Editorial
Procalcitonin direct antibiotic therapy in immunocompromised patients

Procalcitonin (PCT) is a prohormone produced by the C-cells of the thyroid. Once split it becomes calcitonin and is responsible for calcium homeostatic. In response to pro-inflammatory cytokines extrathyroidal nonendocrine tissue produces immature PCT which can be detected in the circulation, reaching a maximum within approximate 12–24 hours after the onset of inflammation. Uniquely, interferon-gamma, which is released during viral infections, inhibits the production of PCT thereby making elevations in PCT useful in detecting bacterial infections as opposed to viral infections.[1] Despite these potential benefits the role of PCT in the intensive care unit (ICU) has not been fully established. The problem is that PCT elevations can take place because of non-infective systemic inflammation, as seen during major trauma or after cardiac bypass, thereby making it difficult to differentiate bacterial from non-bacterial causes.[2] This, together with the 24–48 hour time lag after the onset of an infection, as well as the persistent elevation seen after a major episode of systemic inflammation, limits the diagnostic accuracy of PCT.

Despite these limitations the use of PCT algorithms to direct antibiotic duration and discontinuation in ICU patients has shown great success reducing the number of patients receiving antibiotics as well as shortening antibiotic duration.[3] Interestingly, a recent individual patient meta-analysis found that in the 2252 patients who received PCT-guided therapy, the morality rate was 21.1% as opposed to 23.7% in the 2230 patients who received standard of care (adjusted odds ratio 0.89, 95% CI 0.8 to 0.99; p=0.03). In addition, those who were in the PCT arm had their antibiotics discontinued earlier than the control arm.[4] PCT clearly has a role to play here and has been widely adopted in many local ICUs.

However, all these trials excluded patients with severe immuno-compromise and as a result there is very little data to guide PCT use in this subpopulation. It is into this gap that the paper by Naidoo and colleagues speaks.[5] In their study, conducted at a tertiary level intensive care unit (ICU) in KwaZulu-Natal, they examined the relationship between PCT and ICU morality, length of stay, and ventilation duration in patients admitted to ICU with a diagnosis of community acquired pneumonia. As a secondary outcome, they explored the ability of PCT to predict aetiology as well as organ dysfunction. Out of the 100 patients enrolled in the study 62% were HIV positive and had a median CD4 count of 64 cell/µL. A PCT elevated > 10 ng/ml was predictive of a higher morality than those in whom the PCT decreased or remained unchanged and was also associated with a greater need for inotropic support and acute renal failure.[5]

The study was well conducted with a good yield on formal microbiological cultures and in a population with profound respiratory impairment.[5] This provides us with real-world practical data on how PCT performs in a South African population and highlights the wide variety of microorganisms causing community acquired pneumonias in our ICUs. A concern in this study is the use of repeated univariate testing without p-value correction, which may have increased the risk of false positives. It may have been more appropriate to conduct a logistic regression analysis with multiple predictors to both spare power and to understand the strength of the association with PCT in the presence of other risk factors.[5]

What is striking in this study was that there was no association between admission or 48hour PCT categories and the microorganisms cultured, except in those with a PCT > 10 ng/ml where there was a higher incidence of bacterial infections.[5] This raises a concern that the PCT directed antibiotic guidelines and their thresholds which have been developed in different study populations may not be relevant in an ICU population such as this. This study has clearly identified a gap in our understanding of PCT kinetics in immunocompromised patients and can serve as a great starting point from which to further explore this question. The authors are to be congratulated on taking this important first step.

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