

Question #249: Dx: In unspecified Neonates, c reactive protein and sepsis

ID: 249

Question asked on: 2006-01-26 10:38:05

Clinician: (hidden)

Status: closed

Assigned librarian: (hidden)

We have 2 newborn babies that have elevated CRP (c reactive protein). One clinically appears well and we want to know if we need to treat with abx for 5 days simply based on the elevated CRP level.

Type of question: Diagnosis

P: In unspecified Neonates

I: c reactive protein

C: cbc

O: sepsis

Updated by (Librarian) on 2006-01-27 08:54:15

New status: open

Bottom line:	The proportion of newborns who are treated with antibiotics for mild to moderate clinical signs and/or OB risk factors can be reduced if a diagnostic algorithm that includes measurements of IL-8 and CRP is applied in addition to clinical judgment. This strategy seemed to be safe.
Search:	c-reactive protein AND sensitivity and specificity AND bacterial infections Limit: newborn
Citation(s):	1: Pediatrics. 2004 Jul;114(1):1-8. Erratum in: Pediatrics. 2004 Dec;114(6):1746. Measurement of interleukin 8 in combination with C-reactive protein reduced unnecessary antibiotic therapy in newborn infants: a multicenter, randomized, controlled trial. Franz AR, Bauer K, Schalk A, Garland SM, Bowman ED, Rex K, Nyholm C, Norman M, Bougateg A, Kron M, Mihatsch WA, Pohlandt F; International IL-8 Study Group. Department of Pediatrics, Division of Neonatology and Pediatric Critical Care, University of Ulm, Ulm, Germany. axel.franz@ukb.uni-bonn.de OBJECTIVE: Neonatal bacterial infections carry a high mortality when diagnosed late. Early diagnosis is difficult because initial clinical signs are nonspecific. Consequently, physicians frequently prescribe antibiotic treatment to newborn infants for fear of missing a life-threatening infection. This study was designed to test the hypotheses that a diagnostic algorithm that includes measurements of interleukin 8 (IL-8) and C-reactive protein (CRP) 1) reduces antibiotic therapy and 2) does not result in more initially missed infections compared with standard management that does not include an IL-8 measurement. METHODS: Term and preterm infants who were <72 hours of age and had clinical signs or obstetric risk factors suggesting neonatal bacterial infection but stable enough to wait for results of diagnostic tests were enrolled into the study. A total of 1291 infants were randomly assigned to receive antibiotic therapy according to the guidelines of each center (standard group) or to receive antibiotic therapy when IL-8 was >70 pg/mL and/or CRP was >10 mg/L (IL-8 group). The primary outcome variables were 1) the number of infants treated with antibiotics and 2) the number of infants with infections missed at the initial evaluation. RESULTS: In the IL-8 group, fewer infants received antibiotic therapy than in the standard group (36.1% [237 of 656] vs 49.6% [315 of 635]). In the IL-8 group, 24 (14.5%) of 165 infants with infection were not detected at the initial evaluation, compared with 28 (17.3%) of 162 in the standard group. CONCLUSIONS: The number of newborn infants who received postnatal antibiotic therapy can be reduced with a diagnostic algorithm that includes measurements of IL-8 and CRP. This diagnostic strategy seemed to be safe. http://pediatrics.aappublications.org/cgi/reprint/114/1/1
Methods:	The study was a randomized controlled, multi-center study. A total of 1291 patients were randomly assigned to 1 of 2 diagnostic algorithms using sealed opaque envelopes. In the IL-8 group, therapy was initiated when IL-8 was >70 pg/mL and/or CRP was >10 mg/L. The standard group was evaluated and treated according to the standard guidelines for evaluation of newborn infants with suspected bacterial infection of each center. IL-8 measurements were not included. The decision to start antibiotic therapy was based on the combination of clinical signs, obstetric risk factors, and lab values that included CRP.
Validity:	Was there an appropriate reference standard? yes Was the comparison of the test to the standard blinded? yes Was the comparison independent (everyone got both)? Was the test given to an appropriate spectrum of patients? yes
Results:	In the IL-8 group, fewer infants received abx therapy than in the standard group (36.1% vs 49.6%; P < .0001). This 13.5% reduction (lower limit of the 1-sided 95% CI:9%) occurred only in infants without bacterial infection and therefore was a reduction of unnecessary antibiotic therapy. The proportion of initially missed infections was similar in both groups. With 95% certainty, the implementation of the diagnostic algorithm that included IL-8 and CRP will not increase the proportion of initially missed infections by >3.9%. This study confirms that IL-8 and CRP should always be measured together to optimize the sensitivity. (Table 4) Although IL-8 has a higher sensitivity when measured in the first 12 hours of life and CRP has a higher sensitivity later, the sensitivity for bacterial infection in either age group is greater when both parameters are measured together.
Applicability:	Questions for the physician to consider: Were patients sufficiently similar to those this clinician sees? Was the intervention practical in this clinician's setting? Was the comparison equivalent to the standard of practice? Were the outcomes measured the ones the clinician is interested in?
Notes:	I apologize for the delay. I answered this question yesterday, but there seems to have been a technical problem -- when I checked today the answer was not in the database. Most of the studies I found were about the duration of therapy rather than indications for therapy. Although this is a review article, it does give the sensitivity and specificity for CRP. : Adv Neonatal Care. 2003 Feb;3(1):3-13. Related Articles, Links The role of C-reactive protein in the evaluation and management of infants with suspected sepsis. Hengst JM. Variety Club Intensive Care Nursery, Department of Neonatology, Blank Children's Hospital, 1200 Pleasant St, Des Moines, IA 50309, USA. iowahengst@aol.com C-reactive protein (CRP) is a nonspecific, acute-phase protein that rises in response to infectious and noninfectious inflammatory processes. Good evidence exists to support the use of CRP measurements in conjunction with other established diagnostic tests (such as a white blood cell (WBC) count with differential and blood culture) to establish or exclude the diagnosis of sepsis in full-term or near-term infants. This article reviews the immunologic function of CRP and the history of CRP testing. The 3 methods for measuring CRP and the sensitivity and specificity of this diagnostic test are analyzed. Guidelines for the use of CRP in the evaluation and management of infants with suspected sepsis are presented. Quantitative serial CRP levels, obtained 24 hours after the onset of signs and symptoms of infection, with serial measurements 12 to 24 hours apart, offer the most sensitive and reliable information. At least 2 CRP levels, obtained 24 hours apart, with levels < or = 10 mg/L, are needed to identify infants unlikely to be infected. The use of CRP to exclude infection may allow clinicians to discontinue antibiotics at 48 hours in select infants, limiting extended unnecessary antibiotic exposure.

Updated by (Clinician) on 2006-01-27 10:51:32

New status: open

Is there any way to get the full text of the review article at the end (The role of C-reactive protein in the evaluation and management of infants with suspected sepsis. Hengst JM.)

Thanks! These articles are very helpful.

Updated by (Librarian) on 2006-01-30 12:12:20

New status: open

Unfortunately UIC does not own this journal -- either in print or electronically. You will have to do an Interlibrary Loan to get it.

Updated by (Librarian) on 2006-01-30 12:12:35

New status: closed