Measurement and determination of Procalcitonin (PCT)

Medical Services Advisory Committee

Record Status
This is a bibliographic record of a published health technology assessment. No evaluation of the quality of this assessment has been made for the HTA database.

Citation

Authors' objectives
An application requesting MBS listing of a commercial immunoluminometric assay (ILMA) used to determine the concentration of procalcitonin (PCT) in human serum and plasma for for diagnosing life threatening infections and sepsis in patients and monitoring the course and control of antibiotic therapy was received from B.R.A.H.M.S Pty Ltd by the Department of Health in April 2009. Procalcitonin (PCT), a glycoprotein, is a peptide precursor of the hormone calcitonin. However the exact origin and mechanisms of PCT remain largely unknown. In microbial infections and severe systemic inflammatory responses, the serum level of PCT markedly increases approximately three hours after a pro-inflammatory stimulus or bacterial induction, reaching maximum values after 6-8 hours. Serum levels have been shown to reach levels >0.1 ng/mL in localised infection (e.g., lower respiratory tract infections (LRTIs)) and between 10 and 100 ng/mL or greater in severe sepsis. The increase in serum PCT levels in response to bacterial infection has been shown to correlate with the severity of the infection and with mortality. Measured serum and plasma PCT levels are interpreted based on the clinical setting, the site and extent of infection, and co-morbidities. Increased levels of PCT may not always be related to systemic bacterial infection; the level of PCT has also been shown to markedly increase in: - neonates <48 hours of age (physiological elevation). - patients undergoing treatment with OKT3 antibodies and other drugs stimulating the release of pro-inflammatory cytokines. - patients with invasive fungal infections, acute attacks of plasmoidium falciparum malaria - patients with prolonged or severe cardiogenic shock, prolonged severe organ perfusion anomalies, small cell lung cancer, medullary C-cell carcinoma of the thyroid. - patients with severe systemic inflammatory conditions such as inhalational injury, pulmonary aspiration, severe burns, pancreatitis, heat stroke, mesenteric infarction), multi-trauma, extensive surgery, and infections such as pneumonitis. The measurement of PCT is a two-site immunoassay used to determine the concentration of PCT in human serum and plasma. All assays are based on the formation of a —sandwich‖ antigen-antibody complex. The intended purpose of the measurement of PCT is to determine the concentration of PCT in human serum and plasma in patients suspected of bacterial infection and to guide microbial therapy.

Authors' conclusions
Routine measurement of PCT, with corresponding obligatory guidelines for antimicrobial therapy, for patients presenting to the ED with query LRTI or exacerbation of chronic obstructive pulmonary disease (ECOPD), alongside clinical assessment and other measures of sepsis, usually resulted in a reduction in the use of antibiotics. However, only one of the trials set in the ED was powered to address the question of whether this reduction in antibiotic therapy had any consequences for patients, and it reported non-significant increases in mortality and disease specific complications. The routine use of a PCT test for every person with a query LRTI, in the emergency department, would result in a large number being requested. The available evidence does not justify the routine measurement of PCT and use of a PCT-guided algorithm for antimicrobial therapy in the ED, as used in these trials. The routine measurement of PCT, with corresponding obligatory guidelines for antimicrobial therapy, as an indicator of sepsis alongside clinical assessment for patients in an ICU setting may not result in a reduction in antibiotic therapy. It was unclear whether following a PCT-guided algorithm for initiating or ceasing antibiotic therapy would have consequences for patients, as the majority of the studies in the ICU setting were not powered to answer this question. The one study that was powered to detect 28-day mortality reported no difference in survival, but did report that patients in the PCT-guided arm suffered increased rates of organ-related harm and had prolonged admission to ICU. The routine use of a PCT test in the ICU setting, often recommended on a daily basis, would result in a large number being requested. The available evidence does not justify the routine measurement of procalcitonin, and use of a PCT-guided algorithm for antimicrobial therapy
in the ICU setting. The routine measurement of PCT, with corresponding obligatory guidelines for antimicrobial therapy, for patients presenting to their GP with symptoms of respiratory tract infection (RTI), alongside clinical assessment, resulted in a reduction in the use of antibiotics in the two studies evaluated. However, neither of the trials was powered to measure any consequences to patients that may result from a reduction in antibiotic therapy. The routine use of a PCT test for every person who presents to their GP with the symptoms of RTI would result in a large number being requested. The evidence does not justify the routine measurement of PCT and use of a PCT-guided algorithm for antimicrobial therapy in the general practice setting. Consistent information regarding the accuracy of levels of PCT needed to reliably differentiate between infectious and non-infectious SIRS appears to be lacking.

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Address for correspondence
MDP 106, GPO Box 9848, Canberra ACT 2601 AUSTRALIA Email: msac.secretariat@health.gov.au

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