Case of congenital nonobstructive, nonhaemolytic jaundice

Successful long-term phototherapy at home

Phototherapy is the only treatment of value in cases of Arias type I congenital nonobstructive, nonhaemolytic jaundice, unresponsive to phenobarbitone administration (Callahan et al., 1970; Gorodischer et al., 1970; Karon et al., 1970; Land et al., 1970; Altay and Say, 1973; Arrowsmith et al., 1975). However, the daily duration of exposure to light necessary to maintain bilirubin at safe levels may be so long that it interferes with normal parental attention to the infant. Even continuous light therapy may not prevent a gradual rise in serum bilirubin level after a certain age (Karon et al., 1970; Altay and Say, 1973). On the other hand, cholestyramine has been found to reduce the amount of phototherapy needed (Arrowsmith et al., 1975).

We describe a case of type I congenital nonobstructive, nonhaemolytic jaundice, successfully treated at home with intermittent phototherapy combined with cholestyramine. Frequent determinations of reserve bilirubin binding capacity were made to control the safety of the treatment.

Case report

A boy was born after a term pregnancy. His parents were unrelated. 2 older sibs had a history of neonatal unconjugated hyperbilirubinaemia which had appeared at the 3rd day of life and spontaneously disappeared at the 9th and 13th days, respectively. Birthweight was 3-66 g and length 49 cm; Apgar score at 1 minute was 10. Jaundice developed on the second day of life, mother's and baby's blood group being O Rhesus positive. There was no anaemia and Coombs's test was negative. Maximum serum total bilirubin level was 29-8 mg/100 ml (509-6 μmol/l) on the 8th day. A fall to 15 mg/100 ml (256-5 μmol/l) occurred after the second exchange transfusion. Continuous phototherapy was then started and the serum bilirubin level was maintained at between 15 and 20 mg/100 ml (256-5 and 342 μmol/l). Withdrawal of phototherapy on the 15th day was immediately followed by a rise in serum bilirubin. Phenobarbitone 10 mg/kg per day was then combined with continuous phototherapy, but did not prevent a further rise in bilirubin level when phototherapy was stopped again after 2 weeks of combined treatment.

He was then transferred to our department, aged 39 days. Neurological development was normal. Liver-function tests were normal. Blood bromsulphthalein retention was 14-1% at 15 minutes and 5-4% at 45 minutes. Serum albumin was 41 g/l. Serum unconjugated bilirubin was 15-6 mg/100 ml (266-8 μmol/l) and conjugated bilirubin 0-6 mg/100 ml (10-3 μmol/l). Hepatic bilirubin UDP-glucuronyl-transferase activity, measured in a needle liver biopsy specimen, was nil (control in 15 adult human specimens: 1-06±0-18 μmol/g per 30 min (Odièvre and Luzeau, 1971).

Methods. Bilirubin determinations were made on venous blood samples, by the method described by Michaelsson (1961). Reserve bilirubin binding capacity was measured by a method using thin-layer chromatography (Trivin et al., 1977). The patient was examined at regular intervals by the same psychologist with the Brunet-Lezine scale.

Results

The results of unconjugated bilirubin determinations are summarised in the Table. When phototherapy was

<table>
<thead>
<tr>
<th>Age of patient</th>
<th>Daily duration of phototherapy (h)</th>
<th>Serum bilirubin levels (mg/100 ml)</th>
<th>Serum reserve bilirubin binding (mg/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 w</td>
<td>18</td>
<td>12-4</td>
<td>16-9</td>
</tr>
<tr>
<td>16 w</td>
<td>18</td>
<td>7-6</td>
<td>25-4</td>
</tr>
<tr>
<td>17 w</td>
<td>14</td>
<td>16-2</td>
<td>18-2</td>
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<tr>
<td>17 w</td>
<td>14</td>
<td>16-3</td>
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<td>18 w</td>
<td>14</td>
<td>15-0</td>
<td>16-0</td>
</tr>
<tr>
<td>19 w</td>
<td>12</td>
<td>12-9</td>
<td>18-8</td>
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<tr>
<td>At home</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>44 m</td>
<td>12</td>
<td>10-7</td>
<td>18-8</td>
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<tr>
<td>10 m</td>
<td>13</td>
<td>16-3</td>
<td>18-5</td>
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<tr>
<td>1 yr 3 m</td>
<td>12</td>
<td>14-5</td>
<td>19-5</td>
</tr>
<tr>
<td>1 yr 6 m</td>
<td>12</td>
<td>12-4</td>
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<tr>
<td>1 yr 9 m</td>
<td>12</td>
<td>13-0</td>
<td></td>
</tr>
<tr>
<td>2 yr</td>
<td>12</td>
<td>14-6</td>
<td></td>
</tr>
</tbody>
</table>

Conversion: Traditional units to SI—Bilirubin: 1 mg/100 ml ≈ 17-1 μmol/l.

given 18 hours a day, serum bilirubin concentration ranged from 9-0 to 20-4 mg/100 ml (15-4-348-8 μmol/l) (mean of 27 determinations: 16-5 mg/100 ml; 282-2 μmol/l). Cholestyramine (4 g/day) supplementation to phototherapy was associated with a highly significant fall in serum bilirubin level, ranging from 7-5 to 13-3 mg/100 ml (128-3-227-4 μmol/l) (mean of 6 determinations: 10-7 mg/100 ml; 183 μmol/l) (P<0.001). Levels were still low during the week after stopping cholestyramine; then the serum bilirubin rose progressively to 18 mg/100 ml (307-8 μmol/l). Cholestyramine was reintroduced and the bilirubin level rapidly fell to 7-6 mg/100 ml (130 μmol/l). It then gradually rose, remaining between 11-0 and 16-5 mg/100 ml (188-282-2 μmol/l), while cholestyramine administration continued, although
the duration of phototherapy was gradually reduced
to 12 consecutive hours per day.

The variations of reserve bilirubin binding capacity
during treatment are summarised in the Table,
showing that this capacity always ranged between
16.0 to 19.5 mg/100 ml (273–6–333·5 μmol/l), except
for a single measurement of 25·4 mg/100 ml (434·3
μmol/l).

Growth remained within normal limits, the
patient being last examined at the age of 27 months.
Developmental and neurological examinations were
also normal; the developmental quotient was 100.

Discussion

Since phototherapy is the only effective means of
controlling hyperbilirubinaemia and preventing
kernicterus in patients with Crigler-Najjar type I
jaundice and must be continued for life, the long-
term efficacy and safety of this therapy must be
considered. Kernicterus may occur in patients
receiving phototherapy because it was started too
late, or because the serum bilirubin is not controlled,
due to decay in light energy output from fluorescent
tubes after 180 hours of use. Superimposed events
such as haemolytic episodes may cause a life-
threatening increase in bilirubin production, or may
interfere with albumin binding of bilirubin. Further
potential hazards include the harmful effects of photo-
degradation products of bilirubin and harmful
biological consequences of phototherapy to the skin
and other organs. Phototherapy thus must be
initiated under circumstances which will allow close
monitoring of the serum bilirubin levels. Sequential
determinations of reserve binding capacity, which
may provide a better index of the risk of kernicterus,
were stable in this patient throughout the study.
Phototherapy should be limited to the minimum safe
period.

In this case cholestyramine administration caused
a fall in serum bilirubin levels when first begun, but
no rise when therapy was stopped. When restarted
the effect was less dramatic but it did coincide with a
fall in the duration of phototherapy required. We are
thus unable to confirm fully Arrowsmith’s assertion
(Arrowsmith et al., 1975) that cholestyramine caused
a substantial fall in bilirubin, but have continued to
administer it to this infant because it reduces the
duration of phototherapy to a level which allows him
to receive sufficient phototherapy during sleep. It is
clearly important that such children, who face not
only the hazard of bilirubin neuropathy but the
emotional hazards of being persistently yellow and
requiring such unusual therapy for life, should be
kept in hospital for as short a time as possible. To
deprive them of the emotional, social, and learning
stimulation of a good home environment may itself
cause significant developmental delay and possible
long-term emotional sequelae.

Summary

Use of cholestyramine made it possible to shorten
the daily duration of phototherapy in a case of
genital nonobstructive, nonhaemolytic jaundice.
Treatment at home was therefore possible, allowing
normal parental care. Developmental and neuro-
logical examinations were normal at the age of 27
months. Frequent determinations of reserve bilirubin
binding capacity may be useful in controlling such
management.

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