International Child Health Review Collaboration

When should Exchange Transfusion be performed in hyperbilirubinaemia?

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The World Health Organization has produced guidelines for the management of common illnesses in hospitals with limited resources. This series reviews the scientific evidence behind WHO's recommendations. The WHO guidelines, and more reviews are available at: http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/PB.htm

This review addresses the question: *When should Exchange Transfusion be performed in hyperbilirubinaemia?*

The **WHO Pocketbook of Hospital Care for Children** recommends that if the Bilirubin level is very elevated and one can safely do an exchange transfusion then one should consider doing so. The level of bilirubin at which this should be considered is given in a table which takes into account postnatal age and prematurity or other risk factors (Pocketbook chapter 3.12.1, page 58).

Introduction:

Severe hyperbilirubinaemia in neonates is associated with the development of bilirubin encephalopathy, or kernicterus. Exchange blood transfusion reduces serum bilirubin levels by removal of the bilirubin itself, and can also reduce haemolysis in haemolytic disease of the newborn. Exchange transfusion is not without significant mortality and morbidity, and is usually employed when phototherapy is unable or unlikely to adequately control the rising bilirubin levels. The objective of this review is to document the evidence surrounding when exchange transfusions should be performed in hyperbilirubinaemia.

Methodology

The search string: (hyperbilirubinemia OR jaundice) AND (exchange transfusion), found 12 systematic reviews and 21 articles using the "therapy" and "specific" filters. All abstracts and most of the original articles were read.
References from the sources articles thought to be potentially useful were also traced.

Results

There were no systematic reviews or RCTs that directly addressed the question.
Three systematic reviews sought to provide evidence-based treatment guidelines for neonatal jaundice [1-3]. Each acknowledges from case series that serum bilirubin concentration alone does not predict kernicterus, and that other factors are likely to modify its influence (such as maturity, and condition of the neonate). No references are provided as to how thresholds for exchange transfusion are determined.
Original threshold levels for exchange transfusion appear to be derived from an early paper which noted that kernicterus did not occur in the institution when a policy of treatment (with phototherapy or exchange transfusion) to avoid serum bilirubin levels of 20mg/dL was instituted [4]. A multicentre RCT in the mid-1970s aiming to evaluate the safety of phototherapy varied the threshold for exchange transfusion depending on gestational age and general condition of the neonate [5]. In this study (n=1339) there was no case of kernicterus, and neurodevelopmental outcomes at 6 years were comparable to the general population. Similar thresholds have been employed in subsequent studies.

Discussion

Indications for exchange transfusion in neonatal hyperbilirubinaemia are historical and not supported by direct trial evidence, but rather indirectly by observing reducing incidences of kernicterus with treatment. Original thresholds have been modified over time as more data has accumulated, particularly regarding health term infants (where thresholds for treatment have been increased). Because of the disabling and irreversible nature of kernicterus, it is unlikely that future trials will be able to provide high level evidence. Careful observation of incidence of kernicterus and/or neurodevelopmental outcomes will be important as guidelines for treatment of neonatal jaundice continue to evolve.

Summary

Indications for exchange transfusion (as well as for phototherapy) are somewhat arbitrary but have evolved slowly over the past 50 years, without increases in the incidence of kernicterus. Recommended threshold levels of serum bilirubin differ between sources, though a level of 20mg/dL (340mmol/L) appears to be a standard threshold with modifications for maturity and general condition of the infant (Grade C evidence).
The treatment guidelines of the American Academy of Pediatrics [2] are comprehensive, reflect modern expert opinion, and are in wide use globally (with some local adaptation). In the absence of direct evidence based guidelines, these are recommended.

References

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