

TO STUDY THE SAFETY AND EFFECTIVENESS OF PHOTOTHERAPY, PHOTOTHERAPY PLUS PHENOBARBITONE IN NEONATAL HYPERBILIRUBENEMIA

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ABSTRACT: INTRODUCTION AND BACKGROUND: Neonatal hyperbilirubenemia is increased levels of bilirubin in the blood of neonates and it is an important cause of morbidity in the developing world.

AIM: The study aims to assess and compare the safety as well as efficacy of Phototherapy alone and Phototherapy plus Phenobarbitone in neonatal hyperbilirubenemia.

METHODOLOGY: This is a prospective observational study which was conducted in NICU of Government General Hospital, Anantapur. The study was carried out to assess the safety and efficacy of Group-A (Phototherapy alone) and Group-B (Phototherapy plus Phenobarbitone) in Neonatal hyperbilirubenemia. In both treatment A and treatment B groups, baseline characteristics were recorded and matched with each, later subjects are evaluated for outcome measures (Peak serum bilirubin levels, duration of phototherapy in hours), need of phototherapy and adverse drug effects) and safety measures (ADR profiles for Phototherapy as well as Phototherapy plus Phenobarbitone). All clinical outcome measures compared with each other by using paired T test to select best treatment option for clinical practice.

RESULTS: There was no significant difference between Phototherapy as well as Phototherapy plus Phenobarbitone group in case of total, direct serum bilirubin levels before and after treatment as well as there is no difference in duration of phototherapy (24hrs,48hrs,72hrs) and for all remaining characteristics we calculated in terms of percentage, mean and standard deviation. The P value has no significance (>0.05)

DISCUSSION: The neonates who have been Treated with Phenobarbitone had shown clinical features like Drowsiness and Dehydration with were been corrected by IV fluids and Artificial mother feed. Mono therapy (phototherapy) is alone sufficient when compared to the combination therapy (in treating cases with phototherapy plus Phenobarbitone). In the present study, no significant side effect of phototherapy was observed, and phototherapy was effective in decreasing bilirubin levels in both groups.

CONCLUSION: Combination of phototherapy with Phenobarbitone did not produce any difference in bilirubin levels when compared to phototherapy alone throughout 72 hrs. But when safety profile is considered Phototherapy is best option, because Phenobarbitone has toxic ADR profile when compared with phototherapy alone.

KEYWORDS: Neonatal hyperbilirubenemia, Phototherapy, Phenobarbitone, Anantapur.

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INTRODUCTION AND BACKGROUND: Neonatal Hyperbilirubenemia is elevated levels of bilirubin in the blood of neonates. It is pragmatic during the first week of life in approximately 60% of term infants and 80% of preterm infants. Hyperbilirubenemia is usually due to a combination of an increased bilirubin load and decreased bilirubin elimination. The normal total serum bilirubin concentration is in the range of 0.2 -1.2 mg/dl. It can be classified as Physiologic or Pathologic hyperbilirubenemia. It can be classified by whether the hyperbilirubenemia is Unconjugated, Conjugated or both.

AIMS & OBJECTIVES:

- To assess and compare the safety of phototherapy, phototherapy plus Phenobarbitone in neonatal Hyperbilirubenemia.
- To evaluate the efficacy of Phototherapy, Phenobarbitone plus Phototherapy in neonatal Hyperbilirubenemia.

METHODOLOGY:

Study Design: It is A Prospective, Comparative, and Observational study to evaluate the efficacy, safety of regimen-A (phototherapy) and regimen-B (phototherapy plus phenobarbitone) used in the treatment of Neonatal Hyperbilirubenemia.

Study Duration: The study was carried out over a period of 6 months from December 2014 to May 2015.

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Site of Study: The study entitled "A comparative study on safety and efficacy of Phototherapy, Phototherapy plus Phenobarbitone in Neonatal Hyperbilirubenemia." Was carried out in Department of Pediatrics government general hospital in Anantapuramu.

Inclusion Criteria: New born Neonates with low birth weight & term neonates. Increased Levels of Bilirubin ranging from normal to abnormal peak levels between 15-20 mg/dl.

Exclusion Criteria: Infants with haemolytic Hyperbilirubenemia, congenital anomalies. Neonates with hematological causes tests.

Data Sources: Data will be collected from mother with direct interview and blood samples will be collected from the selected neonates.

Treatment plan: Study consists of three Regimens.
 a. Phototherapy – Regimen A.
 b. Phototherapy plus Phenobarbitone - Regimen B.

Study Procedure: Babies looking icetric were followed up regularly, history regarding Antenatal Care of the mother and high risk factors of the pregnancy, socio economic factors, any line of treatment during pregnancy, details of delivery and conditions of the neonates after the delivery and Blood samples will be collected and evaluation will be done. Comparison will be done regarding the Safety, Efficacy parameters for Regimen A (phototherapy) Regimen B (Both A+B) by recording the ADRs in examined neonates and which line of treatment option is going to show fast recovery and efficacy.

Outcome Measures: Peak serum bilirubin levels, Duration of Phototherapy (hrs), Need of phototherapy and Adverse drug effects.

STATISTICAL ANALYSIS: Descriptive Statistical studies like paired T-test will be followed.

RESULTS:

Sl. No.	Parameters	Group A (n= 55)	Group B (n=50)
1.	Maternal age, D (Mean±SD)	• 6.16±4.6	• 5.66±4.9
2.	Type of delivery • Caesarean n(%) • Normal n(%)	• N=22(40%) • N=33(60%)	• N=16(32%) • N=34(68%)
3.	Gestational age (wks)	• 3.9±1.6	• 38.3± 1.8
4.	Birth Weight (kg) • (< 2.5 kg) • (>2.5 kg)	• 2.98±0.3 • 2.27±0.19	• 2.95±0.3 • 1.86±0.4
5.	Gender: • Males, (n %) • Females, (n %)	• N=31(56%) • N=24(43%)	• N= 36(72%) • N=14(28%)

6.	Type of phototherapy • Single surface (S/S) • Double surface (D/S)	• N=49(89%) • N=6(11%)	• N= 33(66%) • N=17(34%)
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Table 1: Baseline Characteristics of study population

This study consists of total (n= 105) samples are included among them 55 are under group –A (phototherapy) and 50 are under group –B (phototherapy plus phenobarbitone).

The base line characteristic intended is type of delivery. Again two groups have been divided among total samples. Group A 22 (40%) are caesarean and 33 (60%) are normal. In group A total no of sample is (n=55), out of them 31 are male (n=31) (56%) and 24 are females (n=24) (43%). Group 16 cases (32%) are caesarean and 34 cases (68%) are normal.

As discussed in the table above the most important factor in the study is birth weight. Birth weight is categorized into (<2.5), (>2.5). Overall there are 43 neonates who are <2.5kgs. Again there are 62 neonates who are above 2.5. 18 neonates are subjected to phototherapy and alone and with <2.5kgs as per group A. 37 neonates are subjected to phototherapy and alone and with >2.5kgs as per group A. 25 neonates are subjected to phototherapy + phenobarbitone with <2.5kgs as per group B. 30 neonates are subjected to phototherapy + phenobarbitone with >2.5kgs as per group B. Gestational week also included in the study, who have been delivered after 36 weeks of pregnancy up to 42 weeks & results have been evaluated with mean and Standard Deviation. Next most important is phototherapy, in group A, 49 neonates (89%) neonates have been placed under S/S and 6(11%) neonates have been placed under D/S. In group B 33(66%) neonates have been placed under S/S and 17(34%) neonates have been placed under D/S. Total serum bilirubin is the major laboratory finding to assess the severity of NHB. The Serological investigations for the have been carried out & values are noted.

Total Serum Bilirubin levels (mg/dl)	Group A (n= 55)	Group B (n=50)	P- Value
Mean±S.D	14.4±3.17	14.9±3.13	0.1486

Table 2: Comparison of Total Serum Bilirubin levels in study population. Before treatment

p value > 0.05 considered not significant (paired 't' test).

Comparison of Total Serum Bilirubin levels in study population before treatment for both treatment regimens is done and their mean and standard deviation is calculated. As shown in the table 5.2 the mean scores were observed for group A is 14.4±3.17 for group B is 14.9±3.13, which are considered as not significant by the p- value 0.1486*

Total Serum Bilirubin levels (mg/dl)	Group A (n= 55)	Group B (n=50)	P- Value
Mean±S.D	1.80±0.73	1.96±0.75	0.1536

Table 3: Comparison of Total Serum Bilirubin levels in study population. After treatment

p value >0.05 considered not significant (paired t test).

Comparison of Total Serum Bilirubin levels in study population after treatment for both treatment regimens is done and their mean and standard deviation is calculated. As shown in the table 5.3 the mean scores were observed for group A is 1.80±0.73 for group B is 1.96±0.75, which are considered as not significant by the p- value 0.1536*

Duration of Phototherapy	Group A (n= 55)	Group B (n=50)
24Hrs	N = 20 (36%)	N = 17(34%)
48hrs	N= 32 (58%)	30(60%)
72Hrs	N= 3(5.4%)	3(6%)

Table 4: Duration of phototherapy

As shown in the above table the percentage of population with 24 hrs duration of phototherapy in group A is 36% and group B is 34%., 48 hrs is 58% and 60%., Where as after 72 hrs is only 3% in both groups

DISCUSSION: Neonatal Hyperbilirubenemia is a complication which arises in many new borns soon after the birth. We carried out this Prospective comparative study with Sample size (n= 105) to evaluate the Safety, efficacy of phototherapy, phototherapy plus phenobarbitone in management of hyperbilirubenemia in neonates.

Phototherapy is an important treatment of choice to prevent the complications of unconjugated hyperbilirubenemia. Effective phototherapy decreasing total bilirubin to safe levels quickly can minimize the risk of bilirubin neurotoxicity. A significant reduction was observed in peak serum bilirubin, duration of phototherapy, need of phototherapy and exchange transfusion with use of both Regimens. The limitations of the study were small sample size and loss to follow up.

Levin, Mc Mullin, and Mobarak et al¹, stated that phenobarbitone in the treatment of neonatal jaundice revealed a small but significant reduction of the mean bilirubin level of treated cases 24 hours after starting treatment. But as there were no significant differences in the mean bilirubin levels of the treated and untreated cases at 48 and 72 hours after starting treatment, and as there was no significant difference in the maximum recorded levels between the 2 groups, it was concluded by the authors that phenobarbitone had no place in the management of established neonatal jaundice.

Chawla and parmar et al stated that phenobarbitone used in preterm very low birthweight neonates reduces

peak serum bilirubin, duration of phototherapy, need of phototherapy and exchange transfusion.

Majid H, Behnam Z et al², Adding drugs to phototherapy had a much higher effect in reducing the serum bilirubin level than using phototherapy alone. Besides, clofibrate reduced the duration of phototherapy and hospitalization that is of great importance.

In another study in Mexico Bonifacio et al., 2001 similar evaluation on Icteric newborns was performed using two drugs phenobarbital and clofibrate together. Their results showed that there were no significant differences between the effects of these two drugs in decreasing the serum bilirubin level in infants.

Sinniah D., Tay L. K. et al³, Phenobarbitone has been found to be effective in reducing the serum bilirubin levels of jaundiced normal weight babies and also the need for exchange transfusions. There was no increase in mortality rate in infants treated with phenobarbitone and no serious adverse effects were noted apart from drowsiness and difficulty in feeding which occasionally persisted for as long as 2 days after treatment was discontinued.

Şahin Takcı, Şule Yiğit et al⁴ In the present study, no significant side effect of phototherapy was observed, and phototherapy was effective in decreasing bilirubin levels in intensive light-emitting diode and intensive compact fluorescent phototherapy both groups intensive light-emitting diode and intensive compact fluorescent phototherapy.

Our results on combined therapy (phototherapy plus phenobarbitone) of infants >2-5 kg birthweight are in agreement with the findings Valdes et al. (1971) and Blackburn⁵, Orzalesi, and Pigram et al⁶ (1972) who showed no difference in Total serum bilirubin levels when compared with those treated with phototherapy alone. Also the results showing that combined therapy to be no different from phototherapy alone in case of treatment.

In the present study, no significant side effect of phototherapy was observed, and phototherapy was effective in decreasing bilirubin levels in both groups.

CONCLUSION: Even after comparing both the treatment regimens, combined phototherapy with phenobarbitone did not produce any difference in bilirubin levels as well as in duration of phototherapy when compared with phototherapy alone throughout 72 hrs. It is observed that Phototherapy is safe option in treating Neonatal Hyperbilirubenemia than that of Phototherapy plus Phenobarbitone.

Phenobarbitone has toxic ADR profile when compared with phototherapy ADR profile. Because even though Phototherapy may cause skin rashes, loose stools, electrolyte imbalance but may not be harmful and disappears soon after treatment is discontinued, whereas Phenobarbitone it will affect the suckling during the feeds and the baby feels drowsiness and lethargy. Also phototherapy is simple, effective and low-cost and is mostly acceptable procedure for the reduction of Bilirubin

levels. Due to limited sample size it is difficult to follow-up the patient.

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