C-reactive protein in otherwise well babies with risk factors for sepsis

Neonatal sepsis remains one of the leading causes of death in UK neonates. Early diagnosis is life-saving in these babies; however, over-diagnosis can lead to unnecessary treatment and prolonged hospital stay. Although C-reactive protein (CRP) is routinely used in the diagnosis and monitoring of sepsis, its usefulness is variable. This study assessed the correlation between CRP values and blood/cerebrospinal fluid culture findings in otherwise well infants treated for sepsis due to the presence of risk factors.

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Key points

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1. Large numbers of asymptomatic infants are treated for sepsis because of raised CRP levels.
2. This study shows no strong correlation between CRP levels and culture results in healthy babies who received antibiotics because of risk factors for sepsis.
3. Based on these results, if a clinically well infant has two low/normal CRP results, antibiotics could be stopped before culture results are available.

A diagnosis of neonatal sepsis is usually made using a combination of clinical signs, risk factors and laboratory tests. Early diagnosis is life-saving but too many babies are receiving unnecessary treatment with a prolonged hospital stay.[1,2]

CRP values are routinely used in the diagnosis and monitoring of sepsis, however their usefulness is questioned.[3] Some neonates with culture-proven bacteraemia are known to have normal CRP levels and not all neonates with high CRP levels are shown to have sepsis.[4] Serial low or normal CRPs may be useful in dissuading clinicians from a diagnosis of infection.[5] The usefulness of a raised CRP, in the absence of any clinical signs, is less clear.

The National Institute for Health and Care Excellence (NICE) guideline offers recommendations for the early identification and treatment of infants at risk for early onset sepsis.[6] The guidance outlines a strategy for determining which infants have septic screens based on risk factors and biochemical and clinical parameters. The guideline currently recommends measuring CRP at the beginning of antibiotic therapy in babies with risk factors for sepsis and again at 18-24 hours after presentation. NICE also recommends considering lumbar puncture in all babies with a CRP of 10mg/L or greater.

Identifying and treating symptomatic babies is essential; however, minimising the impact of management pathways on healthy babies is challenging and has led to large numbers of infants who do not have

Maximum CRP level (mg/L)	Number of babies	Number of babies with a positive blood culture result	Number of babies that underwent lumbar puncture	Number of babies with a positive CSF culture result
<2	500	0	0	0
>2-10	415	0	1*	0
>10-20	219	1 (GBS)**	15	0
>20-30	73	0	25	0
>30-50	88	0	32	0
>50	80	1 (GBS)***	76 (4 unsuccessful)	0
Total	1,375	2	149	0

TABLE 1 CRP values, blood culture findings and CSF culture findings in otherwise well infants treated for sepsis because of the presence of risk factors, from 1 September 2013 to 31 August 2015. Key: CRP = C-reactive protein, CSF = cerebrospinal fluid, GBS = Group B Streptococcus. *Maternal fever and GBS-positive blood culture. **Maternal GBS positive blood culture and a sibling with GBS meningitis (maximum CRP level = 18.5mg/L). ***Maternal fever and GBS positive (maximum CRP level = 60.5mg/L).

sepsis receiving full courses of antibiotics, increased lumbar punctures and longer hospital stays.

The aim of this study was to assess if there is any correlation between CRP values and blood/cerebrospinal fluid (CSF) culture results in otherwise well babies on the postnatal ward who were screened and treated for sepsis because of the presence of risk factors.

Materials and methods

At King's College Hospital, London, all infants who are screened and treated for sepsis will have a minimum of two sets of blood tests to look at CRP in addition to one set of blood cultures. Lumbar puncture is considered in all infants with a CRP of >10mg/L.

The study was a retrospective review of electronic patient records looking at all infants who received intravenous antibiotics on the postnatal ward between September 2013 and August 2015. All babies who were receiving antibiotic therapy in the absence of any clinical signs of infection were included, ie those who were screened and treated due to presence of risk factors only. Any babies with clinical signs of infection or requiring admission to the neonatal unit were excluded. Those included remained on the postnatal ward throughout the antibiotic course. Any babies who later required admission to the neonatal unit due to emerging clinical signs and symptoms were excluded.

Data were collected on all CRP values, blood culture and CSF culture results in these infants.

Results

A total of 1,375 well babies were screened and treated for sepsis due to presence of risk factors between 1 September 2013 and 31 August 2015. There were only two positive blood cultures, both of which were Group B Streptococcus (GBS). Their maximum CRP values were 18.5mg/L and 60.5mg/L, respectively. One hundred and forty nine babies underwent lumbar puncture, all of whom had negative CSF cultures. One baby underwent lumbar puncture in view of maternal fever and a maternal GBS-positive blood culture, despite a low CRP level of 6.2mg/L. Blood and lumbar puncture cultures for this baby were subsequently negative. The results are summarised in **TABLE 1**.

Conclusions

In this study there appears to be no strong correlation between the CRP values and culture results in well babies who received intravenous antibiotics because of risk factors for sepsis. CRP values must be interpreted in combination with clinical symptoms and possibly other reliable infection markers. Based on these results, if babies are clinically well and have two low/normal CRP results, it would be reasonable to consider stopping antibiotic therapy and arranging discharge before culture results are available.

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