.
- 10- Benito J, Vázquez MA, Morteruel E, Mintegi S, Sánchez J, Fernández A. Impact of Rapid Viral Testing for Influenza A and B Viruses on Management of Febrile Infants Without Signs of Focal Infection. *Pediatr Infect Dis J* 2006;25:1153-7.
- 11- Bonner AB, Monroe KW, Talley LI, Klasner AE, Kimberlin DW. Impact of the Rapid Diagnosis of Influenza on Physician Decision-Making and Patient Management in the Pediatric Emergency Department: Results of a Randomized, Prospective, Controlled Trial. *Pediatrics* 2003;112:363-7.
- 12- Sharma V, Dowd MD, Slaughter AJ, Simon SD. Effect of rapid diagnosis of influenza virus type a on the emergency department management of febrile infants and toddlers. *Arch Pediatr Adolesc Med* 2002;156:41-3.
- 13- Greenes DS, Harper MB. Low risk of bacteraemia in febrile children with recognizable viral syndromes. *Pediatr Infect Dis J* 1999;18:258-61.
- 14- Mintegi S, González M, Pérez A, Pijoán JJ, Capapé S, Benito J. Lactante de 3-24 meses con fiebre sin foco en urgencias: características, tratamiento y evolución posterior. *An Pediatr* 2005;62:522-8.
- 15- Gargallo E, Ricart S, García JJ, Garrido R, Muñoz C, Gené A, et al. Fiebre en el lactante menor de 3 meses: incidencia de enfermedad bacteriana potencialmente grave y utilidad de los tests de diagnóstico rápido virológico. *Emergencias* 2007;19:173-9.
- 16- Petitjean J, Vabret A, Dina J, Gouarin S, Freymuth F. Development and evaluation of a real-time RT-PCR assay on the LightCycler for the rapid detection of enterovirus in cerebrospinal fluid specimens. *J Clin Virol* 2006; 35:278-84.
- 17- Bourlet T, Caro V, Minjolle S, Jusselin I, Pozzetto B, Crainic R, et al. New PCR test that recognizes all human prototypes of enterovirus: application for clinical diagnosis. *J Clin Microbiol* 2003;41:1750-2.
- 18- Waisman Y, Lotem Y, Hemmo M, Wietzen T, Garty BZ, Mimouni M. Management of children with aseptic meningitis in the emergency department. *Pediatr Emerg Care* 1999;15:314-7.
- 19- Mintegi S, Sánchez J, Benito J, Vázquez MA, Rubio G, Capapé S, et al. Tratamiento extrahospitalario de los niños con meningitis viral. *An Esp Pediatr* 2000;52:430-4.

S. Mintegi Raso

Paediatric Emergency Department. Hospital de Cruces.
University of the Basque Country.