ADVANTAGES OF CONTINUOUS AMBULATORY PERITONEAL DIALYSIS TO THE DIABETIC WITH RENAL FAILURE

C T Flynn, J Hibbard, B Dohrman

Iowa Lutheran Hospital, Des Moines, Iowa, USA

Summary

Among the diabetic patients we have treated with dialysis blood pressure and blood sugar control have been poor and vascular disease progressive. Intermittent peritoneal dialysis did not improve these problems compared with haemodialysis. Continuous ambulatory peritoneal dialysis was undertaken in three patients as a last resort and electively in another two patients. Insulin was given by the intraperitoneal route and none was used systemically. Self-care was taught from the first using the spouse if visual problems were present. Serum creatinine levels fell and haemoglobin levels rose. Blood pressure was controlled without diet or drugs. Blood sugar levels were controlled without symptomatic hypoglycaemia or rebound hyperglycaemia. The procedure had a demoralising effect on helper spouses, and self-care had to be achieved even with severe visual problems. The advantages of continuous ambulatory peritoneal dialysis to the diabetic with renal failure are greatly improved control of blood pressure and blood sugar.

Introduction

We have treated some 26 diabetic patients with chronic renal failure due to diabetes mellitus. Haemodialysis, intermittent peritoneal dialysis and renal transplantation were all associated with blood pressure elevation and poor blood sugar control. In a comparative study of haemodialysis and peritoneal dialysis Quellhorst [1] found that all peritoneal dialysis patients required antihypertensive drugs. In five of our patients treated by peritoneal dialysis we found hyperglycaemia difficult to control by subcutaneous insulin. The consequent thirst caused large weight gains and this seemed the cause of poor blood pressure control. The patients were constantly unwell, required frequent admissions to hospital and extra dialyses. These patients all had severe access problems which forced us to use peritoneal dialysis. Two patients died suddenly after intensive
peritoneal dialysis to remove fluid. When continuous ambulatory peritoneal
dialysis became a recognised procedure we had two patients on peritoneal dial-
ysis and we tried the technique on them as a last resort.

Patients and Methods

The first patient was a 68 year old male in very poor general condition, and he
was treated in hospital and died after one month of a myocardial infarction. The
second patient was much improved and ceased to have frequent admissions to
hospital. We then added insulin directly to the peritoneal solution immediately
before instillation into the peritoneal cavity. The dosage was adjusted to achieve
normal blood sugar values and this was done very easily. Three more patients
were started on intraperitoneal insulin at the time of initiation of continuous
ambulatory peritoneal dialysis. Two patients are legally blind and initially we
trained the spouses to do the treatment.

Results

All four patients are successfully treating themselves at home. We found that
involvement of the spouse in the treatment created serious emotional problems
and delayed rehabilitation and full home care. The husband of one patient died
and although legally blind she would not give up the treatment and learned to
do it herself. A second patient stopped his spouse helping of his own accord and
has achieved full self-care. Using magnifying lenses and spot lights and predrawn
insulin they have successfully managed for several months.

Blood Sugar Control

Table I gives the characteristics of the use of intraperitoneal insulin. It avoids
injections, which is welcome. The administration is very easy, except for those
patients with visual problems. The insulin concentration is highest at the time of
instillation when glucose absorption is greatest and thus the dose varies with the
glucose load. The insulin is presumably absorbed via the portal vein and thus
passes directly to the liver as with normal pancreatic insulin. While the patients

| TABLE I |
| Intraperitoneal Insulin |
| 1 No injections |
| 2 Easy administration |
| 3 Dose varies with glucose load |
| 4 Absorbed via portal vein |
| 5 Wide range of safety |
| 6 Asymptomatic hypoglycaemia |
| 7 No rebound hyperglycaemia |
| 8 Lowered glycohaemoglobin HbA1C levels |
were at home they experienced neither hypoglycaemic nor hyperglycaemic symp-
toms. When blood sugar levels were checked in hospital hypoglycaemia occurred
while finding the correct dose, but was not symptomatic, probably because of the
slow onset. Hyperglycaemia did not occur unless the dose of insulin was omitted.
Rebound hyperglycaemia did not follow hypoglycaemia, giving a wider margin
of safety than with systemic insulin. Lower levels of glycohaemoglobin were
found than previously and were normal in three patients. The dosage of insulin
was found to depend on four variables, blood sugar level, calorie intake, dextrose
concentration in the fluid and the occurrence of peritonitis. If the blood sugar
level was high then it tended not to fall, which indicates the characteristic of
this treatment to maintain a fairly constant level of blood sugar when 4.25 per-
cent dextrose containing peritoneal solution is used. At the same blood sugar level
using the same dose of insulin but with 1.5 percent dextrose solution the blood
sugar will fall. The sugar absorbed will contribute significantly to the caloric
intake of the patient but the oral intake of calories still influences the amount
of insulin required. Peritonitis seemed to increase the need for insulin although
it is somewhat difficult to distinguish from the effect of the treatment main-
taining a constant level once it is achieved. These points are illustrated in Figures
1, 2 and 3.

Figure 1. A The effect of omitting insulin from the peritoneal solution
B The effect of using 1.5% dextrose solution and an unchanged dose of insulin
Each square represents an 8 hour exchange period and the concentration of dextrose
and the dose of insulin are shown
Figure 2. Fall in blood sugar levels when using 1.5% dextrose and unchanged dosage of insulin. Each square represents an 8 hour exchange period and the concentration of dextrose and the dosage of insulin are shown.

**Blood Pressure Control**

All four patients were initially hypertensive and required therapy. With adequate fluid removal all achieved normal blood pressures and in two patients postural hypotension occurred requiring extra salt intake. This blood pressure control, which needed no drugs, was achieved by the fluid and salt loss, but was probably aided by the absence of thirst. There were fluctuations from mild hypertension with oedema to dehydration and hypotension but all the patients gradually learned how to cope with these.

**Spouse Involvement**

The average time for an exchange of peritoneal solution varied from patient to patient but could be done in 30 minutes. The procedure is tedious and repetitive and is done every day of the week. Spouse involvement tended to reinforce the image of helplessness of the patient and also required them to be at the same place at the same time for each exchange, imposing limitations and burdens on their life style. Achievement of self-care despite legal blindness actually provided a great boost to the morale of our two patients.
Blood Sugar
mgm/100 ml

Figure 3. Blood sugar control using intraperitoneal insulin. First period when the patient had Candida peritonitis and two weeks later when the peritonitis was under control. Each square represents an 8 hour exchange period and the concentration of dextrose and the dose of insulin are shown.

Choice of Solution

We use 4.25 percent dextrose containing peritoneal dialysis solutions at 8 hour intervals in all patients regardless of body size. This arbitrary decision was based on several considerations. Firstly, the peritoneal solution comes into equilibrium with creatinine and presumably most dialysable uraemic toxins, and thus excess fluid ultrafiltered represents increased clearance. Secondly, the increased clearance may allow fewer exchanges and reduce the possibilities for contamination that occur with each exchange of solutions. Lastly, the constant use of the same concentration of dextrose allows a more reliable evaluation of the insulin requirement for the patient at home.

Peritonitis

There have been six episodes of peritonitis over 26 patient months of experience. One patient has had staphylococcal, gram negative and candida peritonitis. Two patients have had staphylococcal peritonitis, one of them twice. The candida peritonitis resolved with oral flucytosine and intravenous amphotericin B and required hospitalisation. Staphylococcal peritonitis was treated with either vancomycin or a cephalosporin, using the peritoneal route after an intravenous loading dose. As discussed earlier peritonitis seems to increase the need for insulin...
but does not cause lack of control of the blood sugar levels or require change to systemic insulin.

Effects on Uraemia

In all cases the serum creatinine fell. The average value before continuous ambulatory peritoneal dialysis was 12.2mg per cent and after two months of treatment the average value was 8.1mg per cent. Haemoglobin levels rose from an average of 6.9g to an average of 13.8g/dl. Some of this rise was due to haemoconcentration and when the patient learned to control the fluid weight the haemoglobin tended to fall to an average of 11.2g/dl.

Discussion

Intraperitoneal insulin has been used with intermittent peritoneal dialysis. Crossley and Kjellstrand [2] used 145 units with each two litre exchange as well as systemic insulin. Blumenkrantz et al [3] quote a single peritoneal dialysis in which they used 120 units of insulin in each two litre exchange. There seem to be no follow-up reports. Quellhorst [1] quoted 40 units of insulin to each 10 litres of concentrated peritoneal dialysis solution for use with automated equipment. This is a curiously small amount compared with the present series which averaged 37 units to each exchange. The high doses used with ordinary peritoneal dialysis are presumably needed because the high levels of glucose are maintained by relatively rapid exchanges and Crossley and Kjellstrand [2] estimated that 97 percent of the insulin was not absorbed. The main characteristic of continuous ambulatory peritoneal dialysis is the long dwell time of the solution in the peritoneal cavity. As insulin is absorbed while the volume of dilution of the peritoneal solution remains constant, or more often increases, the concentration of the insulin in the peritoneal solution will decrease with time. The absorbed insulin has a longer half-life, and there is also insulin resistance in uraemia [4]. Our preliminary data are uncertain but indicate that approximately 50 percent of the insulin is absorbed. There is thus a constant infusion of insulin, varying appropriately with glucose load, being absorbed through the portal vein as with pancreatic insulin. Intraperitoneal insulin with continuous ambulatory peritoneal dialysis can thus be perceived as an artificial pancreas [5].

By control of blood sugar levels and abolition of thirst the patients were enabled to take advantage of the fluid losses and achieve normal levels of blood pressure. The control of blood sugar and blood pressure in a diabetic patient with renal failure are unique to continuous ambulatory peritoneal dialysis and constitute the major advantages of this treatment. Peritonitis is the major problem and is common to all patients, not just to diabetics. If this is solved and the treatment is made cheaper, then the promise exists that treatment could be begun earlier than at present in the hope of diminishing the progression of vascular disease.
Open Discussion

BOEN (Chairman) We will take the discussion of the last three papers together.

ANDREUCCI (Naples) It was interesting to see what happens with diabetic patients to the blood sugar, but I have not seen the blood sugar in normal patients on CAPD treatment. With intermittent peritoneal dialysis the patient has time to develop a normal blood sugar shortly after dialysis while with CAPD I suppose they have a high blood sugar all the time.

OREOPOULOS To answer your first question, we do measure blood sugar and we found it normal or slightly elevated. A normal pancreas can control the continuous glucose infusion.

ANDREUCCI Concerning the amino acid solution in the dialysis fluid, why don’t you use protein?

OREOPOULOS Because protein is very hard to find and it would be very expensive.

ANDREUCCI And how can the children grow, losing so much protein with CAPD?

OREOPOULOS Well, there is a misconception about the amount of protein losses. It was initially reported that 13 to 20 grams protein are lost daily but I think that these high levels were due to the fact that they were measured in patients with recurrent peritonitis and in addition they were doing five exchanges. Patients without peritonitis lose 5–6g protein a day, an amount which can be compensated by an increased protein intake of 80 to 100g.

ANDREUCCI To replace proteins lost with dialysis, patients should have a high protein intake, but it is difficult to force children to eat protein, I am afraid.

OREOPOULOS Yes, this is a problem with some children.

ANDREUCCI Patients who had hypotension during CAPD were just patients who were not eating enough and had a low plasma protein concentration?

OREOPOULOS Definitely not. This was present in various patients irrespective of their protein intake.

ANDREUCCI Thank you.
GAHL (Berlin) I wondered about the patient with dialysis dementia. Was this a patient who was primarily selected for CAPD, and how was the outcome, did he show any neurological signs, prior to the dialysis treatment?

OREOPoulos This was an old patient with polycystic kidneys, who had been on intermittent peritoneal dialysis for two years and had a prolonged course with severe osteomalacia, which she still has.

She had been on CAPD for one year when she developed dementia. This patient now is a little better and the disease has not progressed.

MION (Nimes) I would just like to comment on the risk of peritonitis in CAPD. In our experience with intermittent PD, the incidence of peritonitis is in the range of one peritonitis every five patient years which is very low I think, and we felt that it was difficult to treat our patients with CAPD without protecting them against peritonitis. So we have chosen to develop a connecting device with a bacteriological filter (Twin 90, Millipore®), 40 patients (37 treated for more than one month), with a total experience of 159 patient months (average 3.9 month/patient) were started on CAPD since September 1978, using this device. Six peritonitis episodes (one septic, five aseptic) have been observed (one episode every 26.5 months). I feel that this type of device is very important to avoid selecting only the cleanest and the most careful patients for CAPD, as the simplicity of this technique makes it a valuable treatment for the less skilful, less educated and less careful patients.

OREOPoulos Does this affect the inflow rate?

MION Well, slightly, but not too much. I think what affects it more is the size of the tubing: if you use a bigger tubing, then you get very good flow rates.

OREOPoulos And I presume that these were all patients converted from intermittent to CAPD?

MION No, most of them were new patients.

BOEN (Chairman) In connection with peritonitis Dr Thomson, there was one patient who ceased to be on CAPD because of peritonitis. Would you tell us whether this was a sterile peritonitis or bacterial peritonitis?

THOMSON This patient's problem was sterile peritonitis. The consequence was principally patient's inconvenience, rather than impairment of health, and, as mentioned before, sterile peritonitis has not been associated with severe morbidity.

BOEN Have you seen extensive peritoneal adhesion formation with sterile peritonitis?

THOMSON We have experienced this problem in intermittent peritoneal dialysis, but so far not in continuous ambulatory peritoneal dialysis.

ROBSON (Tel Aviv) I have the impression that catheter function is better on CAPD than in intermittent peritoneal dialysis, and I would like to ask Dr Oreopoulos if he, in fact, agrees with this or if he has any data on this?
OREOPOULOS In terms of fibrin clot formation we have almost the same or a slightly higher rate in patients on CAPD, and I have not been impressed about any difference in the catheter function and survival.

THOMSON As I previously mentioned, we have experienced a greater survival of Tenckhoff catheters on CAPD in that we have not lost any from obstruction associated with peritonitis; very different from our experience on IPD.

PARSONS (London). Dr Flynn, do you know where your insulin goes to? Is it lost in the bag or in the peritoneum? We share your experience that you can put 160 units a day into a patient's peritoneal dialysis system without any trouble.

FLYNN Well we have tried to do it. Certainly there is a lot of insulin left in the bag, but whether it is a half or a quarter or so, that is a thing we have not been able to work out. We are presuming that the insulin goes into the portal vein and into the liver, where it is absorbed and this may have an important consequence.

PARSONS What is to stop it going up into the thoracic lymphatics and into the circulation that way?

FLYNN Nothing.

OREOPOULOS I would like to add that a significant amount of insulin is absorbed, since with small increases in the intraperitoneal insulin you can make the patient hypoglycaemic; with only one or two unit changes the patient may become hypoglycaemic.

COLOMBI (Lucerne) I was quite impressed by a decrease of PTH in one of my HD patients, when I changed to CAPD. Have you got any data on PTH levels, changing from IPD to CAPD?

OREOPOULOS We have measured plasma PTH regularly, and I have not seen dramatic changes. I have patients whose radiological evidence of hyperparathyroidism has progressed while on CAPD, so I am not convinced that the hyperparathyroidism problem will be solved only with CAPD.

THOMSON We have had two patients whose bone disease definitely improved and PTH level fell on CAPD.

AHMAD (Liverpool) My question is directed to Dr Thomson. Has he any experience of bilaterally nephrectomised patients on chronic ambulatory peritoneal dialysis (CAPD)? Do they show a similar rise in haemoglobin? My colleague at Liverpool, Dr Forbes, had one patient who had no kidneys and on CAPD showed a rise in haemoglobin.

THOMSON Yes, six of our patients have had bilateral nephrectomy, all for severe reflux with infection. On conversion from IPD to CAPD, haemoglobin concentration rose in four of these patients.

BOEN I would like to ask a question to both of you, Dr Thomson and Dr Oreopoulos, about the practical problems of the transplantation procedure in the
patients who were on CAPD. I believe many of us would like to know whether there are differences between the patients on haemodialysis and on CAPD.

THOMSON No, we have had no problems. We have left the Tenckhoff catheters in-situ in case dialysis has been required after transplantation and we have not had any peritonitis in the post transplant period. We actually had one patient who developed clinical peritonitis one hour prior to the transplantation but this settled rapidly with peri-operative antibiotics.

OREOPOULOS As you noticed we had nine patients on CAPD who were transplanted, and more than 70 patients from intermittent peritoneal dialysis. We leave the catheter in place and we often use it when there is need for dialysis. We have not noticed significant differences in survival and complications.