PRELIMINARY COMMUNICATIONS

Intraperitoneal Insulin for Control of Blood Sugar in Diabetic Patients during Peritoneal Dialysis

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Summary

We have added insulin to peritoneal dialysis fluid in three uraemic diabetic patients. The hyperglycaemia and pronounced fluctuations in blood glucose which complicate peritoneal dialysis in diabetic subjects have not occurred with this technique. Studies with ^{131}I-labelled insulin showed that less than 5% of the intraperitoneally administered insulin was absorbed during a one-hour exchange. While the physiology of the procedure needs further evaluation, this procedure has reduced the morbidity of peritoneal dialysis in diabetic patients and made its management easier.

Introduction

Peritoneal dialysis is an accepted method for the treatment of acute and chronic renal failure. A number of persons with diabetes mellitus and secondary renal failure undergo peritoneal dialysis while awaiting haemodialysis and renal transplantation. Hyperglycaemia is a frequent and troublesome complication of peritoneal dialysis in these patients (Ribot *et al.*, 1966; Chazan *et al.*, 1969). To avoid this we have added insulin to the dialysate. We hoped that insulin would be absorbed in parallel with the absorption of glucose and that more precise control of blood sugar levels would be achieved.

Methods and Patients

Peritoneal dialysis was carried out in patients with diabetic renal failure by use of an electrolyte solution containing 1·5% or 7% glucose (Peridial). To each litre was added 250 units of aqueous sodium heparin and 0·5 ml of 1% lignocaine (lidocaine). In patients who were not hyperkalaemic 4 mEq of potassium chloride per litre was also added to the dialysate. To each 2 l. of dialysate 125 to 145 units of crystalline insulin was added. In each case described 1 l. of 1·5% glucose dialysate and 1 l. of 7% glucose dialysate were used during each exchange. The dialysis cycle was of one hour's duration (10-minute in-flow, 20-minute equilibration, and 30-minute out-flow). In the three cases presented the dialyses lasted 48 hours.

Glucose absorption was evaluated by measuring the difference in glucose content of dialysate before and after passage through the abdominal cavity. Insulin absorption was evaluated by adding 100 μCi of ^{131}I-labelled insulin to 2 l. of dialysis fluid. After delivery of the dialysate into the abdomen and following its drainage, the bottles and tubing were eluated with 30% potassium hydroxide solutions (Weisenfeld *et al.*, 1968). Aliquots of the eluate, the dialysis fluid, and the patient's blood were counted in a Picker automatic well counter.

Blood volume was measured by using ^{51}Cr tagged red cells.

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Case Reports

Case 1. Insulin Free Dialysate.—A 24-year-old woman was admitted because of renal failure. She had developed diabetes mellitus at the age of 2. There was an eight-month history of uraemia, hypertension, and anasarca. On her admission the blood urea nitrogen was 155 mg/100 ml, creatinine 13·8 mg/100 ml, sodium 132 mEq/l., potassium 8·1 mEq/l., and blood glucose 650 mg/100 ml. Because of uraemia and hyperkalaemia peritoneal dialysis was begun. No intraperitoneal insulin was given. During dialysis the patient received only small amounts of intravenous glucose and water. Though the blood sugar was measured every two to four hours and intravenous crystalline insulin was frequently administered the blood glucose ranged from 75 to 675 mg/100 ml during the course of the dialysis (Fig. 1).

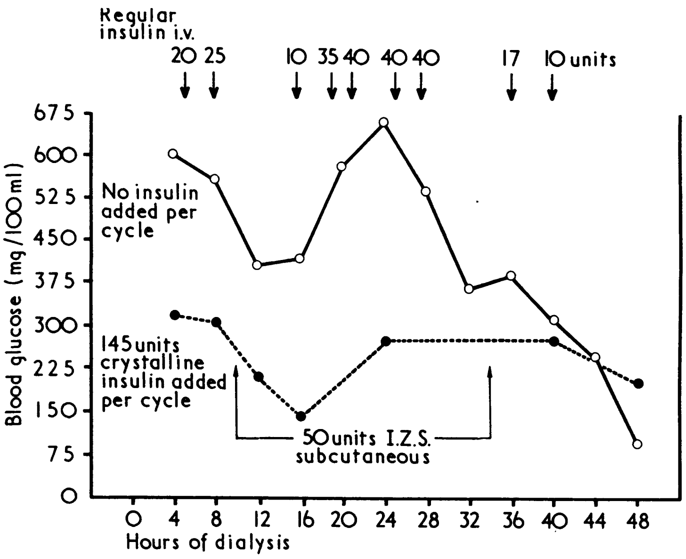

FIG. 1—Upper (continuous) curve represents Case 1. The dosage of insulin given intravenously is shown at top of figure. Despite frequent blood sugar determinations and frequent administration of insulin, great variations in blood sugar occurred. The lower (dotted) curve represents the second peritoneal dialysis of Case 3. A smooth blood sugar curve was obtained without extra insulin.

Case 2. Insulin Added to Dialysate First Part of Dialysis.—A 36-year-old woman with a 20-year history of diabetes mellitus developed rapidly progressive renal failure. On admission the blood urea nitrogen was 193 mg/100 ml and the serum creatinine 11·3 mg/100 ml. During peritoneal dialysis she was maintained on her usual daily dose of 12 units of insulin zinc suspension. During the first 26 hours of treatment 145 units of crystalline insulin was added to each 2 l. dialysis exchange. In the 12 hours before dialysis the blood glucose ranged from 310 to 430 mg/100 ml. During the dialysis the blood glucose values varied from 30 to 100 mg/100 ml. The patient was asymptomatic. Because of hypoglycaemia the last 16 hours of dialysis was accomplished without the use of intraperitoneal insulin. During the latter period the blood glucose ranged from 170 to 600 mg/100 ml (Fig. 2).

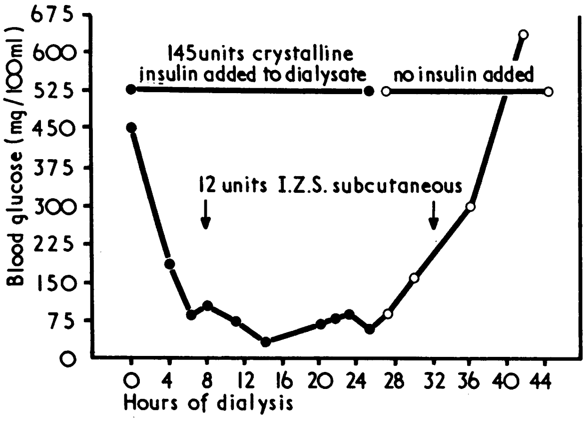

FIG. 2—Blood sugar during peritoneal dialysis of Case 2. With insulin added to the dialysate, a smooth though low blood sugar level was achieved. On stopping insulin the blood sugar rapidly rose to high levels.

Case 3. Effect of Different Dialysate-Insulin Levels.—A 26-year-old man with a 25-year history of diabetes mellitus was admitted for evaluation before renal and pancreatic allotransplantation. There was a three-year history of renal failure. Initial laboratory studies included a blood urea nitrogen of 128 mg/100 ml and creatinine 18·5 mg/100 ml. During peritoneal dialysis crystalline insulin, 120 units, was added to each cycle. Blood glucose values varied from 340 to 460 mg/100 ml during the 48-hour dialysis. Four days later peritoneal lavage was reinstituted. The identical solution and techniques were used with 145 units of crystalline insulin added to each 2 l. exchange. The blood glucose values varied from 150 to 330 mg/100 ml (Fig. 1). During both dialyses the patient received his usual daily dose of 70 units of insulin zinc suspension. Except for the amount present in the dialysate, no supplemental insulin was given during either dialysis. In a 10-day period before treatment the blood glucose values had varied from 137 to 432 mg/100 ml. During the second dialysis the intraperitoneal absorption of insulin was evaluated.

Results and Discussion

Diabetic patients with renal failure are being treated in a number of medical centres with dialysis and renal transplantation. Hyperglycaemia is known to be a serious complication of peritoneal dialysis in this group of patients. Boyer *et al.* (1967) noted that after three one-hour exchanges in non-diabetic patients 32·4 g of glucose was absorbed from 1·5% glucose solution. Even in patients with a normal carbohydrate tolerance pronounced rises in blood glucose can occur and may result in significant extracellular fluid hyperosmolarity and non-ketoacidotic coma (Hutchings *et al.*, 1966; Ribot *et al.*, 1966; Boyer *et al.*, 1967).

Our first case illustrates the problem in the management of diabetes mellitus during peritoneal dialysis. Urine glucose determinations are of no value and frequent blood glucose evaluations are required. In contrast there was no hyperglycaemia during the peritoneal dialysis of the second and third patients when intraperitoneal insulin was administered. Further, the blood sugar level remained very constant during the period of treatment.

The radioimmunoassay of insulin showed that 96% of the infused ^{131}I insulin was recovered in the peritoneal drainage. The remaining 4% was present in the patient's blood (see Table). During the one-hour cycle studied 35 g of glucose was absorbed. The dynamics of the intraperitoneal administration of insulin have not been studied in man. In view of crystalline insulin's low molecular weight, the slow absorption from the peritoneum is difficult to explain. Data from our second patient suggest that the peritoneal absorption of insulin may be proportional to the quantity instilled with the dialysate, as lower blood sugar values were obtained with larger doses of insulin.

Results of Radioimmunoassay of Insulin During Peritoneal Dialysis

Added to dialysate	$61·0 \times 10^6$
Total in potassium hydroxide eluate	$2·4 \times 10^6$
Given intraperitoneally	$58·6 \times 10^6$ (100%)
Recovered in effluent dialysate	$56·1 \times 10^6$
Recovered in potassium hydroxide eluate	$0·2 \times 10^6$
Total recovered	$56·3 \times 10^6$ (96%)
Present in blood	$2·3 \times 10^6$ (4%)

The counts are total counts based on measurements in aliquots minus background.

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MEDICAL MEMORANDA

Lessons from Two Steering Wheels

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Roberts (1967) considered that ruptures of the solid viscera in vehicle occupants were caused by "direct impingement and localized stress concentration" but that the mechanism of rupture of hollow viscera "must be one of shearing resulting from contact in the abdomen between the abdominal wall, which is thrust inward by the steering wheel, and the spinal column." This and similar research evidence has probably influenced the National Highway Safety Bureau of the United States in drafting their proposed new standards for car occupant protection (Docket No. 69-7 Notice 4). Standard 4.4.7 reads: "The force on the abdominal region shall not exceed 2,400 pounds [10·7 kg N] and the pressure on the abdominal region shall not exceed 30 pounds per square inch [2·1 kg/cm²]."

An analysis of abdominal injuries found in 483 necropsies of car occupants we have studied has shown that about 50% of the victims suffered ruptures of the solid viscera (liver, spleen, adrenals, and kidneys in that order) and all also had injuries to other body areas. From the same material there were only 14 patients with ruptures of the intestinal tract—12 of the small bowel and 2 of the stomach. Two drivers had

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