Recent Advances in Management of Neonatal Jaundice

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Topics

- Incidence of neonatal jaundice
- Etiologies of neonatal jaundice
- Current Phototherapy Guidelines
- Prolonged neonatal jaundice
Incidence of Neonatal Jaundice

- **Significant hyperbilirubinemia > 250 umol/L (14.6mg/dL) 2.4% of polyclinic attendance** J Vingson-Guillem et al (NHG ASC 2006)

- **Severe Hyperbilirubinemia > 340 umol/L (20mg/dL) = 5.5/1000 live births** W. Wirral Arch Disease Child health 2007

- **Critical hyperbilirubinemia > 510 umol/L (29.6mg/dL) = 7.1/100,000 live births** Manning Arch Disease Child health 2007
Bilirubin metabolism- conjugation is the rate limiting step
Etiology of Neonatal Jaundice

• Increased bilirubin production
  - ABO isoimmunization
  - Rhesus isoimmunization
  - Glucose-6-Phosphate dehydrogenase deficiency
  - Red cell membrane defect
    (Hereditary Spherocytosis, Pyruvate kinase deficiency)
Etiology: Increased red cells load

- Polycythemia
- Infant of Diabetic mum
- Blood extravasation
Etiology: Decreased clearance

- Defects in bilirubin conjugation
- Inborn errors of metabolism
- Congenital hypothyroidism
Etiology: increased enterohepatic circulation

- Delayed meconium passage
- Intestinal obstruction
- Babies kept nil orally like those with gastrointestinal problems.
UGT 1a1 Mutation

- Dose dependent genetic interaction in neonatal hyperbilirubinemia between Gilbert’s syndrome and G6PD deficient in Jews
- UGT 1a1 with homozygous promoter mutation A(TA)7TAA mutation leads to Gilbert’s
- Defect in conjugation of bilirubin
UGT1a1 mutation - Taiwan

- Huang CS et al *Pediatr Res* 2002 Vol 52; 4; 601-05
- Chinese and Japanese carry Gly71Arg mutation in UGT 1a1 gene
- Most common cause of jaundice is Breast feeding (20%), ABO incompatibility (19%), prematurity (16%)
- Significant association of hyperbilirubinemia (>254 umol/L) in patients with Gly71Arg mutation (44.7% vs 25.7%) p < 0.001
UGT 1a1 mutation - Singapore

- UGT1a1 Haplotype mutation among Asians in Singapore- Zhou YY, Lee Ly et al Neonatology 96(3);150-5
- Cohort study (241 babies)
- 40% Chinese carry the Gly71Arg mutation
- Phototherapy twice as frequent (20%) in mutants
- Incidence of phototherapy shows a statistically significant trend with mutations.
Preventive/Adjunct therapy

• Phenobarbitone
• Induce liver enzymes
• Antenatal drug therapy
• Side effect: Sedation, Steven-Johnson syndrome
3. Management of neonatal jaundice
Management of neonatal jaundice

- Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation
- (Clinical Practice Guidelines) AAP Pediatrics 2004; 114(4) 297-314
- Perform a systematic assessment before discharge for the risk of severe hyperbilirubinemia
- Provide early and focused follow-up based on the risk assessment
- Treat newborns with phototherapy or exchange transfusion to prevent the development of severe hyperbilirubinemia and, possibly, bilirubin encephalopathy (kernicterus).
Risk-based Approach

- **Low risk for kernicterus**
  - Term well babies

- **Medium risk for kernicterus**
  - Premature, evidence of hemolysis, DCT +ve, G6PD deficient, exclusive breastfeeding, cephalohematoma
  - Sepsis, poor APGAR
Transcutaneous bilirubinometer - JM 103


• 849 infants more than 35 weeks which 59.2% whites, 29.8% black, rest other races.
• Black population - correlation was less close (blacks 0.82, whites 0.94, others 0.92)
• JM 103 always over-estimated the results in Black infants, dangerous clinical errors are unlikely to occur
Phototherapy

- Converts bilirubin into water-soluble monomer
- Excreted into stools and urine
- Effective
- Side effects: dehydration, thermal instability, diarrhoea
Threshold for treatment

- **SB > 300**
- **SB > 260**

*Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
* Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
* For well infants 35-37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
* It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.*
Rebound jaundice

- Incidence of Rebound Jaundice = 13.3%
- Hemolytic jaundice
- Prematurity
- Jaundice requiring phototherapy earlier than 72 hours.
Exchange transfusion

- Rapid removal of the bilirubin
- Removal of the baby’s blood with replacement of compatible blood
- Incidence of procedure dropping
  Laurie A. Steiner et al
  *Paediatrics* 2007 Vol. 120 (1); 27-32
- Risks: Mortality, infections, hypocalcemia, metabolite disturbance
Threshold for exchange

- SB > 425
- SB > 340

*Graph showing total serum bilirubin levels over age.*

- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonus, fever, high pitched cry) or if TSB is ≥5 mg/dL (85 μmol/L) above these lines.
- Risk factors - isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (See legend)
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin
- If infant is well and 35-37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.
Intravenous immunoglobulin

- Cochrane review *Alcock GS, Liley H 2003*
- Use in DCT positive hemolytic jaundice
- Nonspecific Binding to Fc portion
- Decrease need for exchange transfusion
- Limited to severe jaundice prior to exchange
Drug therapy

• David Evans *BMJ Clinical Evidence 2006*
• Chelation agents (tin-mesophyrin)
• Experimental (No HSA/FDA approval)
• Long term side effects unknown
Breast-milk jaundice

- **Prolonged neonatal unconjugated jaundice linked to UGT1a1 mutation in Japanese** *Maruo Pediatrics 2000*
- **Similar in Scottish babies.** *Monaghan J Paed 1999.*
- **NHG-SIG grant on correlation of UGT1a1 mutation in prolonged neonatal jaundice in local population.** Poster 50th ESPR 2009, Hamburg
- **Results to be published**
Management of neonatal jaundice

- Common neonatal problem
- Etiology – various etiologies and effect of genetic mutation UGT1a1
- Clinical Practice Guidelines
- Different treatment modalities
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