AN EVALUATION OF VARIOUS REGIMES OF TREATMENT OF HYPERBILIRUBINEMIA OF NEWBORNS

by

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Introduction

From time to time various workers have reported high incidence of hyperbilirubinemia in newborns ranging from 60 to 80 per cent of all newborns (Behrman 1979). The interest in hyperbilirubunemia stems from its potentiality in causing kernicterus. Further, that kernicterus is preventable raises pediatricians' hopes that this can be eliminated as a cause of brain damage. Fortunately, a number of regimes are available today for the purpose. Amongst the regimes available, particularly hopeful is phototherapy as appears from number of reports (Bharucha *et al* 1971; Rao *et al* 1973; Wong and Wood, 1973; Singh and Narayen 1974 and Agrawal *et al* 1976). Further, many agents have been reported to lower bilirubin levels. The present study aims at finding effectivity of phototherapy and whether other agents can potentiate hypobilirubinemic effect of phototherapy to a significant degree or not.

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Material and Methods

This prospective study consists of 70 newborns having jaundice necessitating investigations and treatment. All such cases were included in the study irrespective of age at the onset of jaundice, sex and maturity of newborn. However, the cases where concomitant diseases which are known to accentuate or prolong jaundice, e.g., infections, were present, were excluded from the study.

Each case was examinal and evaluated thoroughly for the evidence of infections, hemorrhages, hematomas, congenital malformations, maturity score etc. History was obtained regarding jaundice in the previous babies in the immediate postnatal life, drugs given to mother during pregnancy and in labour were all noted and entered in the proforma. Cases of severe Rh isoimmunisation were also excluded from the study. In sach case bilirubin estimation was carried out on the day of appearance of jaundice and subsequently on each day. Bilirubin estimation was done for total and direct bilirubin, indirect was obtained by substracting the direct from the total. Rh and ABO grouping, hemoglobin, reticulocyte count and direct Coomb's test were done in each case.

Regimes of Treatment: All the 70 cases were given intermittent phototherapy (IPT). IPT was administered with standard white light and included 6 hours exposure of naked baby with eyes protected by eye patch and 2 hours 'rest period'. The intensity used was about 4,800 lux (Bajpai *et al* 1971) or 420-470 nm. (Behrman 1979). Cases were divided in the following subgroups:

Group I: 20 cases receiving IPT only.

Group II: 10 babies who received phenobarbitone in addition to IPT in the dose of 5 mg per kg. in two divided doses.

Group III: 20 babies who received agar in dose of 250 mg. 6 hourly orally in addition to IPT.

Group IV: 20 babies who received dexamethasone in dose of 0.25 ml. intramuscularly 8 hourly in addition to IPT.

In all cases the therapy was continued for 96 hours, whereever possible, irrespective of fall in bilirubin levels to evaluate side effects, if any, in similar setting. An estimation of bilirubin was obtained 48 hours after stopping the therapy to observe rebound rise of bilirubin, if any.

Time of appearance of jaundice is shown in Table I. In maximum number of cases (63 out of 70) jaundice appeared between 25-120 hours.

TABLE I

Time of Appearance of Jaundice

Time of appearance	Number (n = 70)	Percentage
Within 24 hours	2	2.8
25-120 hours	63	90.1
After 120 hours	5	7.1

The possible etiological factors responsible for jaundice are shown in Table II. Maximum causes were of physiological jaundice. There was 1 case of ABO and 3 cases of Rh isoimmunisation. In 6 cases diagnosis could not be established.

TABLE II

Causes of Jaundice

Disease	Number (n = 70)	Percentage
Physiological jaundice of newborn	60	85.4
ABO isoimmunization	1	1.4
Rh isoimunization	3	4.4
Idiopathic (undiagnosed)	6	8.8

In Table III it is vident that fall in bilirubin observed was, in Group I from 14.6 to 6.2 mg/dl, in Group II from 12.8 to 4.2 mg/dl., in Group III from 14.0 to 7.6 mg/dl—and in Group IV from 13.1 to 5.8 mg/dl within 72 hours. Further no rebound rise was observed.

In Table IV rate of fall of indirect bilirubin per day has been shown. The fall was significant in each category. Thus in first 24 hours daily fall was between 2.5-3.5, in second 24 hours 1.8-2.8 and in third 24 hours 1.8-2.4 mg/dl.

Discussion

It is evident from the present study that phototherapy is a potent hypobilirubinemic procedure. It causes significant fall in the levels ($p = < 0.01$). Many authors agree that IPT is simple, effective and safe (Bharucha *et al* 1971; Wood and Wong, 1973 and Agrawal *et al* 1976).

Different workers from this country and abroad have observed divergent results as regards combining IPT with phenobarbitone. Agrawal *et al* (1976) observed no superiority of combining phenobarbitone with phototherapy. They found no significant augmentation in the

TABLE III

Serum Indirect Bilirubin Levels (mean and range) in Various Regimes of Therapy

Therapy group	No. of cases (n = 70)	Serum bilirubin (mg/dl.) At Initiation	24 hr. after	24 hr. after 48 hr. after	48 hr. after 72 hr. after	96 hr. after	48 hr. after completion	Duration of Therapy
I	20	14.6 ± 3.1 (10.2 — 23.0)	11.2±1.6 (10.2—18.4)	9.8 ± 2.2 (8.2 — 14.0)	6.0±2.0 (4.8—10.2)	3.0±1.0 (0.8—4.2)	2.2 ± 0.4 (1.2 — 3.6)	78 (54—84)
II	10	13.8 ± 1.8 (10.8 — 17.2)	11.2±2.8 (8.2—14.0)	8.8 ± 2.6 (6.4 — 11.0)	5.2±1.8 (3.0—8.0)	3.8±1.8 (2.3—5.2)	1.8 ± 0.8 (1.8 — 0.8)	71 69 (42—78)
III	20	14.0 ± 2.6 (11.8 — 18.2)	12.4±2.4 (9.4—15.4)	10.2 ± 3.4 (8.0 — 12.0)	5.6±1.8 (5.0—8.0	2.4±0.6 (1.0—3.2)	3.2 ± 1.2 (2.2 — 4.6)	71 (48—84)
IV	20	13.1 ± 2.6 11.2 — 16.8	10.8±2.4 (9.6—16.8)	7.8 ± 1.4 (6.8 — 9.6)	5.8±2.4 (4.2—8.8)	1.6±0.6 (0.8—2.2)	2.8 ± 1.6 (1.6 — 3.8)	72 (42—84)

rate of fall with 'photobarb' therapy. Their rate of fall was similar to the present study. It was also observed similarly that initial fall on first day was always more rapid that the fall on subsequent days. Wong and Wood 1973 also did not observe any significant difference. Rao *et al* 1973, on the other hand, found better fall in levels with agar as compared to phenobarbotone, phototherapy and orotic acid. However, in an exhaustive review, Wilson, 1971, cautions against too eager acceptance of phenobarbitone therapy. Sisson, 1971, commented regarding side effects of phenobarbitone and was skeptical about the desirability of enzyme induction effects. He mentioned that phenobarbitone can cut short activity of steroids, alter the clotting mechanisms, adversely affect vitamin D metabolism, suppress REM sleep which represents an interference with normal protein synthesis in brain.

In the present study, phototherapy was observed to be effective. Except for 1 case who required but could not receive exchange transfusion, the rate of fall in all other cases was significant on each day.

RESULTS OF VARIOUS REGIMES OF PHOTOTHERAPY.

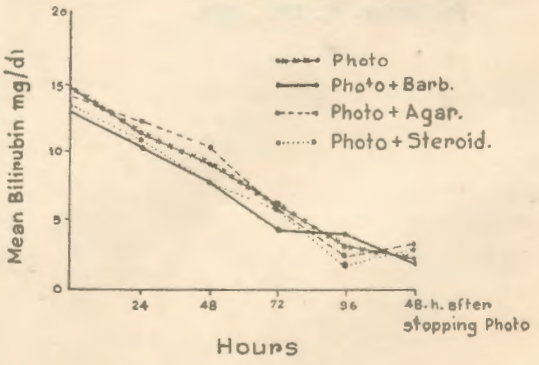

Fig. 1

TABLE IV

Rate of Fall in Levels of Serum Bilirubin Daily on First Three Days of Various Regimes of Therapy

Therapy group	Number of cases (n=70)	Daily rate of fall of bilirubin			'p' value
		First 24 hours	Second 24 hours	Third 24 hours	
I	20	3.6 ± 1.2 (2.8 — 4.4)	2.4 ± 0.9 (1.6 — 3.7)	2.2 ± 0.7 (1.8 — 3.2)	<0.01
II	10	3.2 ± 0.8 (2.6 — 4.7)	2.8 ± 0.7 (2.2 — 3.8)	2.4 ± 0.4 (2.0 — 3.5)	>0.005
III	20	2.8 ± 1.1 (2.4 — 3.8)	1.8 ± 0.5 (2.0 — 3.1)	2.0 ± 0.8 (1.6 — 3.2)	<0.01
IV	20	2.6 ± 0.6 (2.2 — 3.2)	2.2 ± 0.7 (1.6 — 3.3)	1.8 ± 0.4 (1.2 — 2.4)	<0.05

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