Effect of glutamine with auxiliary enteral and parenteral nutrition on feeding intolerance of low birth weight infants

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ABSTRACT

Objective: To analyze the clinical effects of glutamine assisted enteral nutrition and parenteral nutrition on improving the feeding intolerance of low birth weight infants. Methods: A total of 40 cases of low birth weight infants (LBW) in our hospital from May 2013 to June 2015 were selected, which were divided equally into the observation group and the control group according to the different nutritional intervention methods. Patients in the control group received routine enteral nutrition and parenteral nutrition while children of observed group received glutamine assisted enteral and parenteral nutrition. Differences of children's growth and development indicators, nutritional status and levels of calcium and phosphorus, gastrin and motilin levels, mucosal barrier and immune function were compared between two groups. Results: After receiving nutritional intervention, children in the observation group had higher levels of serum leptin, GH, IGF-I and adiponectin than the control group patients, while CORT values were lower. The observation group patients who received nutritional intervention had higher TSF, AMC, TP, ALB, calcium and phosphorus levels than the control group, while the ALP values were lower; children of observation group who received nutrition intervention had higher GAS and MOT levels than the control group; children of observation group after intervention had higher peripheral blood CD3+T, CD4+T and CD4+/CD8+ levels than the control group children, while D-lactic acid and blood ammonia levels were lower. Conclusion: Glutamine assisted enteral nutrition and parenteral nutrition could improve the feeding intolerance of low birth weight infants, and it improved the nutritional status as well as growth and development of children as a whole, and thus had positive clinical significance.

1. Introduction

With the rapid development of assisted reproductive techniques and perinatal medical technology, survival rate of low birth weight infants increases dramatically. Such children are usually with gastrointestinal function hypoplasia and cannot tolerate simple enteral nutrition, so enteral combined with parenteral nutrition is commonly used way. In low birth weight infants who receive the combined nutrition intervention, feeding intolerance occurs from time to time, which seriously affects the patient's normal growth and development, and may even cause complications as organ failure and brain dystrophy when nutritional supplement is not timely given . Glutamine, as an essential amino acid, is oxidative metabolic fuel of intestinal mucosal cells and a variety of fast growth cells. Studies have confirmed that the only gastrointestinal or intravenous supplementation of glutamine can improve children's feeding intolerance . This study mainly analyzed the clinical effect of glutamine assisted enteral nutrition and parenteral nutrition on improving the feeding intolerance of low birth weight infants, hereby reported as follows.
2. Data and methods

2.1 General information

40 cases of low birth weight infants (LBW) in our neonatology department from May 2013 to June 2015 were selected, not limited to genders. 20 cases went into the control group. Enteral nutrition and parenteral nutrition were given in accordance with the China neonatal nutrition support guidelines for the clinical application (2013 update version). The other 20 cases were set as the observation group, who received oral administration of glutamine granules on the basis of the conventional enteral nutrition and parenteral nutrition. The control group had 11 male cases and 9 female cases, weight 1.76-2.18 kg, average (1.95±0.15) kg. The observation group had 10 male cases and 10 female cases, weight 1.73-2.14 kg, average (1.91 ±0.13) kg. There were no significant differences in baseline data between the two groups, P>0.05 and they were comparable.

2.2 Nutrition intervention

Patients in the control group received conventional enteral and parenteral nutrition intervention, which were specifically as follows: enteral nutrition: children with nasogastric feeding in 1-2 mL/kg 5% glucose injection, continued 2 hours each time, 2 times a day. If there was no return, then preterm milk 1-2 mL/kg times was given, and each feeding time was 3 h. If the children gradually accepted, then the amount of milk was increased until it reached completely gastrointestinal feeding. Parenteral nutrition: via the use of unbilical vein catheterization, central venous catheter or peripheral venous route, fluid infusion of 60 mL/kg was given in the first day, and with the increase of the daily age, gradually increased to 150 mL/kg. The intravenous infusion of sugar concentration was less than 12.5%. From the second day, the physiological requirement amount of sodium, potassium and amino acids were supplemented. The initial dose of amino acids in infants was 0.5 g/kg, with daily increasing of 0.5 g/kg; the maximum amount was 3.0 g/kg. Intravenous nutrient was mixed solution under the strict aseptic operation, which was dropped in with 24 h constant speed by infusion pump. With the increase of enteral nutrition, the amount of parenteral nutrition was gradually reduced until the total parenteral nutrition was achieved.

Observe groups of children added glutamine assisted intervention based on enteral and parenteral nutrition, which were specifically as follows: when feeding intolerance occurred, L-glutamine and sodium glutamate granules was joined, 0.1 g/(kg/time) q6h.

2.3 Observation indexes

Serum leptin (Leptin), growth hormone (GH), insulin like growth factor I (IGF-I), cortisol(Cor) and adiponectin (adiponectin) levels were measured by radioimmunoassay. Serum calcium levels were detected by ion-selective-electrode. Phosphorus levels were detected by phosphomolybic acid method. Alkaline phosphatase (ALP) levels were detected by enzymatic method.

2 mL fasting dorsal venous blood was extracted before and 1 month, 3 months, 6 months after the nutritional intervention. Serum gastrin (GAS) and plasma motilin(MOT) levels were detected using radioimmunoassay. After 6 months of intervention, the CD3+T lymphocytes, CD4+T lymphocytes and CD4+CD8+T cell ratio were measured by flow cytometry. The plasma levels of D-lactic acid were determined by enzyme coupled ultraviolet spectrophotometry. Blood ammonia levels were measured by automatic biochemical analyzer.

2.4 Statistical methods

The above mentioned date were analyzed by SPSS 23.0. T-test was used to analyze measuremen data using (Mean±SD). Chi square test was used for count data. When P<0.05 the data was judged as having statistical significance.

3. Results

3.1 Growth and development indexes

Many serum indexes could accurately reflect the children's growth and development, and are also the objective description for effectiveness of nutrition interventions. In this study, we detected the serum leptin, GH, IGF-I, Cor, adiponectin values of two groups of children after nutrition intervention. The results showed that after receiving nutritional intervention, children in the observation group had higher levels of serum leptin, GH, IGF-I and adiponectin than the control group patients, while Cor values were lower (P<0.05), as shown in Table 1.

3.2 Nutritional status and levels of calcium and phosphorus

After nutrition intervention, children’s brachial triceps skinfold (TSF) and arm muscle circumference (AMC) were measured, and blood was extracted to detect the levels of TP, ALB, calcium,

| Table 1 | comparison of the growth and development indexes after nutritional intervention in two groups of children |
| --- | --- | --- | --- | --- | --- |
| Groups | Leptin(µg/ml) | GH(µg/L) | IGF-I(µg/ml) | Cor(µg/ml) | Adiponectin(µg/ml) |
| Observation group(n=20) | 1.37±0.12 | 6.37±0.59 | 4.76±0.45 | 12.73±1.18 | 90.72±0.87 |
| Control group(n=20) | 1.01±0.13 | 4.86±0.47 | 3.11±0.37 | 17.62±1.54 | 72.19±6.83 |
| t | 5.934 | 7.323 | 6.493 | 8.223 | 9.283 |
| P | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 |
phosphorus, ALB. The results showed as follows: the observation group patients who received nutritional intervention had higher TSE, AMC, TP, ALB, calcium and phosphorus levels than the control group, while the ALP values were lower (P<0.05), as shown in Table 2.

3.3 Levels of gastrin and motilin

The radioluminuous assay was used to detect levels of two groups of children’s motilin and gastrin so as to judge changes in gastrointestinal function before and after nutrition intervention. The results showed no statistically significant differences of blood gastrin and motilin levels between the two groups of patients before intervention (P>0.05). After the intervention, both groups of children had higher GAS and MOT values (P<0.05), while the GAS and MOT values of observation group after nutritional intervention were even higher than those of the patients in the control group (P<0.05), as shown in Table 3.

3.4 Mucosal barrier and immune function

The detection results of related blood markers of mucosal barrier and immune function of two groups of children showed as follows: Children of observation group after intervention had higher peripheral blood CD4+T, CD4+T, CD4+/CD8+ levels than the control group children, while D-lactic acid and blood ammonia levels were lower (P<0.05), as shown in Table 4.

Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>TSE(mm)</th>
<th>AMC(cm)</th>
<th>TP(g/L)</th>
<th>ALB(g/L)</th>
<th>calcium(mmol/L)</th>
<th>phosphorus(mmol/L)</th>
<th>ALP(U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group (n=20)</td>
<td>48.2±0.37</td>
<td>10.29±1.32</td>
<td>49.72±4.15</td>
<td>40.62±3.68</td>
<td>2.31±0.20</td>
<td>2.43±0.21</td>
<td>182.49±12.71</td>
</tr>
<tr>
<td>Control group (n=20)</td>
<td>37.1±2.99</td>
<td>8.58±0.59</td>
<td>34.89±3.25</td>
<td>32.01±2.31</td>
<td>1.98±0.14</td>
<td>1.76±0.19</td>
<td>398.67±20.25</td>
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<tr>
<td>t</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>P</td>
<td></td>
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<td></td>
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</table>

Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>Before</th>
<th>1M after intervention</th>
<th>3M after intervention</th>
<th>6M after intervention</th>
<th>Before</th>
<th>1M after intervention</th>
<th>3M after intervention</th>
<th>6M after intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group (n=20)</td>
<td>43.5±3.92</td>
<td>62.17±5.98</td>
<td>109.82±9.82</td>
<td>137.29±11.56</td>
<td>278.37±20.31</td>
<td>421.82±33.96</td>
<td>513.82±46.63</td>
<td></td>
</tr>
<tr>
<td>Control group (n=20)</td>
<td>43.67±4.08</td>
<td>51.58±4.77</td>
<td>63.89±6.05</td>
<td>76.45±6.97</td>
<td>134.67±12.09</td>
<td>189.55±17.62</td>
<td>304.61±29.88</td>
<td>409.72±37.68</td>
</tr>
<tr>
<td>t</td>
<td>0.183</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>0.183</td>
<td>9.304</td>
<td>&lt;0.05</td>
<td>8.241</td>
</tr>
<tr>
<td>P</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4

<table>
<thead>
<tr>
<th>Group (n=20)</th>
<th>CD4+T(%)</th>
<th>CD4+T(%)</th>
<th>CD4+/CD8+</th>
<th>D-lactic acid (mg/dL)</th>
<th>blood ammonia (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>59.82±5.11</td>
<td>30.78±3.25</td>
<td>1.58±0.13</td>
<td>0.87±0.07</td>
<td>18.23±1.72</td>
</tr>
<tr>
<td>Control</td>
<td>53.07±4.98</td>
<td>33.15±2.98</td>
<td>1.31±0.12</td>
<td>1.18±0.12</td>
<td>25.79±2.42</td>
</tr>
<tr>
<td>t</td>
<td>0.935</td>
<td>7.124</td>
<td>5.693</td>
<td>6.182</td>
<td>8.284</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

4. Discussions

With the development of perinatal medicine, the survival rate of premature infants with low birth weight has increased significantly. After that, nutrition intervention and the regular growth and development have become one of the important problems. A large number of studies have shown that the length of stay in hospital and the quality of life of low birth weight infants are closely related to the start time of feeding and the feeding pattern. Early feeding can improve the general situation of the children and promote gastrointestinal function, increase the resistance. But the low birth weight infants usually have limited nutrition reserve and the gastrointestinal function development is not mature to tolerate a lot of enteral nutrition, so on the basis of enteral nutrition, aggressive parenteral nutrition must be combined to provide children with weight gain. A part of children may show feeding intolerance in the process of nutritional intervention. Feeding intolerance indicates that the kid vomiting is more than or equal to 3 times/day, the amount of milk does not increase or even decrease > 3 days, and storage of gastric retention amount is more than or equal to 1/3 of the previous tolerance. Longtime feeding intolerance will pose serious harm to low birth weight infants, and may even cause organ failure due to insufficient nutrient supply. Glutamine (Gln) is the most abundant non essential amino acid in the human body, which is also the oxidative metabolic fuel of intestinal mucosal cells and rapid growth cells. Under the stress, Gln can reduce intestinal permeability, enhance intestinal immunity, prevent intestinal mucosal cell from apoptosis and reduced less bacteria group displacement to play protective effect of intestinal. Glutamine has been routinely used in the treatment of patients with chronic gastritis, but its use in neonates is still at a stage of research. In order to clear the application effect of glutamine in low birth weight infants, the study added glutamine in nutritional intervention of the observation group, specifically analyzing its application effect from the index of
growth and development, nutritional status and levels of calcium and phosphorus, gastrin and motilin levels, mucosal barrier and immune function.

The ultimate goal of positive nutrition intervention is to promote the development of organ function in low birth weight infants, and to promote the improvement of body nutrition and to accelerate the growth of the body. After studying the growth curve of low birth weight infants, it was found that the weight loss was the main feature of the first 4-6 d after birth, the lower the birth weight, the more obvious the decline, and then weight was gradually restored. Early nutrition and environmental stimulation can change the number or the proportion of cells in the tissues permanently, which means reasonable and effective nutrition intervention is very necessary and important to low birth weight infants. Leptin is closely related to the growth and development of children, and with the increase of body weight, the level of leptin in children is increased, and its regulation effect on nutritional balance is played. Insulin like growth factor I (IGF-I) is a single peptide, which can stimulate glycogen, lipid and carbohydrate metabolism, and inhibit fat degradation. Growth hormone (GH) is directly related to the growth and development of children, and the level of GH in children with malnutrition is relatively low. Adiponectin is the newly developed index that has close relationship with children's nutritional as well as the growth and development. Study shows that the level of adiponectin is proportional to the weight of children. The above research results showed that after nutrition intervention, observation group had higher leptin, GH, IGF-I and adiponectin values and lower Cor values, which suggested that glutamine assisted nutrition intervention could promote children's nutrition improvement and growth.

Brachial triceps skinfold (TSF), and arm muscle circumference (AMC), total protein (TP) and albumin (ALB) are all accepted effective indexes reflecting macroscopic trophic state. The results showed observation group with nutrition intervention had increased TSF, AMC, TP and ALB levels, which suggested that the addition of glutamine could promote children's nutritional status improvement. The bone turnover of low birth weight infants is very active, and the calcium and phosphorus reserves are not enough. The study of bone tissue morphology of preterm infants found that bone resorption increased and the bone formation decreased. ALP is membrane protein that has enzymatic activity. It is synthesis by osteoblast and reflects osteoblastic activity. Low birth weight infants' vitamin D and calcium supplies are insufficient and further lead to rising levels of ALP and bone mineralization. In the early stage after premature low birth weight infants are born, bone resorption due to increased calcium can be maintained, with age in days increase serum ALP level was gradually increased and blood phosphorus was decreased. In this study, the observation group was treated with glutamine combined with enteral nutrition intervention, the calcium and phosphorus levels were increased, and the level of ALP was decreased, which indicated that the bone formation activity increased in the children.

Studies have confirmed that gastrointestinal hormones are closely involved in neonatal gastrointestinal structure function development and maturation. Motilin (MOT) and gastrin (GAS) are typical gastrointestinal hormones. Motilin is secreted by the Mo cell and distributed in the small intestine. The motility and transitional of the gastrointestinal tract are mainly regulated by the emeric nervous system and motilin. Gastrin is secreted by G cells in the gastric antrum and duodenal proximal mucosa, which can stimulate the parietal cells to secrete Heil, also play a role in pancreatic and bile secretion, and can slightly stimulate cell secrete pepsin. Studies have confirmed that in very low birth weight infants within 72 h of birth, their blood MOT, GAS levels are significantly lower than those in term infants. Low levels of MOT and GAS are related to feeding intolerance. The study compared blood MOT and GAS levels in children before and after nutrition intervention. The results showed that after the observation group received the positive nutritional intervention, blood MOT and GAS levels were increased significantly. So we speculated that adding glutamine on the basis of enteral and parenteral nutrition intervention could promote gastrointestinal function recovery in low birth body weight infants, and accelerate gastric emptying to improve feeding intolerance, stimulate gastrointestinal growth and development and accelerate the maturation of the gastrointestinal function.

The traditional concept is that glutamine is nonessential amino acid, so parenteral nutrition recipe did not add it. Low birth weight infants have low activity of both glutamine synthetase and glutaminase, so endogenous glutamine cannot be timely and effectively synthesized, resulting in relatively glutamine deficiency state in children. Protein decomposition and regeneration rate of newborn is faster than that of adult, the demand for glutamine is even greater, and so glutamine is necessary for infants. Glutamine is not only oxidation fuel for a high metabolic activity cells, but also provides nitrogen source for lymphocytes and intestinal epithelial cells to synthesize new DNA and RNA. It has been proved that glutamine can increase the number of lymphocytes, enhance the immune function and reduce the incidence of infection in animal models. The study supplemented with glutamine in the observation group, and analyzed its function from the mucosal barrier and immune function. The results showed that the observation group had higher CD3+T, CD4+T, CD4+/CD8+ levels and lower D-lactic acid, blood ammonia levels. CD3+T, CD4+T lymphocytes are main cells of cellular immune function and CD4+/CD8+ ratio can directly determine the state of children humoral immune function. These results all suggested that the addition of glutamine in the treatment of low birth weight infants had strengthened cellular immune function. D-lactic acid and blood ammonia were both intestinal bacterial metabolites; in physiological
state of circulating blood their levels were very low. When the intestinal mucosa biological barrier was destructed, large amounts of lactic acid and blood ammonia were generated and went through the damaged intestinal mucosa into the blood circulation. So, D-lactic acid and blood ammonia levels can reflect the intestinal mucosal injury repair condition. These results suggested that the intestinal mucosal barrier of the observation group was effectively repaired after glutamine treatment, which was the basis of the intestinal absorption of nutrition and improvement of the overall state of the children.

In summary, we can draw the following conclusions: glutamine assisted enteral nutrition and parenteral nutrition can improve feeding intolerance of low birth weight infants and overall improve children's nutritional status and growth and development, and it is worthy of popularization and application in the future clinical practice.

References


