by 4 per minute to 38 and the inflation pressure by 1.4 to 20 cm H₂O. None of these changes was statistically significant, suggesting that the babies had neither improved nor deteriorated.

Discussion

In this study we have been unable to show any improvement in lung mechanics or transcutaneous blood gas measurements after 2 doses of artificial surfactant were delivered to the airways of preterm babies requiring intermittent positive pressure ventilation for IRDS. Blood gas values 12 hours after the study did not indicate that a delayed response was occurring. These findings are at variance with those of Fujiwara et al., but similar to those of Wilkinson et al. There are several possible reasons for this. Firstly, our surfactant may have been inactive. This is unlikely, as many in vitro studies have shown this particular preparation to be highly active; but there are some who claim that artificial surfactants are not as active as natural surfactant. Secondly, the surfactant may not have penetrated far enough into the lungs to achieve a monomolecular layer where required. This too is unlikely as insufflation of the powder certainly deposited surfactant down into the large airways. As the wet surface of the large airways is in direct continuity with the alveoli, any lowering of the surface tension locally would cause the surfactant to spread in the same way that a drop of washing up liquid immediately spreads across the surface of the water. The final insufflation of saline would help to deliver any surfactant deposited in the endotracheal tube, but this too was ineffective. Finally, the dose may have been too small: but 50 mg is a very large dose compared with that required to establish a monomolecular layer throughout the lungs.

We suspect that the improvement seen by the Japanese and Canadian workers may be related to the way the surfactant was given, which included a period of hyperventilation with an anaesthetic rebreathing bag and also instillation of volumes of saline into the lungs—equivalent to as much as 500 ml in the adult. This combination may be useful for the management of conditions in which hyaline membranes have formed in the lungs. We conclude that dry surfactant powder is unlikely to have a useful clinical role in the management of severe IRDS. We consider that other delivery techniques and natural surfactant still need to be explored, but think it unlikely that surfactant deficiency is the main reason for the development of IRDS in the preterm baby and that animal models are not appropriate in this disease.

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Long term phototherapy in Crigler-Najjar syndrome

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SUMMARY A 10 year old girl with type 1 Crigler-Najjar syndrome has been treated with daily phototherapy from birth. Her general physical and neurological development are normal.

Non-obstructive, non-haemolytic congenital hyperbilirubinaemia was described in 1952 by Crigler and Najjar.1 Arias et al.² further clarified the syndrome and identified two main types.

Patients with type 1 have the more severe form,
often associated with kernicterus and neurological damage at an early age. It is inherited as an autosomal recessive; the hyperbilirubinaemia does not respond to treatment with phenobarbitone and there is no bilirubin glucuronide in the bile. In patients with type 2 the disease is milder and the suggested inheritance is as an autosomal dominant; the bilirubin concentration shows some reduction if treated with phenobarbitone and there is some glucuronide in the bile; untreated the prognosis is very much better than for type 1.

Our patient has type 1 Crigler-Najjar syndrome. Her treatment and progress to age 2 years have been reported. We now describe her progress between ages 2 and 10 years.

Case report

At 10 years old our patient weighs 27 kg (25th to 50th centile), height 140 cm (50th to 75th centile), head circumference 54 cm (50th to 75th centile). Her general appearance is that of a normal Asian girl and full physical examination is normal apart from moderate jaundice. She has mild myopia but apart from this the ophthalmological examination is normal. Hearing both clinically and by audiogram is normal. She attends a normal school; her behaviour is normal and psychometric testing is normal (WISCR IQ 96).

Investigations. The following investigations were repeatedly within the normal range: haemoglobin, white blood count, platelets, erythrocyte sedimentation rate, reticulocytes, haemoglobin electrophoresis, serum iron, total iron binding capacity, haptoglobin, serum folate, red cell folate, prothrombin index, total protein, albumin, calcium, phosphate, faecal chymotrypsin, and serum electrolytes.

The following were normal in the year stated: jejunal biopsy (1976); sucrose hydrogen breath test (1980); vitamins A, E, C, B₁, B₂, B₆, B₁₂, and carotene (1980); x-ray films of the wrist, bone age, and an intravenous pyelogram (1974); abdominal ultrasound (1982).

Serum bilirubin levels (American Optical Bilirubinometer), measured twice weekly, varied between 130 and 415 μmol/l. They exceeded 350 μmol/l on 21 occasions. Monthly averaged values are shown in the Figure. The alkaline phosphatase level was raised to between 32-5 and 43 (mean 37-4) KA units during the last 3 years (normal <30 units), and the alanine aminotransferase to between 49 and 95 IU/l (mean 62, upper normal 40 IU/l).

Treatment and progress. The patient has received phototherapy every night since the second day of life, usually for 12 hours but occasionally for the whole day if the bilirubin level has been high. For the first 4 years she was treated in hospital and since then in her own home. Cholestyramine, previously shown to be of benefit, was finally stopped at 9 years without detriment.

Phototherapy. Four different sources of blue light have been used to meet the changing requirements as she has grown older (Table). The first 3 units consisted of fluorescent lamps or tubes fixed over the bed. The fourth unit, which we designed, consists of 10 fluorescent tubes in the base of the bed, under a transparent acrylic sheet on which the patient sleeps. This unit has proved more convenient and acceptable than earlier models because she does not need to be uncovered, and her eyes are shielded from the light by the pillow.

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<td>10-5</td>
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*Measured with an Airshields Radiometer S450 (spectral range about 400–500 nm).
Monitoring of progress. Regular checks of the bilirubin level are performed; blood is collected twice weekly on capillary blood samples by a domiciliary nurse. If the level is above 350 μmol/l the duration of phototherapy is increased to 16 hours. Growth, physical state, haemoglobin level, folic acid, liver function tests, audiograms, visual acuity, and intelligence have been checked regularly and are normal.

Several problems have occurred since phototherapy was transferred to the home at age 4 years. Non-compliance has been suspected, as each admission to hospital produced a significant fall in the bilirubin level. Necessity for nakedness upset the Pakistani family but this objection has been overcome by the underbed light source.

Discussion

Phototherapy is effective in controlling unconjugated neonatal hyperbilirubinaemia and the evidence from a number of studies has been reviewed. It is well known that very high levels of unconjugated bilirubin may cause kernicterus at any age. In view of the high risk of neurological damage, we have tried to control the level of bilirubin with phototherapy from the first days of life. We have managed to keep the bilirubin level below 300 μmol/l for much of the time with occasional levels higher than 350 μmol/l. There has been a tendency for the bilirubin level to rise as shown in the Figure. Relative reduction in surface area, lack of compliance, and a less powerful light source may have contributed to the rise.

Patients with type 1 Crigler-Najjar syndrome often develop kernicterus and die early. There are isolated reports of untreated patients who appeared neurologically normal for several years despite very high unconjugated bilirubin levels but who later, and at times suddenly, developed irreversible neurological damage. Our patient remains neurologically intact and is of average intelligence; her physical development is normal.

Phototherapy alters the physical environment and induces numerous metabolic changes which have been reviewed. Retinal damage has been reported in animals exposed to the blue lights. Tests of visual acuity and ophthalmological examinations have remained normal in our patient. Her eyes were shielded from the light in the early years, however, in recent years she has not tolerated goggles or eye shades.

The cost of phototherapy at home is not excessive, perhaps £500 per year. The major costs have been in prolonged time in hospital initially, subsequent admissions, and the bilirubin estimations. If social circumstances allow, phototherapy can be given in the home from an early age.

At present our patient is growing normally and has shown no obvious ill effects from her prolonged phototherapy although life-long close follow-up will be required. Until phototherapy came into general use in the late 1960s, treatment and survival of such patients was rare. However, with the advent of effective treatment, even though inconvenient and socially restricting, further problems will obviously arise (for example, travel, marriage, and pregnancy).

We believe that by giving regular phototherapy we have reduced her level of unconjugated bilirubin. In view of the well documented history of untreated type I Crigler-Najjar syndrome, we do not feel that stopping phototherapy because of the irreversible damage which would almost certainly follow sooner or later.

We thank Rank Stanley Cox Medical Equipment and Osram (GEC) Ltd for advice and loan of equipment; Mr N J M Lindop for technical assistance; Vallances Limited, Leeds, for provision of a television set for the patient; Mr J Cadranel, principal psychologist, for psychometric testing; the colleagues, nurses, technicians, and others who have helped with the patient's management over the years; Miss S J Littlewood for extra secretarial help.

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