



Determination of the Effect of High-Dose Intralipid in Compared to Its Gradual Dose in Very Low Birth Weight Newborns: A Case-control Study

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MK, AB, AM, NN and BJ designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. All authors managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Objective: The aim of this study was to determine the effect of high dose intralipid in compared to its gradual dose in very low birth weight newborns in Iran.

Methods: This study was a case-control study that conducted on 104 very low birth weight infants (<1500 g) referred to Akbarabadi hospital of Tehran (Iran) in 2016. The infants were randomly assigned to two groups (case group: 52 vs. control group: 52). The control group received intralipid 20% with a dose of 1 g/kg/24 h in the first and second day of the study, then from 3rd day to 3 g/kg/24h was raised. But, the case group received 3 g/kg/24 h of intralipid 20% from the first day and continued until the end of the study. In both groups, the study lasted for up to 30 days. Data were collected and analyzed using SPSS22 software. Also P-Value <0.05 was considered as a significant level.

Results: The results showed mean daily weight gain in case group is higher than control group and this difference was significant statistically (P-Value < 0.05). Also, although the mean of blood sugar,

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triglyceride, HCO₃, the number of positive blood culture and the number of positive CPR in case group were higher than control group, but these differences were not statistically significant (P-Value >0.05).

Conclusion: Given that the better and faster growth of newborns in the intralipid group with high-dose in compared to intralipid group with gradual dose, the use of higher initial doses is recommended in newborns with very low birth weight.

Keywords: Intralipid; high dose; gradual dose; very low birth weight; newborns; Iran.

1. INTRODUCTION

Intestinal nutrition is the preferred method for supplying energy and materials needed of body. This method of feeding is closer to the physiological state, and is also cheaper and has fewer complications [1]. But when intestinal nutrition is not possible or sufficient, parenteral nutrition is used that involves different clinical conditions, such as premature infants [2,3]. The prematurity is one of the major causes of infant mortality and morbidity in neonates in the world [4,5]. Nearly 90 percent of premature infants are born in developing countries that 85% related to Asia and Africa [6]. The preterm birth rate is 5.6% to 13.4% in Iran that varies depending on the geographic area under consideration [7]. The prematurity causes 75% of perinatal deaths and over 50% long-term morbidity [8,9].

On the other hand, postnatal growth failure is one of the most common problems in infants with very low birth weight (<1500 g) that parenteral nutrition can provide calories, amino acids, electrolytes, minerals, essential fatty acids, vitamins and iron for them [10]. The parenteral nutrition can be given through the peripheral or central vessels, but in the case of long-term intravenous feeding, it is better to use the central vessels [11]. Feeding through the peripheral arteries has a few limitations that the most important is disruption in the peripheral vessel pathway when the solution is administered and it is also not possible to use solutions with high osmolarity such as dextrose more than 12.5%. Of course, in the case of lipids because of their little osmolality, they can be injected peripherally with a common IV line with Dextrose and Amino Acid [12,13]. Intralipid is one of the nutritional solutions for parenteral nutrition that has been widely used since 1960. The intralipid have been prepared based on soybean oil, and a mixture of natural neutral triglycerides, mainly fatty acids, which is used from egg yolk phospholipids for emulsifying

and glycerol to regulate tonicity of emulsion [14-16]. Followed by metabolized, these products are used as energy sources and provides about 30-40% of the body's calories [15]. Nutrition with intralipid also increases the production of heat and oxygen consumption. Lack of external source of essential fatty acids or its derivatives during brain and retinal development may lead to long-term neurodevelopmental and visual disturbances [17,18].

Lipid provides the energy needed to make the protein and essential fatty acids for the development of the nervous system. Intralipid are used with caution in preterm infants due to impaired fat tolerance. Also, it may be associated with complications such as impaired oxygenation, bronchopulmonary dysplasia (BPD), and increased free bilirubin and serum triglyceride concentrations [19]. The start time of lipid injection is different in very low birth weight (VLBW), however, studies have shown no difference in morbidity and mortality in terms of start time of lipid injection. However, it is recommended that newborns who are not able to receive intestinal nutrition should receive intralipid before the third birthday [20,21]. This emulsion starts from 0.5 - 1 g/kg of infant weight every 24 hours and increases slightly to provide calories needed by the body and it usually increases its value to 2.5-3.5 g/kg /24 h.

Recent studies have shown that intralipid can be started from 3 g/kg of infant weight every 24 and there is no need for its incremental increase [21,22]. However, studies that compare the effects of high dose intralipid with its incremental increase on mortality and morbidity are limited. So, the present study was designed to compare the effect of high dose intralipid with its incremental increase on hospital clinical outcome in very low birth weight newborns in Iran.

2. MATERIALS AND METHODS

2.1 Study Design and Subjects

This study was a case-control study trial that conducted on 104 very low birth weight infants (<1500 g) referred to Akbarabadi hospital of Tehran (Iran) in 2016. Sampling was easy or available and the very low birth weight newborns were randomly assigned to two groups (case group: 52 vs. control group: 52) using random numbers table. The control group (intralipid group with gradual dose) received intralipid 20% with a dose of 1 g/kg/24 h in the first and second day of the study, then from 3rd day to 3 g/kg /24h was raised. But the case group (intralipid group with high-dose) received 3 g/kg /24h of intralipid 20% from the first day and continued until the end of the study. In both groups, the study lasted for up to 30 days, however, if the infant's weight reached 1800 grams or there was a possibility for oral feeding with milk before 30 days (100 cc/kg), the intralipid injection stopped and was excluded.

2.2 Inclusion and Exclusion Criteria

Inclusion criteria consisted of birth weight < 1500 g, major anomalies, peripartetic asphyxia (Apgar 5 minutes below 6), and lack of sepsis, written and informed consent of the child's parents. Exclusion criteria consisted of parental unwillingness to participate in the study, sepsis, resistant metabolic acidosis to treatment, triglyceride > 200

mg/dl and blood sugar > 200 mg/dl in three turns.

2.3 Data Collection

The data collection tool was a check list includes variables of sex, Apgar score, gestational age, birth weight, blood sugar, triglyceride, PH, HCO₃, type of delivery, CRP and positive blood culture. The researcher has checked the variables daily and recorded in the checklist. The infants were examined daily for blood sugar and weight gain and also the triglyceride level, ABG and CRP were checked 2 times a week.

2.4 Statistical Analysis

Data were collected and analyzed using SPSS22 software. For descriptive analyzes, mean and standard deviation (for quantitative variables) and number and relative frequency (for qualitative variables) were used. For analytical analyzes, Independent T-Test and Chi-Square Test were used to compare quantitative and qualitative variables in two groups under study. Also P-Value <0.05 was considered as a significant level.

3. RESULTS

In the present study, 104 very low birth weight infants referred to Akbarabadi hospital of Tehran (Iran) were examined (case group: 52 vs. control group: 52). Table 1 shows the demographic and baseline characteristic of infants under study.

Table 1. Demographic and baseline characteristics of the two groups of infants under study and its comparison

Quantitative variables		Group	Mean	S.D*	P-value	
Gestational Age		Case	28.60	2	0.539	
		Control	29	1.70		
Apgar Score		Case	8.10	0.9	0.373	
		Control	8.30	0.50		
Birth Weight		Case	1115	127	0.600	
		Control	1130	111		
Qualitative variables		Case		Control		P-value
		Number	%	Number	%	
Sex of Infant	Boy	24	46.1	25	53.9	0.245
	Girl	28	53.8	27	46.2	
Type of Delivery	NVD**	20	38.1	19	36.5	0.455
	CS***	32	61.9	33	63.5	

*S.D : Standard Deviation; **NVD : Normal Vaginal Delivery;

***CS : Cesarean Section

Table 2. Determination of the effect of high dose intralipid in compared to its gradual dose in the two groups of infants under study

Variables	Group	Mean	S.D	P-Value
Blood Sugar (mg/dl)	Case	88.60	13.90	0.721
	Control	87.20	9.33	
Triglyceride (mg/dl)	Case	58.20	6.20	0.288
	Control	55.20	4.50	
HCO ₃	Case	22.70	1.20	0.478
	Control	21.1	0.90	
Daily Weight Gain	Case	23	9.90	<0.001
	Control	15	4.50	
Positive Blood Culture (number)	Case	1	0	1.00
	Control	1	0	
Positive CPR (number)	Case	4	0	1.00
	Control	4	0	

The means (S.D) of gestational age in case and control group were 28.60 (2) and 29 (1.70); respectively and there was no significant statistical difference between the two groups in terms of this variable (P-Value >0.05). Also, the means (S.D) of birth weight in case and control group were 1115 (127) and 1130 (11); respectively and this difference was not significant statistically (P-Value >0.05). Other baseline variables are visible in Table 1. As it is seen, there were no significant statistical differences between the two groups in terms of the baseline variables Apgar score, sex of infant and type of delivery (P-Value > 0.05). Generally, the absence of a significant statistical association between the groups in terms of the baseline variables implies that the randomization process has been done correctly.

Table 2 shows the effect of high dose intralipid with its incremental increase on variables of blood sugar, triglyceride, HCO₃, daily weight gain, positive blood culture and positive CPR in two groups of case and control under study. As it is seen, mean daily weight gain in case group (Mean: 23; S.D: 9.90) was higher than control group (Mean: 15; S.D: 4.50) and this difference was significant statistically (P-Value < 0.001). Also, mean of blood sugar, triglyceride and HCO₃ in case group was higher than control group but these differences were not statistically significant (P-Value >0.05). Also, in this study, the number of positive blood culture and the number of positive CPR were the same in case and control groups, and there was no statistically significant difference (P-Value >0.05) (Table 2).

4. DISCUSSION

The present study was designed to compare of the effect of high dose intralipid with its incremental increase on blood sugar, triglyceride, HCO₃, daily weight gain, positive blood culture and positive CPR in newborns with very low birth weight in Iran. The results of this study showed mean daily weight gain in case group is higher than control group and this difference is significant statistically (P-Value < 0.05). Also, although the mean of blood sugar, triglyceride, HCO₃, the number of positive blood culture and the number of positive CPR in case group are higher than control group, but these differences are not statistically significant (P-Value >0.05).

This finding has been supported by various studies in this regard. In a study by Drenkpohl et al. that aimed to determine whether very low birth weight newborns could tolerate higher rates of infusion of intravenous fat emulsion during the first week of life and maintain their serum triglyceride levels at ≤200 mg/dl, the results showed that very low birth weight newborns can tolerate higher rates of infusion of intravenous fat emulsion solutions without significant adverse effects in the first week of life [10].

In other study by Jorine A. Roelants et al. to determine the effect of early aggressive parenteral nutrition (PN) on long-term outcome in very low birth weight newborns, the findings demonstrated that the he primary use of high-dose amine-acid administration and mixed fat emulsions, although improving the growth, has no positive effect on neuronal growth in very low

birth weight newborns [23]. The study by dit Trolli SE to determine of the effect of cumulative intakes of proteins, carbohydrates, lipids and energy during the first 28 days of life on the weight gain in the first 28 days of life, showed that there is a significant statistical association between the cumulative lipid intake at 14 days of life with the developmental quotient (P-Value: 0.04) [24].

A review study by Ghassan S, et al. with the aim of assessment the studies done on intravenous lipids for preterm infants in order to achieve a comprehensive overview, the results indicated physicians should balance the benefits versus the risks when using 2-3 g /kg /day intravenous lipid infusion for preterm infants. However, this review study concludes that the benefits are much more than the risks and strongly recommended that very low birth weight and extremely low birth weight infants receive 2-3 g/ kg /day intravenous lipid as a continuous infusion in the first 24 hours of life [25]. Also, a systematic review and meta-analysis study by Hester Vlaardingerbroek et al. with the aim of summarizing effects of initiation of lipids within the first 2 d of life and the effects of different lipid compositions on growth and morbidities in low birth weight infants, the findings demonstrated injection of lipids is safe and well tolerated in the first 2 days of life in low birth weight infants, however, its positive impact on growth is not clear according to the type of lipid emulsion [22]. Generally, the very low birth weight infants are vulnerable to insufficient lipid supply, because until the third trimester there is no remarkable increase in utero fat accretion [26]. The increase of adipose tissue begins 25 weeks of pregnancy and continues with rate of 1-3 g/kg /day [27]. The body composition of 1000 g of a preterm infant consists of approximately 0.5% glycogen, 8.5% protein, and 1% fat, which is approximately 10 or 20 g of very low birth weight newborns at birth [28-30]. If the newborn does not receive supplemental lipids, they lose 1.2 g /day of stored fat. Therefore, it seems replacement and injection of supplemental lipids are necessary [25].

5. CONCLUSION

The newborns in the case group (intralipid group with high-dose) had more favorable conditions than the control group (intralipid group with gradual dose). Indeed, the case group had better daily weight gain than the control group. Also, the two groups did not have a significant difference

in terms of important factors such as on blood sugar, triglyceride, HCO₃, positive blood culture and positive CPR. Therefore, given that the better and faster growth of newborns in the intralipid group with high-dose, the use of higher initial doses is recommended in newborns with very low birth weight. Using the same high initial dose and avoiding a gradual dose increase can reduce the risk of personnel errors in the dose used for these patients during treatment.

CONSENT AND ETHICAL APPROVAL

Before the start of the study, the research objectives were explained for the parents and informed consent were obtained from them. Also, researchers at all stages of the study were committed to the principles of the Declaration of Helsinki. The study was approved by the Deputy of Research and Ethics Committee of Iran University of Medical Sciences, Tehran, Iran (Number ethical code: IR.IUMS.REC.2016.9311165004).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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