Screening for bilirubin encephalopathy  
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CRD summary  
This review concluded that a combination of risk factors and early total serum bilirubin measurement had better ability to predict hyperbilirubinaemia than risk factors alone. These conclusions were based on a single study, which combined with limitations in the search, quality assessment and synthesis mean that the authors' conclusions are unlikely to be reliable.

Authors' objectives  
To determine the effectiveness of strategies to prevent chronic bilirubin encephalopathy. In particular the review aimed to determine: (1) whether screening using risk factor assessment and/or bilirubin testing reduced the incidence of acute or chronic bilirubin encephalopathy; (2) whether risk factor assessment accurately identified infants who may benefit from bilirubin testing; (3) whether bilirubin testing accurately identified infants who may benefit from phototherapy; (4) harms of screening; (5) whether treatment reduced the risk of bilirubin encephalopathy in infants identified by screening; and (6) the harms of treatment with phototherapy.

Searching  
MEDLINE was searched from September 2001 to August 2007. Search terms were reported. Bibliographies of existing studies were screened and experts in the area were contacted to identify additional studies. The review was an update of a previous report (see Other Publications of Related Interest) in which searches were conducted to September 2001; studies published before this date were not included in the current review. The review was restricted to English-language studies published in peer-reviewed journals.

Study selection  
Experimental and observational studies with comparison groups (concurrent or historical or before-after comparison) of healthy term or near-term infants (≥35 weeks gestation) were eligible for inclusion if they assessed screening for risk factors or total serum and/or transcutaneous bilirubin (TSB or TcB) or phototherapy or exchange transfusion compared to non screening and assessed different risk levels for developing hyperbilirubinaemia defined by the screening program or no treatment. Eligible studies needed to report rates of acute or chronic bilirubin encephalopathy, rates of serum bilirubin, risk for developing hyperbilirubinaemia or undergoing phototherapy or health outcomes and adverse events related to phototherapy. Studies of adverse events associated with phototherapy case reports and case series were included.

One reviewer screened abstracts for inclusion and a second reviewer reviewed all potentially relevant abstracts. The authors did not state how full-text studies were assessed for inclusion.

Assessment of study quality  
Studies were assessed for methodological quality with criteria defined by United States Preventive Services Task Force. Studies were assigned a rating of good, fair or poor. Criteria included randomisation, definition of outcomes, consideration of potential confounders in cohort studies and intention-to-treat analysis in randomised controlled trials (RCTs) and presence of verification bias in diagnostic accuracy studies.

Two reviewers independently assessed study quality. Disagreements were resolved by a third reviewer. The quality of studies of adverse effects was not assessed.

Data extraction  
Data were extracted from screening studies to calculate sensitivity, specificity, positive and negative likelihood ratios and area under the receiver operating characteristic curve (AUC).
Methods of synthesis
A narrative synthesis was presented due to differences between studies.

Results of the review
Eighteen studies were included in the review. Three studies were considered to be of fair quality and six of poor quality; the quality of the remaining nine studies was not assessed as these were of adverse events.

Did risk factor assessment accurately identify infants who may benefit from bilirubin testing? (three studies, n=6,974):
One retrospective cohort study and one nested case-control study and retrospective cohort study reported in the same paper assessed this question. All studies were rated as fair on the quality assessment. Risk scores were based on personal history. AUC ranged from 0.69 to 0.83.

Did bilirubin testing accurately identify infants who may benefit from phototherapy? (nine studies, n at least 133,923):
Four studies (three fair quality, one poor quality), two prospective and two retrospective cohort studies suggested comparable diagnostic abilities of early total serum bilirubin (TSB) measurements to predict late high TSB measurements. AUC ranged from 0.79 to 0.83 in the two studies that reported data on this.

Two poor-quality studies suggested that TcB measurements less than specific thresholds may predict TSB measurements that did not indicate the need for phototherapy. Verification bias was a problem in one of the studies.

One fair-quality study that compared various screening strategies in predicting later hyperbilirubinaemia suggested that the combination of the modified risk index with early TSB level significantly enhanced prediction compared with using one of the screening strategies alone.

Three poor-quality studies assessed outcomes associated with the implementation of TcB screening and use of hour-specific bilirubin nomogram. These studies were subject to confounding and only provided indirect evidence.

Harms of treatment with phototherapy (nine studies, n at least 510)
One study found an association in children between sizes of melanocytic nevi and exposure to neonatal phototherapy. Adverse events reported included hypo- or hyperthermia, weight loss, gastrointestinal problems, skin rash or erythema and changes in cardiopulmonary parameters. No definitive harm could be attributed to phototherapy based on the included studies.

No studies were identified that assessed whether screening using risk factor assessment and/or bilirubin testing reduced the incidence of acute or chronic bilirubin encephalopathy, harms of screening or whether treatment reduced the risk of bilirubin encephalopathy in infants identified by screening.

Authors' conclusions
Based on retrospective analyses among infants who had both early and late TSB measurements available, the combination of risk factors and early TSB measurements had better diagnostic ability to predict clinically significant hyperbilirubinaemia when compared with risk factors alone.

CRD commentary
The review addressed several defined objectives. Inclusion criteria were reported. The literature search included only one electronic database and was restricted to published English-language studies, which raised the possibility of language and publication biases. The review was an update of an earlier review. Instead of incorporating the findings of the newer studies with those included in the original review, this review was restricted to studies published after the original review. Appropriate steps were taken to minimise bias and errors in the quality assessment; no such steps were taken when screening the results of the searches. Details were lacking on methods used for assessment of full-text papers for inclusion and data extraction. A formal quality assessment was conducted and some relevant criteria were considered. It was unclear exactly how the gradings of fair and poor quality were achieved, which made these difficult to interpret. A narrative synthesis was appropriate given the differences between studies, but this lacked clarity and was
difficult to interpret. Some relevant study details were summarised in tables, but these also lacked clarity and contained limited data on outcomes and participants.

The authors’ conclusions were based on a single study and did not consider the other studies included in the review, which combined with the limitations discussed above mean that the authors’ conclusions are unlikely to be reliable.

Implications of the review for practice and research
Practice: The review did not state any implications for practice.

Research: The authors stated that a prospective independent validation study that compared multiple screening strategies (such as risk factors only, early TSB only and combinations of these) in the same infants would be informative. Future studies on preventive and screening strategies should actively monitor potential harms from implementing such strategies in both infants and their family members. Prospective controlled studies were required to clarify the relationship between exposure to neonatal phototherapy and the development of melanocytic nevi.

Bibliographic details

Original Paper URL
http://www.ahrq.gov/clinic/uspstf/uspshyperb.htm

Other publications of related interest


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Subject indexing assigned by CRD

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.