Serum procalcitonin for prediction of renal parenchymal involvement in children with urinary tract infections: a meta-analysis of prospective clinical studies
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CRD summary
The review found that in children with culture-proven urinary tract infection serum procalcitonin greater than 0.5ng/mL predicted renal parenchymal involvement (defined by Tc-99m dimercaptosuccinic acid scintigraphy) reasonably well. Limitations in review methodology together with apparent clinical heterogeneity and a wide range of reported sensitivity and specificity values mean that the authors' conclusions should be interpreted cautiously.

Authors' objectives
To determine whether serum procalcitonin (PCT) is a useful marker of acute renal parenchymal involvement (RPI), as determined by acute-phase Tc-99m dimercaptosuccinic acid (DMSA) renal scintigraphy, in children with culture-proven urinary tract infection.

Searching
PubMed and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to February 2009. Search terms were reported. Bibliographies of relevant articles were handsearched for additional studies.

Conference abstracts and studies published in languages other than English, Spanish, French, German, Italian or Greek were excluded.

Study selection
Prospective studies of children of any age with confirmed urinary tract infection were eligible for inclusion. Included studies were required to report baseline levels of procalcitonin in children with and without RPI. Children had to be assessed with DMSA scintigraphy within 14 days of presentation.

Ages of children in the included studies ranged from one week to 16 years and 68% of participants were female. Follow-up investigations conducted in addition to DMSA scintigraphy were renal ultrasound and voiding cystourethrography. A positive procalcitonin result was defined as serum procalcitonin greater than 0.5ng/mL to 0.6ng/mL.

Two reviewers independently assessed studies for inclusion.

Assessment of study quality
Assessment of methodological quality of included studies was based on the 14-item QUADAS tool. Eleven items were assessed in this review: representative patient spectrum; acceptable reference standard; delay between tests; partial and differential verification bias; incorporation bias; blinded interpretation of the index test and reference standard; clinical review bias; reporting of uninterpretable results; and explanation of withdrawals from the study. Items were rated as yes (positive), unclear or no (negative).

Quality assessment of included studies was performed using Review Manager version 5.0 software. The authors did not state how many reviewers performed quality assessment.

Data extraction
Data were extracted on numbers of true positive, false negative, false positive and true negative results for a procalcitonin cut-off of 0.5ng/mL to 0.6ng/mL, together with corresponding sensitivity and specificity values with 95% confidence intervals (CIs). Measured serum procalcitonin levels and available data on sensitivity, specificity and positive and negative predictive values of serum procalcitonin at different diagnostic cut-off values were extracted.

The authors did not state how many reviewers performed data extraction.
Methods of synthesis
A pooled estimate of the diagnostic odds ratio (DOR) was calculated using a random-effects model and a summary receiver operating characteristic (sROC) curve was plotted.

Between-study heterogeneity was assessed using $\chi^2$ and $I^2$ tests.

Results of the review
Ten prospective cohort studies (n=627, range 33 to 100) were included in the review. Blinding of study investigators for interpretation of both index test and references standard was unclear in most studies. Full details of quality assessment results were reported online.

Nine studies assessed a procalcitonin cut-off value of 0.5ng/mL and one study assessed a cut-off of 0.6ng/mL. At these cut-off values, sensitivity ranged from 0.59 (95% CI 0.41 to 0.75) to 1.00 (95% CI 0.82 to 1.00) and specificity ranged from 0.23 (95% CI 0.05 to 0.54) to 0.90 (95% CI 0.77 to 0.97).

The pooled estimate of DOR was 14.25 (95% CI 4.7 to 43.23). Significant between-study heterogeneity was noted ($\chi^2$ test, p < 0.001 and $I^2$ test 80%). When the two studies that reported a DOR with confidence intervals that included values of 1 (which indicated no significant diagnostic utility) were excluded from the analysis, the $\chi^2$ test showed no significant heterogeneity and the $I^2$ value was 36%; the pooled estimate of DOR excluding these two studies was 26.73 (95% CI 10.29 to 69.39).

Sensitivity analysis indicated that for studies that enrolled only children with febrile urinary tract infection, the DOR was 9.56 (95% CI 3.01 to 30.39).

Authors’ conclusions
In children with culture-proven urinary tract infection, a serum procalcitonin value of greater than 0.5ng/mL predicted the presence of RPI (defined by DMSA scintigraphy) reasonably well.

CRD commentary
The review addressed a clearly stated research question defined by appropriate inclusion criteria. The literature search was limited to two bibliographic databases and reference screening. Language and publication status restrictions further limited the capacity of the likely retrieval rate of the search and left open the possibility of language and publication biases. Measures were taken to reduce error and/or bias in the selection of studies for the review; it was unclear whether similar measures were applied throughout the review process. Methodological quality of included studies was assessed and discussed along with relevant study details. Given the evidence of statistical heterogeneity between studies as well as the apparent heterogeneity in clinically important factors (such as age and gender distribution), use of a pooled estimate of DOR was of questionable value. The apparent clinical heterogeneity and wide range of reported sensitivity and specificity values mean that the authors’ conclusions should be interpreted cautiously.

Implications of the review for practice and research
Practice: Procalcitonin may help identify those children with urinary tract infection who require more intense evaluation and management.

Research: The authors made no recommendations for research.

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