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Procalcitonin (PCT) test (immunoassay)

Submission to the WHO EDL 2019


We as members of the parallel WHO EML Antibiotic Working Group, have some concerns regarding the listing of this test on the WHO EDL due to:

- The absence of high-quality studies comparing C-reactive protein (CRP) guided treatment algorithms with PCT-guided algorithms makes it difficult to judge in how far PCT is really superior to CRP, a cheaper biomarker already listed on the EDL. A small randomized trial in two intensive care units in Brazil did not find a difference in PCT vs CRP algorithms on antibiotic use.[1]
- The evidence on the role of PCT in reducing mortality in patients with sepsis is very low / moderate according to the 2017 Cochrane review, the sample size being too small to derive definite conclusions and generalize the results. [2] Furthermore the results are mainly driven by studies financed by companies producing the test.
- The usage of PCT in sepsis is advisable in clinical practice mainly as a serial test while a single measurement at sepsis diagnosis will not impact at stewardship level and/or duration of therapy. Since clear evidence and recommendations on PCT use for de-escalation in patients with sepsis is missing, this increases the risk of inappropriate usage and inadequate antibiotic stewardship.
- A recent patient level meta-analysis of 26 trials of patients with respiratory infections (RTI) assigned to receive antibiotics either according to a PCT based strategy or control found that patients assigned to the PCT arm not only had lower antibiotic exposure (5.7 vs 8.1 days), fewer side effects (16 vs 22%) but also lower 30-day mortality (9 vs 10%, adjusted OR 0.83 [95% CI 0.70-0.99]).[3] The meta-analysis has attracted some criticism (e.g. adherence to the algorithm was not taken into account) and the explanations for the finding of lower mortality remains somewhat unsatisfactory.[4, 5] Some authors have questions the usefulness of PCT for respiratory tract infections where there is already good evidence for short treatment durations (e.g. community acquired pneumonia; 43% of patients in the PCT group) or withholding antibiotic treatment (such as upper RTI, 8% in the PCT group or acute bronchitis, 9%), especially given that the duration of antibiotic treatment for this started on antibiotics in the PCT group was still longer than recommended for most indications (8.0 days).[6]
- In “real life” settings use of PCT without additional antibiotic stewardship interventions is not likely to be successful. A recently published RCT in 14 US hospitals where patients with lower respiratory tract infections were randomized either to a PCT algorithm or usual care without additional antibiotic stewardship interventions did not result in significant differences in antibiotic exposure (4.2 versus 4.3 days).[7]

Conclusions/recommendations

- Currently, the role of PCT is not routinely recommended in the diagnosis and management of patients with sepsis and community-acquired pneumonia in most international guidelines
March 2019

- We suggest NOT to list the PCT in the revised version until its exact role and integration in a comprehensive stewardship policy is derived from new randomised clinical trials in diverse settings.

- A full WHO guidance document on when and how to use PCT should be developed and current listing in the WHO EDL could be a waste of resources without improving antibiotic use.

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References