



COMPARATIVE STUDY OF FLUID THERAPY WITH NO FLUIDS IN NEONATES WITH HYPERBILIRUBINEMIA.

Paediatrics

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ABSTRACT

Background: Treatment modalities for Neonatal jaundice include: Phototherapy, exchange transfusion, suppression of ISO-immunization by I.V I g, competitive inhibition of heme-oxygenase, induction of hepatic conjugation, inhibition of entero-hepatic circulation. Fluid therapy is other treatment modality. Do to paucity of literature regarding the role of extra fluids we decided to evaluate the beneficial effects of fluid supplementation in neonates with jaundice who need either phototherapy (PT) or exchange transfusion (ET).

Material and methods: A total of 200 neonates, with hyperbilirubinemia were included in this study ,randomized into two groups (case group n=100; control group n=100).The case group was given I.V fluid supplementation with N/4 saline in 5% dextrose for a period of 8hrs, in addition to oral-feeds (Breast/formula feed). At the end of 8hrs period, the I.V fluid was discontinued. While the control group was continued on oral feeds and no IV fluids. Samples were obtained for serum osmolality, DCT, Reticulocyte-Count, Blood group, PBF (peripheral blood film), serum bilirubin etc in all babies included in the study. All infants received LED phototherapy. Comparison of the rate of decrease in bilirubin, length of hospital stay and the rate of exchange transfusion was done.

Results: On the basis of decremental decrease in serum bilirubin levels 6 hourly, we found that there was statistically significant decremental decrease over the first 6 hours in study group when compared with control group (p-value=<0.001).Results of rate of exchange transfusion and duration of phototherapy were also statistically significant (p-value=<0.001).

Conclusion: We recommend prolonged fluid administration especially to clinically dehydrated neonates which is not currently practiced, as the same leads to more rapid decrease of serum bilirubin and much less duration of phototherapy and hospital stay.

KEYWORDS

Neonatal jaundice, Phototherapy, Exchange transfusion, Fluid supplementation.

INTRODUCTION

Treatment modalities for Neonatal jaundice include: Phototherapy, exchange transfusion, suppression of ISO-immunization by I.V I g, competitive inhibition of heme-oxygenase, induction of hepatic conjugation, inhibition of entero-hepatic circulation.

Fluid therapy is other treatment modality which when given in full term neonates with hyperbilirubinemia in addition to phototherapy, decreases the serum bilirubin at a much faster rate [1], because, the photo products responsible for decline in serum bilirubin are excreted in both urine and bile, maintaining adequate hydration and good urine output should help in improving the efficiency of phototherapy [2]. We decided to evaluate the beneficial effects of fluid supplementation in neonates with jaundice who need either phototherapy or exchange transfusion as there is paucity of literature regarding the role of extra fluids.

MATERIAL AND METHODS

This was an open labelled prospective study conducted in the NICU (Neonatal Intensive Care Unit) over a period of 15 months at Sher-i-Kashmir Institute of Medical Sciences Srinagar (SKIMS) which is a tertiary care institute. Studied population included babies with gestational age > 35 weeks with hyperbilirubinemia within phototherapy and or exchange zone. All procedures involving human patients were approved by the Ethics Committee of SKIMS.

Also, an informed consent was obtained from either parent of all included children. Patients were randomly divided into case group and control group. Sick infants, or infants with major congenital malformations, conjugated hyperbilirubinemia, age>14 days as well as infants already receiving I.V fluids for any other reason were excluded. Samples were obtained for serum osmolality, DCT, Reticulocyte-Count, Blood group, PBF (peripheral blood film), serum bilirubin etc in all babies included in the study.

The case group was given I.V fluid supplementation with N/4 saline in 5% dextrose for a period of 8hrs, in addition to oral-feeds (Breast/formula feed). At the end of 8hrs period, the I.V fluid was discontinued, and the oral feed (expressed breast milk/ formula feed) was continued till the duration of phototherapy. While the control group was continued on oral feeds and no IV fluids. In both the groups, the weight was monitored 24 hrly.

All infants received LED phototherapy. Comparison of the rate of decrease in bilirubin, length of hospital stay and the rate of exchange transfusion was done.

Statistical methods:

Statistical software SPSS (version 20.0), Microsoft excel were used to carry out the statistical analysis of data. Continuous variables were analyzed by using student's independent t-test for parametric data and Man-Whitney U test for non parametric data. Normalcy of the data was checked by using shapero-wilk and box- plots. Categorical variables were analyzed by using chi-square and or Fishers exact test. A P-value of less than 0.05 was considered statistically significant.

RESULTS

The 200 neonates were randomized into two groups (case group n=100; control group n=100). There were 56 males,44 females in case group and in control group there were 58 males and 42 female and the difference was statistically insignificant with [p-value=0.775].

In our study, the mean age of patients in case group was 5.8±2.73 days and 5.7±2.4 days in control group and the difference was statistically insignificant (p-value=0.935).

The median birth weight (IQR) was 2.9(0.54) in case group while it was 2.7(0.32) in control group and the difference was statistically insignificant (P-value=0.090). Similarly the median weight(IQR) at admission was 2.82(0.50) in case group while in control group the

median weight (IQR) was 2.68(0.35) with no statistical significance (p-value=0.197).

Among the study group, 3 were found positive/deficient for G6PD while in control group 4 were found positive/deficient (p-value=1.000).

In study group, there were 6 cases who had history of oxytocin administration to their mothers at the time of labour while in control group 12 cases has history of oxytocin administration to their mother's at the time of delivery and the result was statistically insignificant (p-value=0.138).

The median (IQR) reticulocyte count of cases was 1.30(1.2) and in controls the median (IQR) reticulocyte count was 1.30(1.05) and the difference was statistically insignificant (p-value=0.750).

In our study we found that 5 neonates among study group underwent exchange transfusion while in the control group 15 neonates underwent exchange transfusion. The results were statistically significant [Table - 1] with p-value=0.018.

Table-1: Comparison of DVET

DVET	Cases (%) N=100	Controls (%) N=100	P-value
Done	5(5%)	15(15%)	0.018
Not done	95(95%)	85(85%)	

During our study, we found that the neonates in study group required less duration of phototherapy as compared to control group [Table - 2].

Table-2: Duration of phototherapy

Duration of phototherapy	Cases n=100	Controls n=100	P-value
Median(IQR)	21(10)	30.5(16)	<0.001

As per our study, the median (IQR) duration of phototherapy in study group was 21hrs (10) while the control group required 30.5hrs (16). The difference between the two was statistically significant (p-value=<0.001). On the basis of decremental decrease in serum bilirubin levels 6 hourly, we found that there was statistically significant decremental decrease over the first 6 hours in study group when compared with control group (p-value=<0.001) [Table -3].

Table-3: Serum Bilirubin Decrement

Rate of decrement of Serum Bilirubin	Cases N=100	Controls N=100	P-value
0-6hrs (Mean±sd)	4.06±1.58	2.71±0.92	<0.001
6-12hrs (Mean±sd)	2.41±1.45	2.10±0.98	0.083
12-18hrs (Mean±sd)	1.44±0.79	1.51±0.76	0.485

In our study group we found that during the first 6 hours of phototherapy, the mean decrease in serum bilirubin was 4.06(mg/dl) ±1.58 while in the control group the mean decrease in serum bilirubin was 2.71(mg/dl) ±0.92. As per our study the decremental decrease in serum bilirubin from 6-12 hrs in case group was 2.41±1.45 and that of control group was 2.10±0.98 and the difference was statistically insignificant (p-value=0.083). The decremental decrease in serum bilirubin from 12-18hrs in case group was 1.44±0.79 while in control group the decrement was 1.51±0.76 and the difference was statistically insignificant (p-value=0.485).

DISCUSSION

In our study, we decided to focus on infants with TSB>= 18mg/dl (380micromol/l), because of high rate of exchange transfusions and frequent need for phototherapy.

In our study, the mean age of cases was 5.8 days while that of controls was 5.7 days. In our study, among cases 56% were males and 44% females while in controls 58% were males and 42% were females, with no statistical significance, (p-value=0.775). Regarding the mode of delivery whether LSCS or NVD our study showed statistically insignificant co-relation between the two groups and the result was consistent with the study conducted by Mital Patel et al (2012) [3] and S-Mehta/Kumar et al (2005) [4].

As per our study, the median weight (IQR) at admission of cases was 2.9(0.54) kg while median weight (IQR) of controls was 2.7(0.32) kg with no statistical significance. (P-value=0.0090). Mital Patel et al (2012) [3] also found no statistical significance. The study conducted

by S-Mehta/Kumar et al (2005) [4] also found no statistical significance with respect to median weight of cases and controls at admission. According to our study, 3% cases were found positive for G6PD while in control group the percentage was 4% and there was no statistical significance (p-value=1.00) and the findings were consistent with the study conducted by S-Mehta/Kumar et al (2005) [4]. Results of median (IQR) reticulocyte count and median (IQR) serum osmolality show no statistical significance. This was also close with the findings of S-Mehta/Kumar et al (2005) [4].

The number of babies who underwent exchange transfusion among cases were 5% and among controls 15% babies underwent exchange transfusion, which was statistically significant (p-value=0.081), similar results were noticed in the study of S-Mehta/Kumar et al (2005) [4] in which 6 babies underwent exchange transfusion in case group while in control group 18 babies underwent exchange transfusion which were statistically significant (p-value=0.001). As per the study conducted by Mital Patel et al (2012) [3] they also found statistically significant reduction in cases who underwent exchange transfusion as compared to controls with (p-value=.03).

As per our study, the median (IQR) duration of phototherapy in cases was 21(10) hrs while in controls it was 30.5(16) hrs, which was statistically significant (p-value=<0.001). Similar results were seen by the study of S-Mehta/Kumar et al (2005) [4] with mean duration in cases where 49hrs± 19 and in controls were 65hrs±25 with p-value=(0.01) and in study conducted by Mital Patel et al (2012) [3] the mean duration of phototherapy in cases was 48hrs while in controls it was 62 hrs with statistically significant results (p-value=0.002). Over all after comparing the mean/median duration of phototherapy with other similar studies, we found that the median duration of phototherapy in our study was much less than other studies. The reason may be the extended fluid administration in our study that was 8 hours while in study of S-Mehta/Kumar et al (2005) [4] the duration of fluid administration was 6 hours, though both the studies showed statistically significant decrease in duration of phototherapy. So our recommendation is administration of fluids for prolonged period which is not the current practice. In our study we chose to provide the babies with severe hyperbilirubinemia I.V maintenance fluids in addition to oral supplementation in case group for first 8hrs of hospital stay while the oral supplementation was continued after stopping the IV maintenance fluid. The control group was given only oral supplementation throughout the hospital. One of the mechanisms that could have helped is expansion of intravascular volume leading to slight dilutional lowering of TSB. The more important effect would be enhanced biliary and bowel function [5]. Oral supplementation of feeds that accompanied and followed the initial I.V supplementation possibly helped decrease enterohepatic circulation and reabsorption of bilirubin from the gut [6]. Many believe that breast feed infants can auto regulate and increase milk intake while receiving phototherapy; however we did not find any significant increase in breast feeding frequency or volume over the study period. On comparing the decremental decrease in serum bilirubin 6 hourly, we found in our study that there was mean serum bilirubin decrease of 4.06 (mg/dl) ± 1.58 in cases and mean serum bilirubin decrease of 2.71(mg/dl) ±0.92in controls, and it was statistically significant (p-value=<0.001). The case group showed statistically significant rate of decrement of bilirubin during the first 6 hours. According to our study, there was statistically insignificant rate of decrement of serum bilirubin from 6-12 hours (p-value=0.083) and 12-18 hours (p-value=0.485). According to the study conducted by Mital Patel et al (2005) [4] they found statistically significant decremental decrease in serum bilirubin both during the 0-6 hr period (p-value<0.001) and 6-12hr period (p-value<0.001). According to study conducted by S-Mehta/Kumar et al (2005) [4], they found statistical significant percent fall in TSB over the first 24 hours period (p-value=0.02). Also regarding the decremental decrease in the serum bilirubin the study conducted by Reza Saedi et al (2009) [7] also found statistically significant decremental decrease in the serum bilirubin during the first 24 hours of phototherapy (p-value=.02). The reason for this would be that the babies they included in study may be severely dehydrated or they might have administered the fluids at higher rate than ours.

CONCLUSION

We recommend prolonged fluid administration especially to clinically dehydrated neonates which is not currently practiced, as the same leads to more rapid decrease of serum bilirubin and much less duration of phototherapy and hospital stay. There were fewer chances of

complications in cases as compared to controls due to decreased rate of exchange transfusion.

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