PARENTERAL NUTRITION (PN) IN THE MANAGEMENT OF VERY LOW BIRTHWEIGHT (VLBW) BABIES-A RANDOMIZED CONTROLLED TRIAL

Umesh V. Vaidya
Sheila A. Bhave
Anand N. Pandit

ABSTRACT

Eighty five very low birth weight (VLBW) babies with birthweight less than 1250g were randomly assigned such that 43 received parenteral nutrition (PN) with aminoacid based glucose electrolyte solution (Vamin) and lipid emulsion (Intralipid) in the first 16 days of life. The other 42 (control group) received conventional intravenous dextrose with or without electrolytes plus enteral milk regimen. Baseline clinical parameters and neonatal problems encountered in the two groups were similar. There was no significant difference in the mortality rate in the two groups (48.9% in PN group and 42.9% in control group: \( \chi^2 = 0.3, p > 0.05 \)). The commonest cause of mortality in both the groups was septicemia (163% and 26.1% in PN and control groups, respectively). Local complications, sepsis and fluid electrolyte disturbances were similar in the two groups. Azotemia (25.6%), hyperlipidemia (9.3%), metabolic acidosis (9.3%) and prolonged cholestasis (14%) were commoner in the PN group but were reversible with early recognition. Time taken to regain birthweight was also similar in the two groups (\( \chi^2 = 14.2 \) and 15.2 days for PN and control groups, respectively). Thus, PN failed to improve the survival or early weight gain in the routine management of the VLBW babies in our unit.

Key Words: Parenteral nutrition, Very low birthweight babies, Management.

From the Department of Pediatrics, K.E.M. Hospital, Pune 411 011.
Reprint requests: Dr. Sheila Bhave, Department of Pediatrics, K.E.M. Hospital, Pune 411011.
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in view of the expense and expertise involved, it is necessary for us to have a clear idea of the value and indications of PN in neonates.

Over the past 6 years, PN has been used in over 100 children and neonates at our centre in KEM Hospital, Pune(6). Cost and complications have reduced significantly with continuous experience and indigenisation(7). The specific aim of this study was to evaluate the role of PN (if any) in the reduction of mortality and morbidity in the routine management of VLBW babies in our setting.

Subjects and Methods

Eighty five VLBW babies with birthweight <1250 g who survived the first 48 hours were randomly assigned to parenteral nutrition group (PN) or conventional intravenous fluid therapy (control group) in the first 15 days of life. Aminoacid solution (Vamin) was initiated on the 3rd day of life in a dose of 0.5 g/kg/day and increased daily up to a maximum of 3 g/kg/day. Lipid emulsion (Intralipid) was started on the 5th day of life in a dose of 0.5 g/kg/day and increased to a maximum of 3 g/kg/day. Lipid administration was deferred in babies with hyperbilirubinemia (serum bilirubin >10 mg/dl). Electrolytes, minerals and vitamins were added as per standard recommendations(8). Enteral feed in the form of expressed breast milk or formula (Dexolac, Wockhardt) was initiated and increased as per the tolerance with suitable fluid adjustments in parenteral feeds. Technique, protocol and monitoring of PN were as previously described(6,9).

Control group received intravenous 10% dextrose at 60 ml/kg on day 1, which was increased to 120-150 ml/kg by the end of the first week. Enteral feeds similar to PN group babies were started and advanced as per tolerance up to a maximum of 200 ml/kg/day with suitable reduction in intravenous fluids. Enteral feeds in both groups were by intermittent gavage feeding.

The outcome variables analysed in the two groups were mortality, morbidity and related complications. Sample size calculation was done using EPI INFO statistical software assuming an event rate (mortality) in the controls as 50% and expecting a 10% reduction in mortality in the PN group (one tailed test, 95% confidence limit). Chi square test and Fisher exact tests were used to test statistical significance in the two groups.

Results

Of the 85 VLBW babies (birthweight < 1250 g) enrolled for this study, 43 were included in the PN group and 42 in the control group, i.e., conventional intravenous fluid plus enteral feeding group. There were no significant differences in the baseline variables (mean birthweight, gestational age and percent SGA) and in the neonatal problems encountered (respiratory distress syndrome, apnea, hypoxic ischemic encephalopathy) in the two groups (Table I).

The mean duration of administration of PN was 8.7 ± 0.5 days (range 2-16 days). The mean maximal protein and lipid intakes in the PN group were 2.6 ± 1.2 and 3 ± 1.5 g/kg/day. All babies received PN by peripheral sites except for four, who required a central catheter (umbilical) because of non-availability of peripheral sites.
In the control group, the mean duration of intravenous fluids (10% dextrose) was 8.4 ± 6.7 days. The mean age at initiation and type of enteral feeding (expressed breast milk/formula) did not differ in the 2 groups (3.6 ± 3.5 days in PN group and 2.6 ±1.7 days in the control group).

There was no significant difference in the overall mortality rate in the 2 groups (Table I). Septicemia was the commonest cause of mortality in both the groups. The incidence of fatal intracranial and pulmonary hemorrhage was higher in the PN group, whereas NEC was responsible for death in two control babies as against none in the PN group. The mean duration of time to regain birthweight (after the initial postnatal weight loss) in the survivors was 15.2 ± 8.6 days (range 0-33 days) and 14.2 ± 10.3 days (range 0-41 days) for the control and the PN group, respectively (p >0.05).

The local and systemic complications encountered in the two groups are seen in Table II. There were no significant differences in the number of babies with complications due to infection and fluid imbalance. However, local and metabolic complications, particularly azotemia and hyperbilirubinemia were commoner in the babies receiving PN as compared to controls. All were

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PN group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight (g)</td>
<td>Mean</td>
<td>1116±101</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>(900-1245)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>Mean</td>
<td>31.5 ±2.8</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>(28-40)</td>
</tr>
<tr>
<td>SGA(%)</td>
<td>58.1</td>
<td>54.7</td>
</tr>
<tr>
<td>Days required to regain birthweight</td>
<td>Mean</td>
<td>14.2±10.3</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>(0-41)</td>
</tr>
<tr>
<td>Mortality n (%)</td>
<td>21 (48.9)</td>
<td>18 (42.9)*</td>
</tr>
</tbody>
</table>

* Chi square 0.3, p >0.05.
reversible with early recognition. Hyperlipidemia, seen in 4 VLBWs (9.3%) during fat administration, reduced rapidly by controlling the lipid intake. Cholestasis which occurred in 6 (14%) babies receiving PN continued for prolonged periods lasting for 13-286 days. This cholestasis (though prolonged), resolved spontaneously in all but one baby, who died of hepatic dysfunction at the age of 27 days with post-mortem liver biopsy findings of giant cell transformation, hepatic necrosis and proliferation of bile ducts.

**Discussion**

A number of theoretical advantages suggest the indication of parenteral nutrition in VLBW babies. The various feeding difficulties, gastrointestinal immaturity and frequent occurrence of illnesses such as apnea and respiratory distress, hamper the initiation and establishment of adequate enteral feeding(3,10). At the same time the greatly increased demands and poor stores(11) are such that a 1000 g baby is not expected to survive beyond 7 days on intravenous fluids alone(12). It is, therefore, surprising that well designed clinical trials have failed to show convincing survival advantages of routine PN policy over conventional enteral feeding with or without intravenous fluids(5,13,14). In the present study too, there was no significant difference in the mortality in the two study groups, being over 40% in both (Table I). The chief causes of death in both groups were also similar, viz., septicemia, intracranial and pulmonary hemorrhage and respiratory distress with or without apnea. In the absence of other supportive measures such as ventilation, these conditions are known to have a poor outcome in VLBW babies with birthweight <1250 g(15,16). It is, therefore, perhaps, not fair to evaluate PN in VLBWs by mortality figures alone.

On the positive side, this study also demonstrates that the technique of PN, by itself did not confer a greater risk of mortality in this high risk group in our unit. Complication rates in the PN group too, were not significantly higher.

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**TABLE II—Complications During the Study.**

<table>
<thead>
<tr>
<th>Complications (n)</th>
<th>PN Group (n=43)</th>
<th>Control Group (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Cutaneous gangrene</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Abscess</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Infective</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Fluid Imbalance</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**Metabolic Abnormalities**

- Electrolyte imbalance 2 4
- Hypoglycemia 5 4
- Hyperglycemia 2 1
- Hyperbilirubinemia 11 7
- Ca & PO₄ abnormalities 3 2
- Azotemia 11 1
- Hypertriglyceridemia* (>200 mg/dl) 4 -
- Elevated transaminases* 2 -
- Cholestasis* 6 -
- Metabolic acidosis* 4 -

**Others**

- Thrombocytopenia 2 -
- Bleeding diathesis 1 -

* Parameters monitored only in the PN group.
than in control group. With stringent monitoring protocols and continuous training of staff, die PN related complications have reduced in our unit to rates comparable to western centres particularly, for sepsis(3,17), cholestasis(18) and metabolic disturbances(19,20). NEC did not develop in any of the PN group patients as against two in our control group and though the numbers are small, this observation has also been reported in the other similar controlled studies(13,14).

Though routine supplementation of PN in VLBW babies cannot be recommended on the basis of this study, it does not absolve NICUs from developing this important technique in their units. PN has already proven its critical life saving value in various neonatal conditions such as severe congenital anomalies of gut, NEC and intractable diarrheas(21,-23). In our unit too, the most gratifying results of PN were in surgical neonates with successful surgical corrections, viz., tracheoesophageal fistula and duodenal atresia(6). Importantly, various studies have suggested at least two compelling reasons for the use of PN in carefully selected situations: (i) PN is capable of supporting normal to supra normal rates of growth in LBW babies(24); and (ii) PN can be given for prolonged periods with only minimally added morbidity(25).

In conclusion, routine supplementation of PN in VLBW babies for the first week or two of life offers no survival advantage or disadvantage over a policy of enteral feeding plus intravenous fluids. Safe parenteral feeding back up services, however, must be available in situations were enteral feeding is precluded for prolonged periods.

Acknowledgements

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REFERENCES


