Effectiveness of Multicomponent Lipid Emulsion in Preterm Infants Requiring Parenteral Nutrition: A Two-Center, Double-Blind Randomized Clinical Trial

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Background: Very-low-birth-weight infants are largely dependent on parenteral nutrition after birth. Parenteral nutrition-associated liver disease is often observed in long-term parenteral nutrition with pure soybean oil lipid emulsion. A novel multicomponent lipid emulsion may prevent liver injury, improve growth, and decrease morbidity in preterm infants.

Objective: To compare the effects of a multicomponent lipid emulsion with a conventional pure soybean oil lipid emulsion on the incidence of neonatal cholestasis, neonatal growth, neonatal morbidity, and the biochemical assessment of liver enzymes.

Material and Method: Preterm infants weighing less than 1,250 g were allocated using a double-blind method. Both groups received parenteral nutrition, based on the same protocol. The study group received multicomponent lipid emulsion, while the control group received the standard pure soybean oil lipid emulsion. Serum levels of bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transpeptidase (GGT) were measured before enrollment, and at week 1, 2, and 3. Clinical data on neonatal outcomes were collected until the day of discharge.

Results: Each group was comprised of 22 preterm infants. The mean total parenteral nutrition (TPN) days were 12.5±8.1 and 10.5±5.9 in the study group and the control group respectively. There were no significant differences in laboratory parameters, including liver enzymes and GGT between the two groups. The incidence of cholestasis was 4.5% in the study group, and 9% in the control group, which was not statistically significant. No differences were observed in neonatal growth or neonatal morbidity including sepsis, bronchopulmonary dysplasia, retinopathy of prematurity, and necrotizing enterocolitis between the two groups. Eight infants (36%) in the study group experienced growth failure before discharge compared with 12 infants (54%) in the control group.

Conclusion: Multicomponent lipid emulsion appeared to be safe and well tolerated in preterm infants. No beneficial effects on the prevention of liver dysfunction were seen based on the type of lipid emulsion.

Keywords: Preterm, Parenteral nutrition, Cholestasis, Intravenous lipid emulsion, Growth

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Postnatal growth restriction (PNGR) is a common finding during neonatal hospitalization in very low birth weight infants at discharge\(^{(1,2)}\). The main cause of PNGR is insufficient administration of protein and calories especially during the early days of life. This is a cause of concern as initial suboptimal nutritional management and PNGR both have been associated with impaired neurodevelopment\(^{(3,4)}\). Preterm infants are born with limited nutrient stores. Their nutritional status is further compromised by gastrointestinal immaturity and conditions such as feeding intolerance or suspected necrotizing enterocolitis. This often results in delayed enteral feeding. Therefore, during the first few postnatal days, very-low-birth-weight infants are largely depended on parenteral nutrition (PN). Among PN ingredients, intravenous lipid emulsions serve as a major source of non-protein energy and provision of required essential fatty acids\(^{(5,6)}\). The conventional lipid emulsion, widely used in Thailand for many years, is prepared from soybean oil, which is rich in omega 6 polyunsaturated fatty acids (omega 6 PUFAs) and phytosterols, which contribute to hepatotoxicity\(^{(7,8)}\). Excess omega 6 PUFAs and their metabolites result in proinflammatory eicosanoid production and have the potential to increase lipid peroxidation\(^{(9)}\). The risk of lipid peroxidation is
of particular concern in premature infants, who are often exposed to oxidative stress under intensive care conditions. Existing evidence strongly supports a pathogenetic role of inflammation and oxidative stress on parenteral nutrition-associated liver disease (PNALD)\(^{(10)}\). Subsequent development of lipid emulsions have focused on reducing the amount of soybean oil and replacing it with other oils including coconut oil (rich in medium chain triglycerides [MCTs]), olive oil (rich in omega 9 fatty acids) and fish oil (rich in omega 3 fatty acids). Each type of lipid has potential benefits. The MCTs are eliminated faster from the bloodstream than the long chain triglycerides and are less susceptible to lipid peroxidation\(^{(11,12)}\). The advantage of olive oil is thought to stem from the presence of omega 9 monounsaturated fatty acids (MUFAs), which preserve immune function\(^{(13)}\). Moreover, olive oil is rich in alpha tocopherol, which is a major antioxidant. The omega 3 fatty acids from fish oil are metabolized to anti-inflammatory eicosanoids, which can prevent inflammatory response\(^{(14)}\). Several recent studies have shown that the multicomponent lipid emulsions improve growth\(^{(15)}\), lower incidence of PNALD\(^{(16,17)}\), reduce the risk for retinopathy of prematurity (ROP)\(^{(18)}\), and decrease bronchopulmonary dysplasia (BPD)\(^{(19)}\).

The authors hypothesized that the use of multicomponent lipid emulsions for PN of preterm infants may have favorable effects on inflammation, reduce oxidative stress-induced morbidity in prematurity (such as cholestasis, BPD, and ROP), and improve neonatal growth. To test this hypothesis, the present study compared the effects of two lipid emulsions on the incidence of parenteral nutrition-associated cholestasis, the biochemical assessment of liver enzymes, and morbidity in very-low-birth-weight infants in two hospitals.

**Material and Method**

**Study population**

A double-blind randomized controlled trial was performed between December 2013 and December 2015 at the neonatal intensive care unit of Thammasat Hospital and Nopparat Rajathanee Hospital, both in Bangkok. The infants with gestational age of less than 30 weeks and birth weight of less than 1,250 g who required PN for at least seven days were eligible for the study. Written informed consents were obtained from the parents. Exclusion criteria were evidence of congenital infection, perinatal asphyxia, congenital anomalies, an intraventricular hemorrhage (IVH) grade greater than 2, thrombocytopenia, shock or circulation failure, and renal or hepatic disorders.

**Sample size estimation**

Power analysis indicated that 22 infants in each group would provide 70% power to detect a postulated 40% reduction (from 0.6 in control group to 0.2 in the study group) in the incidence of cholestasis using a 0.05 level test of significance.

**Study design and methods**

Enrolled infants were randomly assigned to a multicomponent emulsion composed of 30% soybean oil, 30% MCTs, 25% olive oil, and 15% fish oil (study group) or to a pure soybean oil (control group) within 48 hours after birth. The infants were stratified by birth weight (less than 1,000 g or 1,000 g and heavier) to ensure a balance of infants in each allocation. Blocks of four stratified randomization by treatment centers were used. The allocations were kept in sequentially numbered, opaque, sealed envelopes. The investigators and the patient care teams were blinded to the treatment allocation and remained throughout the study and the analysis.

**Nutritional intervention**

Lipids were first administered at a dose of 1 g/kg/day within 24 hours after birth for both groups; lipid dosage was increased by an increment of 0.5 g/kg/day until the maximal dose of 3.5 g/kg/day were reached. The other macronutrients and micronutrients were provided using the same products and protocol in both groups. Protein was first administered at a dose of 1 g/kg/day and was increased by 1 g/kg every 24 hours until reaching the maximal dose of 4 g/kg/day. Parenteral lipid and amino acid administration were temporarily stopped when either plasma triglyceride (TG) concentrations exceeded 250 mg/dL or when urea concentrations exceeded 35 mg/dL respectively. Minimal enteral feeding was initiated on the day of birth, and intake was advanced with 20 mL/kg/day of breast milk or preterm formula. PN was stopped when the oral feeding reached 120 mL/kg/day.

**Data collection and analysis**

Baseline data including gestational age, sex, birth weight, route of delivery, the numbers of prenatal steroid doses (0, 1, or 2), and Apgar score were recorded. Nutritional intake was recorded daily until the infants successfully progressed to full enteral feeding.
The primary outcomes were the incidence of cholestasis and the assessment of biochemical signs of hepatic dysfunction including alanine aminotransferase (ALT), aspartate aminotransferase (AST), total and direct bilirubin, gamma-glutamyl transpeptidase (GGT), and alkaline phosphatase (ALP). Cholestasis was defined as a direct bilirubin level of greater than 2 mg/dL. A diagnosis of cholestasis was confirmed if two consecutive measurements showed an elevation of direct bilirubin of greater than 2 mg/dL. All participating infants' blood samples were obtained before enrollment, and at week 1, 2, and 3 for liver function tests and GGT. Plasma TG was taken on day 5 and day 8 to assess lipid clearance or tolerance.

Secondary outcomes included: 1) death, 2) BPD defined as the need for supplementary oxygen or any form of respiratory support at 36 weeks postmenstrual age, 3) duration of ventilator support (days), 4) necrotizing enterocolitis (NEC) stage >1 on Bell’s staging system(20), 5) ROP as defined by the International Classification of Retinopathy of Prematurity(21), 6) hemodynamically significant patent ductus arteriosus (PDA) diagnosed by echocardiography as needing treatment by medication or surgery, 7) sepsis defined as a positive blood culture, 8) IVH, all grades, and severe IVH (grade 3 and 4) of Papile classification(22), 9) duration of hospital stay (days), and 10) growth parameters assessed using in-hospital growth rates, the gain in head circumference and height from birth until discharge, the diagnosis of extrauterine growth restriction (EUGR) by the time of discharge defined as a weight that is less than the tenth percentile for corrected gestational age(23).

The study protocol was approved by the Human Research Ethics Committee of Thammasat University and Nopparat Rajathanee Hospital. The trial was registered in Clinical Trials.gov (Clinical Trials.gov Identifier: NCT02663453).

**Statistical analysis**

Data were expressed as median and ranges for non-normal distributions or means and standard deviations for normal distributions. Comparable categorical data between the two groups were analyzed using the Chi-square test or Fisher’s exact test when appropriated. Comparable continuous data between the two groups were analyzed using an independent sample t-test, and non-parametric variables were calculated by the Mann-Whitney U test. Multilevel linear regression with fixed effects modelling was performed to compare the differences in serum total and direct bilirubin, ALP, AST, ALT, and GGT concentrations. A p-value less than 0.05 was considered significant. The statistician was blinded to the type of lipid therapy.

**Results**

Forty-four infants met the criteria for enrollment (22/22 in the study/control group), 35 of 44 (17/18 in the study/control group) completed the study. Fig. 1 is a flow diagram describing the study population. The demographics at baseline are displayed in Table 1. No differences was observed between the two groups. The age at the start of the study was 23.5±13.8 hours in the study group and 22.4±13.6 hours in the control group. There was no difference regarding the number of days required to reach full enteral feeding (14.9±7.3 days vs. 12.4±5.5 days respectively, \( p = 0.247 \)). The two groups were similar in mean duration of PN and lipid emulsion. During the double-blind treatment period, the infants received 1.6±0.6 g of lipids per kg per day in the study group, compared to 1.7±0.6 g per kg per day in the control group. The intravenous intakes of protein, carbohydrates, and total energy did not differ significantly between the groups (Table 2).

![Fig. 1](image-url) Flow diagram showing the numbers of recruitment, loss of participants, and final number of study participants.

**Primary outcomes**

One infant (4.5%) in the study group and two infants (9%) in the control group developed cholestasis. These three infants received PN longer than 14 days (23 days for the study group, and 28 and 20 days for the two in the control group). The effects of two types of lipid emulsion on biochemical parameters of liver dysfunction, including ALT, AST, total bilirubin, direct bilirubin, GGT, and ALP taken on Day 0, Week 1, Week 2, and Week 3, when adjusted for baseline, were
not different between the two groups (Fig. 2). On Day 5, with lipid dosage amounting up to 2 g/kg/day and Day 8 when administered 3.5 g/kg/day, the mean serum TGs were not significantly different between the two groups (mean 160±157 mg/dL vs. 168±125 mg/dL, \( p = 0.861 \) on Day 5, and 158±143 mg/dL vs. 118±65 mg/dL, \( p = 0.268 \) on Day 8 in the study group and the control group, respectively).

**Secondary outcomes**

Of the 44 infants (22/22 in the study/control group), 35 (20/15) had respiratory distress syndrome, 20 (11/9) received surfactant replacement therapy, 23 (13/10) developed significant PDA, and 15 (7/8) were diagnosed as having IVH, with 3 (2/1) having greater than grade 2 IVH. The occurrence of respiratory problems in the first week was slightly higher in the study group. Death occurred in eight (4/4) infants. Morbidity incidence by BPD, NEC, ROP, and sepsis was 19 (10/9), 4 (2/2), 13 (7/6), and 2 (1/1) in the study/control group respectively. The duration of respiratory support with mechanical ventilator was longer in the study group compared to the control group (20.9±23.4 and 8.9±15.0 days, respectively, \( p = 0.050 \)). The mean duration of hospitalization was slightly longer in the study group 80.6±32.8 days, compared to 69.7±20.8 days in the control group, but not statistically significant \( (p = 0.243) \). For the growth parameters, there was no difference observed in total weight gain at time of discharge, and no apparent difference in head circumference and height from birth to the time of discharge. At the time of discharge, 20 infants (8/12 in the study/control group) were diagnosed as having EUGR (36% vs. 54%) respectively (Table 3).
### Table 1. Baseline demographic data of infants in the study group and control group

<table>
<thead>
<tr>
<th></th>
<th>Study group (n = 22)</th>
<th>Control group (n = 22)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female n (%)</td>
<td>14 (63.6)</td>
<td>14 (63.6)</td>
<td>1.000</td>
</tr>
<tr>
<td>BW (g), mean ± SD</td>
<td>947±208</td>
<td>1,060±119</td>
<td>0.034</td>
</tr>
<tr>
<td>GA (week), mean ± SD</td>
<td>27.6±2.2</td>
<td>28.4±1.2</td>
<td>0.178</td>
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<tr>
<td>Multiple birth, n (%)</td>
<td>7 (31.8)</td>
<td>6 (27.3)</td>
<td>0.741</td>
</tr>
<tr>
<td>Cesarean section, n (%)</td>
<td>13 (59.1)</td>
<td>9 (40.9)</td>
<td>0.228</td>
</tr>
<tr>
<td>5 minutes Apgar, median (range)</td>
<td>8 (3, 10)</td>
<td>8 (4, 10)</td>
<td>0.793</td>
</tr>
<tr>
<td>Prenatal steroid (0/1/2), %</td>
<td>59/9/32</td>
<td>36/23/41</td>
<td>0.256</td>
</tr>
<tr>
<td>PROM, n (%)</td>
<td>2 (9.1)</td>
<td>5 (22.7)</td>
<td>0.216</td>
</tr>
<tr>
<td>Age at entry (hours), mean ± SD</td>
<td>23.5±13.8</td>
<td>22.4±13.6</td>
<td>0.777</td>
</tr>
<tr>
<td>Time to full enteral feeding (days), mean ± SD</td>
<td>14.9±7.3</td>
<td>12.4±5.5</td>
<td>0.247</td>
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</tbody>
</table>

BW = birth weight; GA = gestational age; PROM = premature rupture of membrane

### Table 2. Details of parenteral nutrition intake

<table>
<thead>
<tr>
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<th>Study group (n = 22)</th>
<th>Control group (n = 22)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of PN (days)</td>
<td>12.5±8.1</td>
<td>10.5±5.9</td>
<td>0.378</td>
</tr>
<tr>
<td>Duration of lipid emulsion (days)</td>
<td>11.9±8.1</td>
<td>9.9±5.9</td>
<td>0.366</td>
</tr>
<tr>
<td>Lipid intake (g/kg/day)</td>
<td>1.6±0.6</td>
<td>1.7±0.6</td>
<td>0.583</td>
</tr>
<tr>
<td>Amino acid intake (g/kg/day)</td>
<td>2.9±0.8</td>
<td>2.7±0.7</td>
<td>0.261</td>
</tr>
<tr>
<td>Glucose intake (g/kg/day)</td>
<td>7.1±1.6</td>
<td>7.4±1.6</td>
<td>0.471</td>
</tr>
<tr>
<td>Total energy (kcal/kg/day)</td>
<td>50.9±0.7</td>
<td>51.9±9.5</td>
<td>0.740</td>
</tr>
</tbody>
</table>

PN = parenteral nutrition

The data are presented as the mean ± SD, the p-values are based on Student t-tests

### Table 3. Neonatal outcomes of infants in the study group and control group

<table>
<thead>
<tr>
<th></th>
<th>Study group (n = 22)</th>
<th>Control group (n = 22)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPD, n (%)</td>
<td>10 (45.5)</td>
<td>9 (40.9)</td>
<td>0.070</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>4 (18.2)</td>
<td>4 (18.2)</td>
<td>1.000</td>
</tr>
<tr>
<td>IVH grade &gt;2, n (%)</td>
<td>2 (9.1)</td>
<td>1 (4.5)</td>
<td>0.493</td>
</tr>
<tr>
<td>Late onset sepsis, n (%)</td>
<td>1 (4.5)</td>
<td>1 (4.5)</td>
<td>0.972</td>
</tr>
<tr>
<td>Length of hospital stay (days)*</td>
<td>80.6±32.8</td>
<td>69.7±20.8</td>
<td>0.243</td>
</tr>
<tr>
<td>NEC, n (%)</td>
<td>2 (9.1)</td>
<td>2 (9.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>RDS, n (%)</td>
<td>13 (59.1)</td>
<td>10 (45.5)</td>
<td>0.365</td>
</tr>
<tr>
<td>RDS need surfactant therapy, n (%)</td>
<td>11 (50.0)</td>
<td>9 (40.9)</td>
<td>0.545</td>
</tr>
<tr>
<td>ROP, n (%)</td>
<td>7 (31.8)</td>
<td>6 (27.3)</td>
<td>0.556</td>
</tr>
<tr>
<td>ROP need surgery, n (%)</td>
<td>2 (9.1)</td>
<td>2 (9.1)</td>
<td>0.667</td>
</tr>
<tr>
<td>Time on ventilator (days)*</td>
<td>20.9±23.4</td>
<td>8.9±15.0</td>
<td>0.050</td>
</tr>
<tr>
<td>EUGR at discharge, n (%)</td>
<td>8 (36.4)</td>
<td>12 (54.5)</td>
<td>0.241</td>
</tr>
<tr>
<td>Weight gain birth to discharge (gm/day)*</td>
<td>19.7±3.9</td>
<td>18.8±3.9</td>
<td>0.471</td>
</tr>
<tr>
<td>Head circumference gain (cm/week)*</td>
<td>0.7±0.2</td>
<td>0.7±0.2</td>
<td>0.587</td>
</tr>
<tr>
<td>Height gain (cm/week)*</td>
<td>0.9±0.2</td>
<td>0.8±0.2</td>
<td>0.090</td>
</tr>
</tbody>
</table>

BPD = bronchopulmonary dysplasia; IVH = intraventricular hemorrhage; NEC = necrotizing enterocolitis; PDA = patent ductus arteriosus; RDS = respiratory distress syndrome; ROP = retinopathy of prematurity; EUGR = extrauterine growth restriction

* The data are presented as the mean ± SD
Discussion

Premature infants with low birth weight, receiving PN for longer periods, are at risk for developing cholestasis and PNALD(24,25), therefore, monitoring of total and direct bilirubin and liver enzyme levels during the administration of PN is crucial. In the present study, we failed to demonstrate any beneficial effects of the multicomponent emulsion on biochemical markers of liver injury, but others have observed lower GGT(26) and lower concentration of bilirubin(27). This difference may be explained because the infants need to be on PN for extended period of time before the negative effects on liver function become apparent. Most of infants in the present trial did not require PN beyond the second week of life. Consequently, their inflammatory response might have not yet developed. The rate of neonatal cholestasis in the study group (4.5%) is about half the rate of infants in the control group (9%). The difference did not attain statistical significance, obviously due to the low overall rate of cholestasis in the preterm infants included in the study. The intervention had no effect on the clinical outcomes, as there were no differences between the groups regarding BPD, NEC, ROP, and infection rate, nor was the growth rate in hospital affected. The time on ventilator and the mean duration of hospitalization were longer in the study group due to more infants had respiratory distress syndrome with subsequently developed significant PDA compared to the control group. There appeared to be a trend toward a lower incidence of extrauterine growth retardation at the time of discharge, but no statistical significance could be determined due to the small number of infants studied. Larger controlled studies are needed to determine whether the new lipid emulsion results in improving neonatal growth or other long-term benefits.

Conclusion

Administration of the standard soybean oil and the new lipid emulsion containing soybean oil, MCT, olive oil, and fish oil were safe and well tolerated in preterm infants without notable adverse effects. While the biochemical markers of liver injury and neonatal outcomes were comparable in both groups, there was slightly more growth improvement in the study group at time of discharge. Further trials, with both longer duration and larger sample size, are necessary.

What is already known on this topic?

PNALD is often observed in long-term PN with pure soybean oil lipid emulsion. Few studies have examined the effect of multicomponent lipid emulsion on the prevention of liver injury and morbidity in preterm infants.

What this study adds?

Administration of multicomponent lipid emulsion was safe and well tolerated in preterm infants. No beneficial effects on the prevention of liver dysfunction were seen based on the type of lipid emulsion.

Acknowledgement

The authors wish to acknowledge the assistance in statistical analysis of Professor Jayanton Patumanond MD, Clinical Research Center, Faculty of Medicine, Thammasat University. The authors also would like to thank the paramedical staffs of the neonatal units for their support of the clinical trial.

Potential conflicts of interest

None.

References


ประสิทธิผลของการให้ไขมันทางหลอดเลือดดำชนิดที่มีน้ำมันหลายชนิดเป็นองค์ประกอบในทารกเกิดก่อนกำหนดโดยวิธีการสุ่มและปกป้องในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติและโรงพยาบาลนพรัตนราชธานี

วิทยา เตราะสินธิ, ติวทรัพย์ พิชญมาลัย, ศิรวัน ศิริพานิช, อนุชา คุรุระ

ภูมิหลัง: การให้สารอาหารทางหลอดเลือดดำมีความจำเป็นในทารกเกิดก่อนกำหนดที่มีปัญหาความเจ็บป่วยและวันสารอาหารทางปากไม่ได้ตามลำดับเวลาของชีวิต ทารกที่ได้รับสารอาหารทางหลอดเลือดดำเป็นแนวทางมักเกิดการทำงานของตับผิดปกติ การให้ไขมันทางหลอดเลือดดำชนิดใหม่ที่มีน้ำมันหลายชนิดเป็นองค์ประกอบอาจช่วยลดภาวะแทรกซ้อน ทำให้อัตราการเจริญเติบโตดีขึ้น และลดอัตราการเกิดภาวะทุพพลภาพได้

วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิผลของการให้ไขมันทางหลอดเลือดดำชนิดที่ต่างกันต่อความกิจกรรมการเกิดภาวะแทรกซ้อน neonatal cholestasis การเปลี่ยนแปลงของการทำงานของตับโดยประเมินจาก liver function test, gamma-glutamyl transpeptidase (GGT), อัตราการเจริญเติบโต และอัตราการเกิดภาวะทุพพลภาพ

วัตถุประสงค์: ทารกเกิดก่อนกำหนดอายุครรภ์น้อยกว่าหรือเท่ากับ 30 สัปดาห์ และน้ำหนักแรกเกิดน้อยกว่าหรือเท่ากับ 1,250 กรัมที่แพทย์ผู้ดูแลประเมินว่ามีความจำเป็นต้องได้รับสารอาหารทางหลอดเลือดดำนานกว่า 7 วัน จะถูกสุ่มเป็น 2 กลุ่มละ 22 ราย ทารกกลุ่มทดลองจะได้รับไขมันทางหลอดเลือดดำชนิดที่มีน้ำมันหลายชนิดเป็นองค์ประกอบ ในขณะที่ทารกกลุ่มควบคุมจะได้รับไขมันชนิดที่มีน้ำมันแต่เดิมเป็นองค์ประกอบอย่างเดียว โดยทีมผู้ดูแลทารก ผู้วิจัย และผู้วิเคราะห์ข้อมูลจะไม่ทราบชนิดของไขมันที่ทารกได้รับ นอกจากนี้ทารกทั้ง 2 กลุ่มจะได้รับการติดตามอัตราการเจริญเติบโต การเกิดภาวะแทรกซ้อน อัตราการเกิดภาวะทุพพลภาพ และติดตามการทำงานของตับด้วยค่าเอนไซม์ที่เกี่ยวข้องทั้งสัปดาห์ที่ 1, 2 และ 3

ผลการศึกษา: ทารกกลุ่มละ 22 ราย ได้รับสารอาหารทางหลอดเลือดดำใกล้เคียงกัน คือ 12.5±8.1 วัน และ 10.5±5.9 วัน ในกลุ่มทดลองและกลุ่มควบคุมตามลำดับ นอกจากนี้ 高新区เดิม neonatal cholestasis 1 ราย ในกลุ่มทดลอง และ 2 ราย ในกลุ่มควบคุม ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติในการประเมินการทำงานของตับ อัตราการเจริญเติบโต และการเกิดภาวะทุพพลภาพ เช่น โรคปอดเรื้อรัง, late onset sepsis, retinopathy of prematurity ในทารกทั้งกลุ่ม ร้อยละ 36 ของทารกในกลุ่มทดลองได้รับการวินิจฉัยว่ามีภาวะเจริญเติบโตช้าหลังเกิดเทียบกับร้อยละ 54 ในกลุ่มควบคุม

สรุป: ไม่พบผลในการป้องกันภาวะทำงานของตับผิดปกติจากการให้น้ำมันหลายชนิดเป็นองค์ประกอบทางหลอดเลือดดำในทารกเกิดก่อนกำหนด