Phototherapy

Short and long-term complications

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Drew, J. H., Marriage, K. J., Bayle, V. V., Bajraszewski, E., and McNamara, J. M. (1976). *Archives of Disease in Childhood*, 51, 454. **Phototherapy: short and long-term complications.** Use of phototherapy for hyperbilirubinaemia in 300 consecutively treated infants has shown that minor complications are common. With a knowledge of these complications and measures taken to minimize their effects, phototherapy appears to be safe in the short term. The long-term follow-up study showed that growth, and in particular head circumference, was not affected. There was, however, a higher incidence of squints and abnormal developmental performance in those infants treated with phototherapy. This may not have been due to phototherapy usage per se. However, because of these findings, it is suggested that phototherapy should not be used indiscriminately for hyperbilirubinaemia until the results of further long-term studies are available.

Phototherapy has been used for over 10 years to treat a large number of newborn infants with hyperbilirubinaemia (Cremer, Perryman, and Richards, 1958; Broughton *et al.*, 1965). Controlled studies have shown it to be effective (Lucey, Ferreiro, and Hewitt, 1968; Porto and Hsia, 1969). Reports of complication during usage have been few and none have been considered significant (Lucey, 1970; 1972). Significant complications have not been noted in the few long-term follow-up studies reported (Hodgman and Teberg, 1970; Lucey, 1972), but because information on the long-term effects is inadequate, the safety of phototherapy has not been definitely established. The results of a long-term study of infants treated with phototherapy are reported.

Patients and methods

During the 35 months from February 1971 to December 1973, 300 infants were treated with phototherapy for hyperbilirubinaemia. Phototherapy was begun when the serum bilirubin level was 12 mg/100 ml or greater in term infants and 10 mg/100 ml or greater in preterm infants. If the cause of jaundice was not diagnosed before the start of phototherapy the following

investigations were performed on capillary blood samples: Hb, white cell count and blood smear, blood group and direct Coombs's test. Urine was collected, cultured, and tested for the presence of reducing substances. Other investigations were performed when warranted. The infants were nursed in incubators naked except for occlusive covering over the eyes of 2 mm thick black felt lined on each side by white Leukosilk (Beiersdorf, Hamburg). The infants received continuous light from a phototherapy unit comprising 12 20-watt Phillips white fluorescent tubes. Each infant was turned at intervals of three-quarters of an hour and the temperature was recorded hourly. Serum bilirubin levels were measured before beginning phototherapy, and at least at 24-hour intervals; when the level fell below 10 mg/100 ml phototherapy was discontinued. Adequate fluid intake was ensured by complementing breast feeds with glucose or other artificial feeds and by reducing the interval between feeds to a maximum of 3 hours.

Each infant was examined daily for any untoward signs. A record was kept of the colour, consistency, and frequency of stools. In order to determine if any long-term effects of phototherapy usage occurred, a follow-up study was conducted on those infants who had attained one year of age. Randomly selected infants managed in the same nursery over the same period who were not treated with phototherapy, served as controls for neurological, developmental, and visual assessments. Each mother was interviewed regarding

the child's susceptibility to illness and particularly questioned about any skin problems that had occurred. Weight and length were recorded on the charts adapted from those of Tanner, Whitehouse, and Takaishi (1966); head circumference was plotted on the Composite International and Interracial Graphs developed by Nellhaus (1968). Tests of visual acuity and refractive error were given, and the fundus was visualized by a trained ophthalmologist. Acuity was determined by using objects of various sizes and colours. Developmental progress was evaluated by a Denver Developmental Screening Test (DDST) using the method reported by Frankenburg, Goldstein, and Camp (1971).

Results

The mean duration of phototherapy treatment was 35 hours, range 18–144 hours. Complications occurring during treatment in the 300 consecutively treated newborn infants are shown in Table I.

TABLE I

Complications during phototherapy usage in the 300 infants

Complications	Infants	
	No.	%
Fever	150	50
Diarrhoea	81	27
Irritability	57	19
Rash	35	12
Bronze baby syndrome	1	0.3

5 infants in the series died. At necropsy examination no evidence of bilirubin encephalopathy or damage attributable to phototherapy was observed. 89 infants were approximately one year or more of age. 54 (61%) of these and 67 (74%) of the 90 control infants were assessed in the longitudinal study. The incidence of prematurity (Table II), postmaturity, and dysmaturity, and the sex ratio were similar in the light-treated and control groups. The age range at assessment of the treated infants was 8 to 24 months, mean 15 months. One child of 8 months was seen before the age of one year as the parents were emigrating. Table III

TABLE III
Significant findings in light-treated and control infants on long-term follow-up

Findings	Light-treated group	Control group
Abnormal DDST	4	1
Convulsions	—	1
Squint	5	1
Retrolental fibroplasia	1	—
Ventricular septal defect	1	—
Atrial septal defect	1	2
Funnel chest	—	1
Total in series	54	67

DDST, Denver Developmental Screening Test.

shows the overall incidence of major abnormalities detected.

General health. The susceptibility to childhood illness and the incidence of skin problems in the two groups of infants were remarkably similar. Physical examination in the majority of infants in both groups was normal. A few minor physical abnormalities, such as umbilical hernias, functional heart murmurs, and capillary haemangiomas were present in both groups. The significant physical abnormalities found are shown in Table III. One control child had convulsed but development was satisfactory. The aetiology of the convulsion was not determined.

Developmental performance. 4 (7%) of the treated infants and one (2%) control infant scored abnormally on the DDST. In the 4 treated infants the significant intellectual delay could be attributed to other causes.

Case 1. Born at 32 weeks of gestation, after a normal pregnancy; birthweight 1290 g. This baby developed severe recurrent cyanotic attacks.

Case 2. The result of a pregnancy complicated by twins. Spontaneous labour began at 41.5 weeks of gestation and this infant was the second

TABLE II

Gestational ages of the 2 groups of infants in 4-week cohorts

Group	Gestational ages (w)				
	<28	28.1–32	32.1–36	36.1–40	>40
Light-treated	1 (1.8)	9 (16.7)	12 (22.3)	28 (51.8)	4 (7.4)
Control	1 (1.5)	12 (17.9)	15 (22.4)	33 (49.3)	6 (8.9)

Numbers in parentheses represent percentages.

twin, born by a breech extraction. Birthweight was 2466 g and the only abnormality noted was 'dysmaturity'. He was admitted to the special care nursery at 5 days of age with a serum bilirubin level of 23 mg/100 ml, fitting, and hypotonic. He now shows evidence of intellectual retardation and a hearing deficit.

Case 3. Born at 29 weeks of gestation; birthweight 1040 g. This infant's early postnatal period was complicated by severe recurrent cyanotic episodes.

Case 4. The product of a pregnancy complicated by an episode of antepartum haemorrhage. A caesarean section was performed at 36.5 weeks of gestation and the infant suffered severe neonatal asphyxia requiring 12 minutes of assisted ventilation before respiration was established. Birthweight was 3000 g.

Eyes. All infants gave normal responses upon testing of gross vision. The child with mild retrolental fibroplasia (Table III) had received

prolonged oxygen therapy for hyaline membrane disease and was premature (born at 32 weeks of gestation). Nothing specific was found in the fundi of the children with squints (Table III).

Growth. Weights and lengths were plotted (Fig. 1) for individual infants treated with phototherapy. Only one subject (an infant with proven sucrase-isomaltase deficiency) fell significantly behind on any parameter. The reference chart for head circumference gives the mean ± 2 SD, corresponding to the 50th, 98th, and 2nd centiles (Fig. 2). No treated infant fell below the 2nd centile at follow-up.

Discussion

Before 1958, jaundice in the newborn was treated principally by exchange transfusion (Cremer *et al.*, 1958), this therapy being applied only when the serum bilirubin level approached that thought to place the infant at risk of bilirubin encephalopathy (values of 18 mg/100 ml in the preterm infant and 20 mg/100 ml in the term infant) (Campbell, 1964). More recently it has been appreciated that hypoxia, acidosis, hypoglycaemia, and sepsis may lower the

FIG. 1.—Weight and length of light-treated infants at follow-up.

FIG. 2.—Head circumference of light-treated infants at follow-up.

threshold at which unbound bilirubin causes cerebral damage, and that future intellectual performance may be threatened by serum bilirubin levels insufficient to cause the complete picture of kernicterus (Odell, Storey, and Rosenberg, 1970). When the mortality of exchange transfusion of approximately 1% (Panagopoulos, Valaes, and Doxiadis, 1969) is also taken into account, treatment for increasing icterus before exchange transfusion becomes necessary is obviously desirable. Phototherapy is one approach now widely used. Phototherapy with a light source in the range 425–475 nm has effectively reduced the level of bilirubin in newborn infants in a number of trials, the reduction being proportional to the energy of light applied (Mims *et al.*, 1973). The exact mode of its action is uncertain; present knowledge suggests that light causes the degradation of bilirubin to more polar, and therefore more water-soluble, products, so allowing increased biliary excretion. Phototherapy may also open up an alternative pathway which allows the passage of unconjugated bilirubin directly into the bile (Ostrow, 1972).

Recognized short-term complications of phototherapy include pyrexia, loose bowel actions, irritability, feeding difficulties, a 'flea bite' rash on the face, trunk and limbs, and the occasional case of the 'bronze baby' syndrome (Kopelman, Brown, and Odell, 1972); the latter is thought to occur when parenchymal liver disease prevents the usual prompt excretion via the bile of the products of photocatabolism. Rare cases of haemolytic anaemia due to photo-oxidant damage to red cells in the presence of raised bilirubin levels have also been reported (Kopelman *et al.*, 1972; Odell, Brown, and Kopelman, 1972). When the incidence of complications during phototherapy treatment was reviewed the high incidence of minor complications was apparent, though none necessitated the withdrawal of treatment (except the one case of the 'bronze baby' syndrome which occurred in a 840 g severely dysmature infant born at 36 weeks of gestation).

It has been suggested that photo-decomposition products could be neurotoxic. A convincing body of experimental animal work exists which is reassuring (Diamond and Schmid, 1968; Ballowicz, 1971), though adequate long-term studies in humans are rare. Hodgman and Teberg (1970) reported that developmental performance and neurological findings in 23 infants subjected to phototherapy compared favourably with those in 23 control infants. In the present series there was an increased incidence of an abnormal DDST in those infants treated with phototherapy. When the histories of

the 4 treated infants with an abnormal DDST were scrutinized, other reasons were apparent to explain the results. The effect might not be due to the photo-decomposition products, but the result is interesting and must be considered seriously.

Retinal damage from intense light exposure has been reported in animals (Noell *et al.*, 1966; Kuwabara and Gorn, 1968). Sophisticated work by Dobson, Cowett, and Riggs (1975), which included electroretinography, suggested that no permanent damage to rod function occurs. In the present series there was a higher incidence of children with squints in the light-treated group. Other coarse tests of visual function were normal. Again this result may not be clinically significant, nor might it be a cause and effect of phototherapy. Obviously further work is required in this area.

The original animal studies of Ballowicz *et al.* (1970) suggested that growth retardation occurred in Gunn rats subjected to phototherapy, but this was retracted by the author in 1971 upon further study. Teberg and Hodgman (1971) reported the results of a 2-year follow-up on 30 infants from an original study of 98. They found 10 of 14 light-treated infants had head circumferences 2 SD below normal as compared to 5 of 16 controls. This study was repeated on another 97 infants (Wu *et al.*, 1971) and in that study weight, length, and head circumference were the same in light-treated and control infants. This has been verified by Lucey (1972) in a study of 39 light-treated and 33 control infants reviewed at ages of 4 to 6 years. The present series suggests that no significant effect of phototherapy on growth occurs.

This study suggests that although phototherapy is a useful therapeutic agent complications during its usage are common. However, provided a knowledge of these complications exists and measures are taken to minimize their effects, phototherapy is safe in the short term. It should be pointed out that subtle metabolic consequences of usage are not yet completely determined. Less is known about the long-term effects but this study suggests growth is not affected. The effects on intellectual and visual performances require further study.

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