Plasma insulin and glucose levels in diabetic patients undergoing continuous ambulatory peritoneal dialysis using insulin only in the dialysate[1]

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Eight diabetics undergoing continuous ambulatory peritoneal dialysis were followed for 18 months. The best control of hyperglycemia was achieved with insulin only in the dialysate. To study the plasma glucose levels and the absorption of insulin, blood was drawn every two hours from 8:00 AM until midnight and the next morning at 8:00 AM in 4 patients. Plasma glucose, total insulin, free insulin, and insulin antibody levels were measured. The hemoglobin A_1C levels were obtained in all but patient 4. Although the total insulin levels were erratic, the free insulin levels appeared consistent throughout the 24-hour period.

Index terms: Hyperglycemia, drug therapy • Insulin, administration and dosage

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Because of the enormous costs involved in hospital dialysis, patients with end-stage renal failure are increasingly electing home dialysis. This allows them a considerably better life-style with freedom to pursue normal activities. Consequently, more diabetic patients are placed on continuous ambulatory peritoneal dialysis (CAPD).

Over the last 18 months, we followed 8 diabetics with end-stage renal disease who were undergoing CAPD. Multiple subcutaneous injections of insulin alone and combined with small amounts of insulin in the dialysate resulted in wide swings of plasma glucose levels. As did Flynn and Nanson,[1] we found that the best control of hyperglycemia was achieved with insulin in the dialysate alone, as measured by the finger-stick method with the Stat-tek made

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Table 1. Standard orders for insulin added to dialysate during training

	Blood sugar	Insulin (R)
Exchange 1	>400	30
Dialysate 4.25%	>300	25
	>200	20
	>100	15
	<100	10–15
Exchange 2 and 3	>400	25
Dialysate 4.25%	>300	20
	>200	15
	>100	10–15
	<100	5–10
Exchange 1	>400	20
Dialysate 1.5%	>300	15
	>200	10–15
	>100	5–10
	<100	5–10
Exchange 2 and 3	>400	20
Dialysate 1.5%	>300	15
	>200	10–15
	>100	5–10
	<100	5–10
Exchange 1	>400	25
Dialysate 2.5%	>300	20
	>200	15–20
	>100	10–15
	<100	5–10
Exchange 2 and 3	>400	20–25
Dialysate 2.5%	>300	15–20
	>200	10–15
	>100	5–10
	<100	5–10
Exchange 4	>400	15
Dialysate	>300	10
	>200	5–10
	>100	5–10
	<100	2–5

1. Add one third of the total subcutaneous insulin dose to the first exchange to cover morning hyperglycemia and breakfast.
2. Split the remaining two thirds of the subcutaneous dose and add one-half to the next two exchanges to cover lunch and supper.
3. The insulin added to the last exchange should not include any of the previous subcutaneous insulin dose and should be the smallest amount of insulin added, no matter what the concentration of the dialysate.

before each exchange. Yet, we still did not know what the glucose levels were during the time that the dialysate was dwelling in the patients or what the insulin levels were. We thus selected 4 diabetic patients at random who were coming in for monthly evaluation and determined their glucose and insulin levels throughout the day.

Methods

Patients

Four insulin-dependent diabetic patients (3 men and 1 woman; age range: 32 to 45 years old) with end-stage renal failure undergoing CAPD were chosen at random. They had been undergoing dialysis from two to seven months.

Training

The method of peritoneal dialysis has been described previously.[2] Four exchanges with use of dialysate solutions with dextrose concentrations of 1.5, 2.5, or 4.25 g/2-liter bag were performed each day.

All training is done on an outpatient basis in five to eight days. During the training period, the nurses adjust the insulin dosage according to the standard orders listed in *Table 1*. The plasma glucose levels are based on finger-stick determinations measured on the Stat-tek dextrometer. Insulin dosage varies with the concentration of the dialysate and time of day of the exchange. At the end of the training period, the insulin requirements are reviewed by a physician. After the training period, the patient is expected to check his plasma glucose level by the finger-stick method with a dextrometer before each exchange. There are no carbohydrate restrictions in the diet.

Plasma glucose and insulin determinations

Patients were asked to follow their usual routine of four exchanges. Plasma glucose and insulin levels were determined from peripheral vein blood every two hours from 8:00 AM until midnight and then the next morning at 8:00 AM. Quantitation of free, total, and antibody-bound insulin was done via the method described by Gennaro and Van Norman.[3]

Results

Plasma glucose level

In general, patients had symptomatic hypoglycemia when plasma glucose levels were ≤60, but none was more significantly hypoglycemic clinically than the average diabetic. *Table 2* compares the results of subcutaneous insulin combined with small doses of insulin in the dialysate versus insulin in the dialysate only. Variation in the daily

plasma glucose levels of the patients in the study is shown in *Table 3*. The plasma glucose level in patient 1 varied from 70 to 268 mg (average, 164 mg); in patient 2, from 56 to 303 mg (average, 160 mg); in patient 3, from 85 to 265 mg (average, 155 mg); and in patient 4, from 50 to 200 mg (average, 118 mg). Control of hyperglycemia is indicated by the following glycosylated hemoglobin levels: 8.3% in patient 1, 8.8% in patient 2, and 9.4% in patient 3. The hemoglobin A_1C level was not available for patient 4.

Insulin levels

The insulin antibody levels were 9.9% in patient 1, 37.3% in patient 2, 9.3% in patient 3, and 4% in patient 4. The total and free insulin levels are shown in graphs A through D (*Figure*). The total insulin levels in patient 1 varied from 135 to 227 μU/mL (average, 154 μU/mL); in patient 2, from 529 to 861 μU/mL (average, 648 μU/mL); in patient 3, from 90 to 118 μU/mL (average, 101 μU/mL); and in patient 4, from 137 to 197 μU/ml (average, 174). The free insulin levels in patient 1 varied from 14 to 31 μU/mL (average, 21 μU/mL); in patient 3, from 5 to 9 μU/mL (average, 6 μU/mL); and in patient 4, from 9 to 24 μU/mL (average, 18 μU/ml).

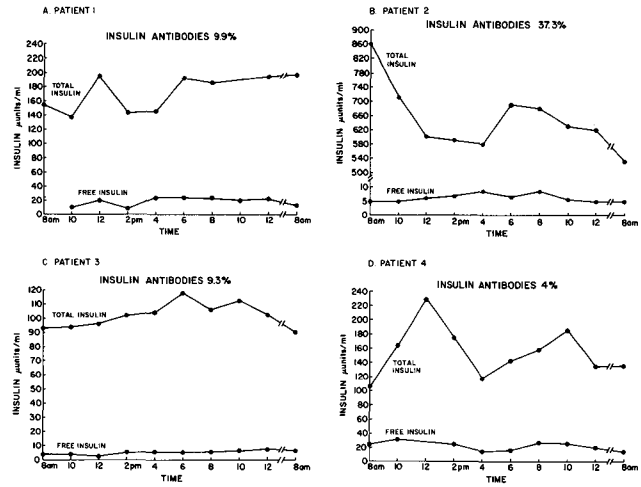

Figure. Total and free insulin levels.

Discussion

The intraperitoneal route of insulin administration has been advocated previously.[4,5] The route of absorption is presumed to be through the portal system into the liver. Flynn and Nanson[1] have referred to this method of insulin delivery as the "artificial pancreas." Our data indicate that we have achieved good clinical control of hyperglycemia in diabetics with end-stage renal disease on CAPD by using insulin in the dialysate only. These patients have had no carbohydrate restrictions and have eaten a relatively unrestricted diet. Variations in diet usually re-

Table 2. Comparison of results of CAPD with subcutaneous insulin and dialysate insulin versus CAPD with dialysate only

	Exchange	Time	% Dialysate instilled	Dialysate insulin (R)	Stat-tek	Subcutaneous insulin
CAPD with subcutaneous insulin and dialysate insulin	1	8 AM	4.25	26	175	32 L, 8 R
	2	1 PM	1.5	26	400+	–
	3	6 PM	4.25	25	200	–
	4	11 PM	1.5	10	175	–
CAPD with dialysate insulin only	1	7 AM	4.25	60	135	–
	2	1 PM	1.5	35	140	–
	3	6 PM	4.25	35	100	–
	4	12 AM	1.5	10	135	–

Table 3. Plasma glucose levels (mg)

Time	8 AM	10 AM	12 AM	2 PM	4 PM	6 PM	8 PM	10 PM	12 PM	8 AM
Patient 1	70	176	208	139	159	124	236	268	284	61
Patient 2	207	219	232	303	135	87	56	88	123	143
Patient 3	85	188	168	265	229	148	130	129	85	130
Patient 4	188	199	179	144	88	68	50	49	64	151

sulted in increases or decreases in insulin. Patient 1 had eaten chocolate ice cream after his third exchange, which explains the elevations in his evening plasma glucose levels. Patients 2 and 3 were adjusting to using a 2.5% solution for the first time.

An advantage of our method is that during the training period, patients are not hospitalized to establish insulin requirements as is done at some other institutions.[6] Our nurses have had no difficulty in adjusting the insulin dose according to the standard orders. By not hospitalizing these patients, we have decreased the cost of the training program. In general, patients who are hospitalized for such a training program spend approximately seven to 10 days in the hospital at a cost of $375 per day.

The degree of insulin antibodies varied widely from one patient to another. Although the total insulin levels were high and probably are the reflection of the insulin bound to antibodies, the free insulin levels were measurable and appeared fairly constant throughout the day. Patient 2, with the highest elevation of insulin antibodies, had had two episodes of diabetic ketoacidosis in the nine months before CAPD, but has had no further episodes after CAPD. The constant delivery of insulin, as seen by the steady level of measurable free insulin, may account for this. After patient 2 had been on CAPD for 20 months, her repeat insulin antibody level had decreased to 6%.

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