METABOLIC EFFECTS OF CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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Summary

Prospective studies concerning protein, carbohydrate, and lipid metabolism were performed in 10 CAPD patients. After 2–4 months on CAPD the mean nitrogen balance was positive (3.14 ± 1.98g N/day) and was correlated with protein and energy intake as well as with the increase in body weight. Plasma free amino acid concentrations were normal, but the tyrosine/phenylalanine ratio was decreased compared with healthy subjects. In spite of the excessive glucose load, there was no further deterioration in glucose tolerance. Serum concentrations of TG and CHOL were increased due to a rise of VLDL-TG and VLDL-CHOL.

Introduction

Since the technique of continuous ambulatory peritoneal dialysis (CAPD) was proposed for the treatment of chronic renal failure by Popovich and co-workers in 1976 [1], an increasing number of patients are being treated with this method. There are several reports of good clinical results [2–4], but little is known about potentially harmful, or beneficial metabolic effects in long-term treatment with CAPD. We here report the first results of a prospective study on protein, lipid and carbohydrate metabolism in patients treated with CAPD.

Material and Methods

Since December 1978, 28 patients (28–71 years) with glomerular filtration rate < 5ml/min have been treated with CAPD for a total of 208 patient months. On May 31, 1980, 22 patients were still treated with CAPD, performed according to the technique introduced by Oreopoulos [5], using four exchanges of 2L dialysate (Dianeal©) per day. The patients were encouraged to consume a diet providing at least 1.2g of protein/kg body weight (BW) per day and with an energy content of at least 145kJ/kg BW per day.

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Metabolic studies were performed in selected patients before CAPD; when the patients had been treated with IPD for more than 10 days. The studies were repeated after 2–4 months.

Results

_Nitrogen balance_

Nitrogen balance studies were performed in 10 patients (age 28–62, 52.9 ± 11.3, mean ± SD; BW 58–81 kg, 66.1 ± 7.5) after 2–4 months' treatment with CAPD. The patients were admitted to the renal ward, and were provided with an individual balance diet, strictly defined with regard to nitrogen and energy content. The

![Graph showing nitrogen intake, nitrogen losses, and the nitrogen balance in 10 patients after treatment with CAPD for 2–4 months (mean ± SD)](image)

Figure 1. Nitrogen intake, nitrogen losses and the nitrogen balance in 10 patients after treatment with CAPD for 2–4 months (mean ± SD)
diet was composed so as to correspond to the normal dietary habits of the patients, as assessed by our dietician. Nitrogen losses were directly determined in dialysate, urine, and stools. After an adaptation period of 3–7 days on the diet, nitrogen balance was calculated for the next seven days.

The protein intake varied between 0.76 and 2.07g/kg body weight per day, and the total energy intake (including uptake of glucose from the dialysate) was 120−222kJ/kg BW per day. The nitrogen balance was 17.3−122.4mg nitrogen/kg BW per day, corresponding to a nitrogen balance of 3.14 ± 1.98g N per day (mean ± SD) (Figure 1). Hence the nitrogen balance was positive in all patients, even when extra-renal and extra-ileal losses were taken into consideration. A positive correlation was found between the nitrogen balance (mg N·kg⁻¹·day⁻¹) and the protein intake (g·kg⁻¹· day⁻¹) as well as the total energy intake (kJ·kg⁻¹· day⁻¹) (y = −44.2 + 67.4x; r = 0.80, and y = −78.2 + 0.75x; r = 0.63, respectively). A positive correlation was also found between the per cent change in BW (Δ%/month) over two months and nitrogen balance (gN/day) (y = 0.61 + 0.33x; r = 0.72).

**Plasma free amino acids**

Plasma free amino acids were determined in six patients after an overnight fast. In contrast with untreated uraemic patients and patients treated with IPD [6, 7] and HD [8], the CAPD patients had normal concentrations of all amino acids and the ratios glycine/valine and essential amino acids/non-essential amino acids were normal. However, the ratio tyrosine/phenylalanine was lower in CAPD patients (0.93) than in healthy subjects (1.03; p < 0.01), although less reduced than in untreated uraemic patients and patients on IPD.

**Carbohydrate metabolism**

In 10 patients, undergoing N-balance studies, the uptake of glucose from the dialysate was 56.4−81.9% (71.6 ± 8.2) of the total amount of glucose in dialysate. The uptake was 77.8−254.0g glucose/day (126 ± 53.0).

Oral glucose tolerance tests with determinations of serum insulin and glucagon were performed in nine patients before start of CAPD and after 2–4 months’ treatment (Figure 2). The results do not indicate any impairment in glucose tolerance and the insulin and the glucagon response remained essentially unchanged.

**Lipid metabolism**

TG and CHOL in serum and in VLDL-, LDL-, and HDL-lipoprotein fractions were determined in 12 patients before and after 2–4 months’ treatment with CAPD. The patients were in the fasting state and the dialysate had been drained 10 hours before sampling. After 2–4 months treatment with CAPD the concentrations of TG and CHOL were increased due to a rise in VLDL-TG and VLDL-CHOL (Table I). No impressive fall in HDL-CHOL was observed.
Figure 2. Oral glucose tolerance test; 1g glucose/kg BW (OGTT) and determination of serum immunoreactive insulin (S-IRI) and immunoreactive serum glucagon in nine patients before (OGTT 1) and after (OGTT 2) 2—4 months' treatment with CAPD. The patients were in fasting state and dialysate had been drained 10 hours before sampling.
TABLE I. Cholesterol and triglyceride concentrations (mmol/L) in serum and in lipoprotein fractions in healthy subjects, in patients before CAPD (treated with IPD for 1–2 weeks), and in patients after 2–4 months'CAPD treatment (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Serum</th>
<th>VLDL</th>
<th>LDL</th>
<th>HDL</th>
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<tr>
<td></td>
<td></td>
<td>CHOL</td>
<td>TG</td>
<td>CHOL</td>
<td>TG</td>
</tr>
<tr>
<td>Healthy</td>
<td>61</td>
<td>6.47 ± 1.19</td>
<td>1.76 ± 0.64</td>
<td>0.50 ± 0.31</td>
<td>0.95 ± 0.52</td>
</tr>
<tr>
<td>Uraemia</td>
<td>12</td>
<td>6.23 ± 1.39</td>
<td>2.13 ± 1.05</td>
<td>0.89 ± 0.60*</td>
<td>1.23 ± 0.92</td>
</tr>
<tr>
<td>before CAPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uraemia</td>
<td>12</td>
<td>7.42 ± 1.48*◊</td>
<td>3.29 ± 1.75‡◊</td>
<td>1.56 ± 0.97‡◊</td>
<td>2.20 ± 1.47‡◊</td>
</tr>
<tr>
<td>after CAPD</td>
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</tbody>
</table>

Significance of difference compared with healthy subjects:  
* p < 0.05  
† p < 0.01  
‡ p < 0.001

Significance of difference compared with results before CAPD:  
◊ p < 0.05 (Student's paired t-test)
Middle molecules were determined in plasma in 14 patients after 2–4 months' treatment with CAPD by using an automatic middle molecule analyser [9, 10]. The plasma concentration of peak 7c was found to be significantly lower than in conservatively treated patients (p < 0.001) or in IPD-patients (p < 0.001).

Comments

The finding that CAPD results in positive N-balance is in agreement with a recent study by Giordano and co-workers, who observed positive N-balance in eight patients on a diet providing 1.2g protein/kg BW [11]. In our study positive N-balance was also observed in two patients with considerably lower protein intake (0.8g protein/kg BW per day).

A positive correlation was found between N-balance and protein intake as well as between N-balance and the total energy intake, thus, emphasising the important role of adequate nutrition for improvement of the metabolic status of these patients. A positive correlation was also found between changes in body weight and N-balance. This indicates that the retention of nitrogen was associated with an increase in lean body mass with build-up of body protein, as suggested by other investigators [12].

It has been observed that patients on IPD have pathological plasma free amino acid concentrations [6, 7, 13]. The fact that CAPD patients after 2–4 months' treatment had essentially normal plasma amino acid concentrations supports the conclusion that their nutritional status had improved.

Exhaustion of the pancreatic β-cells, due to uptake of considerable amounts of glucose from the dialysate, is a potential hazard in CAPD. We did not see any deterioration of glucose tolerance or hormonal response to glucose after CAPD; however, our time of observation was short and it cannot be ruled out that long-term CAPD treatment may be deleterious in this respect.

Hyperlipidaemia, or more specifically hyperlipoproteinaemia, is a common finding in patients suffering from chronic renal insufficiency [14]. Recent studies have shown that more than 50% of patients with long standing uraemia have elevated serum TG levels. Studies of isolated serum lipoproteins in uraemia have revealed a pathological increase of the VLDL-fraction (mainly a rise in TG), high levels of LDL-TG, and low concentrations of HDL-CHOL [15].

Administration of high amounts of carbohydrates to healthy subjects usually results in elevated VLDL-TG and low HDL-CHOL [16–18]. Thus, CAPD may induce similar or even more extreme disturbances in lipid metabolism than those previously observed in uraemic patients [15]. Our preliminary results indicate that CAPD interferes with lipid metabolism after 2–4 months' treatment and induces changes in lipoprotein composition considered to be atherogenic [19–21]. It should, however, be pointed out that we did not observe the fall in HDL-CHOL reported by other investigators [22].

The remarkably good clinical results with CAPD regarding control of uraemic symptoms, weight gain, improvement in haemoglobin concentration [22] and well-being are in favour of the middle molecule hypothesis, since CAPD is more
efficient than IPD or HD for removing middle molecules. Follow-up studies are now being performed to elucidate which metabolic risk-factors are of clinical importance over longer periods of treatment.

Acknowledgments

This work has been supported by grants from the Swedish Medical Research Council (projects numbers B80-19X-1002-15C and B80-17X-4210-07), Stockholm, Sweden, and Travenol International Services Inc, Brussels, Belgium. Dr Lindholm has been granted a research fellowship by the Stockholms Läns Landsting and the Förenade Livs, Stockholm.

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Open Discussion

BUCHT (Gothenburg) In the abstract you have written that there is a slight increase in the total body potassium. You said nothing of the kind in your lecture. How do you measure total body potassium in your material and what are your actual figures for potassium?

LINDHOLM We found that the total body potassium measured by total body counter, using $^{40}\text{K}$ was initially slightly increased, but when a greater number of patients had been investigated we found no significant change in total body potassium.

LEGRAIN (Paris) Could you comment a little more about how you measure your stool nitrogens.

LINDHOLM We collect all stools for each day and then it is analysed by the Kjeldahl technique.

LEGRAIN Increased intestinal nitrogen output in patients on CAPD has recently been reported by Blumenkrantz et al.

LINDHOLM We found that the mean nitrogen losses in the stools of these patients were 1.48g nitrogen per day.

DORHOUT-MEES (Utrecht) What is the basis for your last conclusion that the nitrogen balance was better for CAPD than in haemodialysis. Did you compare these with a comparable group of haemodialysis patients?

LINDHOLM In this study we did not compare nitrogen balance in haemodialysis patients.

DORHOUT-MEES How did you know then?

LINDHOLM We have had no opportunity to measure the nitrogen balance before and after CAPD. However, we consider it as a fact that patients on haemodialysis often exhibit a negative nitrogen balance when the protein intake is less than 1g protein per kg per day. Two of the patients studied had a protein intake of less than 0.8g protein/kg/day.

However I would again like to point out that we do not state that nitrogen balance was better in these patients compared with haemodialysis patients.