

## PCT-guided antibiotic treatment improves outcomes in sepsis patients



Procalcitonin (PCT)-guided antibiotic treatment in ICU patients with infection and sepsis patients results in improved survival and reduced antibiotic treatment duration, according to results of a new meta-analysis published in the journal Critical Care.

Early identification of sepsis and appropriate initial management including the start of antibiotic treatment and fluid resuscitation improves outcomes. In addition, monitoring of patients during treatment both for timely escalation of therapy in case of treatment failure and de-escalation in case of a favourable treatment response has an important impact on patient recovery. Given that clinical signs for monitoring patients with sepsis can be ambiguous, the use of additional biomarkers mirroring specific physiopathological pathways has been proposed.

PCT has emerged as a sensitive biomarker that provides prognostic information in patients with infections, and thus may improve sepsis management. However, the clinical utility of PCT levels in guiding antibiotic treatment decisions in patients with sepsis remains unclear. An international team of researchers therefore performed a patient-level meta-analysis of 11 randomised controlled trials (RCTs) to assess the safety of using PCT to guide antibiotic decisions in ICU patients with infection and different sepsis severities and with the involvement of different organs.

For this meta-analysis, the researchers in February 2018 updated the database of a previous individual patient data meta-analysis which was limited to patients with respiratory infections only. The researchers used individual patient data from 11 trials that randomly assigned patients to receive antibiotics based on PCT levels (the "PCT-guided" group) or the current standard of care (the "controls"). The primary endpoint was mortality within 30 days. Secondary endpoints were duration of antibiotic treatment and length of stay.

After analysing all pertinent data, the international research team reported these key findings:

- Mortality in the PCT-guided group (n = 2,252) was significantly lower compared with the control group (n = 2,230) (21.1% vs. 23.7%; adjusted odds ratio 0.89, 95% confidence interval (CI) 0.8 to 0.99; p = 0.03).
- These effects on mortality persisted in a subgroup of patients meeting the sepsis 3 definition and based on the severity of sepsis (assessed on the basis of the Sequential Organ Failure Assessment (SOFA) score, occurrence of septic shock or renal failure, and need for vasopressor or ventilatory support) and on the type of infection (respiratory, urinary tract, abdominal, skin, or central nervous system), with interaction for each analysis being >0.05.
- Procalcitonin guidance facilitated earlier discontinuation of antibiotics, with a reduction in treatment duration (9.3 vs. 10.4 days; adjusted coefficient –1.19 days, 95% CI –1.73 to –0.66; p < 0.001).

"Whether the reduction in antibiotic exposure fully explains the mortality effects seen in our data needs to be investigated in future trials," the authors note. "These findings have substantial clinical and public health implications."

Limitations of this analysis include incomplete adherence to the PCT algorithm among the included trials, exclusion of immunocompromised patients in most trials, and heterogeneity among trials with regard to patient populations and follow-up of patients. In addition, cost-effectiveness analyses need to be undertaken to determine whether using PCT-guided care is a cost-effective intervention, the authors say.

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