Utility of procalcitonin and C-reactive protein for the diagnosis of invasive infections of infants younger than 90 days with fever without source

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Objective: To compare the performance of procalcitonin (PCT) and C-reactive protein (CRP) for the diagnosis of invasive bacterial infections (IBI) of infants under 3 months of age with fever without source (FWS).

Methodology: A sub-analysis of a prospective study of RiSEUP - SPERG Network, of infants younger than 90 days with FWS, seen between October 2011 and September 2013 in 19 Spanish pediatric emergency departments; of these, we selected 15 hospitals that quantify PCT levels. Children were excluded if lacked any of the required data (leukocyte count, CRP, PCT, hemoculture, or urine culture collected by sterile method) or informed consent. Patients were followed-up. The performances of CRP and PCT were studied and compared with area under curve (AUC); post-test probability for different cutoffs was calculated.

Results: We treated 3,497 infants younger than 90 days with FWS. After application of the exclusion criteria, 2,785 were analyzed (84.8%). 608 patients (21.8%, 545 urinary tract infections) were diagnosed with serious bacterial infection (SBI). Diagnosed with IBI (2.8%) were the following: 25 occult bacteremia, 29 urinary infections with bacteremia, 14 sepsis, 11 bacterial meningitis and 1 cervical adenitis with bacteremia.

The frequency of SBI without IBI was similar for well-appearing infants (468/2488, 18.8 %) and for ill-appearing infants (60/297, 20.2%). The IBI frequency was higher in ill-appearing infants (25/297, 8.4 %) than for well-appearing infants (55/2480, 2.2 %) with statistically significant difference [$p < 0.001$, odds ratio 0.24 (95% confidence interval –CI- 0.15 - 0.34)].

In well-appearing infants with FWS (2488, 55 IBI), AUC of the PCT (0.79, 95 % CI 0.72 - 0.86) was higher than AUC of CRP (0.74, 95% CI 0.66 - 0.82) for diagnosing IBI. For this group of patients:
* PCT ≥ 0.5. Likehood Ratio+: 3.99 (95% CI 3.15-5.05), post test probability 8.2%. Likehood Ratio –: 0.47 (95% CI 0.34-0.65), post test probability 1%.

* PCT ≥ 2. Likehood Ratio+: 9.69 (95% CI 6.74-13.94), post test probability 17.9%. Likehood Ratio –: 0.61 (95% CI 0.49-0.76), post test probability 1.4%.

* CRP ≥ 20. Likehood Ratio+: 2.63 (95% CI 2.09-3.3), post test probability 5.6%. Likehood Ratio –: 0.52 (95% CI 0.37-0.72), post test probability 1.2%.

* CRP ≥ 50. Likehood Ratio+: 5.56 (95% CI 4.04-7.64), post test probability 11.1%. Likehood Ratio –: 0.59 (95% CI 0.47-0.76), post test probability 1.3%.

Conclusion: PCT is of greater utility than CRP for either the detection or ruling-out of IBI for well-appearing infants under 3 months of age with fever without source. In clinical practice, the results of PCT and CRP must be interpreted in accordance with the objective: rule out or diagnose an IBI.