The role of Intralipid in prolonged parenteral nutrition. I. As a caloric substitute for glucose


ABSTRACT Three stable patients were studied in order to assess the role of intravenous fat solutions (Intralipid) in long-term home parenteral nutrition. The standard source of nonprotein calories (NPC) in these patients was 60% glucose. Replacing 40% of NPC by Intralipid was effective in maintaining nitrogen balance and allowed total infusion time to be reduced from 12 hr to 8 hr. The serum triglyceride level was significantly elevated when glucose was used as the sole source of NPC, whereas serum cholesterol was significantly elevated when 40% of NPC were supplied by Intralipid. Am. J. Clin. Nutr. 29: 255-257, 1976.

An increasing number of patients now depend upon lifelong home parenteral nutrition for their total or almost total supply of nutrients essential to a healthy life. Unfortunately, patients in the United States have had to rely upon glucose for their source of nonprotein calories (NPC), thus obligating them to overnight infusions of 12 to 14 hr in order to get 2,000 cal as glucose. More rapid infusion led to significant glucosuria and/or complaints by the patients of nausea and abdominal pain. The time free from infusion has not allowed full patient rehabilitation, as it is the exception rather than the rule for a patient requiring 12- to 14-hr infusions 5 to 7 times per week to be able to resume full-time employment, even though healthy in all other respects (1). The present studies were performed to determine whether Intralipid as a 10% soybean oil emulsion, when isocalorically substituted for 40% of the total glucose NPC, could overcome these drawbacks to prolonged parenteral nutrition without adversely affecting the nutritional status of the patient or producing other serious side effects.

Methods

Subjects Three stable patients requiring prolonged parenteral nutrition were studied in the metabolic unit of the University of Washington Hospital Clinical Research Center after their informed consent was obtained. These patients had normal weight for height, normal serum total protein, albumin, transferrin, electrolytes, and renal function, and no evidence of significant infection or presence of other catabolic stresses.

Protocol The study was designed so that each subject served as his own control. Period I (days 1 to 7) provided 600 or 700 g of glucose, 85 g of crystalline amino acids, and appropriate electrolytes and vitamins at a stable continuous infusion rate over each 24 hr. The total amount of glucose infused corresponded to that amount previously determined in each patient to provide a stable weight or slight weight gain. In each patient this amount of nutrients supplied 35 to 45 cal/kg body weight and 1.5 g protein/kg body weight. In period II (days 8 to 14) the same amount of nutrients was given at a stable rate over 12 hr/day with the subject fasting for the other 12 hr. In period III (days 15 to 21) all nutrients remained the same except the caloric source: 60% of total NPC were supplied as glucose and 40% of total NPC were supplied as fat and infused over 12 hr/day.

Two of the subjects were studied during period IV, in which the regimen was the same as period III, except that the infusion time was shortened from 12 to 8 hr to determine whether substitution of fat could permit the patient to tolerate this short an infusion period and still maintain nitrogen balance.

During the study periods and the preceding 3 days, the

1 From the Department of Medicine, University of Washington, Seattle, Washington 98195.
2 Supported by National Institutes of Health Grant AM-16849. (A portion of this work was conducted through the Clinical Research Center facilities of the University of Washington, National Institutes of Health Grant 8M01 RR.37.)
subjects were allowed ad libitum oral intake of water and unsweetened beverages, except for the days of blood collection, in which they were allowed only water. There were no restrictions on patient activity, and all were encouraged to participate in physical therapy even when on infusion.

Procedures

All nutrients except Intralipid were prepared daily in the hospital pharmacy and infused through an indwelling central venous feeding catheter (2) with the rate controlled by a peristaltic pump (Fig. 1). Intralipid was infused through separate tubing and pump, but into the same catheter. The connection between infusion tubing occurred immediately proximal to the indwelling catheter. At the end of the intermittent infusions the catheter was filled with 1 to 1.5 ml of heparin, 1,000 U/ml, and capped. It is estimated that approximately 0.75 ml of heparin was given intravenously at the end of each intermittent infusion, since the volume required to fill the catheter is approximately 0.75 ml.

Statistics

Statistical evaluation was by paired differences, Student's t test, with a P value of <0.05 being considered significant.

Results

Nitrogen balance

The average daily nitrogen balance results are presented in Table 1. The nitrogen retention in period I (continuous infusion of nutrients over 24 hr/day) was greater than that attained in period II, III, or IV. No difference was seen among periods II, III, and IV. There was no significant difference among the values of the following parameters measured at the end of each period: body weight, serum electrolytes, acid-base status, alkaline phosphatase, serum glutamic oxaloacetic and pyruvic transaminases, total bilirubin, blood urea nitrogen, creatinine, prothrombin time, fibrinogen level, complete blood count and platelet count, reticulocyte count, total protein, albumin, or transferrin levels. Weight remained stable, and the laboratory values were within the normal range throughout the study except for the presence of an elevated alkaline phosphatase in subject 3 before and during his second study.

Plasma lipid values

The fasting plasma levels of cholesterol, triglyceride, and the 20:3/20:4 fatty acid ratio are shown in Table 2. The fasting cholesterol level was significantly higher (P < 0.01) during those periods in which Intralipid supplied 40% of the total NPC, whereas the triglyceride level was significantly elevated (P < 0.01) during the periods in which glucose served as the sole source of NPC. As expected, an abnormal 20:3/20:4 fatty acid ratio present during a regimen devoid of fat was corrected after 7 to 14 days of intravenous fat.

Discussion

In an attempt to develop a home parenteral nutrition regimen that would interfere the least with the lifestyle of a patient requiring total parenteral nutrition, Intralipid was substituted for 40% of the total NPC. In this preliminary report, it appears that the use of Intralipid in such a manner enabled patients to infused in as short a period as 8 hr their total daily nutritional requirements without significant interference with nitrogen balance or many other major determinants of good health and nutrition (weight, laboratory values, etc.). As can be seen in Table 1, there was no significant difference in the nitrogen balance during period III versus period IV. It is anticipated that such a program will allow patients greater freedom from the nutrient infusion apparatus and encourage them to become fully rehabilitated, including more time available for full-time employment, as well as serial and recreational activities.

This study documents the fact that a continuous infusion of a given amount of calories
TABLE 1
Results of nitrogen balance (g/day) with IV intake of 85 g protein and 2,000 nonprotein calories

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>I (100% glucose, 24-hr infusion)</th>
<th>II (100% glucose, 12-hr infusion)</th>
<th>III (60% glucose, 40% fat, 12-hr infusion)</th>
<th>IV (60% glucose, 40% fat, 8-hr infusion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.9</td>
<td>1.0</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td>2</td>
<td>2.1</td>
<td>0.6</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>3</td>
<td>2.3</td>
<td>1.1</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.8 ± 1.0</td>
<td>0.9 ± 0.3</td>
<td>1.2 ± 0.9</td>
<td>0.8 ± 1.0</td>
</tr>
</tbody>
</table>

* N.S., not significant.

TABLE 2
Plasma lipids during parenteral nutrition

<table>
<thead>
<tr>
<th>Plasma lipids</th>
<th>Glucose 100% Fat 0%</th>
<th>Glucose 60% Fat 40%</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>156 ± 15</td>
<td>315 ± 100</td>
<td>120-260</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>164 ± 20</td>
<td>74 ± 30</td>
<td>60-135</td>
</tr>
<tr>
<td>20:3/20:4</td>
<td>1.14</td>
<td>0.15</td>
<td>&lt;0.4</td>
</tr>
</tbody>
</table>

and protein is more effective as far as nitrogen retention is concerned than if it is infused over a shorter time per 24 hr (Table 1). The reason for this difference is not clear. Perhaps it occurs as a result of a constant stimulation of insulin secretion and an enhanced degree of anabolism during the continuous infusion state. However, all speculation must be tempered by the fact that although the differences in nitrogen balance are statistically significant, they may not be caused only by the timing of the infusion. It is likely that the patients were not as active physically when on continuous infusion and hooked to the infusion apparatus as when they were on infusion 12 hr and off 12 hr/day. A greater expenditure of calories when on intermittent infusion also may explain the difference in nitrogen balance. A more definite answer awaits a study designed to control more variables than the ones described in this paper.

The long-term use of Intralipid for home parenteral nutrition should allow greater patient rehabilitation. However, it may pose a hazard to the patient’s well-being. The significantly elevated fasting cholesterol level with this type of therapy is disturbing and might place patients so treated at an increased risk of atherosclerotic disease (Table 2). However, the use of glucose alone also may favor progressive atherosclerosis since it produces a state of sustained elevation of fasting triglyceride levels. Perhaps an optimal ratio of glucose to fat calories can be found that will minimize the elevation of both cholesterol and triglyceride.

The authors are indebted to Dr. Michael Wells of the University of Arizona Medical Center, Tucson, Arizona, for measurement of plasma fatty acid levels.

References