



The effect of intravenous fluid therapy in icteric neonates during phototherapy: A randomized clinical trial

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DOI: 10.5455/jrmds.2017529

ABSTRACT

Jaundice is the most prevalent neonatal clinical complication. One of the causes of this disease is the insufficiency of mother's milk to feed the neonate. Therefore, fluid therapy is considered as one of the useful intervention to alleviate jaundice. This study was designed to examine the effect of intravenous fluid therapy on icteric neonates who are also treated by phototherapy. A clinical research was conducted on 100 icteric neonates hospitalized in the hospitals of the city of Kashan during the year 2014. They were randomly assigned into two equal groups of intervention and control groups. The case group was treated by photo plus fluid therapy whereas the control group was treated by the phototherapy only. The bilirubin level of neonates was measured at admission, 6, 12 and 24 hours after the start of the treatment in both groups. The rebound bilirubin level was measured 12 hours after the termination of the phototherapy. The results of analysis indicated that there was no significant difference in the bilirubin decrease between the photo plus fluid therapy and the phototherapy-only group after 6, 12 and 24 hours of treatment ($p > 0.05$). However, when the bilirubin level of the treated group was very high there was a significant difference between the bilirubin decrease of the photo plus fluid therapy and the phototherapy group alone after 6, 12 and 24 hours of treatment ($p < 0.05$). The level of bilirubin rebound in the photo plus fluid therapy was more than the control group and needed-phototherapy again; therefore, the time for the phototherapy in the photo plus fluid therapy was longer than the control group. Despite the fact that using fluid therapy in the group with very high level of bilirubin causes decrease of bilirubin level, it leads to the increase of bilirubin rebound and the need to use phototherapy again. Therefore, this treatment is useful for the cases of severe jaundice that require blood transfusion even though it results in longer periods of phototherapy and the length of hospitalization.

Keywords: Icter, Fluid therapy, Phototherapy, Neonate

HOW TO CITE THIS ARTICLE: Mohammad Reza Sharif, The effect of intravenous fluid therapy in icteric neonates during phototherapy: A randomized clinical trial, J Res Med Dent Sci, 2017, 5 (2): 56-60, DOI: 10.5455/jrmds.2017529

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Received: 12/12/2016

Accepted: 20/05/2017

INTRODUCTION

Jaundice is the most prevalent type of clinical complications that threatens the neonates [1]. In 60 percent of term and 80 percent of preterm neonates face this problem [2]. Typically, icter appears in skin and mucus due to the residing of bilirubin [3]. The increase in the rate of bilirubin production, decrease in the uptake of liver, disturbance of conjugation and increase in the cycle of enterohepatic bilirubin are the main causes of non-conjugated hyper bilirubinemia [4].

This disease has not only economic, social and psychological burden due to the hospitalization of the neonate but also causes permanent neurological damage at the presence of kernicterus as well as high mortality rate. For the first time, a nurse in England in 1956 noticed the effectiveness of light in decreasing the level of bilirubin in neonates. Later on, researchers noticed that bilirubin molecules absorb light and through the change in their photo isomer easily excrete in urine and liver [5]. Following the recognition of the photobiology of bilirubin, phototherapy sets were constructed and used as a non-invasive mean of treatment of neonate jaundice and is widely currently used [6].

Despite the widespread use of phototherapy, the search to find other means of treatment for

reducing the neonate jaundice continues [7, 8]. There is a type of phototherapy set known as intensive phototherapy set that uses 8 florescent lamps (4 in the upper and 4 in the lower part) that conducts phototherapy from two sides [9]. Tan and associate compared the effectiveness of this set with the conventional one and concluded that the intensive set was more effective in decreasing the serum bilirubin level [10].

The side effects of phototherapy include skin problems (erythematic rashes, sensitivity to light), eye damages (toxic effects of light on retina, cornea scratches and the likelihood of conjunctivitis), hyperthermia, increase in skin blood flow and increase in invisible fluid loss, long term effect on sexual and endocrine development, disturbances in DNA repairing mechanism in skin epithelial cells, diarrhea, weight loss, hypocalcaemia, thrombocytopenia, and PDA [7]. Phototherapy causes the increase of skin evaporation in open areas, in the other hand, one of the causes of jaundice is the insufficiency of mother's milk. Thus, fluid therapy is purposed as a beneficiary intervention in jaundice [9].

In addition, considering the fact that phototherapy results in conversion of bilirubin to lumirubin that eventually is excreted through urination, fluid therapy also results in increase in the volume of urine and thus facilitates the excretion of this substance [10]. There are reports that show the effectiveness of serum therapy in treatment of severe jaundice [11]. The result of studies conducted in India show that serum therapy can be effective in treating the sever cases of jaundice and decrease the need for blood change in neonates [12]. Ebrahimi and associates demonstrated that fluid therapy results in faster rate of decrease in bilirubin level and shortens the length of staying in hospital [13], however, Torkman and associates did not find any significant effect of serum therapy on the decrease rate of bilirubin nor the course of hospitalization [14].

Iranpour and associates confirmed these findings [15]. Considering the fact that serum therapy has its own disadvantage including the possibility of infection, it seems like it should be employed for the server cases of jaundices associated with dehydration [12]. Due to the fact that the majorities of the neonates hospitalized are icteric cases and the mothers of these neonates face physical problems in addition to the economic burden to stay in hospital, it seems

reasonable to find means by which to shorten the healing process for the neonates. The family as well as the treatment service will benefit from this approach. Since there are conflicting reports in regard to the serum therapy effectiveness for reducing the bilirubin level, this research was designed to examine the effectiveness of fluid therapy to reduce the level of bilirubin in icteric neonates who undergo phototherapy in the city of Kashan-Iran in year 2014.

MATERIALS AND METHODS

The icteric neonates who were undergoing intensive phototherapy in hospitals of the city of Kashan during the year 2014 constituted the population for this research. Following the approval of ethical committee of the Kashan University of Medical Sciences (No: 91125), the human consent form was completed by the guardian of the neonates. The inclusion criterion was gestational age over 38 weeks, age over 24 hours after the birth to less than two weeks, the total bilirubin level more than 15 mg/dl and indirect hyper bilirubinemia. The exclusion criterion included the need to fluid therapy except icter, preterm and low birth weight neonates, hemolytic jaundice, sepsis and prolonged icter.

A total of 100 neonates diagnosed for indirect hyper bilirubinemia were selected and randomly assigned into two equal groups (n=50). One of the groups received intravenous fluid containing dextrose 10% preservative mixed with 30 milli equivalent per liter of sodium and 20 milliequivalents per liter of potassium. Another group as the control group received no intravenous fluid. The neonates in both groups also received phototherapy for their jaundice. The level of bilirubin was measured at the start, 6, 12 and 24 hours after the treatment. When the level of bilirubin reached 13 mg/dl, phototherapy was stopped and the time of phototherapy was recorded.

Twelve hours after the termination of the phototherapy, the bilirubin level was measured, in cases that the level of bilirubin exceeded 14 mg/dl, phototherapy restarted and continued until it reached to 13 mg/dl or lower. The length of retreatment by phototherapy was added to the phototherapy duration. In addition, the bilirubin level was considered as the base for dividing the two groups as very high and high level. One group with 15 to 22 mg/dl was defined as the high group and another group

with bilirubin level with 23 to 29 mg/dl served as the very high group. During the entire time of treatment, the neonates received complete nutrition. Following the collection of data recorded in recording forms, data analysis was performed by using SPSS: PC version 16.0.

RESULTS

There were 49 boys and 51 girls examined in this research. 23 boys and 27 girls in the intervention group and 26 boys and 24 girls were the subjects of the intervention and control group. There was no significant difference between the proportion of girls and boys (p=0.54). The mean age of the neonates in intervention and control group was 5.74 ± 2.9 and 5.44 ± 2.40 days, respectively. There was no significant difference between the age of both groups (P>0.05). In the intervention group, 26 neonates were fed by mother's milk and 24 were fed by a combination of mother plus formula milk. This condition was 30 and 20 cases in the control group, respectively. There was no significant difference in regard to the feeding of neonates (P=0.42) The mean of bilirubin at the beginning of the treatment was 21.47±3.11 (mg/dl) and 22.01±3.03 (mg/dl) in the intervention and control group, respectively. The result of analysis showed that there was no significant difference in bilirubin level between these two groups at the start of treatment (p=0.37). The level of bilirubin decreases in the intervention compared to the control group in 6, 12, and 24 hours after the treatment was higher, but these differences were not statistically significant. These results are presented in table 1. The neonates were divided into two groups of high (15-22 mg/dl) and very high (23 - 29 mg/dl) bilirubin level. The bilirubin decreases

in the high-level group was not statistically significant while the decrease in the very high bilirubin level was statistically significant after 6, 12 and 24 hours following the treatment (P=0.05).

These results are presented in table 2. The increase of bilirubin rebound after 12 hours following the session of phototherapy in the fluid therapy group was 1.64± 1.5 whereas this value for the control group was 0.48 ± 0.81 mg/dl. The value of change in the fluid therapy was significantly more than the control group (p=0.001). Overall, 8 neonates in the fluid therapy required phototherapy again since the bilirubin rebound was noticeable, while only 2 neonates in the control group needed phototherapy again. This proportions were significantly different (p=0.004). The photo plus fluid therapy group received 26.5 ± 5.57 hours of phototherapy compared to the control group who received 24.29 ± 4.22 hours (p=0.003). In the control group, 2 neonates needed blood transfusion while no neonate needed such treatment in the fluid therapy group.

DISCUSSION AND CONCLUSION

The result of this research showed that using fluid therapy for the very high bilirubin cases of disease leads to significant decrease in bilirubin level, but in cases of not very high-level bilirubin, it is ineffective. Iranpour and associates (2004) showed that adding fluid therapy to the phototherapy for the term icteric neonates who were fed by the mother milk had no significant effect [15].

Table 1: Bilirubin decrease after 6, 12 and 24 hours following the treatment in both groups

Bilirubin change Post time(hr.)	Photo + fluid therapy			Photo therapy-only			PV
	N	Mean	SD	N	Mean	SD	
6	50	4.23	1.64	50	4.12	1.36	0.71
12	50	7.09	2.32	48	6.64	1.87	0.30
24	46	12.24	3.22	44	11.81	2.51	0.47

Table 2: Bilirubin decrease after 6, 12 and 24 hours following the phototherapy in both groups with high and very high level of bilirubin

Bilirubin change Post time(hr.)		Photo + fluid therapy			Photo therapy-only			PV
		N	Mean	SD	N	Mean	SD	
6	HI	27	3.00	0.86	27	3.42	0.90	0.08
	Very HI	23	5.68	1.03	23	4.95	1.37	0.04
12	HI	27	5.31	1.27	27	5.42	1.21	0.76
	Very HI	23	9.16	1.30	21	8.22	1.30	0.02
24	HI	23	9.51	1.52	23	10.02	1.43	0.24
	Very HI	23	14.97	1.80	21	13.76	1.91	0.03

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In addition, Saini (2011) reported that fluid therapy had no significant effect on non-hemolytic neonateicter[16]. This result was confirmed by the research conducted by Torkaman and associates (2007) who did not report any significant reduction in bilirubin in neonates with high level of bilirubin [14].

However, in Ebrahimi's study (2003) it was shown that the decrease in bilirubin level in the phototherapy plus fluid therapy group was higher than the only phototherapy group [13]. This result is in agreement with the result of the study reported by Saeidi[17]. The result of a research conducted in India showed that serum therapy is an effective treatment for the severe cases of jaundice and reduces the need for blood transfusion [12]. Mehta (2005) and Balasubramanian (2012) also claimed that using fluid therapy reduces the need for blood transfusion [18, 19].

The present research result indicated that when neonates are treated by photo plus fluid therapy compared to the phototherapy alone, rebound of bilirubin following the termination of phototherapy has occurred to a point that additional phototherapy has been needed. The rebound of bilirubin has not been discussed in the literature. The duration of phototherapy in intervention group has been longer than the phototherapy alone group because the increase of bilirubin rebound and the need to repeat the phototherapy extends the time of phototherapy. Patel (2008) also points out that fluid therapy leads to longer period of hospitalization [20]. Contrary to this view, Metha (2005) and Ebrahimi (2003) report that fluid therapy results in shorter period [18, 13], whereas Saiedi (2014) and Torkama (2007) stated that fluid therapy had no significant effect on the length of hospitalization [17, 14]. It was concluded that despite the fact that fluid therapy results in decrease of bilirubin level in severe cases of jaundice and reduces the need for blood transfusion, however, it led to increase in bilirubin rebound and the need for phototherapy again. As other researchers claimed [21], there is still insufficient evidence to conclude firmly that fluid therapy is the routine intervention in icteric neonates and its use should be limited to the cases that the level of bilirubin is very high in order to reduce the need for blood transfusion. It was concluded

that more research about the rebound of bilirubin and phototherapy again is needed.

Acknowledgement

This study was funded by a research grant (No: 91125) from the under deputy of research of Kashan University of Medical Sciences.

IRCT Number: IRCT2013022711145N5

Funding source

Vice Chancellor of Research and Technology in Kashan University of Medical Sciences

Authors contribution

Mohammad Reza Sharif developed the study concept and design and the acquisition of data, interpretations of data, and drafting of the manuscript. Davood Kheirkhah developed the protocol, analysis of data and drafting of the manuscript.

Conflict of interest

The authors have no conflict of interest to disclose.

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