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Riboflavin (Vitamin B_2) Treatment of Neonatal Pathological Jaundice

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The effect of traditional blue-light and riboflavin combined with blue-light was compared in newborns affected by ABO incompatibility, admitted for exchange transfusion. During the period of preparation for the intervention 14 patients were treated with blue light alone and 14 patients with riboflavin combined with phototherapy. A single dose of 10 mg/kg riboflavin was administered intravenously. The duration of treatment was three hours in both groups. The effect of phototherapy was markedly enhanced by the additional riboflavin, by the end of the 3-hour period a significant fall of serum bilirubin was demonstrated in the 14 patients treated with blue light and riboflavin while in the patients treated with phototherapy alone the bilirubin level continued to rise. There was no difference in the activity of the antioxidant enzymes superoxide dismutase and catalase, and in lipid peroxidation between the groups.

Kostenbauder and Santvordeker [10, 26] have shown that riboflavin sensitises bilirubin against the effect of light, enhancing thus its photocatabolism. This observation led to clinical trials of the drug [6, 7, 19, 22, 31]. Later Meisel et al [19] showed that riboflavin does not affect the albumin-bilirubin binding, i.e. its application carries no risk of bilirubin displacement from its albumin binding. In an earlier paper we reported on the favourable effect of riboflavin in preventing jaundice. In this study we have attempted to demonstrate that phototherapy combined with riboflavin, proven to be effective in preventing hyperbilirubinaemia, is suitable for producing a rapid decrease in the high bilirubin level.

Patients and Methods

The material consisted of 28 term babies affected by ABO incompatibility. Only newborns free of all symptoms but hyperbilirubinaemia, with a bilirubin level above the level of indication for exchange transfusion [24] were selected. The trial was carried out during the 3-hour period necessary for preparing the exchange transfusion. 14 patients were treated with blue light alone, another 14 patients with riboflavin plus phototherapy. Vitamin B_2 (Beflavin, La Roche) was diluted by a three-fold volume of physiological saline and a single intravenous dose of 10 mg/kg was injected slowly. Serum bilirubin was determined at the time of introducing therapy, this value was regarded as the 0-hour level. The determination was repeated after three hours (3-hour value) and the mean values of the two groups were then compared statistically.

TABLE I

Data of newborn infants treated with blue light alone, or riboflavin combined with phototherapy

Group of treatment	Mean ± SD		Serum bilirubin, micromol/l		Degree of statistical significance
	Birthweight, g	Age, hours	0 hour	3 hours	
Blue light alone n = 14	3405±467	49.7±28.8	349±77	381±92	NS
Blue light plus riboflavin n = 14	3271±588	50.8±26.7	367±66	280±51	$p<0.01$
Degree of statistical significance	NS	NS	NS	$p<0.01$	

The activity of the antioxidant enzymes superoxide dismutase (SOD) and catalase and the degree of lipid peroxidation (LP) were determined at 0 and 3 hours by biochemical methods [2, 15, 21, 23].

RESULTS

Table I shows the mean bilirubin level of the newborns treated with blue light alone and with riboflavin plus phototherapy, determined at initiation and termination of treatment. It can be seen that the two groups did not differ in birthweight, age at admission and mean initial bilirubin level. The mean bilirubin level was somewhat higher than the initial level in the group treated with phototherapy alone; the difference was, however, not significant. In all cases treated with riboflavin and blue light there was a decrease in the bilirubin level by the end of the 3-hour period. The difference between the mean 0-hour and 3-hour values was significant statistically. There was no significant difference between the two groups in respect of SOD activity (Fig. 1). The mean initial activity of catalase was significantly higher in the group treated with the combination of riboflavin and phototherapy (Fig. 2). LP was similar in the two groups, no significamt difference has been found (Fig. 3).

DISCUSSION

Earlier, a decisive role was attributed to oxidation in the process of bilirubin photocatabolism. It was thought that the energy of light induces formation of singlet oxygen ($^1O_2$), this in turn leads to photoxidation of the bilirubin molecule [8, 16]. It was thus anticipated that the catabolic effect of riboflavin on bilirubin is mediated by its capacity of producing $^1O_2$ [20, 22, 26]. Recent observations have, however, shown that isomeration and not oxidation is the basic factor in bilirubin breakdown [12, 13, 14, 17, 18, 27]. It has turned out that $^1O_2$ formed by the photodynamic reaction plays a minor role, this process may affect the bilirubin catabolism via oxidation of other compounds [3, 5, 11, 26]. In vitro studies have shown that changes in the structure of DNA can be in-

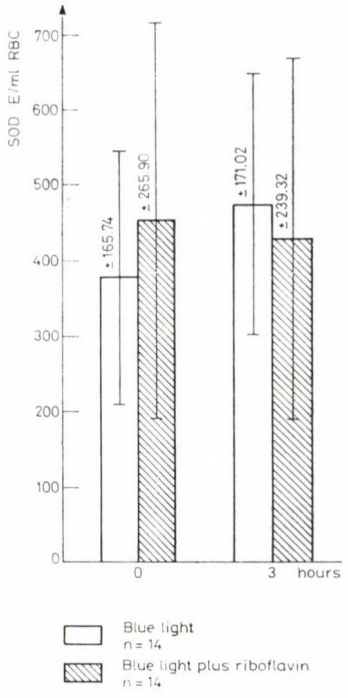

FIG. 1. Superoxide dismutase activity in patients treated with phototherapy alone and with blue light plus riboflavin, before initiation (0 hour) and after completion (3 hours) of therapy

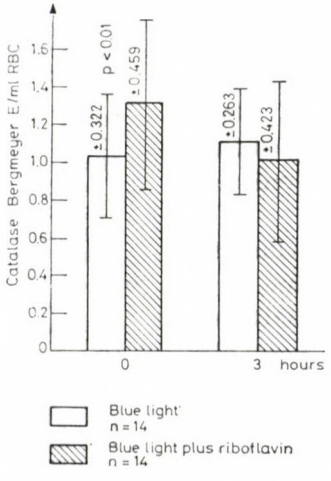

FIG. 2. Catalase activity in patients treated with phototherapy alone and with blue light plus riboflavin, before initiation (0 hour) and after completion (3 hours) of therapy

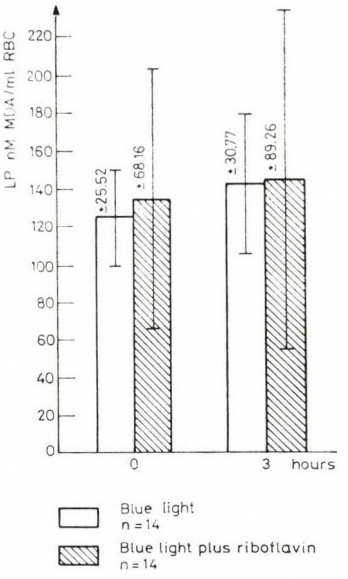

FIG. 3. Lipid peroxidation in patients treated with phototherapy alone and with blue light plus riboflavin before initiation (0 hour) and after completion (3 hours) of therapy

duced by light used in phototherapy [30]. This phenomenon, attributed to the effect of singlet oxygen, can also be seen if irradiation occurs in the presence of bilirubin or riboflavin [9, 25, 28, 29]. This is the reason for warnings of certain authors against the therapeutic use of riboflavin [10, 22, 26, 28, 30, 32]. Others regard phototherapy itself risky [4, 28, 30]. It is also known that exchange transfusion may enhance the toxicity of oxygen [1].

In our material no detrimental effect of riboflavin plus blue light has been demonstrated in SOD and catalase activity or lipid peroxidation. The figures showed that a rapid fall in bilirubin level can be achieved by riboflavin combined with phototherapy during the period of preparation for an exchange transfusion. The method may be useful if prolongation of this preparation period is inevitable.

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