Procalcitonin algorithms for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms

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CRD summary
This review found that measurement of procalcitonin to inform antibiotic prescription decisions for patients with respiratory tract infections or sepsis reduced antibiotic exposure without worsening mortality. The review was well-conducted and the authors’ conclusions are likely to be reliable.

Authors’ objectives
To evaluate the evidence for use of algorithms based on procalcitonin levels to guide decisions on antibiotic use in patients with respiratory tract infections or sepsis.

Searching
EMBASE, MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to 2011 (month not specified). Search terms were reported. No language restrictions were imposed. Reference lists of relevant systematic reviews and clinical trials were screened. The authors searched clinical trial registries and contacted experts in the field to identify additional studies.

Study selection
Randomised controlled trials (RCTs) that evaluated measurement of procalcitonin levels to inform decisions regarding antibiotic therapy in adults with respiratory tract infections or sepsis were eligible for the review.

Included trials were performed in primary care, emergency department or intensive care unit/in-patient settings. Trials used a variety of different algorithms based on procalcitonin levels, mostly to recommend discontinuation of antibiotics. Control treatments were not reported. Most trials recruited patients with respiratory tract infections; patients with sepsis were also included in some trials. Primary outcomes included mortality, length of stay and measures of antibiotic use.

Two reviewers independently selected studies for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Trial quality was assessed based on adequacy of: sequence generation; allocation concealment; blinding of physicians, patients and outcome assessors; risk of attrition bias; and freedom from selective outcome reporting.

It appeared that validity was assessed by two reviewers independently and disagreements were resolved by consensus.

Data extraction
Odds ratios (ORs) and 95% confidence intervals (CIs) for mortality were extracted or calculated. Measures of antibiotic use (prescription rate and duration) were extracted and used to calculate the relative reduction for the procalcitonin group compared with the control group.

Data were extracted by two reviewers independently. Disagreements were resolved by consensus.

Methods of synthesis
Pooled odds ratios and 95% confidence intervals were calculated using the Peto method. Heterogeneity was assessed using the Cochran Q test and $I^2$. Sensitivity analyses were performed to compare the results of trials at high versus low risk of bias as indicated by validity assessment. Data on antibiotic use were synthesised narratively by type of setting. Publication bias was investigated using funnel plots.
Results of the review
Fourteen RCTs with 4,467 participants were included in the review. Risk of bias was considered low for three trials and high for the rest.

Mortality did not differ significantly between procalcitonin and control groups across all trials (OR 0.91, 95% CI 0.73 to 1.14), in primary care (OR 0.13, 95% CI 0 to 6.64; two RCTs), in the emergency department (OR 0.95, 95% CI 0.67 to 1.36; six RCTs) and in intensive care unit/in-patient (OR 0.89, 95% CI 0.66 to 1.20; six RCTs) settings.

Measures of antibiotic use were consistently lower in the procalcitonin groups. This was attributed to lower prescription rates in less acutely ill patients and shorter duration of treatment in more acutely ill patients.

There was no evidence of significant heterogeneity or publication bias.

Authors’ conclusions
Measurement of procalcitonin to inform antibiotic prescription decisions appeared to reduce antibiotic exposure without worsening mortality for patients with respiratory tract infections or sepsis.

CRD commentary
The review question and inclusion criteria were generally clear, although control treatments were not specified and reported. The search covered a range of relevant sources without language restrictions and included some effort to locate unpublished studies. Publication bias was assessed using a standard method. Measures were taken to reduce the risks of errors and bias during the review process. Study quality was assessed appropriately and the results were used in the synthesis. Appropriate methods were used to synthesise the studies and to investigate heterogeneity.

This was a well-conducted review and the authors' conclusions are likely to be reliable. The recommendations for practice and further research seem appropriate.

Implications of the review for practice and research
Practice: The authors stated that procalcitonin-based algorithms should not be considered as the criterion standard of care and should supplement rather than replace clinical assessment.

Research: The authors stated that further trials of procalcitonin-based algorithms were required and presented proposed algorithms for evaluation in large multicentre trials in USA populations.

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