HAEMO- AND PERITONEAL DIALYSIS TREATMENT OF PATIENTS WITH DIABETIC NEPHROPATHY — A COMPARATIVE STUDY

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Summary

Thirty-two patients with advanced chronic renal insufficiency due to juvenile onset diabetes mellitus were submitted to dialytic treatment, 16 with intermittent haemodialysis and 16 with peritoneal dialysis. Both groups were similar with respect to onset of diabetes, course of renal insufficiency, as well as start and duration of dialysis treatment (382 and 389 patient months respectively). Patients on haemodialysis showed a more rapid progress of retinopathy and neuropathy, whereas the control of hypertension proved to be more difficult with peritoneal dialysis. A reduced peritoneal dialysance of urea, demonstrated in patients with diabetic nephropathy, could be improved by dipyridamole administration, whereas this drug showed no effect on the dialysances of urea and inulin in patients with chronic renal insufficiency of non-diabetic origin. There were no differences between the survival rates of the two groups which were substantially lower than in non-diabetic dialysis patients.

Introduction

End-stage diabetic nephropathy, some years ago a reason for exclusion from dialytic treatment because of the high risks, is now one of those late complications of diabetes mellitus which in general can be treated successfully by dialysis or transplantation. The results of dialytic treatment, however, are significantly different; one-year survival on haemodialysis treatment varies between 22 and 86 per cent [1]. Transplantation has been preferred to haemodialysis by some investigators because of the aggravation of retinopathy resulting in blindness in the course of haemodialysis [2,3]. The contradictory data concerning survival and development of extra-renal complications of diabetic nephropathy prompted this comparative study involving 32 patients with juvenile onset diabetes and advanced renal insufficiency. The course of illness of 16 patients with diabetic end-stage kidney disease on long term haemodialysis was compared to that of an equal number of patients on peritoneal dialysis.
treatment. Because of diabetic vascular disease a diminished diffusion of metabolic waste products across the wall of intestinal capillaries and thus a reduced efficiency of peritoneal dialysis was to be expected. The influence of drugs on peritoneal dialysates of substances with different mol wt, therefore, had to be investigated.

Patients and Methods

Sixteen patients with end-stage renal disease caused by juvenile onset diabetes mellitus were treated by long term haemodialysis (group A) and 16 patients by peritoneal dialysis (group B). The age at onset of diabetes was 21.1 years on average in group A and 24.6 years in group B. Residual renal function (GFR) was 2.9 ± 0.8 ml/min and 3.1 ± 0.9 ml/min respectively. During 382 patient months 4,966 haemodialyses were performed in group A and during 389 months 5,057 peritoneal dialyses in group B. Patients of both groups were treated three times weekly, the mean duration of haemodialysis being 6 hours and of peritoneal dialysis 12 hours each. Gambro Lundia major dialysers were used for haemodialysis, heparin was given in order to achieve a whole blood partial thromboplastin time of about 110–120 sec. Eighty litres of dialysis fluid were consumed per peritoneal dialysis. Dialysis fluid was composed for haemodialysis as follows: Na 140, K 2.0, Ca 3.5, Mg 2.0, Cl 112.5, Acetate 35.0 mEq/L (292 mOsm/L), and for peritoneal dialysis: Na 132, K 2.0, Ca 3.5, Mg 1.5, Cl 104, Lactate 35 mEq/L, Glucose 16.5 g/L (359 mOsm/L). Blood pressure was measured at the start of each procedure and mean pre-dialysis blood pressure values were calculated per month of treatment. Ophthalmoscopy for the judgement of retinopathy, as well as measurements of the vibration sensitivity threshold and nerve conduction velocity (n. peronaeus) were performed at intervals of three months. Among others the following pre-dialysis blood parameters were measured monthly: Hgb, Hct, Protein, Creatinine, BUN, Cholesterol, Triglycerides, and Glucose.

In 9 patients of group B and 9 patients with chronic renal insufficiency of non-diabetic origin (group C) 0.3 mg/kg body weight of dipyridamole were injected i.v. once free dialysis fluid flow was established. Two weeks later sodium nitroprusside (6 mg/L) was added to the dialysis fluid for 20 cycles after the tenth exchange in patients of both groups (1 exchange = 2 L/30 min).

A prime dose of inulin followed by a continuous infusion had been given to all patients two hours before the start of dialysis procedure. Blood samples were withdrawn at the beginning of every fifth exchange throughout dialysis, and dialysate samples were taken from every dialysate outflow cycle.

Dialysances of inulin and creatinine were calculated according to the equation:

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D_x = \frac{V_D \cdot [x]_D}{t \cdot [x]_B}
\]

where \(V_D\) is the volume of dialysate outflow, \([x]_D\) and \([x]_B\) are the concentrations of \(x\) in the dialysate and blood, and \(t\) is the time of each cycle. Inulin
was measured in serum and dialysis fluid according to Walser et al [4].

Results

In the course of treatment considerable differences concerning blood and serum parameters developed between patients of group A and group B (Figure 1); whereas haematocrit values were constantly lower in group A than in group B, serum protein levels were significantly higher in group A and serum creatinine values significantly higher in group B. There were no differences between the

![Graph showing changes in serum creatinine, phosphorus, protein, and haematocrit values over 24 months of treatment for PD and HD groups.](image)

Figure 1. Changes of serum creatinine, phosphorus and protein concentration as well as of haematocrit values in patients of group A (haemodialysis=HD) and group B (peritoneal dialysis=PD) in the course of a 24 month treatment period. n=9 (PD) and 9 (HD), X±SE
Figure 2. Behaviour of hypertension, diabetic retinopathy and neuropathy in patients of group A (haemodialysis) and group B (peritoneal dialysis) in the course of a 21 month treatment period. White bars = number of patients alive. Hypertension = RR > 140/90 mmHg pre-dialysis monthly on average, or requiring antihypertensive drug therapy.
two groups with regard to serum phosphorus levels. Mean serum triglyceride values were significantly higher in group B than in group A whereas serum cholesterol concentrations did not show any differences.

The influence of dialysis treatment on blood pressure, diabetic retinopathy and neuropathy is shown in Figure 2. Hypertension, demonstrable at the start of treatment in 13 haemodialysis and 12 peritoneal dialysis patients, could be controlled in most patients of group A by haemodialysis alone, but persisted during peritoneal dialysis treatment thereby requiring additional drug therapy. Deterioration of retinopathy occurred in all patients of group A but only in 5 patients of group B.

The percentage of patients with a deterioration of neuropathy rose during the course of treatment more steeply in group A than in group B.

In the course of treatment pericarditis appeared in 5 patients of group A and 2 patients of group B. Cardiac infarction occurred in 4 patients of group A and 3 patients of group B. Fundus bleeding, occurring in 6 patients of group A and none in group B, induced bilateral blindness in 4 patients. Fistula thrombosis occurred in 6 and fistula infection in 5 patients of group A; peritoneal (Tenckhoff) catheter occlusion in 8 and peritonitis in 11 (pos. cult. 6, neg. cult. 5) patients of group B. Mean peritoneal catheter survival was 48.6 months.

Figure 3. Changes of $D_{\text{urea}}$ and $D_{\text{inulin}}$ induced by nitroprusside i.p. and dipyridamole i.v.
in patients with chronic renal insufficiency of non-diabetic origin and patients with diabetic nephropathy on maintenance peritoneal dialysis treatment. $n=9$, $x \pm SE$
Six patients of group A and 5 patients of group B died during the observation period. Causes of death were in group A cardiac infarction (3 patients), hyperkalaemia (2), cardiac insufficiency (1), and in group B pneumonia (2), cardiac infarction (2), and hyperosmolar coma (1).

As Figure 3 shows, nitroprusside i.p. and dipyridamole i.v. influenced peritoneal dialyses of urea and inulin in group B and C. Nitroprusside induced a significant increase in D\textsubscript{inulin} in patients with non-diabetic chronic renal insufficiency whereas dipyridamole improved D\textsubscript{urea} in diabetics.

Discussion

In reviewing the complications arising from dialysis treatment of end-stage diabetic nephropathy a discrimination has to be made between two groups: those complications developing as a consequence of the underlying disease and those resulting from the dialytic treatment. In comparable groups of patients with renal insufficiency due to juvenile onset diabetes mellitus hypertension could be more effectively influenced by haemodialysis than by peritoneal dialysis. Blood pressure could be normalised in most patients by haemodialysis alone whereas normotension was achieved in most peritoneal dialysis patients only after drug therapy. Retinopathy, however, deteriorated in all cases during haemodialysis therapy.

This observation supports the thesis of Goldstein and Massry [5], according to which a deterioration of vision cannot be avoided by control of hypertension. The high rate of fundus bleeding in haemodialysis stresses the significance of a strict control of heparinisation by repeated measurements of coagulation parameters.

Peripheral neuropathy of diabetic and/or uraemic origin already existed in 60 out of 68 patients with end-stage renal failure as reported by Goldstein and Massry [5], in 6 cases it worsened on haemodialysis. In our patients a deterioration of neuropathy could be observed mainly in haemodialysis and to a lesser degree in peritoneal dialysis.

Comty et al [6] observed a high incidence of pericarditis in patients with diabetes mellitus on haemodialysis treatment. In our study, episodes of pericarditis were detected in 5 patients on haemodialysis and 2 patients on peritoneal dialysis. Sensibility to infections and an increased tendency to bleeding may contribute to the frequency of pericarditis during haemodialysis therapy. A high incidence of peritonitis was to be expected in diabetic patients on peritoneal dialysis. In non-diabetic patients Tenckhoff et al [7] had reported a frequency of 0.61% and von Hartitzsch et al [8] an incidence of 0.32%. The data obtained from our study show a peritonitis incidence in diabetes of 0.2% and support the assumption that with adequate techniques peritonitis can be avoided in diabetes mellitus as well.

Control of hyperglycaemia is an important precaution to prevent fluid overload, hypertension [6] and hyperkalaemia [9]. In contrast to the information given by Slifkin et al [10] and Comty et al [6], control of hyperglycaemia was a major problem in about 10% of our patients.

It has to be assumed that the unusual incidence of hyperkalaemic deaths in
our haemodialysis patients was caused by uncontrollable fluctuations of blood glucose and therefore of potassium in these two patients. Efforts to prevent hyperglycaemia in the course of peritoneal dialysis by replacement of glucose by sorbitol were abandoned after the occurrence of severe cerebral side reactions [11]. Meanwhile, the addition of insulin to the glucose-containing peritoneal dialysis fluid has provided a better control of serum glucose levels [12].

First year mortality of patients with diabetic nephropathy on haemodialysis therapy has recently been reported to be between 22.6 and 33.3% (6), 19% (10), and 54% (5). In both groups of our patients 75% survived the first and 69% the second year of treatment. This contrasts with the data presented in the Combined Report on Regular Dialysis and Transplantation in Europe, 1976 [13], in which survival rates of patients with diabetes mellitus are substantially lower, independent of the method of dialytic treatment.

A significantly lower peritoneal urea clearance in patients with vascular disease than in those with normal vasculature was reported by Maher et al [14]. The results reported by these authors, in particular the increase of C\textsubscript{urea} after dipyridamole and the ineffectiveness of this drug in a control group, were confirmed by our investigations. Nitroprusside, another vasoactive drug, improved the dialysance of inulin in non-diabetics, as had been described by Nolph et al [15] in non-diabetic patients, but did not influence dialysances or urea and inulin in diabetics. On the basis of these observations it would appear that dipyridamole in diabetic nephropathy as well as in patients with systemic vascular disease increases the removal of small molecular uraemic substances, perhaps by preventing platelet aggregation and fibrin deposition.

References

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Open Discussion

PARSONS (London) I share your experience of less bleeding in the retina using peritoneal dialysis for these patients and I want to ask you whether you believe this is due to the anticoagulant used in haemodialysis or whether you are removing something on peritoneal dialysis which prevents retinopathy progressing?

QUELLHORST I think the lower incidence of bleeding occurring in peritoneal dialysis is due to less anticoagulation.

BLUMENKRANTZ (Los Angeles) It is the opinion of many ophthalmologists that ischaemia of the retina during haemodialysis with rapid fluctuations in blood pressure is the more common cause of the progressive retinopathy often observed in these unfortunate patients. Episodes of hypotension are much less common in patients undergoing peritoneal dialysis. To my knowledge no controlled, randomised prospective trial has yet been performed to confirm that diabetic patients on peritoneal dialysis do indeed have a lower incidence of retinopathy.

JONES (London) You briefly mentioned diabetic control during peritoneal dialysis. I wonder if you would enlarge on the precise technique that you used to achieve that? Could you describe the method of insulin administration that you employed during peritoneal dialysis?

QUELLHORST According to the recommendations of Tenckhoff’s group we added crystalline insulin, 40 units per 10 litres of dialysis fluid containing glucose in a concentration of 1.5%.