Nitrogen balance in obese patients receiving a very low calorie liquid formula diet¹

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ABSTRACT

Eleven obese patients were placed on a liquid formula diet containing 320 kcal (1.34 MJ), 31 g protein, 44 g oligosaccharides, 1.5 g fat, vitamins, and essential minerals for a period of 4 weeks under metabolic ward conditions. The diet was well tolerated, and mean weight loss was 2.49 kg/week during the 4-week period. Nitrogen excretion diminished in all patients during the period of treatment, but nitrogen balance remained slightly negative in most patients, mean daily deficit being 1.3 g N/day at the end of the study. The rate at which nitrogen was lost declined in a biphasic fashion, a slower second phase after an initial rapid period of adjustment to the diet. During the study a mean of 4.1 ± 1.4% SD of calculated total body nitrogen was lost. Potassium excretion studies did not reveal significant potassium losses. The amount of nitrogen lost was correlated with the urinary creatinine excretion, suggesting that nitrogen loss during reduced dietary intake of protein is largely dependent on the size of the lean body mass. Am. J. Clin. Nutr. 32: 1612-1616, 1979.

The management of the overweight patient is often a difficult and frustrating task for the physician. Diet, drugs, behavioral therapy, and surgery have all been advocated but are frequently associated either with poor results or serious side effects. Reduction of caloric intake, however, remains the cornerstone of the rational treatment of obesity. In its most extreme form—total starvation—rapid weight loss may be achieved (1), but this is not without danger if continued for long periods. Fatal lactic acidosis in a diabetic (2), fatal volvulus (3), and cardiac deaths have been reported (4-6). Recently Baird et al. (7) and Howard and Baird (8) have suggested that a diet containing small amounts of protein and carbohydrates, with minerals and vitamins may prevent the serious complications of total fasting while allowing a similar rate of weight loss. In this investigation we studied the effects of their diet on obese patients who were admitted to a metabolic ward. The main aim of the study was to determine the efficacy, acceptability to the patient and safety (as judged by its effects on nitrogen and electrolyte balance) of such a diet.

Patients and methods

Eleven patients were admitted to the metabolic ward for a period of 32 days. All patients were more than 40% above mean desirable body weight for sex and height according to Metropolitan Life Insurance tables (Table 1). During the first 4 days of the admission the patients received a diet isocaloric to their home ambulatory intake. Blood was taken for hematological, electrolyte, urea, creatinine, uric acid, lipid and enzyme determinations at the beginning and the end of the study. Thyroid hormone levels were also measured together with serum uric acid at weekly intervals as part of an ongoing study of the effects of obesity and weight reduction on thyroid function (9). On the 5th day the patients were given carmine red as a fecal marker and started on a liquid formula diet containing 320 kcal (1.34 MJ) as 31 g milk proteins, 44 g oligosaccharides, 1.5 g fat to supply essential fatty acids, vitamins and minerals (including 71 mmole sodium and 57 mmole potassium). The patients were given the diet in three equal portions, the dried powder being made up to approximately 200 ml with water immediately before drinking. The patients were allowed free access to black coffee and tea and diet lemonade containing 1 kcal per drink. The mean daily potassium intake in coffee and tea was 10 mmole potassium. Physical activities were not restricted during the study and all patients participated in a daily period of supervised physical exercise during 60 min/day. Their activities were kept constant during the course of the study.

Urine was collected in 24-hr periods and preserved with 10 ml glacial acetic per volume and stored at -20

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NITROGEN BALANCE IN OBESE PATIENTS

TABLE I
Patients investigated under metabolic ward conditions—body weight, total body nitrogen calculated from the daily creatinine excretion, and percentage of total body nitrogen lost while on the diet

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Height</th>
<th>Weight</th>
<th>Calcd total body % N</th>
<th>% N lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>F</td>
<td>43</td>
<td>158</td>
<td>99.8</td>
<td>1809 g</td>
<td>4.4</td>
</tr>
<tr>
<td>JT</td>
<td>M</td>
<td>32</td>
<td>174</td>
<td>110.0</td>
<td>2605</td>
<td>6.8</td>
</tr>
<tr>
<td>H</td>
<td>F</td>
<td>40</td>
<td>169</td>
<td>106.9</td>
<td>1685</td>
<td>5.8</td>
</tr>
<tr>
<td>Bo</td>
<td>F</td>
<td>47</td>
<td>158</td>
<td>83.7</td>
<td>1702</td>
<td>4.0</td>
</tr>
<tr>
<td>Be</td>
<td>F</td>
<td>53</td>
<td>177.5</td>
<td>137.6</td>
<td>918</td>
<td>5.2</td>
</tr>
<tr>
<td>DU</td>
<td>F</td>
<td>62</td>
<td>153</td>
<td>105.8</td>
<td>1654</td>
<td>2.0</td>
</tr>
<tr>
<td>P</td>
<td>F</td>
<td>48</td>
<td>169</td>
<td>89.3</td>
<td>1761</td>
<td>3.6</td>
</tr>
<tr>
<td>K</td>
<td>F</td>
<td>42</td>
<td>171</td>
<td>87.5</td>
<td>1461</td>
<td>2.7</td>
</tr>
<tr>
<td>MT</td>
<td>F</td>
<td>17</td>
<td>159</td>
<td>87.6</td>
<td>1984</td>
<td>3.7</td>
</tr>
<tr>
<td>Br</td>
<td>F</td>
<td>25</td>
<td>167</td>
<td>98.3</td>
<td>1955</td>
<td>3.7</td>
</tr>
<tr>
<td>D</td>
<td>F</td>
<td>52</td>
<td>169</td>
<td>103.3</td>
<td>1784</td>
<td>4.1</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>42</td>
<td>166</td>
<td></td>
<td>1784</td>
<td>4.1</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td>13</td>
<td>7</td>
<td></td>
<td>416</td>
<td>1.4</td>
</tr>
</tbody>
</table>

C until the end of the study. Feces were collected in paint cans and stored at −20 C until the measurements were made. Body weight, temperature, pulse rate, and blood pressure were recorded daily. Fecal and urinary nitrogen were measured by a modified Kjeldahl method. Serum and urinary electrolytes, urea, creatinine, uric acid, serum cholesterol, triglycerides and enzymes (alkaline phosphatase, SGOT, and SGPT) were measured by routine automated techniques.

Calculations
Total body nitrogen at the start of the diet was derived from the urinary creatinine excretion using the equation of Forbes and Bruining (10), lean body mass (kg) = 7.38 + 0.02908 creatinine (mg/24 hr). One kilogram lean body mass was considered to contain 40 g nitrogen (1). The urinary creatinine excretion rates used in the calculation were taken during the 2nd week, to exclude the effects of dietary creatine and creatinine (11). Total net nitrogen loss during the course of the dietary period was measured and expressed as a percentage of body nitrogen (Table 1). Integumental nitrogen and potassium losses were not taken into consideration in the calculation. The rate of nitrogen excretion was found to diminish in a biexponential fashion (Fig. 1). An indication of the time it would take to reach nitrogen balance was derived graphically by extrapolating the nitrogen excretion curve to an excretion rate of 5 g N/day (the amount present in the diet).

Results

Acceptability
The patients tolerated the diet well, with mild complaints of tiredness after moderate physical exercise, some cold intolerance, a tendency to sleep longer and constipation. Sensations of hunger disappeared in most patients within 2 to 3 days of starting the diet.

Effectiveness
Mean weight loss was 2.49 kg/week during the 4-week period (Fig. 2). This rate is slightly higher than that found by Howard and Baird (8) and by us in a preliminary outpatient study (9).

Metabolic effects
Hemoglobin levels, hematocrit, leucocyte count, serum sodium, potassium, chloride, calcium, magnesium, phosphate, urea, creatinine, and enzyme levels did not change significantly between the beginning and end of the admission. Serum cholesterol dropped from 6.6 ± 1.5 μmole/liter (mean ± SD) to 5.1 ± 1.3 μmole/liter (P < 0.005), whereas serum triglyceride levels did not change significantly for the group. Serum uric acid levels rose at the start of the diet but tended to fall towards the end. This was associated with a reduction in urinary uric acid excretion. Arterial pH and bicarbonate were measured during the course of the diet in six patients and were found to remain normal, suggesting that ketosis was mild. Nitrogen excretion (Fig. 2) diminished in all patients during the course of treatment, but the nitrogen balance remained negative in most patients, mean daily nitrogen deficit being 1.3 g/day during the last week of the trial. The total amount of nitrogen excreted during the 4th week did not correlate with the amount of weight lost during this period, nor with the initial body weight of the patient, nor with
Examination of the pattern of excretion of nitrogen revealed in all patients a biphasic curve in the adjustment to the reduced nitrogen intake, an initial rapid loss phase being followed by a slower rate of change (Fig. 1). Extrapolation of the slow phase suggests that if the patients continued to diminish nitrogen excretion in this fashion they would take...
between 18 and 68 days to achieve nitrogen equilibrium. During the course of the 4 weeks the patients were calculated to have lost 4.1 ± 1.4% of their total body nitrogen.

Daily potassium losses fluctuated in all patients, but apart from slight excess losses during the first week of the trial, potassium excretion approximated intake (Fig. 1). The slightly positive balance found does not take potassium losses through perspiration into account.

Discussion

This study confirms the patient acceptability of very low calorie liquid formula diets in the management of obesity. All patients commented favorably on the simplicity of preparation and the lack of hunger while on the diet. Its efficacy, at least on a short-term basis, could also be confirmed (7–9). Side effects were mild and nonspecific, being seen in patients treated with other forms of caloric restriction. Regarding the safety of such a preparation, acidosis was not observed and potassium losses were minor. Nitrogen balance remained negative to a varying degree in most patients. The discrepancy between our findings and the initial reports of nitrogen balance being achieved in patients using this diet (7, 8) is possibly partly due to the failure of these authors to take fecal and integumental nitrogen excretion into account. A more important explanation, however, lies in the fact that their patients were studied after their patients were studied after

intake and would vary during the course of the study (14). Our conservative estimate of nitrogen loss showed that a mean of 4.1% of estimated total body nitrogen was lost during 4 weeks of the study. This mean value of 73 g nitrogen, although considerable, is markedly lower than the estimated 200 g lost during a similar period of total fasting (15). It may, however, be higher than that shown by patients receiving 1.2 to 1.4 g protein per kilogram ideal body weight in the form of a so-called protein-sparing modified fast (16). Nitrogen excretion was found to correlate with creatinine excretion. As creatinine excretion in the presence of normal renal function is mainly dependent on lean body mass (10) this finding suggests that the rate of adjustment to this diet will depend on the size of the lean body mass. The safety of drastic weight reduction schemes such as protein diets (17, 18) has recently been questioned (19). Although nitrogen loss cannot be excluded as a contributing factor to the sudden deaths seen during treatment with liquid protein collagen hydrolysate diets, a more likely candidate is potassium depletion (20). The absence of significant potassium loss seen with this diet suggests that it might be a safer alternative than total fasting or liquid protein diets. At present we consider that such diets should only be used under strict medical supervision.

The diets used in this study were kindly supplied by Dr. R. W. de Bruin, Organon, Oss, The Netherlands. This study would not have been possible without the efficient participation of the staff of the metabolic ward and the cooperation of the patients studied.

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