Intravenous supplementation of L-amino acids and dextrose in low-birth-weight infants

The effect of intravenous 3.4 per cent L-amino acid and 10 per cent dextrose supplementation on mortality rate, weight gain, and biochemical blood values was examined in 54 low-birth-weight newborn infants. At 24 to 48 hours of age, the infants were assigned according to birth weight to Group I (701 to 1,000 Gm.), Group II (1,001 to 1,250 Gm.), or Group III (1,251 to 1,500 Gm.). Each group was subdivided randomly into amino acid-treated infants (A) and control subjects (C). There was no significant difference in the case fatality rates between infants in Subgroups A and C. Serial determinations of serum electrolytes, CO₂ combining power, and hematocrit were similar in Groups A and C. Serial blood urea nitrogen concentrations in Group A infants were significantly higher than those in Group C infants. Plasma amino acids showed undue elevations in methionine and glycine concentrations in some of the infants who received supplemental amino acids. At 21 days, a significantly greater increase in weight was observed in Group IIA (178 ± 26 Gm.) compared to Group IIC (54 ± 51 Gm.). Similarly, weight increase in Group IIIA (206 ± 27 Gm.) was significantly greater than that in Group IIIC (58 ± 24 Gm.). Infants in Groups IIA and IIC reached a discharge weight of 2,041 Gm. at 45 ± 11 days and 55 ± 9 days, respectively. Infants in Group IIIA reached the discharge weight significantly earlier than those in Group IIIC (41 ± 1 and 49 ± 2 days, respectively).


From the Departments of Pediatrics, Cook County Children's Hospital, The University of Illinois College of Medicine, and the Infant's Aid Perinatal Research Laboratory, Mount Sinai Hospital, The Chicago Medical School, and the Hektoen Institute.

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*Reprint address: 700 S. Wood St., Chicago, Ill. 60612.

The provision of optimal nutrition for low-birth-weight infants remains a significant problem. Generally, adequate oral intake cannot be promptly established. Moreover, the danger of aspiration precludes the use of this route in most instances. Total parenteral alimentation¹ has been used in small premature infants.² The complexities and the potentially serious complications of this technique³ render it impractical for routine use in these small infants.
Table I. Composition of solution
(per 100 ml.)

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextrose (Gm.)</td>
<td>10.5</td>
</tr>
<tr>
<td>L-Amino acids (Gm.)*</td>
<td>3.4</td>
</tr>
<tr>
<td>Sodium (mEq.)</td>
<td>2.9</td>
</tr>
<tr>
<td>Chloride (mEq.)</td>
<td>1.8-3.8</td>
</tr>
<tr>
<td>Lactate (mEq.)</td>
<td>2.5</td>
</tr>
<tr>
<td>Potassium (mEq.)</td>
<td>2.0</td>
</tr>
<tr>
<td>Calories</td>
<td>55.6</td>
</tr>
<tr>
<td>Milliosmoles</td>
<td>890</td>
</tr>
</tbody>
</table>

*PreAmine, McGaw Laboratories, Glendale, Calif.

The purpose of this study was to evaluate the effects of a modified form of parenteral alimentation on mortality rate, weight gain, and biochemical blood values in premature infants who weighed less than 1,500 Gm. at birth. Since most of these infants were able to receive some of their caloric requirement by mouth, intravenous supplementation rather than complete parenteral alimentation was employed. In order to prevent or reduce serious complications, the infusion was given via a peripheral vein rather than an indwelling catheter in the superior vena cava.

MATERIALS AND METHODS

Fifty-four newborn premature infants born at Cook County Hospital were included in this study. At 24 to 48 hours of age, the infants were divided according to birth weight into Group I (701 to 1,000 Gm.), Group II (1,001 to 1,250 Gm.), or Group III (1,251 to 1,500 Gm.). Each group was subdivided randomly into amino acid-treated infants (A) and control subjects (C). There were 15 infants in Group I, 20 in Group II, and 19 in Group III. There was no significant difference in the clinical features among the infants in Subgroups A and C in the individual groups.

The composition of the solution given to the Subgroup A infants is shown in Table I. Sodium lactate was added because of the high content of cationic amino acids in the solution. The solution was prepared daily by one individual using sterile technique, vacuum bottles, and special mixing sets. A constant infusion pump and Millipore filters were employed. The intravenous line was not used for any other purpose. Vitamins were given by mouth.

Control infants were given the usual intravenous maintenance solution used in our nursery, 5 per cent dextrose in 0.2 per cent saline and potassium chloride as needed.

All infants were fed the same formula in amounts depending on what could be tolerated. The formula contained 2.8 Gm. of protein per 100 ml. The total fluid intake (oral plus intravenous) was increased by 15 ml. per kilogram daily until a maximum of 150 ml. per kilogram per day was established.

Blood urea nitrogen, sodium, chloride, potassium, CO₂ combining power, and hematocrit were determined on the first day of the study and every third day thereafter until the infants were 21 days of age. Blood glucose was determined periodically using the glucose oxidase method. Urine was tested for glycosuria at least twice a day. Serum osmolality was determined by freezing point depression using an "Advance Model" osmometer. Serum protein was determined by the method of Lowry and associates and albumin by electrophoresis. Column chromatography was used for the quantitation of plasma amino acids.

RESULTS

Mortality rate. At 21 days, there was no significant difference in the mortality rate between the amino acid-treated and the control groups. Six of 8 infants in Group IA and 6 of 7 infants in Group IC died. There were three deaths in Group IIA, one in Group IIC, and one in Group IIIA. There were no deaths in Group IIIC.

Autopsies were performed in the 10 amino acid-treated and 7 control infants. Intraventricular hemorrhage was the most common cause of death (6 in Group A and 2 in Group C). Hyaline membrane disease and primary pulmonary atelectasis were also common (3 in Group A and 4 in Group C). The data suggest that there may be a higher incidence of central nervous system hemorrhage in the amino acid-treated infants, particularly in those who weighed less than
1,000 Gm. at birth. Since the number is small, further studies are required for confirmation. There were only three survivors in Group I. The data from these three infants cannot be analyzed and are therefore excluded from subsequent analysis.

**Biochemical data.** The serial concentrations of blood glucose, serum potassium, sodium, chloride, osmolality, hematocrit, and blood pH were not significantly different in Subgroups A and C. Blood glucose concentrations varied from 25 to 165 mg. per 100 ml. in the Subgroup A infants, and glycosuria (2+ or 3+) was observed in only 3 of 434 urine samples.

**Blood urea nitrogen.** During amino acid infusion, blood urea nitrogen concentrations in Subgroups A were significantly higher than those in Subgroups C. By the eighteenth day of the study, the mean blood urea nitrogen concentration in Group IIIA was not significantly different from that in Group IIIC. This coincided with the discontinuation of amino acid infusion in the majority of the infants (Fig. 1).

**Serum albumin.** The initial serum albumin concentrations were similar in all groups. Weekly serum albumin determinations are shown in Fig. 2. In Group IIC, there was a decrease of serum albumin during the first two weeks. No similar decrease was observed in Group IIA. There was no significant difference in the serum albumin concentrations among the infants in Groups IIIA and IIIC.

**Plasma amino acids.** Initially, there was no significant difference in the mean concentra-
tions of the individual amino acid in infants in Subgroups A and C. However, there was a marked and persistent increase of plasma methionine in the Subgroup A infants throughout the study period (26.42 ± 8.15 µm per milliliter in Subgroup A and 5.87 ± 3.20 µm per milliliter in Subgroup C during the first week; 40.30 ± 11.98 µm per milliliter in Subgroup A and 4.12 ± 1.17 µm per milliliter in Subgroup C during the second week). In 8 of the Subgroup A infants, plasma methionine varied from 5 to 30 times the normal mean. In the first week of the study, there was a transient but significant increase of plasma ornithine and lysine in Subgroup A. In two infants in Subgroup A, there was a transient increase of plasma glycine up to three times the normal mean.

Caloric intake. Total caloric intake in the various groups is shown in Fig. 3. The intake in Group IIA was significantly higher than that in Group IIC in the first few days of life. On the other hand, the intake in Group IIIA was significantly higher than that in Group IIIC throughout most of the study period. There was no significant difference in the daily oral caloric intake in Subgroups A and C, and there was no significant difference in the volume of oral or intravenous fluid given to Subgroups A and C. However, the total protein intake (including amino acids) was significantly higher in Subgroups A throughout most of the study period.

CLINICAL OUTCOME

Regaining of birth weight. Amino acid–treated infants regained their birth weight earlier than control infants. Group IIA infants regained their birth weight in 10 ± 1.5 days and Group IIC, in 14 ± 2.6 days. Group IIIA infants regained their birth weight in 8 ± 1.8 days and Group IIIC, in 16 ± 2.0 days. The difference was significant in Group III infants (p < 0.01).

Weight gain. At 21 days of age, the amino acid–treated infants gained significantly more weight than the control subjects. Group IIA gained 178 ± 26 Gm. and Group IIC, 54 ± 50 Gm. (p < 0.05). Group IIIA gained 206 ± 27 Gm. and Group IIIC, 58 ± 24 Gm. (p < 0.001).

Time required to reach discharge weight. Infants who received L-amino acids and 10 per cent dextrose reached a satisfactory condition and the discharge body weight of 2,041 Gm. sooner than the control subjects. Infants from Group IIA attained a body weight of 2,041 Gm. at a mean age of 45 ±
11 days and those from Group II C at 55 ± 9 days (not significant). Infants from Group II A attained a body weight of 2,041 Gm. at a mean age of 41 ± 1.1 days, and those from Group II C at 49 ± 2.0 days. The difference in Group III was significant (p < 0.005).

DISCUSSION

Benda and Babson demonstrated significantly greater weight gain in small premature infants by the infusion of a “high-calorie” solution containing alcohol through peripheral veins without apparent complications. In this study, the provision of additional calories in the form of amino acids and dextrose via peripheral veins resulted in significantly greater weight gain in infants weighing 1,001 to 1,500 Gm. at birth as compared to control subjects of similar birth weight. These findings are in agreement with those reported by Bryan and associates, who used 10 per cent dextrose in 5 per cent fibrin hydrolysate in the infusate. They attributed the greater weight gain to the amino acids in the infusate, since total caloric intake was similar in both the experimental and control groups. In our study, a significant difference in total caloric intake was generally observed between Subgroups A and C. The greater weight gain observed in the amino acid-treated infants was not accompanied by clinical edema, anemia, or hypoproteinemia, suggesting a true gain in body tissue. In fact, serum albumin concentrations were higher in group IIA than in Group IIC.

The significantly higher blood urea nitrogen in the amino acid–treated infants is most likely a reflection of the higher protein (amino acid) intake. However, renal function may be a contributory factor as the blood urea nitrogen in Group IIA was higher than that in Group IIIA, and both of them received similar amounts of protein (amino acids) per kilogram of body weight. It may be suggested, therefore, that the amount of intravenous amino acids given to these infants might have been excessive.

The high plasma methionine in eight of the amino acid–treated infants may be a reflection of their inability to metabolize methionine normally. This probability is strengthened by the presence of only trace amounts of cystine in their plasma. Excessive methionine has been reported to produce damage in multiple tissues in rats and disaggregation of polyribosomes and inhibition of in vitro protein synthesis in immature rat brain. Two infants had transient elevation of plasma glycine up to three times the normal mean. These observations emphasize the need to monitor plasma amino acids in infants receiving prolonged amino acid infusions. Since the glycine content of FreAmine is approximately ten times and methionine content twice that in human breast milk, it seems advisable to reduce the content of these amino acids in FreAmine.

In this study, no serious complications were observed. This is in sharp contrast to the numerous complications reported with the use of total parenteral alimentation in low-birth-weight infants. Moreover, since most infants are able to receive some oral or nasogastric feedings, it is unnecessary to provide a nutritionally complete intravenous fluid. Total parenteral alimentation should be reserved for infants who are unable to tolerate any oral intake for prolonged periods of time.

There was no evidence in this study to suggest that intravenous supplementation of amino acids and dextrose to oral feedings was beneficial to survival. However, such combined feedings should prevent prolonged starvation or semistarvation with its potential detrimental effects. In addition, this method may be of practical value in permitting earlier discharge of these infants from the hospital.

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