Research Article

Efficacy of oral fenofibrate in the management of unconjugated hyperbilirubinemia in neonates- A prospective study

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Abstract

Background: Fenofibrate is one of the commonest drugs to treat hyperlipidemia in adults. It also has the ability to induce bilirubin conjugation apart from its hypolipidemic action. **Objective:** To study the efficacy of oral fenofibrate in reducing bilirubin levels in neonates with significant unconjugated hyperbilirubinemia. **Materials and methods**: A prospective study was conducted ina tertiary care hospital at Tumkur, Karnataka between June 2013 and April 2014 following up a cohort of 100 neonates. Efficacy of oral fenofibrate was determined by comparing 50 neonates who received oral fenofibrate as well as phototherapy (exposed group) with those who received phototherapy alone (unexposed group), by measuring direct and indirect bilirubin levels at 12, 24, and 48 hours. **Results:** There was no significant difference in bilirubin levels at 12 (p=0.22), 24 (p=0.08) and 48 hours (p=0.07) respectively among the two groups. **Conclusion:** Oral fenofibrate did not prove efficacious in reducing bilirubin levels in neonates with significant unconjugated hyperbilirubinemia.

Keywords: Oral fenofibrate, Neonatal Hyperbilirubinemia, Significant unconjugated hyperbilirubinemia.

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INTRODUCTION

Neonatal jaundice is the result of an imbalance between bilirubin production and elimination. The ability of newborns to conjugate bilirubin is significantly impaired in the first few days, even a small increase in the rate of production can contribute to the development of hyperbilirubinemia. Increased heme catabolism is an important mechanism responsible for hyperbilirubinemia in the first 4 days after birth. In neonates, this becomes more significant because of high Red Cell mass and relative immaturity for bilirubin conjugation.[1,2] This free bilirubin deposits in the skin and mucous membranes and produces jaundice. It may also deposit in the brain where it has been implicated in causing transient dysfunction and, occasionally, permanent neuronal damage.[3] "Kernicterus" refers to neurological consequences of the deposition of unconjugated bilirubin in brain tissue by damaging and scarring of the basal ganglia and brain stem nuclei.[4] There are several non-pharmacological and pharmacological modalities for treating hyperbilirubinemia. Phototherapy has emerged as the most widely used non pharmacological therapy for the treatment and prophylaxis of neonatal unconjugated hyperbilirubinemia, but it has several untoward complications such as deleterious effect to eyes, high temperature, loose stool and bronze baby syndrome.[5] Pharmacological agents introduced for treatment of

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unconjugated neonatal jaundice include Phenobarbitone, Metalloporphyrins and D–penicillamine but, so far they have not been proved very effective and safe in clinical use.[6] Fibrates have been used for several years as a hypolipidemic drug.[7] Fibrates also increase bilirubin conjugation and excretion via induction of glucuronyl transferase activity.[8] Its potency to induce bilirubin conjugation is many times more than Phenobarbitone.[9] The present study was designed to assess the efficacy of oral Fenofibrate on significant hyperbilirubinemia of neonates during the first week of life.

METHODOLOGY

A prospective study was conducted ina tertiary care hospital at Tumkur, Karnataka between June 2013 and April 2014 after approval from the Institution Ethics committee. Accordingly, a total of 100 neonates with birth weight more than 2000 grams and total bilirubin level between 15 to 25 mg% after 48 hours of birth were included in study after obtaining an informed parental consent. Jaundiced newborns with congenital anomalies, systemic disorders, septicemia, dehydration, conjugated bilirubin>2mg/dl and hemolytic disease were excluded from the study.

Significant hyperbilirubinemia was defined as peak serum bilirubin level >15mg/dl, from 2nd to 7th postnatal day, since specific treatment was usually considered at or above this level in healthy term newborns. At birth, the demographic and anthropometric parameters of 100 neonates were recorded and bilirubin levels estimated. Among the 100 neonates, 50 neonates who received oral fenofibrate (5mg/kg) as well as phototherapy (exposed group)and 50 neonates who received phototherapy alone (unexposed group) were followed up at 12, 24 and 48 hours and serum direct and total bilirubin levels were measured at the respective hours of birth. The efficacy of oral fenofibrate was studied by comparing the mean bilirubin levels between the exposed and unexposed group.

STATISTICAL ANALYSIS

Data entry was done in Microsoft Excel 2010 and any significant differences in mean bilirubin levels were estimated using Student Independent T test in STATA version 11. P value of < 0.05was taken as significant.

RESULTS

There was no significant difference in bilirubin levels at 12 (p=0.22), 24 (p=0.08) and 48 hours (p=0.07) respectively among the exposed and unexposed group. [Table 1]

Table 1: Indirect and direct bilirubin levels among exposed and unexposed groups

Time since birth (hours)	Oral fenofibrate + Phototherapy	Only Phototherapy	P value*
At birth			
Indirect	19.82	23.06	0.35
Direct	1.57	1.60	0.69
12 hours			
Indirect	15.42	16.10	0.22
Direct	1.50	1.70	0.45
24 hours			
Indirect	12.50	13.37	0.08
Direct	1.50	1.51	0.88
48 hours			
Indirect	10.78	11.01	0.07
Direct	1.38	1.32	0.40

*Student Independent T-test

DISCUSSION

Management of significant unconjugated hyperbilirubinemia at neonatal period is a challenging task considering the prevailing risks in management with conventional treatment procedures including phototherapy in addition to being controversial, expensive and time consuming. Hence there is ongoing research for easier, cost-effective and rapid management techniques. Fenofibrate is one of the commonest drugs to treat hyperlipidemia in adults. However, apart from its hypolipidemic action, it also has the ability to induce bilirubin conjugation.[2]A study by Bijay K *et al*[10] showed that a comparison of therapy with single oral dose of Fenofibrate (10mg/kg) and phototherapy (Group B) with phototherapy alone (Group A) on bilirubin levels. Total serum bilirubin levels in group B at 24th, 36th and 48th hours after starting the treatment were significantly lower than those in group A. The mean time of phototherapy needed in group B was also lower than that in group A. In a study done by Mohammad zadeh *et al*[11], single dose of clofibrate (100mg/kg) in newborns with marked hyperbilirubinemia produced a drop in bilirubin levels after 12 hours compared to control group with no difference in 24 and 48 hours. In the present study we found no significant reduction in bilirubin levels at 12, 24 and 48 hours. Phototherapy and exchange transfusion remain as consistently used effective modalities for lowering neonatal hyperbilirubinemia.

CONCLUSION

Oral fenofibrate did not prove efficacious in reducing bilirubin levels in neonates with significant unconjugated hyperbilirubinemia. Further drug trials are required to establish cost-effective modalities for the management neonatal hyperbilirubinemia.

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