Noninvasive techniques to detect fetal anemia due to red blood cell alloimmunization: a systematic review


Authors' objectives
To estimate the diagnostic value of foetal ultrasonography and Doppler blood flow velocity in the evaluation and prediction of foetal anaemia.

Searching
MEDLINE and EMBASE were searched from 1970 to 2000; the search terms were reported. The Cochrane Library and relevant specialist registers of the Cochrane Collaboration were also searched. Recent issues of specialist obstetrics journals were handsearched, as were the reference lists of primary studies and review articles.

Study selection
Specific interventions included in the review
Studies of foetal ultrasound parameters, or Doppler studies indicative of foetal haemoglobin, were eligible for inclusion. The studies evaluated foetal spleen perimeter measurement using ultrasound and the following Doppler measurements: ductus venosus maximum systolic velocity; middle cerebral artery maximum and mean velocity; umbilical vein mean velocity; thoracic aorta mean and maximum velocity; umbilical vein maximum velocity in combination with the thoracic aorta mean velocity; and umbilical artery Purcelot index combined with the thoracic aorta maximum velocity.

Reference standard test against which the new test was compared
Studies that used foetal haemoglobin concentration obtained from foetal blood samples (in utero or postpartum) were eligible for inclusion. The studies used different cut-offs to define foetal anaemia.

Participants included in the review
Studies of women with pregnancies affected by red cell alloimmunisation were eligible for inclusion. This included alloimmunisation resulting from Rh, Kell, or rarer antigens (anti-c).

Outcomes assessed in the review
The studies had to report sufficient data to construct 2x2 tables of test performance. The primary outcomes for the review were likelihood ratios (LRs).

How were decisions on the relevance of primary studies made?
Two authors independently reviewed the identified studies. Potentially relevant studies were identified by scanning the titles and abstracts obtained from the searches. The full text of these articles was retrieved, and the final decision about inclusion was made on the basis of information contained in the full text. Any disagreements regarding inclusion were resolved through discussion, or by referral to a third reviewer when agreement could not be reached.

Assessment of study quality
The studies were assessed for: prospective recruitment, appropriateness of the sample, description of the diagnostic intervention, blinding (diagnostic review bias) and reference standard. This information was used to grade studies according to a hierarchy of evidence consisting of 6 levels. Only studies fulfilling levels 1 to 4 were included in the review. Excluded studies (level 5 and 6) were those in which the reference standard was not applied to all patients, the reference standard was not applied independently, or the study relied on expert opinion with no explicit appraisal. Two independent reviewers performed the validity assessment and resolved any disagreements by consensus.
Data extraction
The results from each study were extracted as 2x2 data comparing the results from the diagnostic test with the reference standard. The sensitivity, specificity, LRs, and pre- and post-test probabilities were calculated for each study. For studies that included cells with 0 values, 0.5 was added to all cells to allow the calculation of LRs.

Methods of synthesis
How were the studies combined?
The authors planned to pool the LRs. However, this was not possible because of the heterogeneity of the methods and cut-off levels among the included studies. A narrative synthesis was therefore reported.

How were differences between studies investigated?
Differences between the studies were discussed.

Results of the review
Eight studies (362 pregnancies) reporting 11 evaluations were included. Four studies were prospective and four did not report whether the study was prospective. Five studies enrolled consecutive patients; this was not reported in the other three studies.

The positive LRs ranged from 0.83 (negative LR 1.14) to 10.50 (negative LR 0.24). The negative LRs ranged from 0.02 (positive LR 8.45) to 1.14 (positive LR 0.83). These results suggested that ultrasound is a poor test for both ruling in and ruling out foetal anaeemia.

Authors’ conclusions
The literature reporting noninvasive techniques to predict foetal anaemia was methodologically poor and a standard approach to the evaluation of the techniques was lacking. A recommendation for practice cannot be generated without further rigorous research.

CRD commentary
This was a well-conducted and clearly presented review. The objective was clearly stated and was supported by well-defined inclusion criteria. A reasonable literature search was conducted, although attempts to locate unpublished studies were not made; thus, the review may be subject to publication bias. Details of the review process were reported, and these included appropriate steps to minimise bias. A detailed quality assessment was performed and the results of this were discussed. Adequate details of the studies were tabulated. The decision not to pool the results was appropriate given the heterogeneity between the studies. The authors’ conclusions are supported by the results presented.

Implications of the review for practice and research
Practice: The authors stated that a recommendation for practice could not be generated without further rigorous research.

Research: The authors did not state any implications for research.

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