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Some studies on Physiological Jaundice of the Newborn

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INTRODUCTION

The incidence of icterus as a physiologic phenomenon merits a special place in any study of the disorders of the newborn. The term physiological jaundice has been challenged by workers like Claireaux (1960) and Mekay and Smith (1964). Lucey (1960) states that the term physiological jaundice lacks precise definition, it is a diagnosis which must be made by exclusion.

The theory of haemolysis as the cause as the cause of hyperbilirubinaemia was originally propagated by Goldbloom and Gettlieb (1929), Yllpo (1913) and Hirsch (1913) who ascribed a major role to the liver in the causation of so-called physiological jaundice. They held that though the bilirubin came from the excessive haemolysis in the postnatal period, the main factor determining the appearance of jaundice is a functional immaturity of the liver which renders it unable for the first few days of life to excrete the extra load of bilirubin. Later Snelling (1933), Ross *et al* (1937) and Mollison (1948) supported that immaturity of liver is the chief factor in the causation of physiological jaundice. Finally, in 1954 Billing *et al* postulated a possible metabolic block in the excretion of bilirubin. Brown *et al* (1958) demonstrated that there is a delay in the maturation of the glucuronide conjugating system in newborns. Walker (1957, 1968) showed a deficiency of the glucoronating enzyme in the hepatic cells and less availability of the substrate uridine diphosphate.

The immaturity of the enzyme and restricted availability of the substrate are temporary and develop to normal in the first few days of life.

So the precise mechanism of the causation of 'physiological jaundice' is better understood now. There is little, however, which can be done from the point of view of treatment, and much less from the point of view of prevention. With this object in mind, we decided to undertake this study, in the hope that some newer facts could emerge from the present study, especially with the use of an indigenous drug, Liv.52 (The Himalaya Drug Co.).

MATERIAL AND METHODS

This work was carried out in a total of 346 newborns delivered at the Maternity Hospital of G.S.V.M. Medical College, Kanpur. Those babies were excluded from the study, who were less than 2½ lb (1125 gm) at birth, who died before the cause of jaundice could be established, and also babies with jaundice due to other recognisable causes such as haemolytic disease, infection, congenital anomalies of the biliary system and drugs.

A detailed history was taken regarding the use of drugs in the antenatal period, infection, nature and duration of delivery, history of hypothermia in mother and jaundice in previous sibs as well as history of diabetes in mother.

All the babies were examined for the detection of jaundice in good sunlight and mild cases were noticed by pressing the skin of the newborn. The time and site of appearance of icterus, its further

progression and disappearance were carefully recorded. A thorough clinical evaluation was done daily to exclude other known causes of jaundice in the neonatal period as mentioned above.

Rh and ABO blood groupings were carried out in every cord blood collection and also in mother's blood. Serum bilirubin estimations of total, conjugated and unconjugated fractions were carried out by the method of King & Wootton (1959) in every cord blood sample and their subsequent determinations were undertaken on 4th and 8th days only in jaundiced babies. A group of neonates without jaundice were selected for analysis of bilirubin fractions on the 4th and 8th day to provide control figures. The Methaemoglobin Reduction Test – a field screening procedure for detection of deficiency of the enzyme G6-P-D in the red blood cells as described by Brewer *et al* (1960) was introduced late in the study to exclude G6-P-D deficiency as the cause of neonatal jaundice. Haemoglobin per cent, reticulocyte count, Coomb's test, etc. were carried out when necessary.

A total of 346 newborn babies were included in the work to evaluate the effect of Liv.52 drops on the natural course of 'physiological jaundice'. Out of them 136 newborns were administered the drug on random selection starting from the first feed till the 8th day of life in a dose of 5 drops t.i.d. A parallel study was also carried out among 210 babies to establish the natural course of the physiological jaundice. The criteria for diagnosis in the present study were a mild jaundice appearing on the 2nd or 3rd day of life and the baby being otherwise healthy.

Table I: The incidence of physiological jaundice

	Babies receiving Liv.52 drops	Controlled study without Liv.52 drops
Total	136	210
Jaundiced	36	75
Percentage Jaundiced	26.47	35.71

They were divided into two groups:
Group I: 210 babies who were studied for the natural course of 'physiological jaundice'.
Group II: 136 babies who were administered Liv.52 drops, to study its effect on `physiological jaundice'.

Liv.52, an indigenous drug (Himalaya Drug Co.) was used in the groups of babies as outlined above in a dose of 5 drops t.i.d. In Group I no drug was given whether jaundice appeared or not; in Group II the drug was administered for a period of eight days and from the first feed.

In a series of 210 newborns (Group I) male children showed more jaundice, the incidence being more in summer months. The highest incidence of jaundice was in babies of low birth weights, i.e. 1500 to 2000 gm., severity increasing with lower birth weights. Jaundice appeared on the second or third day of life and cleared on the eighth day. Lesser the birth weight, higher was the value for cord blood total bilirubin.

Composition of Liv.52 drops:
Each ml contains:

Exts.	Capparis spinosa	17 mg
	Cichorium intybus	17 mg
	Solanum nigrum	8 mg
	Cassia occidentalis	4 mg
	Terminalia arjuna	8 mg
	Achillea millefolium	4 mg
	Tamarix gallica	4 mg

Table II: Effect of Liv.52 drops on incidence of jaundice in treated and control groups (Liv.52 drops given to alternate babies in a series of 72 babies)			
	Babies receiving Liv.52 drops Treated group	Babies not receiving Liv.52 drops Control Groups	Total
Total	36	36	72
Without jaundice	27	18	45
With jaundice	9	18	27
Percentage jaundiced	25.0	50.0	37.5

The above Table II shows that the incidence of jaundice was only half as much in the group that received Liv.52 drops than in the control.

Table III: Effect of Liv.52 drops on incidence of jaundice (Liv.52 drops given at random among 70 cases) Treated and control groups			
	Babies receiving Liv.52 drops Treated	Babies not receiving Liv.52 drops Control	Total
Without jaundice	24	24	48
With jaundice	7	15	22
Total babies	31	39	70
Percentage jaundiced	22.58	38.46	31.43

Table III indicates that in babies receiving Liv.52 drops as a preventive drug only, 22.58% of babies developed 'physiological jaundice' while the incidence of jaundice was about one and half times higher in babies not receiving Liv.52 drops (38.6%). The administration of Liv.52 drops from the first day of life considerably reduced the incidence of physiological jaundice, lessened its severity and reduced the morbidity.

Note: the criteria of assessing clinical severity of jaundice is as follows:
Mild: Mild jaundice on face extremities without any complication like lethargy, refusal to feed or dehydration.
Moderate: Moderate jaundice in the whole of the body with sluggishness.
Severe: Marked jaundice in whole body with refusal to feed and may show dehydration.

Table V indicates that none of the babies receiving the drug developed severe jaundice and 19.40% showed mild degree of icterus as against 4.48% of the babies exhibiting moderate intensity.

Table IV: Incidence and clinical severity of jaundice in 75 jaundiced babies not receiving Liv.52					
Birth weight in gm	Mild	Moderate	Severe	Total cases of jaundice	Per cent
1500 – 2000	5	6	9	20	26.7
2000 – 2500	26	9	4	39	52.0
2500 – 3000	10	2	1	13	17.3
3000 & above	2	1	–	3	4.0
Total cases in each group	43	18	14	75	–
Percentage	57.33%	24%	18.67%	100%	

Table V: Clinical severity of jaundice in 67 babies receiving Liv.52 drops					
Weight in gm	Mild	Moderate	Severe	Total	Percentage
1500 – 2000 6 children	–	1	–	1	16.67
2000 – 2500 34 children	6	2	–	8	23.53
2500 – 3000 20 children	6	–	–	6	30.00
Above 3000 7 children	1	–	–	1	14.29
67 children	13	3	–	16	23.88
Percentage of incidence	19.40	4.48	–		

Comparing Tables IV and V in the birth weight group of 1500-2000 gm only 16.67% babies on Liv.52 developed jaundice. In the 2000-2500 gm 23.53% and 2500-3000 gm 30% showed icterus whereas in the control group in the 1500-2000 gm birth weight 26.7% were jaundiced, in the 2000-2500 gm group 52% and 2500-3000 gm 17.3%.

Table VI: Comparison of mean 4th day serum bilirubin in newborns who developed jaundice 38 babies on Liv.52 and 75 not on Liv.52						
Birth weight in gm	Receiving Liv.52			Not receiving Liv.52		
	Treated Group			Control Group		
	Total bilirubin in mg%	Conjugated		Total bilirubin in mg%	Conjugated	
		Value mg%	% of total bilirubin		Value mg%	% of total bilirubin
1	2	3	4	5	6	7
1500–2000	6.95 (9 cases)	1.40	20.14	7.36 (20 cases)	0.89	12.09
2000–2500	5.23 (20 cases)	1.10	21.03	5.62 (39 cases)	0.87	15.48
2500–3000	3.82 (8 cases)	0.92	24.08	5.62 (13 cases)	0.79	14.06
3000 and above	4.6 (1 case)	0.90	19.56	7.38 (3 cases)	0.56	7.59
Total mean	5.15 (38 cases)	1.08	20.97	6.50 (75 cases)	0.77	11.85

Then Table VI shows that the mean total bilirubin is lower on the 4th day when Liv.52 drops are administered to the baby with the first feed. It is also evident that conjugated bilirubin fraction is higher in babies receiving Liv.52 drops than those not receiving the drug.

Table VII: Comparison of mean bilirubin value on the 4th day among babies without jaundice						
Birth weight in gm	Receiving Liv.52			Not receiving Liv.52		
	Treated Group			Control Group		
	Total bilirubin in mg%	Conjugated		Total bilirubin in mg%	Conjugated	
		Value mg%	% of total bilirubin		Value mg%	% of total bilirubin
1500–2000	2.01 (14 cases)	0.91	45.27	2.25 (7 cases)	0.80	35.56
Over 2000–2500	1.75 (52 cases)	0.75	42.86	1.50 (23 cases)	0.56	37.33
Over 2500–3000	1.35 (19 cases)	0.68	50.37	2.79 (7 cases)	0.79	28.32
Over 3000	1.12 (2 cases)	0.56	50.00	0.80 (1 case)	0.30	37.50
Total mean	1.56 (38 cases)	0.72	46.15	1.84 (38 cases)	0.61	33.15

Table VII shows that mean total serum bilirubin was 1.56 mg% on the 4th day in babies (without jaundice) receiving Liv.52 and 1.84 mg% in babies not receiving Liv.52.

The conjugated fraction was 46.15 as compared to that of 33.15 in those who were not receiving the drug. So the drug may be used with advantage in the management of hyperbilirubinaemia in low birth weight neonates.

DISCUSSION

The present study exhibited that 29.62% of the first born and 37.8% of later born neonates became icteric. Barton and associates (1962) have also observed the same pattern, their figures being 21% in the first born and 30% in 286 later born infants.

Tovey *et al* (1959) reported a higher incidence of jaundice in premature babies. In 1962 Barton *et al* also found that 51% of babies born before 35 weeks of gestation developed jaundice, but only 14% of those born after this time. We found an incidence of 57.14% in babies below 38 weeks of gestation, 36.70% in 38.40 weeks gestation group and 13.34% in babies older than 40 weeks. This significant effect of gestational maturity on the incidence of jaundice can be explained by the immaturity of the liver.

Since long, workers have tried to treat or prevent this neonatal episode but none of their methods has proved satisfactory. Exchange transfusion is the only way of managing an infant with severe hyperbilirubinaemia. Brown (1968) has suggested avoidance of factors like anoxia, drugs etc, which aggravate hyperbilirubinaemia. In 1957 Cremer and later Blondhfien (1960) reported lessening of physiological jaundice by fluorescent light. In 1958 and 1959 Danoff *et al* showed encouraging results by oral glucuronic acid but this was contradicted by Schmid (1958), Jeliu *et al* (1959), Dyer and Mecue (1959) and Singh *et al* (1959). Grollman and Odell (1962) could not find any substantial benefit by intermittent peritoneal dialysis in jaundiced babies.

In 1968 Chafekar undertook a study to see the effect of Liv.52 drops on physiological jaundice. He analysed on clinical grounds alone that babies receiving the drug showed less morbidity and were better on the whole.

In the present study 142 babies (Table II & III) were divided into two series to note any effect of Liv.52 on the incidence of physiological jaundice. In one group 25.0% of the babies (alternate babies) receiving the drug showed icterus (compared to 50.0% in the control group) and in another series (random selection) 22.58% of the babies getting the drug were icteric as against 38.46% in the control group. Among jaundiced babies none developed severe icterus and 4.48% showed moderate jaundice as compared to 18.7% severe and 24% moderate in the 75 jaundiced infants not on Liv.52. The total mean bilirubin percentage value on the 4^{th} day among jaundiced babies was low (5.15%) in those who were getting Liv.52 drops as against babies not receiving the drug (6.50%). The mean percentage of conjugated fraction was higher (20.97%) in jaundiced babies receiving Liv.52 than those jaundiced babies not receiving the drug (11.85%). In the birth weight group of 2000-2500 gm, the conjugated fraction rose to 21.03% from 15.48% by the administration of the drug. This increased fraction of conjugated bilirubin was also conclusively shown on the 4^{th} day bilirubin estimations in the newborns who did not develop icterus but were receiving the drug.

Thus, it is evident from observations made in this study that the combination of indigenous drugs, Liv.52, has a definite place in the prevention and management of the `physiological jaundice'. The drug definitely improves the clinical condition, shortens the period of morbidity and in a good number of cases, prevents the jaundice from appearing.

On the basis of the above observations and investigations this inference can be drawn that this indigenous drug Liv.52 helps in this `episode' by promoting the conjugating power of the neonatal liver and this in turn accelerates the excretion of bilirubin through the gut thereby lessening the

severity of hyperbilirubinaemia. This drug may, therefore, be of greater value in low birth weight infants who are more prone to severe hyperbilirubinaemia.

SUMMARY AND CONCLUSION

In this study of 346 new-borns, undertaken at the G.S.V.M. Medical College, Kanpur, the incidence of so-called 'physiological jaundice' of the newborn was found to be 35.71%.

Infants of low birth weight are more prone to develop 'physiological jaundice'.

The lesser the weight of the infant at birth, the higher is the risk of developing severe hyperbilirubinaemia. In the birth weight group 1500-2000 gm, 9 out of 20 (45%) jaundiced babies showed severe icterus.

In an analysis of bilirubin fractions, it was found that the percentage composition of conjugated bilirubin was about one-fourth in the blood on the 4^{th} day in jaundiced babies as compared to that on the 8^{th} day. This observation proves that the neonatal liver has less ability to conjugate bilirubin.

Administer of Liv.52 drops from the first day of life, considerably reduced the incidence of 'physiological jaundice'. Liv.52 administration from the first day of life also reduced the morbidity in 'physiological jaundice' and clinical severity of jaundice was also minimised. Babies receiving the drug were better on the whole, than those not getting it.

Our clinical as well as biochemical observations showed that the severity of `physiological jaundice' was markedly reduced in the low birth weight group of neonates. So, this indigenous drug Liv.52 may be used with benefit as an adjunct in the management of hyperbilirubinaemia in low birth weight neonates. The morbidity period was also reduced in all the physiologically jaundiced neonates receiving Liv.52.

The percentage composition of conjugated fraction of bilirubin was more on the 4^{th} day and 8^{th} day in babies receiving Liv.52 (jaundiced and unjaundiced) than that of those not getting the drug. This observation explains the mechanism of action of Liv.52, that it, in some way, helps in the conjugation of bilirubin by improving the hepatic function. So this indigenous drug may be used with benefit as an adjunct in the management of hyperbilirubinaemia in low birth weight neonates.

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