Eur J Pediatr (1998) 157: 132–137

NEONATOLOGY

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Fibre optic versus conventional phototherapy for hyperbilirubinaemia in preterm infants

Received: 14 May 1996 and in revised form: 20 June 1997 / Accepted: 23 June 1997

Abstract Studies comparing efficacy of fibre optic phototherapy to conventional phototherapy are performed mostly in term infants and give conflicting results. This randomized prospective study compares efficacy of fibre optic phototherapy using the Ohmeda Biliblanket device to conventional fluorescent phototherapy in preterm infants. A total of 124 preterm infants with a nonhaemolytic hyperbilirubinaemia were evaluated. Stratification at randomisation was performed according to birth weight (< 1000 g, 1000–1500 g or 1500–2000 g). Fifty-six infants received fibre optic and 68 conventional phototherapy. Efficacy was assessed by comparing the required duration of phototherapy.
Median duration of phototherapy was 118 h and 114 h in the fibre optic and conventional groups respectively, the difference in which was not statistically significant.
The median durations were also not significantly different within the separate weight groups. The number of infants requiring exchange transfusions was similar in both treatment groups.

Conclusion The efficacy of fibre optic phototherapy in preterm infants is comparable to conventional phototherapy.

Key words Neonatal hyperbilirubinaemia · Fibre optic phototherapy · Biliblanket Preterm infants

Introduction

Since its introduction over 30 years ago, phototherapy has proven to be an effective treatment of neonatal hyperbilirubinaemia [4]. The few modifications that occurred during these years concerned the source of light (fluorescent vs halogen bulbs) and the colour of the bulbs (white, blue or green) [13, 19, 20]. The light source, however, during conventional phototherapy is placed at a distance from the baby. This means that the infants require eye patches, depriving them from visual stimuli and limiting the mother-baby interaction. Due to the glare, visual assessment of the infant is difficult and nursery personnel have reported headaches, nausea and eye irritation [7].

New techniques have enabled us to deliver phototherapy directly to the skin. The infant is placed on a flat mat containing optic fibres connected to an external portable illuminator. This way, eye patching is

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not required and glare is avoided. Furthermore higher irradiance levels can be used because of the external illuminator. However, comparative studies of fibre optic phototherapy in term infants showed conflicting results, some claiming superior efficacy to conventional phototherapy [12], others the opposite [8, 17]. Only two studies have evaluated fibre optic phototherapy in preterm infants [5, 17].

In one study the fibre optic device was not set at the maximum irradiance level [17] and in both studies preterm infants were not divided into different weight groups to estimate the influence of birth weight on efficacy.

In our study the efficacy of fibre optic phototherapy was compared to conventional phototherapy in preterm infants using the Ohmeda fibre optic Biliblanket system (Ohmeda Critical Care, Columbia, U.S.A.). The evaluated system's fibre optic irradiance level is greater than that of the conventional setup as used in our unit. We therefore hypothesized that the efficacy of the Biliblanket system would exceed that of the conventional device. In order to determine the influence of body weight on the efficacy, infants were divided into three birth weight groups, at entry into the study.

Methods

All preterm infants with a birth weight below 2000 g and a non-haemolytic hyperbilirubinaemia needing phototherapy were considered eligible for the study. Patients who received phototherapy before admission or who met the exchange transfusion criteria before entering the study, were excluded. Informed consent was obtained from one or both parents. Infants were divided into three groups depending on birth weight: (1) <1000 g; (2) 1000–1500 g; (3) 1500–2000 g. Within each weight group the patients were randomly assigned using sealed envelopes to receive one of the following two forms of phototherapy: (1) the fibre optic Ohmeda Biliblanket device, consisting of a halogen lamp illuminating a flat mat using a fibre optic attachment containing 2400 optic fibres which are woven into the mat, or (2) conventional phototherapy consisting of four overhead fluorescent lamps (Philips TLK 40 W/03; Eindhoven, The Netherlands) arranged in an arc 40 cm above the infant. During fibre optic phototherapy the mat, covered with a disposable sheet, is in direct contact with the skin. The size of the illuminating part of the mat is 11×13 cm. The Biliblanket device provides light in the 400–550 nm range and the conventional lamps in the 380–480 nm range. The irradiance level averaged 35 and 16 $\mu W/cm^2$ per nm, for the fibre optic and conventional device respectively. Irradiance levels were measured on a monthly basis using a Spectroline DM-450× radiometer (Spectronics Corporation, Westbury, NY, U.S.A.). If levels declined by more than 20% from baseline values the lamp was replaced. Infants were completely unclothed during either form of phototherapy. Eye pads were only used during conventional phototherapy.

If bilirubin concentrations increased above predetermined levels despite single phototherapy, double phototherapy was started using a conventional fluorescent lamp as described above regardless of the initial form of phototherapy.

Bilirubin concentrations at which single or double phototherapy was initiated or terminated depended on postnatal age (during the first 72 h) and birth weight. Values were presented in six specially designed graphs for the following birth weight groups: 600–799, 800–999, 1000–1250, 1250–1500, 1500–1750 and 1750–2000 g. Graphs also contained the bilirubin values at which an exchange transfusion should be performed. The limits of the bilirubin values at which phototherapy had to be initiated or exchange transfusion should be performed, increased with birth weight. Figures 1 and 2 show the bilirubin concentrations to initiate single and double phototherapy related to postnatal age and birth weight group.

Before infants entered the study, blood was drawn for blood typing, Coombs test and haematocrit in order to detect a possible haemolytic hyperbilirubinaemia. After initiation of phototherapy, capillary blood was sampled at least once every 24 h to monitor the serum bilirubin. Urine was checked twice daily for bilirubin using Ames reagent Strips (Multistix 10 SG; Miles Inc., Diagnostics Division, Elkhart, U.S.A.). When bilirubin was present a serum direct-acting bilirubin was also estimated. Bilirubin levels were determined with the Jensdrassik-Grof procedure [9].

Efficacy was assessed by comparing the required duration of treatment. The duration of phototherapy was evaluated and compared using the Kaplan-Meier method and the log rank-test [10]. Data were primarily analysed according to the intention to treat principle [11].

In this analysis patients are only excluded if they had been entered into the study without fulfilling the entry criteria. A secondary analysis was performed in which the patients in whom phototherapy was stopped while the specified criteria for stopping had not been met, were evaluated as if they left the study at that time (censored phototherapy duration) [10]. In all analyses, the phototherapy duration of patients who had died while still receiving phototherapy were treated as censored observations. Because this analysis essentially led to the same conclusions as with the primary analysis, only the intention to treat analysis is reported. $P = 0.05$ (two-sided) was considered the limit of significance.

Results

Between November 1991 and June 1993 a total of 132 infants entered the study. Retrospectively 4 patients (3 in

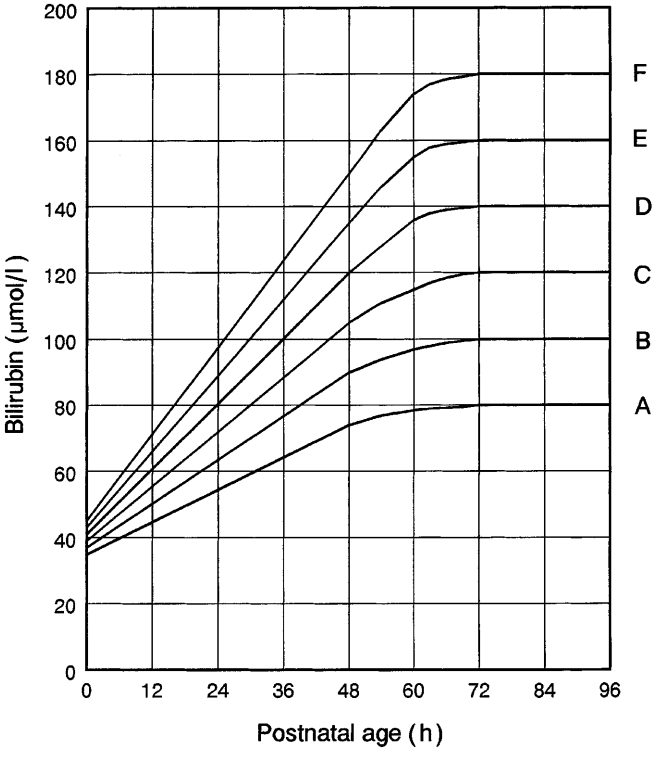

Fig. 1 Graphic presentation of bilirubin concentrations to initiate single phototherapy related to postnatal age. The six curves present the following birth weight groups: *A*: 600–800 g, *B*: 800–1000 g, *C*: 1000–1250 g, *D*: 1250–1500 g, *E*: 1500–1750 g and *F*: 1750–2000 g

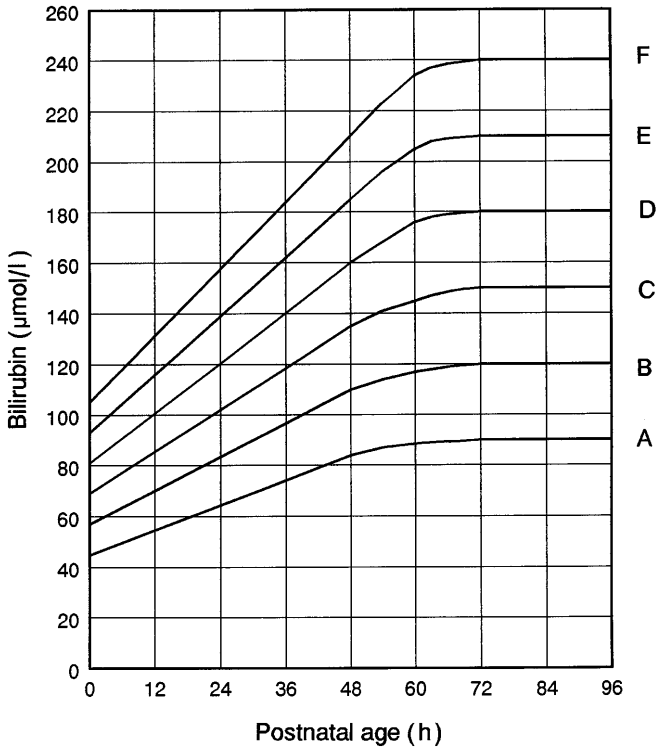

Fig. 2 Graphic presentation of bilirubin concentrations to initiate double phototherapy related to postnatal age. The six curves present the following birth weight groups: *A*: 600–800 g, *B*: 800–1000 g, *C*: 1000–1250 g, *D*: 1250–1500 g, *E*: 1500–1750 g and *F*: 1750–2000 g

the fibre optic and 1 in the conventional group) were excluded because they either met exchange transfusion criteria before entry (2), received phototherapy before admission (1) or had evidence of haemolytic anaemia (1). Furthermore, from four patients (three in the fibre optic and one in the conventional group) insufficient data were available to evaluate outcome due to administrative problems.

A total of 124 patients were evaluated and form the basis of this report. Characteristics of the studied infants are listed in Table 1 . There were no significant differences in gestational age, birth weight and the number of small for gestational age infants between the two treatment groups or within each birth weight group. Four patients died while still receiving phototherapy at that time (2 in the fibre optic and 2 in the conventional group). The causes of death were persistent pulmonary hypertension of the neonate (1), lung hypoplasia (1) and hyaline membrane disease complicated by severe barotrauma (2). In 11 patients, 6 in the fibre optic and 5 in the conventional group, phototherapy had been stopped prematurely, before criteria had been met. Three patients (two in the fibre optic and one in the conventional group), had received phenobarbital for neonatal convulsions. Two patients, one in each group, had been treated with a partial exchange transfusion because of polycythaemia. One patient in the conventional group developed a conjugated hyperbilirubinaemia with a maximum direct-acting bilirubin of 28% of the total serum bilirubin con-

Table 1 Characteristics of studied groups (*SGA* Small for gestational age). Values presented as mean ± SD

Groups[b]	Fibre optic[a]						Conventional					
	1	2	3	Total			1	2	3	Total		
No. (M/F)	17 (10/7)	23 (14/9)	16 (8/8)	56 (32/24)			22 (9/13)	27 (17/10)	19 (14/5)	68 (40/27)		
SGA infants (No.)	8	7	1	16			14	6	2	22		
Birth weight (g)	844 ± 130	1258 ± 143	1697 ± 129	1258 ± 356			871 ± 100	1258 ± 171	1713 ± 121	1253 ± 353		
Gestational age (weeks)	27.3 ± 2.3	30.3 ± 2.8	31.1 ± 1.5	29.6 ± 2.8			28.6 ± 2.1	29.9 ± 1.8	31.8 ± 1.2	29.9 ± 2.1		
Age at start (h)	16.1 ± 9.4	25.7 ± 19.8	33.3 ± 19.9	25.0 ± 18.3			18.9 ± 8.6	29.2 ± 14.8	35.9 ± 22.8	27.7 ± 16.9		
Haematocrit (l/l)	0.47 ± 0.07	0.52 ± 0.09	0.49 ± 0.06	0.49 ± 0.08			0.50 ± 0.09	0.51 ± 0.08	0.49 ± 0.09	0.50 ± 0.09		
Bilirubin (µmol/l)												
start	74 ± 18	96 ± 38	118 ± 48	96 ± 40			71 ± 14	97 ± 33	114 ± 33	93 ± 32		
maximum	99 ± 18	139 ± 35	188 ± 48	142 ± 49			96 ± 33	126 ± 25	168 ± 39	128 ± 42		
stop	71 ± 29	89 ± 20	129 ± 43	94 ± 38			67 ± 17	95 ± 23	117 ± 30	91 ± 30		

[a] Biliblanket fibre optic mat (Ohmeda)
[b] Birth weight groups 1 = < 1000 g, 2 = 1000–1500 g, 3 = 1500–2000 g

centration. Because analysis was based on the intention to treat principle all patients were included.

Eleven patients (5 in the fibre optic and 6 in the conventional group) had been transported back to the referring hospital because of improved clinical condition, while still receiving phototherapy treatment at the time of transfer. Further phototherapy treatment was continued according to the local hospital criteria and the duration thereof was documented. These patients were also included in the analysis.

Kaplan-Meier curves showing the percentage of patients still on phototherapy along time for both modalities are shown in Fig. 3. The median duration in the fibre optic group was 118 h, which did not differ significantly ($P = 0.17$) from the value of 114 h in the conventional group. Also no significant differences were found within the three separate weight groups (Fig. 4). The weight groups themselves did not differ significantly from each other regarding required duration of treatment. An additional conventional lamp was initiated in 29 patients (52%) in the fibre optic group and 27-patients (40%) in the conventional group ($P = 0.21$) after a mean time of respectively 28 and 26 h. The required duration of the second lamp did not significantly differ between the fibre optic and the conventional group ($P = 0.13$), with median duration respectively 54 and 48 h. Seven patients had required exchange transfusions, 4 in the fibre optic (7%) and 3 in the conventional (4%) group ($P = 0.70$).

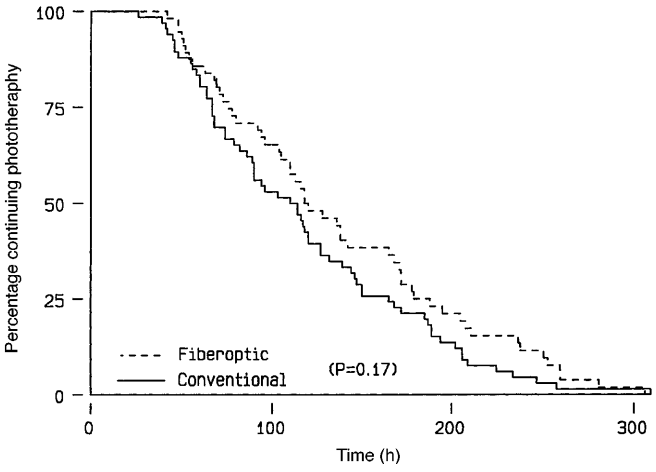

Fig. 3 Percentage of patients still on phototherapy versus time according to fibre optic and conventional treatment

Discussion

Several studies have evaluated the efficacy of fibre optic phototherapy, a new modality for treatment of neonatal hyperbilirubinaemia. Studies using the Wallaby phototherapy system (Fibre optic Medical Products Inc., Allentown, Pa., U.S.A.) showed different results [8, 12]. These efficacy studies were done in term infants. Two studies used the Ohmeda Biliblanket device and also looked at preterm infants [5, 17]. One study reported that fibre optic phototherapy was less effective as compared to conventional blue light phototherapy [5]. The other reported equal efficacy of fibre optic phototherapy compared to conventional treatment in preterm infants. The decline rate of bilirubin during fibre optic treatment however, was still inferior to conventional phototherapy [17]. Although the author in this study stated that the fibre optic device was set at maximal power, the manu-

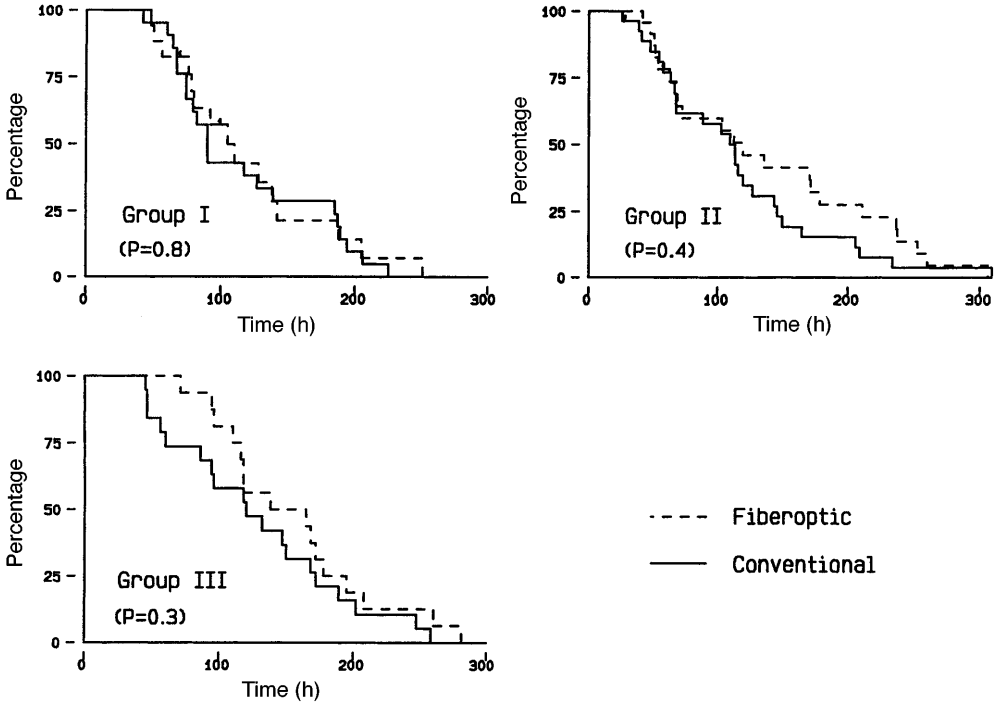

Fig. 4 Percentage of patients still on phototherapy versus time according to fibre optic and conventional treatment in the three separate birth weight groups

facturer noted that according to the reported irradiance levels the investigators only used the lower two levels. It was suggested that the use of the high irradiance level might have improved efficacy.

In our study we compared the efficacy of fibre optic phototherapy to our conventional setup in preterm infants, using the Biliblanket system with the maximum irradiance level. Bilirubin levels were determined once every 24 h. We find it ethically unacceptable to sample more often without a clinical reason. As the sampling interval was applied to both treatment groups we feel it did not influence the comparison of efficacy. Although not stated in the protocol, in practice all the infants were sampled at 800 a.m. together with other needed blood tests. The influence of fluctuations of bilirubin levels during the day was therefore minimal.

Additional blood sampling was only performed if there was a clinical reason as estimated by the attending physician. As all attending physicians share a consistent approach in managing the treatment of hyperbilirubinaemia, differences in additional sampling between the two treatment groups is very unlikely.

In some patients phototherapy was terminated prematurely, but they were equally presented in the two treatment groups. Some patients were transported back to the referring hospital because of improved clinical condition. It is not our policy to prolong the admission for research reasons only. Again patients were equally presented in the two treatment groups. All patients were included in the final analysis which was based on the intention to treat principle. We found no significant difference in efficacy of the fibre optic phototherapy compared to conventional phototherapy in preterm infants. This despite the fact that higher irradiance levels are used compared to the conventional phototherapy and a dose-response relation has been demonstrated [15]. Because the size of the fibre optic mat used in the Biliblanket system is relatively small, the area of exposure is smaller as compared to the conventional setup. Therefore with increasing body weight the fraction of body surface exposed to the fibre optic light will becomes less. This could partly explain the reported inferior efficacy of fibre optic therapy in the term infant as compared to conventional phototherapy [8, 17]. In addition, much of the spectral emission of the Biliblanket device was in the green region, which is less effective than the blue light [16].

To estimate the importance of body weight in the preterm infant we divided the study population into three birth weight groups.

Although it has been shown that gestational age also has an impact on efficacy of phototherapy [18], we decided to divide by birth weight for the following reasons: (1) birth weight is more accurate than gestational age; (2) in current practice criteria to start and stop phototherapy are usually presented in graphs depending on birth weight and not gestational age [1, 6]. Table 1 shows that the gestational age did not differ significantly within each birth weight group. Although the differences in efficacy were not significant we also found a trend towards less efficacy of the fibre optic therapy compared to the conventional setup with increasing birth weight (Fig. 4).

Although no different between the treatment groups, the need for an additional lamp and the need to perform an exchange transfusion were relatively high. The reason for this high "failure rate" are the strict criteria used to start an additional lamp and to perform an exchange transfusion. The basis for these strict criteria was a national collaborative survey on hyperbilirubinaemia in preterm infants and outcome at 2 years of age [2]. They concluded that mild to moderate hyperbilirubinaemia in preterm infants was associated with impaired neurodevelopmental outcome. When we would have applied more conventional criteria this "failure rate" would have been much lower.

The median duration of phototherapy in the fibre optic and conventional treatment group was 118 and 114 h respectively. This relatively long duration of therapy can also be explained by the strict criteria used to start and stop phototherapy. The mean postnatal age at which phototherapy was initiated was approximately 24 h at a mean bilirubin level of approximately 95 μmol/l. As shown elsewhere, bilirubin has still to reach his maximum level at this stage, especially in premature infants weighing less than 2000 g [4].

Phototherapy will lower this maximum level and shorten the time in which it is reached. In most other studies [5, 8, 12, 17] the postnatal age at start of phototherapy ranged between 60 and 80 h, with a bilirubin level ranging between 230 and 250 μmol/l.

Several studies have mentioned that the parents and the nursery personnel find fibre optic phototherapy more comfortable as compared to the conventional phototherapy [14, 17]. We did not formally interview our nursing personnel about their reaction to the fibre optic phototherapy. However, the general impression leads us to believe that the fibre optic phototherapy was highly appreciated. Better visual assessment and the absence of eye patches were considered the main advantages. Moving of the infants away from the fibre optic mat was the only disadvantage mentioned. This problem can be solved by attaching the fibre optic mat to the back of the infant using a special designed sheet.

Our study demonstrates that in the preterm infant the efficacy of fibre optic phototherapy using the Ohmeda Biliblanket system is comparable to conventional phototherapy. Because of the small size of the fibre optic setup as compared to the large lightbanks of conventional phototherapy, it appears very useful in the combination phototherapy in the preterm infant. Using the fibre optic system as the first choice of phototherapy in preterm infants is a more arbitrary choice.

Further comparative studies evaluating the occurrence of known side-effects during phototherapy treatment (i.e. hyperthermia and dehydration) [3] could facilitate this choice.

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