REVIEW OF THE USE OF PHOTOTHERAPY IN NEONATAL JAUNDICE

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Roanna is a fourth-year medical student spending a year in Lancaster, having completed her first three years in Liverpool. This review was conducted as part of a special study module she completed during her third year. She is interested in how treatment plans can be modified depending on resources available (eg, UK compared to developing countries), particularly in vulnerable groups.

INTRODUCTION

Although use of phototherapy is widespread in treatment of neonatal jaundice, there are few published studies, and National Institute for Clinical Excellence (NICE) guidelines are two years away.[1] To address the situation, this review seeks to highlight what studies are available and make recommendations for further work.

Definition

Neonatal jaundice is the yellow discolouration of skin and sclera caused by hyperbilirubinaemia.[2] It is often first noticed in the face and spreads down the body.[3] Tiredness and poor feeding are associated signs.[3] It occurs in about 60% of term and 80% of pre-term babies within the first week of life.[1]

There are two main types of jaundice:

- ***Unconjugated hyperbilirubinaemia*** is potentially toxic but may be physiological or pathological. If left untreated, high levels may lead to kernicterus.[4]
- ***Conjugated hyperbilirubinaemia*** is not always toxic but always pathological.[4]

Aetiology and Risk Factors

There are many causes of hyperbilirubinaemia. Premature infants are more susceptible.[5]

Causes of hyperbilirubinaemia include: [3,5]

breast milk jaundice
physiological jaundice
rhesus incompatibility
glucose 6 phosphate deficiency
spherocytosis
pyruvate kinase deficiency
congenital infection
infection, eg urinary tract infection
haemolysis
polycythemia
Crigler-Najjar syndrome
hypothyroidism
haemolytic anaemia
high GI obstruction
bile duct obstruction
neonatal hepatitis

Pathophysiology

In neonates, bilirubin production may increase because of increased red cell mass, combined with shortened cell life.[6] Decreased bilirubin excretion may occur because of low concentrations of the enzyme ligandin in hepatocytes.[7] Ligandin normally binds to bilirubin, so low concentrations decrease hepatic excretory capacity.[7] Excretion of bilirubin in neonates is also reduced because the activity of glucuronyl transferase (normally responsible for making bilirubin soluble by attaching to it and making the bilirubin polar) is slower.[4]

Complications

The main complication of neonatal jaundice is kernicterus,[8] where free unconjugated bilirubin crosses the blood-brain barrier[9] and can be deposited in the brain (specifically in the basal ganglia, hippocampal cortex, subthalamic nuclei, and cerebellum)[2] causing neurotoxic effects and potentially death. Hearing loss, loss of muscle tone, seizures and permanent central nervous system damage can result.[8]

Treatment

There are three main treatments:

- ***Feeding methods***[10,11]
  Breast feeding can cause jaundice; however, increasing breast feeding to every $2^1/_2$ hours can decrease jaundice as it helps to reduce dehydration. Often infants will also receive supplementation with formula feeds. This is normally first-line treatment as it is cheap and very easy to implement.
- ***Phototherapy***[5,6]
  Bilirubin levels higher than 260μmol/L at 25-48 hours after birth (see table 1) are treated with phototherapy. There are a variety of different methods. During treatment with phototherapy, four-hourly blood tests are taken to measure total serum bilirubin levels which are a more reliable indicator of the extent of hyperbilirubinaemia than examining the colour of the neonate. Phototherapy works by chemically breaking down bilirubin in the neonate rather than relying on the liver.

Age (hours)	Total serum bilirubin level (μmol/L)		
	Consider phototherapy	*Phototherapy*	*Exchange and intensive phototherapy*
25-48	≥170	≥260	≥430
49-72	≥260	≥310	≥510
>72	≥290	≥340	≥510

Table 1 Criteria for phototherapy[5,12]

- **Exchange transfusion**[9,11]
  This is normally only used in severe neonatal jaundice when total serum bilirubin fails to decrease towards 0.8μmol/L, often occurring with Rhesus haemolytic

disease or sickle cell anaemia. It involves repeatedly replacing 5-10ml of neonatal blood with that of a donor until the entire volume of the neonatal blood is exchanged twice.

DISCUSSION

Phototherapy method 1: Coloured lights with different wavelengths

The key study is a 14-month Danish randomised controlled trial comparing turquoise and blue fluorescent lamps starting in 2002.[13] The most effective wavelengths to breakdown bilirubin are those matching the maximum absorption of the plasma bilirubin-albumin complex at 460nm.[16] This corresponds to blue light (450-495nm).[14]

Most studies compared blue light with green (495-570nm) and, as expected, found blue to be more efficacious.[14] However, blue light has more potential mutagenic effects and penetrates less because it has a shorter wavelength, being closer to the ultraviolet end of the spectrum. As a compromise, the key study compared turquoise with blue, finding it equally effective.[13] Turquoise light was found to decrease bilirubin by the same concentration as blue light and was actually more efficient (by 30%) when taking into account light irradiance. This suggests turquoise would be more appropriate overall.

The study highlighted other factors affecting the outcome:

- The length of phototherapy time. Although continuous phototherapy is normally used, this does not include baby feeding time which will vary individually.
- The distance of lamps from baby. The key study used 32cm,[13] but in other studies it varied from 'as close as possible' to 45cm. Providing heating effects do not cause problems, the minimum distance would give maximum irradiance, and if used could make the treatment appear more efficacious than studies with lamps further away.

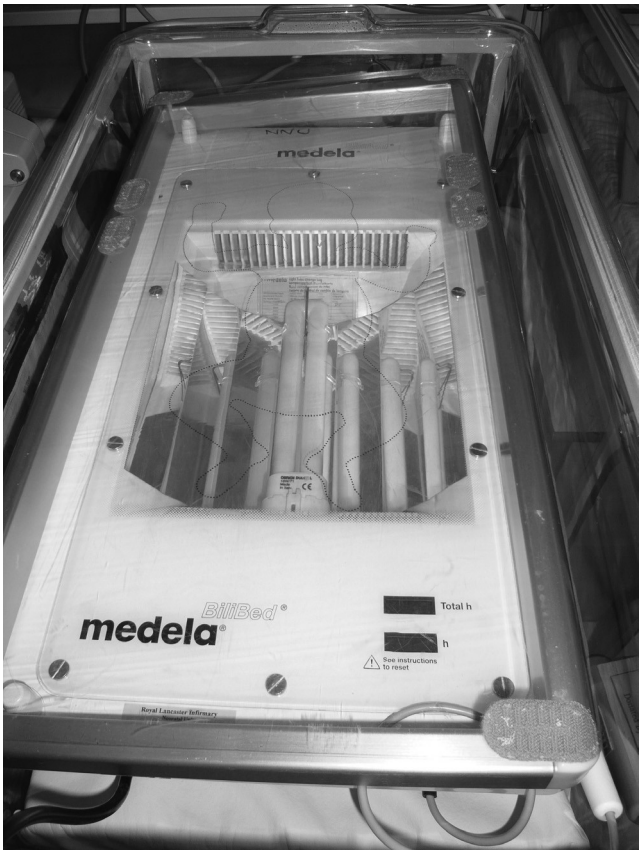
Phototherapy method 2: Fibre Optic *vs* conventional phototherapy

The key study is a randomised prospective study over 13 months from 1996 in Holland, comparing conventional phototherapy with a fibre optic mat on which the baby lies.[15] The advantages of fibre optic mats are reduction of side effects (the baby does not need eye patches and staff experience fewer visual problems), so if both treatments were equally effective, fibre optic mats would be preferred. This was found to be the case, so fibre optic mats are recommended instead of conventional treatment, although they probably do not confer extra benefit to smaller infants.

Phototherapy method 3: Compact fluorescent lights (CFL) *vs* standard phototherapy (SPT)

CFL aims to centre the light to focus more accurately, reduce scattering and increase irradiance. It was expected to be better in terms of effectiveness and acceptability to nursing staff than SPT.

The key study is a randomised controlled trial in India, published in 2006.[16] The authors were unblinded of necessity (as were all key studies). However, the placebo effect would not be expected to be significant as neonates would be unaware of their treatment and the outcome measured was both quantitative and independent (time taken to reduce bilirubin levels).



Bilibed phototherapy system on the neonatal unit at the RLI

Despite initial optimism and manufacturer's claims, the study found no difference between CFL and SPT in the treatment time needed. In fact, infants receiving CFL were more likely to need exchange transfusions, contraindicating use of CFL, though this was probably due to the small sample size. An additional sub-analysis of those with ABO incompatibility and glucose-6-phosphate dehydrogenase (G6PD) deficiency found no statistical differences in the effects of the treatment in infants with these conditions. As the standard lights are cheaper to buy (though per hour cost is unknown), and given there is an issue with increased exchange transfusions with CFL for no overall increase in effectiveness, CFL treatment would currently not be recommended.

Phototherapy method 4: Use of white reflecting curtains

In developing countries, cost is a major consideration in treatment availability, and compromises may be needed, eg using white light (cheaper) instead of the standard blue. It was therefore hoped that light intensity could be increased by using white curtains to reflect light back and increase irradiance cheaply.

The key study is a randomised controlled trial carried out in Malaysia over three months in 2005.[17] Results showed a reduction of 22 hours in treatment needed to reduce bilirubin concentration to the guideline levels. This was actually a huge difference from 35 hours (conventional) to 12 hours (with curtains). Even after four hours, results with white curtains were significantly better.

Two other studies suggested a rebound effect may occur which would need further investigation.[14,18] The key study found that 24 hours after completion no rebound effect was evident.[17] f this is the case, in addition to use of the strategy in developing countries, reflecting curtains seem appropriate worldwide.

SUGGESTIONS FOR FURTHER RESEARCH

Despite extensive literature searches to obtain more authoritative studies there is little current published research in this field. In the light of this, recommendations for further research are:

- randomised controlled trials with larger sample sizes to confirm the results with turquoise light and light reflecting curtains
- estimation of the optimum distance of the infant from the phototherapy lights
- repetition of trials with contradictory evidence
- establishing optimum treatment in neonates with ABO incompatibility or G6PD deficiency

CONCLUSION AND RECOMMENDATIONS

Until NICE guidelines are published (minimum two years from now), recommendations in the UK, including the Morecambe Bay area, for 'standard cases' are either:

- turquoise lights as close as possible to the neonate with light reflecting curtains, or
- fibre optic mat

No benefit was found with use of compact fluorescent lights, so standard length bulbs should be used. If cases of neonatal jaundice are due to ABO incompatibility or G6PD deficiency, continue with standard treatment until research establishes appropriate guidelines.

Recommendations for developing countries should be:

- white light (cheaper), and
- light reflecting curtains

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