Assessment of Nutritional Proteins During the Parenteral Nutrition of Cancer Patients

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ABSTRACT

Albumin, prealbumin, retinol-binding protein, and transferrin were all measured on the sera of 39 cancer patients before and during parenteral nutrition (PN). At the outset of PN, the concentrations of all of these proteins were low, as compared to reference values, and thus quantitatively reflected the degree of malnutrition. Prealbumin proved to be the most interesting parameter during PN: (1) during an initial period it rapidly reflects the nutritional input, and (2) after two weeks of PN it allows differentiation of patients whose prealbumin level rises regularly during PN and will survive from those patients whose prealbumin level drops after the initial period and will die during or within the month following PN. Prealbumin thus offers a means for biochemical monitoring of PN as well as having a prognostic value.

Introduction

Assessment of the nutritional status of cancer patients is essential, yet objective evaluation remains difficult despite various suggested procedures: anthropometric measurements, definition of corporal zones, immunological and biochemical tests. Following the work of Schwartz, Copeland, and Solassol, parenteral nutrition (PN) has proven effective for the treatment of cancer patients. Of the various biochemical nutritional parameters, the carrier proteins (albumin, prealbumin, transferrin, and retinol-binding protein) appear of interest for the evaluation of nutritional status. The purpose of this study was measurement of these proteins in cancer patients undergoing PN in order: (1) to evaluate the respective sensitivity of these proteins as concerns the malnutrition of cancer patients; (2) to analyze their variations during PN; and (3) to define the parameter(s) with the best prognostic value.

Materials and Methods

Patients

Thirty-nine patients (22 men, 17 women) aged 22 to 81 years (mean 64.6) and hospitalized for treatment of cancer or cancer-related complications underwent PN. Two patient groups were defined: group G1 (22 patients who lived at least one month after PN or within the month after PN had been stopped) and group G2
TABLE I

Distribution of Cancer Patients in Groups G1 and G2 by Sex, Age, Weight Loss, Liver Involvement and Duration of PN

<table>
<thead>
<tr>
<th></th>
<th>Group G1</th>
<th></th>
<th>Group G2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total: 22</td>
<td>Males (10)</td>
<td>Females (12)</td>
<td>Total: 17</td>
</tr>
<tr>
<td>Age mean ± SD</td>
<td>67.4 ± 9.8</td>
<td>66.9 ± 11.7</td>
<td>69.2 ± 8.6</td>
<td>61.5 ± 14.5</td>
</tr>
<tr>
<td>Weight loss &gt; 10 percent</td>
<td>11</td>
<td>5</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Liver metastasis (n°)</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Duration of PN days mean ± SD</td>
<td>24.3 ± 12.6</td>
<td>27.7 ± 16.3</td>
<td>21.5 ± 8.6</td>
<td>29.1 ± 21.2</td>
</tr>
</tbody>
</table>

PN = Parenteral nutrition

(17 patients who died during PN or within the month after PN had been stopped). Each of these groups is defined in tables I and II and indicates the treatments applied during the course of PN. Ten patients had no anti-cancer treatment.

The indications for use of PN were as follows: (1) weight loss and difficulty in eating (anorexia, vomiting, digestive stenosis), (2) preparation for abdominal surgery, (3) optimization of the patient’s condition for radiotherapy and/or chemotherapy, and (4) treatment of a complication (fistula, radiation-induced colitis).

PN was carried out by insertion of a catheter into a deep vein. Commercial perfusion solutions were employed: 10 to 30 percent glucose serum; nitrogen solution containing 25 g of nitrogen per liter; lipid emulsion; oligoelements (solution containing 0.018 mmol Fe, 0.007 mmol Cu, 0.18 mmol Mg, 0.044 mmol Zn, 0.076 mmol fluoride, 0.025 μmol Co, and 0.012 μmol iodine for 40 ml); electrolytes (Na, K, Ca); and the vitamins listed in table III. Inputs were adapted to the patient’s clinical state; the general supply was 200 calories per gram of nitrogen. Caloric supplies were an average of 40.04 Kcal per kg per day (18.0 to 64.8 Kcal per kg per day) while nitrogen inputs were on the average 0.199 g per kg per day (extremes 0.069 to 0.424 g per kg per day).

TABLE II

Distribution of the Various Cancers and the Main Treatments Practiced During Parenteral Nutrition*

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Group G1</th>
<th></th>
<th>Group G2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total: 22</td>
<td>Surgery RT</td>
<td>Chemotherapy</td>
<td>Other</td>
</tr>
<tr>
<td>21 Digestive</td>
<td>13</td>
<td>6</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8 Head and neck tumors</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2 Ovary</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Hematosarcomas</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Kidney</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Uterus</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Thyroid</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Peritoneum</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Certain patients had associated treatments

RT = radiotherapy patients

* Azonutril 25, R Bellon, France.
† Intralipide kabivitrum, France.
‡ Obtained from Aguettant, France.
TABLE III
Vitamins Supplied During Parenteral Nutrition

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A Retinol</td>
<td>B1 Thiamine</td>
<td>B2 Riboflavin</td>
<td>B6 Pyridoxine</td>
</tr>
<tr>
<td></td>
<td>500 mg/week</td>
<td>200 mg/week</td>
<td>20 mg/week</td>
<td>250 mg/week</td>
</tr>
<tr>
<td></td>
<td>B3 Cyanocobalamin</td>
<td>1 mg/month</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C Ascorbic acid</td>
<td>1 g/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D2 Ergocalciferol</td>
<td>600,000 IU/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D Panthenol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>500 mg/week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>H Biotin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 mg/week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Folic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>100 mg/week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F Nicotinamide</td>
<td>1 g/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PP Phytomenadione</td>
<td>100 mg/week</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

0.340 g per kg per day). The average duration of PN was 26.4 days (9 to 105 days).

BIological METHODS

Blood samples were obtained before or during the first four days of PN and then periodically every week. Sera were stored at −20°C until analyzed. Sera were also obtained from 46 healthy blood donors (26 men, 20 women) aged 41 to 81 years (mean 60.8, similar to that of our cancer patient population) in order to establish precise reference values for each protein.

Albumin was measured automatically. Prealbumin, retinol-binding protein and transferrin were measured by radial immunodiffusion. Reference values obtained from controls are listed in table IV. Data were assessed by statistical analysis of variance and Student’s t-test.

Results

In table V are listed the values for nutritional proteins in controls and cancer patients (groups G1 and G2) before and during PN. All concentrations were significantly lower for our cancer populations than for the controls. Furthermore, these values were clearly lower in G2 than in group G1 (except for retinol-binding protein in group G2) even though the differences were not significant. During refeeding, prealbumin was the only protein that rose; all of the other nutritional parameters dropped. However, variations between the initiation of PN and on-going PN measurements were not significant.

Prealbumin was found to be the best parameter, with the lowest concentrations before PN as compared to the reference values: −41 percent and −52 percent, respectively, for group G1 and group G2. Repeat prealbumin measurements obtained during PN are presented in figure 1. Following an initial two week period during which prealbumin rose in both groups, levels continued to rise slightly in group G1 patients, i.e., survivors, before stabilizing after the third week, whereas in group G2 patients, the concentrations dropped. Comparison of the mean prealbumin value for each group before and after the 15th day of PN reveals a positive variation in group G1 and a negative one in group G2. The distributions of these variations are significantly different (figure 2).

Discussion

This study confirmed the value of measuring carrier proteins such as albumin (Alb), prealbumin (Palb), transferrin (Tf), and retinol-binding protein (RBP) when dealing with malnourished cancer patients. All of these biological parameters were considerably lower in these patients.
NUTRITIONAL PROTEINS IN CANCER

TABLE V

Nutritional Proteins in Controls and Cancer Patients Before and During Parenteral Nutrition (PN)

<table>
<thead>
<tr>
<th>Albumin g/l</th>
<th>Prealbumin g/l</th>
<th>Transferrin g/l</th>
<th>RBP mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>34.8 ± 2.19</td>
<td>0.280 ± 0.40</td>
<td>3.24 ± 0.42</td>
</tr>
<tr>
<td>Cancer patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before PN</td>
<td>26.7 ± 6.53</td>
<td>0.190 ± 0.086</td>
<td>2.08 ± 0.63</td>
</tr>
<tr>
<td></td>
<td>(-24)</td>
<td>(-41)</td>
<td>(-36)</td>
</tr>
<tr>
<td>G1</td>
<td>25.62T ± 5.08</td>
<td>0.190 ± 0.072</td>
<td>1.99 ± 0.57</td>
</tr>
<tr>
<td></td>
<td>(-26)</td>
<td>(-29)</td>
<td>(-39)</td>
</tr>
<tr>
<td>During PN</td>
<td>22.71 ± 2.05</td>
<td>0.134 ± 0.065</td>
<td>1.92 ± 0.52</td>
</tr>
<tr>
<td></td>
<td>(-35)</td>
<td>(-52)</td>
<td>(-41)</td>
</tr>
<tr>
<td>G2</td>
<td>22.19 ± 3.48</td>
<td>0.171 ± 0.060</td>
<td>1.70 ± 0.46</td>
</tr>
<tr>
<td></td>
<td>(-36)</td>
<td>(-39)</td>
<td>(-48)</td>
</tr>
</tbody>
</table>

Tp < 0.05 with respect to controls

\*p < 0.05 with respect to controls

RBP = Retinol-binding protein

Nutritional protein values in controls and cancer patients at the beginning and during PN. Before = value obtained three days before starting PN or during the first four days of PN; During = mean value after the seventh day of PN. Figures in parentheses give the percentage with respect to the mean value for the control population.

than in healthy controls, and they thus quantitatively reflect the state of malnutrition. These findings concur with the conclusions of other authors.9,10

Numerous investigators have attempted to determine the prognostic value of such parameters.3,4,6,7,13,14 In our case, prealbumin turned out to be the most valuable protein: (1) it was the most sensitive nutritional parameter even though it had no prognostic value when measured at the beginning of refeeding; (2) it rapidly reflects the nutritional input during PN and thus allows surveillance of the response to nutrition; this concurs with the findings of Shetty18; and (3) the fact that prealbumin levels continue to rise in patients who survive (group G1) but show a secondary drop for G2 patients gives this protein a prognostic value, as previously reported by Milano and Coll13 in connection with colorectal cancers. This drop in prealbumin after two weeks of PN appears to be the negative indication of a fatal outcome at short term. This observation concurs with that of Eriksson for transferrin.6

The value of prealbumin measurements probably results from this protein’s physico-chemical properties: a high trypto-

![Figure 1](image-url)
phan content and a short half-life (two days)\textsuperscript{9,15,19} which allows rapid variations. It is also interesting to note that group G2 patients required the highest energy and nitrogen inputs: 45.9 cal per kg per day and 23.6 gN per day versus only 36.8 cal per kg per day and 18.7 gN per day for group G1. This finding emphasizes the limits of PN for cancer patients, since the greatest nutritional support was required for patients who did not survive. This situation differs from that generally observed for surgical patients or those in intensive care units\textsuperscript{12} and, thus, reinforces the interest of using biochemical criteria to evaluate PN for cancer patients.

References