

recurrence of pulmonary interstitial emphysema after the initial attempt should not preclude a second attempt.

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Serum bilirubin kinetics in intermittent phototherapy of physiological jaundice

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SUMMARY Thirty four term babies with physiological jaundice were subjected to continuous phototherapy and to two regimens of intermittent phototherapy. The difference in serum bilirubin kinetics between the three groups of treated babies was insignificant; a schedule of one in four hours of irradiation achieved the same treatment effect as continuous phototherapy.

Over the past 20 years phototherapy has become the most common treatment for neonatal hyperbilirubinaemia. The question of subtle, long term side effects, however, has not been adequately answered and it is theoretically important, therefore, that infants should be subjected to the least amount of irradiation without sacrificing the overall efficiency of the treatment. Various schedules of intermittent phototherapy have been investigated. Because most earlier studies¹⁻³ were concerned with the prophylaxis of hyperbilirubinaemia and treatment was started early without consideration of the individual variation of bilirubin kinetics, the results were not surprisingly controversial. Using a new mathematical approach to study the serum bilirubin kinetics *in vivo* this report compares the efficiency of three different regimens of phototherapy in jaundiced, term Chinese infants.

Patients and methods

Jaundiced term infants born in the Tsan Yuk

Maternity Hospital, Hong Kong with a birthweight of 2.5 kg or more were enrolled in the study. Infants with jaundice of known causes were excluded. When the serum bilirubin concentration reached 190 to 205 $\mu\text{mol/l}$ (11.5 to 12 mg/dl) the babies were randomised into one of three groups receiving different regimens of phototherapy—group A underwent continuous phototherapy; group B received four hours of phototherapy followed by four hours off, and group C underwent one hour of phototherapy and three hours off.

Phototherapy was administered by a bank of 8 fluorescent lamps (Duro-vita lite, 20 W) in standard units. Irradiance was measured every morning by an IL 444 Radiometer (Spectrum 420-470 nanometer, International Light Inc, USA) at the centre of the mattress. A reading of $350 \mu\text{W}/\text{cm}^2 \pm 5\%$ was considered satisfactory and in case of deviation either the lamps were replaced or the distance between mattress and lamps was adjusted.

The total serum bilirubin concentration was measured 6 to 8 hourly by spectrophotometric technique (AO Bilirubinometer, American Optical Corporation). Phototherapy was stopped when the serum bilirubin concentration had fallen to 170 $\mu\text{mol/l}$ (10 mg/dl). The change in the serum bilirubin concentration with time was represented by a bilirubin growth curve which was constructed by the least square method.⁴ A polynomial of third degree ($SB = a + b \times T + c \times T^2 + d \times T^3$ where SB=interpolated serum bilirubin concentration; a,b,c,d=coefficients of the polynomial equation; and T=time) was found to be a satisfactory mathe-

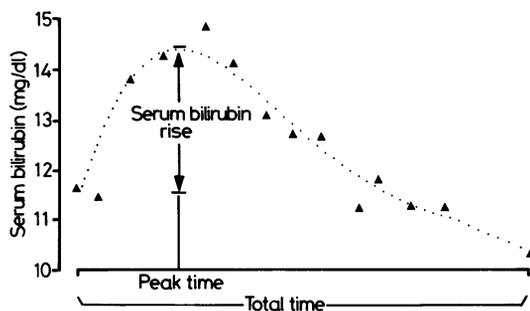


Figure Serum bilirubin growth curve

Arrows denote the start and the end of phototherapy. Broken line represents the fitted polynomial to the actual serum bilirubin readings (▲).
 Conversion—traditional units to SI: bilirubin 1 mg/dl=17 μmol/l.

mathematical model as all curves have a correlation coefficient of greater than 0.8 and a significantly large variance ratio F (F=mean square due to regression/residual mean square) (P<0.01). The peak serum bilirubin concentration and the time of this peak are the coordinates of the highest turning point of the growth curve. All the parameters analysed were derived from the polynomial (Figure) and analysis of variance was used to test the difference between the three groups. The non-parametric Kruskal-Wallis test was performed when the data within the group were either not normally distributed or the variances between groups were non-homogeneous.

Results

Thirty four babies allocated to three treatment

groups were studied (Table). All the clinical and laboratory parameters analysed were strictly comparable for the three groups. The correlations between the variables were also examined. As expected, two pairs of variables (the time of the peak bilirubin concentration and the total period of treatment; the difference between the peak bilirubin concentration and the concentration at the beginning of treatment and the rate of increase in the serum bilirubin) showed good correlation (regression coefficients 0.7 and 0.9, respectively). Significant positive correlation between the peak bilirubin concentration and that at the beginning of treatment and between the rate of decline in the bilirubin concentration and the peak concentration, and negative correlation between the peak bilirubin concentration and that at the beginning of phototherapy were shown. Therefore, further analysis of covariance for the peak serum bilirubin concentration, the difference between the peak serum bilirubin concentration and that at the beginning of phototherapy (covariate, serum bilirubin at the beginning of phototherapy), and the rate of decline in the serum bilirubin concentration (covariate, peak serum bilirubin concentration) was necessary. Again no significant difference between the groups was shown.

The group means and medians for actual phototherapy were tested by analysis of variance. The difference in the means was highly significant (P<0.001) and the P value by the non-parametric Kruskal-Wallis test was also less than 0.001. The total dose of irradiation is directly proportional to the duration of phototherapy and therefore the difference in the three groups achieved exactly the same significance.

Table Statistical analysis of clinical parameters

Clinical parameter	Group A (n=13)	Group B (n=9)	Group C (n=12)	P value	Statistical method
Gestational age (weeks), mean (SD)	39.5 (1.4)	40.0 (1.8)	40.2 (1.3)	ns	ANOVA
Birthweight (kg), mean (SD)	3.26 (0.33)	3.10 (0.43)	3.29 (0.44)	ns	ANOVA
Haemoglobin (g/dl), mean (SD)	18.5 (2.0)	19.6 (1.9)	18.1 (1.5)	ns	ANOVA
Serum bilirubin at onset (μmol/l), mean (SD)	201.8 (27.4)	193.2 (34.2)	198.4 (12.0)	ns	ANOVA
Peak serum bilirubin (μmol/l), mean (SD)	229.1 (29.1)	239.4 (23.9)	227.4 (10.3)	ns	ANOVA, ANOCO
Rise in serum bilirubin (μmol/l), mean (SD)	27.3 (22.2)	46.2 (29.1)	29.0 (18.8)	ns	ANOVA, ANOCO
Rate of increase in serum bilirubin (μmol/l/hr), mean (SD)	0.82 (0.43)	1.25 (0.66)	0.89 (0.65)	ns	ANOVA
Rate of decline in serum bilirubin (μmol/l/hr), mean (SD)	1.08 (4.10)	1.49 (0.87)	1.09 (0.56)	ns	ANOVA, ANOCO
Time of peak in serum bilirubin (hr)	33.2 (25.0)	34.1 (13.2)	36.2 (32.0)	ns	ANOVA
Total period of treatment (hr)	89.9 (54.2)	86.7 (28.9)	100.0 (61.0)	ns	ANOVA
Fractional irradiation (%)	100	50	25		
Total hours of irradiation					
Mean (SD)	89.9 (54.2)	43.4 (14.5)	25.0 (15.3)	<0.001	ANOVA
Median	78.8	35.5	22.4	<0.001	K-W
Total irradiation (Joules/cm ²)					
Mean (SD)	64.7 (38.9)	31.2 (10.1)	18.8 (10.8)	<0.001	ANOVA
Median	56.7	25.5	16.1	<0.001	K-W

ANOVA=Analysis of variance; ANOCO=analysis of covariance; K-W=Kruskal-Wallis test.

Discussion

Particularly relevant to our study was the report of Vogl *et al*⁵ of the effectiveness of intermittent phototherapy on preterm infants using a short exposure time of 15 minutes in every 30, 45, or 75 minutes. Employing a different time schedule the results of our study on term infants with physiological jaundice are similar. Because all the parameters can be estimated more precisely by the polynomial model, statistical comparison between groups becomes more reliable. Neither the peak serum bilirubin concentrations nor the rates of decline after the peak has been reached were statistically different in the three groups. This result lends support to the hypothesis of two step photodegradation of bilirubin *in vivo*.⁶ The first step is the photochemical reaction at the skin site which is completed in nanoseconds. Simultaneously, unexcited bilirubin from the body pool migrates slowly into the skin loci and photo products out of the skin. This is considered to be the limiting factor in the rate of removal of unconjugated bilirubin *in vivo*. The time required for the second step to be completed has been estimated to be one to three hours. Therefore there may be only marginal improvement by irradiation during the second phase. The chief advantage of intermittent treatment is the reduction of total irradiance. In our study infants of group C received only 28% of the irradiance given to those in group A. Our data suggests at an irradiance of 350

$\mu\text{W}/\text{cm}^2$ a regimen of one hour of phototherapy and three hours off is as effective as continuous exposure in term infants with physiological jaundice. Besides its simplicity in application, it is also economically attractive for developing countries where the need is great and resources are scarce. Furthermore, this regimen is less disruptive to the establishment of infant maternal bonding and breast feeding because the infants are not confined to the incubators during the whole course of treatment.

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Mebendazole in the treatment of hydatid cysts

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SUMMARY We report two children with ruptured, multiple hydatid cysts treated with mebendazole. Long term follow up has confirmed the success of this treatment.

Surgical intervention in ruptured or multiple hydatid cysts may meet with failure; treatment with mebendazole is justified in these cases but almost all published reports have been in adults.¹⁻³ We report two children with multiple, ruptured hydatid cysts who were successfully treated with mebendazole.

Case reports

Case 1. A 13 year old boy was admitted to hospital in August 1977 because of paroxysmal cough which resulted in vomiting. Chest radiography showed a ruptured hydatid cyst on the right upper lobe (Figure). Casoni skin test was positive and Weinberg (complement fixation) test and echinococcal antibodies determined by immunoelectrophoresis were negative. Surgery was advised but his parents refused permission.

In June 1980 he was readmitted to hospital having suffered two episodes of haemoptysis during the