Short Communication

J Babol Univ Med Sci
Vol 19, Issu 12; Dec 2017. P:7-11

An Evaluation of Changes in Liver Function Tests in Extremely Premature Infants Receiving Intravenous Feeding

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J Babol Univ Med Sci; 19(12); Dec 2017; PP: 7-11
Received: May 25th 2017, Revised: Sep 17th 2017, Accepted: Oct 3rd 2017

ABSTRACT

BACKGROUND AND OBJECTIVE: Considering the fact that oral feeding is delayed too much in extremely premature infants due to respiratory and digestive problems, these infants usually suffer from severe weight loss and muscular dystrophy in the absence of intravenous feeding. On the other hand, intravenous feeding has several complications such as cholestasis and liver damage. The aim of this study was to determine the effects of intravenous feeding on blood biochemical parameters in premature infants.

METHODS: This cross-sectional study was performed on 26 preterm infants (gestational age of 27 to 33 weeks and weighing from 800 to 1900 grams) receiving intravenous feeding in Alavi Hospital in Tabriz during the year 2016. Blood biochemical parameters were measured by spectrophotometry with an auto-analyzer apparatus before and after feeding.

FINDINGS: At the end, the activity of alkaline phosphatase (712.86±299.73 vs. 476.04±173.53) and gamma-glutamyl (81.79±46.23±vs. 59.5±5.42) increased significantly and the activity of total bilirubin (1.45±0.79 vs. 7.16±5.04) and direct bilirubin (0.21±0.15 vs 0.49±0.31) showed a significant decrease ($p<0.05$). However, the changes of aspartate transferase and alanine transferase were not significant at the end of the feeding period. No symptoms of cholestasis were observed in any of the infants.

CONCLUSION: The results of the study showed that intravenous feeding has no effect on cholestasis.

KEY WORDS: *Liver Function Tests, Intravenous Feeding, Prematurity*.

Please cite this article as follows:

Aramli S, Yaghoubi H, Khalafi J, Shahizadeh S. An Evaluation of Changes in Liver Function Tests in Extremely Premature Infants Receiving Intravenous Feeding. J Babol Univ Med Sci. 2017;19(12): 7-11.

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[DOR: 20.1001.1.15614107.1396.19.12.1.4]
[DOI: 10.18869/acadpub.jbums.19.12.7]

Introduction

According to the World Health Organization, premature infants are infants who are born alive before 37 weeks from the first day of the last menstrual period (1). Pre-term birth means birth before 37 weeks, is associated major diseases and is observed in all developed countries (2). This prematurity increases the risk of infectious diseases and morbidity and is a major health problem for all countries, and exorbitant expenses are imposed for the care and treatment of these patients (1).

Total parenteral nutrition (TPN) is a nutritional method that provides nutritional needs for metabolism and growth, and can be used when a person cannot get food through fluids or mouth. In this method, a mixture of fluids including macronutrients (protein, carbohydrate and fat) and micronutrients (electrolytes, minerals, and vitamins) are entered into the infant's vessel. In fact, the goal of TPN is to provide adequate nutrition to prevent negative energy, and nitrogen balance, compensate for the lack of essential fatty acids, and support the normal growth rate without increasing the symptoms of the disease (3). However, the use of TPN is accompanied by complications. One of the most important complications is cholestasis, in which the normal flow of bile is suppressed and obstruction of bile ducts leads to a lack of absorption of lipids and fat-soluble vitamins. Since TPN is used for more than two weeks, liver function tests should be performed for extra low birth weight infants to observe changes such as cholestasis and liver disease (4).

Since oral nutrition is delayed in extremely premature infants because of respiratory and digestive problems, these infants usually suffer from severe weight loss and muscular dystrophy in the absence of intravenous feeding. On the other hand, intravenous nutrition in infants has several complications such as cholestasis and liver complications. Therefore, the present study was conducted to evaluate the effect of intravenous nutrition on blood biochemical parameters in premature infants.

Methods

This cross-sectional study was approved by the Ethics Committee of Ardabil University of Medical Sciences (IR.ARUMS.REC.1394.109). Informed consent was obtained from parents of premature infants less than 1500 g who were admitted to the intensive care unit of Alavi Hospital in Ardabil and were unable to feed orally from November 2015 to November 2016. Experiments were performed on 26 premature infants including 14 male infants and 12 female infants in two stages, beginning of intravenous feeding and its end. For this purpose, 60 cc/kg dextrose saline (Samen Pharmaceutical Company) was started and gradually increased to 150 cc/kg. In order to supply amino acids, 1 g/kg Aminoven 10% Solution (Fresenius KABI, Sweden) was injected into the dextrose saline and increased to 3 g/kg in two days. In order to provide the trace elements, 1 cc/kg Peditrace solution (Fresenius KABI, Sweden) was injected.

To provide the required vitamins, vial of lyophilized soluvit (Fresenius KABI, Sweden) was used. This was done by adding 10 cc sterile distilled water to the vial of soluvit, and 1 cc/kg of this vial was prepared and injected into the dextrose saline.

Sampling and preparation: A sample of venous blood (2 cc) was collected from subjects at the beginning of feeding, and a sample was immediately collected at the end of feeding. After collecting venous blood from the subjects, the needle was removed from the syringe and blood samples were poured into the gel tube. The samples were then transferred to the laboratory and 5 to 10 minutes after blood was clotted in the tube, samples were inserted into the centrifuge machine (Hitachi, Germany), and were centrifuged for 3 minutes at 3500 RPM to separate serum from clot. Finally, the serum was transferred to a simple tube using the sampler and kept in the refrigerator until the tests were started.

Measurement of Biochemical Parameters of Blood: To measure all parameters, Pars Azmoon Kit (Iran) was used. Measurement of aspartate aminotransferase and alanine transferase was done by IFCC without adding pyridoxal-5-phosphate, alkaline phosphatase by standard method of German biochemical association, gamma-glutamyl transferase by enzymatic method and finally, total and direct bilirubin was measured by photometric method using 2,4-dichloroaniline. Experimental analysis was carried out using an auto-analyzer (BT-3500, Italy). Data were analyzed by paired t-test in SPSS Ver.23 software and $p < 0.05$ was considered significant.

Results

The gestational age of the mothers of infants was 30.3±1.3 weeks. The birth weight of infants, pre-feeding weight and post-feeding weight was

[DOR: 20.1001.1.15614107.1396.19.12.1.4]
[DOI: 10.18869/acadpub.jbums.19.12.7]

1488±272.4, 1325±203.6 and 1472.1±228.6 g, respectively. The time spent with TPN (day) was 18.1±5.1 for dextrose saline, 8.5±4.9 for Peditrace, 13.4±5.3 for soluvit and 14.2±5.7 for amino acid. The results showed that there was a significant increase in alkaline phosphatase and gamma-glutamyl transferase activity at the end of the period, and total and direct bilirubin decreased significantly ($p \leq 0.05$). However, there was no significant difference in the activity of aspartate aminotransferase and alanine transferase at the beginning and end of intravenous feeding. On the other hand, total bilirubin in females and both types of bilirubin with alkaline phosphatase in males showed significant difference at the beginning and end of the experiment ($p<0.05$) (Table 1).

Table 1. Mean biochemical parameters of premature infants, beginning and end of intravenous feeding

Analytes Gender	Beginning of feeding Mean±SD	End of feeding Mean±SD	P-value
Regardless of gender			
AST(IU/l)	35.34±15.88	35.23±17.77	0.475
ALT(IU/l)	15.09±13.03	15.23±7.14	0.96
ALK.P(IU/l)	476.04±177.53	712.86±299.73	0.001
GGT(IU/l)	59.5±25.42	81.79±46.23	0.036
Bill.T(mg/dl)	7.16±5.04	1.45±0.79	0.000
Bill.D(mg/dl)	0.49±0.31	0.31±0.15	0.015
Weight(gram)	1472.11±228.68	1325±203.67	0.018
Male			
AST(IU/l)	34.89±19.33	36.94±19.48	0.782
ALT(IU/l)	15.26±16.03	16.06±7.97	0.869
ALK.P(IU/l)	430.47±142.76	706.18±293.71	0.004
GGT(IU/l)	65.47±26.9	96.88±53.11	0.15
Bill.T(mg/dl)	7.97±6.11	1.45±0.82	0.001
Bill.D(mg/dl)	0.33±0.18	0.31±0.15	0.031
Weight(gram)	1262.5±396.51	1534.64±232.77	0.036
Female			
AST(IU/l)	35.86±11.44	33.23±16.16	0.65
ALT(IU/l)	14.89±9.07	14.27±6.25	0.848
ALK.P(IU/l)	509.7±209.42	720.65±319.55	0.069
GGT(IU/l)	52.52±22.7	64.19±29.94	0.294
Bill.T(mg/dl)	6.27±3.47	1.45±0.79	0.000
Bill.D(mg/dl)	0.36±0.12	0.29±0.1	0.148
Weight(gram)	1287.08±166.34	1399.16±209.84	0.161

Discussion

The most important finding of this study was the lack of suffering from cholestasis in infants, despite some significant changes in some of the studied parameters. Since the studied infants did not suffer from cholestasis, no significant changes were observed in AST, ALT, which was consistent with the study of Laciege et al. In 1985, which did not show a significant difference in AST in the reference range (5). However, it is not consistent with the study of Mihan et al. and Jolin—Dahel et al., who observed that the increase in aminotransferases was associated with intravenous nutrition (6, 7).

In this study, Bill T had a significant decrease considering the normal and physiological course in infants. However, although ALK.P, GGT and Bill D had significant numerical and statistical changes in the end of intravenous feeding, they were in the normal range, which is consistent with studies by Laciege et al. in 1985 about alkaline phosphatase, Dale et al. in 1999 (8), and Jolin—Dahel et al. in 2013 (7) about direct bilirubin and study of Mihan et al. in 1997 (7) about alkaline phosphatase and gamma-glutamyl transferase. Serum alkaline phosphatase and AST were measured weekly in the study of Laciege et al. The amount of alkaline phosphatase activity increased, but the changes in AST were not significant and this enzyme was within the reference range (5). In the study of Mihan et al., an increase in ALK.P, AST, ALT, and GGT was observed in the presence of intravenous nutrition (7).

In the study of Dale et al. in Konya, Turkey, entitled "TPN-dependent cholestasis in infants undergoing surgery", including 54 infants, 16 infants who suffered from cholestasis had a mean 7.1 direct bilirubin, and 38 infants who did not suffer from cholestasis had a mean 1.1 direct bilirubin and it was concluded that TPN is one of the risk factors for cholestasis (8).

But recently, in a study by Jolin—Dahel et al. in Canada in 2013, including 87 infants and feeding period more than 14 days, 18 infants suffered from cholestasis with conjugated bilirubin higher than 2.92 mg%, while AST, and ALT were high (6), which is not consistent with the results of this study. Opposite to previous studies, the development of cholestasis by intravenous feeding was not concluded this study. Alkaline phosphatase and gamma-glutamyl transferase enzymes had a significant increase in the end of intravenous feeding, but these values were within the reference range.

Total and direct bilirubin faced a significant reduction at the end of intravenous nutrition, which is a natural and physiological course. Aspartate transferase,

[DOR: 20.1001.1.15614107.1396.19.12.1.4]
[DOI: 10.18869/acadpub.jbums.19.12.7]

and alanine transferase enzymes did not change significantly at the end of intravenous nutrition. Because of the technical limitations, lack of long-term access to the central vein and the prevalence of sepsis in the section, intravenous lipids were not used for intravenous feeding. Use of all intravenous nutritional compounds, including intra-lipid, with more samples and control of biochemical parameters at specified intervals for the diagnosis and prevention of cholestasis, as well as the use of gastrointestinal stimulation or Priming Feeding Gut are suggested.

Acknowledgments

Hereby, we express our deepest sense of gratitude and indebtedness to Research Deputy of Ardabil University of Medical Sciences, as well as personnel of ICU and Laboratory of Alavi Medical Center.

[DOR: 20.1001.1.15614107.1396.19.12.1.4]
[DOI: 10.18869/acadpub.jbums.19.12.7]

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[DOR: 20.1001.1.15614107.1396.19.12.1.4]

[DOI: 10.18869/acadpub.jbums.19.12.7]