Procalcitonin Use in Critical Care

AIM: To provide guidance on the use of procalcitonin in critical care. It must be noted that procalcitonin should be used as an adjunct and not a replacement for sound clinical judgement.

KEY POINTS

Patients presenting with acute respiratory tract infections, systemic inflammatory response syndrome or sepsis frequently exhibit symptoms that are not specific to each disease. Sepsis is common among intensive care unit (ICU) patients with overall ICU mortality rates in the region of 26% (Sakr et al 2018). Bacteria are the most common cause of sepsis, but systemic viral and fungal infections can also occur (NICE 2015).

Early, appropriate antimicrobial therapy is vital in achieving the best possible outcome for patients with sepsis and septic shock (SSCG 2016). However clinical signs and routine laboratory parameters such as white cell count and C-reactive protein, whilst sensitive, lack the specificity required when diagnosing bacterial infection (Reinhart and Meisner 2011).

The need to distinguish between infectious and non-infectious as well as different pathogens has led to the emergence of the diagnostic biomarker procalcitonin (PCT) (Schuetz et al 2019).

PROCALCITONIN

PCT is a 116 amino acid polypeptide prohormone synthesised by thyroid C-cells and released into its mature form calcitonin. Thus, serum PCT is typically undetectable in healthy people when standard assays are used.

WHY DOES PROCALCITONIN INCREASE?

In the presence of bacterial pathogens, PCT is released from multiple tissues providing useful information about the presence of bacterial infection (UpToDate 2020). Conversely, viral cytokines attenuate PCT levels, thereby providing a useful distinction between bacterial and viral infections (Meisner 2014 and Schuetz et al 2019).

PROCALCITONIN KINETICS

Serum PCT levels rise approximately 2 to 4 hours after the onset of bacterial stimulus with levels peaking at 24 to 48 hours.

Peak levels correlate with the severity of infection and therefore provide prognostic information and can assist in decisions to obtain further diagnostic testing (Schuetz et al 2019). Higher levels are observed in patients with septic shock and sepsis. After reaching peak levels, plasma PCT will decline by 50% at 1 to 1.5 days with effective treatment (Meisner 2014). Elimination rates of PCT may be reduced with renal dysfunction. A low PCT does not exclude the possibility of bacterial infection as the initial test may have been taken early in the stages of the infective process.

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NON-INFECTIOUS ELEVATIONS IN PROCALCITONIN

- Severe burns and major trauma
- Major Surgery (cardiac and major abdominal)
- Multi-organ failure (prolonged severe perfusion deficits)
- Treatments which stimulate proinflammatory cytokines
- Severe liver and renal dysfunction
- Massive tumour necrosis
- Tumour Lysis Syndrome
- Rhabdomyolysis
- Autoimmune disorders
- Cardiogenic shock

THE INDICATIONS FOR PROCALCITONIN MEASUREMENT

- Confirmation or exclusion of diagnosis of sepsis, severe sepsis, or septic shock.
- Severity assessment and follow up of systemic inflammation mainly induced by microbial infection.
- To guide antibiotic therapy and in terms of commencement, escalation of therapy in case of treatment failure or de-escalate in the case of favourable treatment response.

SENDING A PROCALCITONIN SAMPLE

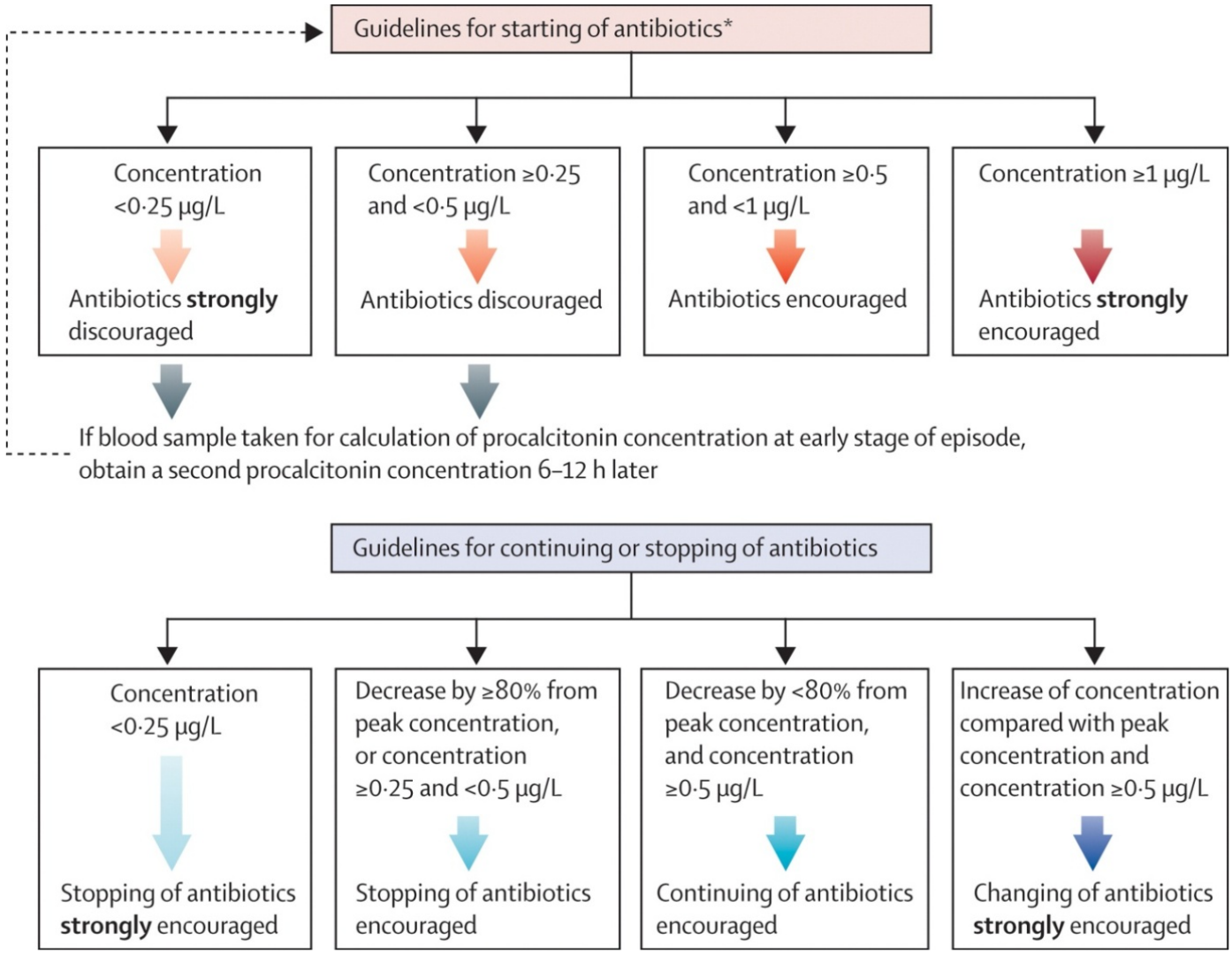
Request is available from WebICE under the Biochemistry tab as Procalcitonin is sent in a standard Gold (aka Yellow) top blood bottle.

Important Notes	Tube Colour	Tube Type	Information
The sample should be inverted about six times to ensure the blood and gel mixes to activate the clotting process. **The samples must not be shaken to mix the blood**	 Gold	Serum Separating Tube (SST)	This tube type is used for the vast majority of Biochemistry, Immunology and Serology tests. Please check the website if unsure of the correct sample type.

A PCT test should be authorised by the Consultant Intensivist, ideally during the morning ward round. The test is available 24 hours a day, though the need out-of-hours should be small.

HOW TO INTERPRET PCT RESULTS

Guidelines for starting, continuing, or stopping of antibiotics according to procalcitonin concentrations.



Derived from Bouadma et al (2010) the PRORATA study Lancet; 375: 463-474.

EVIDENCE

Reduction in antibiotic duration and safety of PCT guided therapy in ICU patients

A recent meta-analysis of 11 randomised controlled trials comparing PCT-guided antibiotic treatment with standard care (non-PCT guided) in critically ill patients with sepsis of any type (Wirz et al 2018) found mortality was significantly lower in the 2252 PCT-guided patients compared with the 2230 standard care group (21.1% vs 23.7%). In addition, the meta-analysis also found that in sepsis patients, PCT use led to an earlier discontinuation of antibiotics with a reduction in treatment duration 9.3 days vs 10.4 days.

A Cochrane systematic review and meta-analysis (Schuetz et al 2017) of 26 randomised controlled trials including patient data from 6708 patients, with varying severities of respiratory infections investigated the effect of PCT-guided antibiotic decision making. The review demonstrated that PCT use in the context of respiratory infections reduced antibiotic exposure (from 8.1 days to 5.7 days), antibiotic side effects (decreased from 22.1% to 16.3%) and mortality (10% vs 8.3% p=0.037).

The multi-centred Stop Antibiotics on guidance of Procalcitonin (SAPS) randomised controlled trial (de Jong et al 2016) compared PCT-guided antibiotic treatment with standard care and found the use of PCT resulted in lower antibiotic exposure (5 days vs 7 days) and significantly lower mortality 1 year (36% vs 43%).

The recent single-centre PROGRESS trial (Kyriazopoulou et al 2021) investigated whether PCT guided early discontinuation of antibiotic treatment would reduce the incidence of death by multi-drug resistant organisms (MDROs) and acquisition of clostridium difficile. The study revealed a lower 28-day mortality in the PCT guidance arm compared with standard care (15.2% (19/125) vs 28.2 (37/131 p=0.02). In addition, the PCT guided group had a lower incidence of adverse events specifically, diarrhoea and acute kidney injury.

Document Details	
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External references used

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Amendments History

No	Date	Amendment
1		
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