HAEMODIALYSIS OR RENAL TRANSPLANTATION IN THE TREATMENT OF END-STAGE DIABETIC NEPHROPATHY

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Summary

We have reviewed 27 diabetic patients treated between 1971 and 1981 by haemodialysis and/or by transplantation.

Overall patient survival is 43 per cent at five years (vs 78 per cent in non-diabetics of similar age). Two year patient survival is identical (73%) with haemodialysis and after transplantation. One year graft survival is 55 per cent. Progression of extrarenal diabetic complications is similar in haemodialysis and after transplantation. Recurrence of diabetic glomerulosclerosis was documented in two grafts.

Haemodialysis thus offers a suitable alternative for diabetic patients who cannot be transplanted.

Introduction

Diabetic nephropathy is a frequent cause of end-stage renal failure, second only to glomerulonephritis and pyelonephritis. Treatment by dialysis and transplantation has been made increasingly available over the last few years, the number of diabetic patients treated in Europe increasing from 37 in 1972 to 1920 in 1979. Initial reports claimed better survival for diabetic patients treated by transplantation than by haemodialysis. Accordingly, most groups including ours, selected for treatment only those patients fit to be transplanted.

More recently it has been suggested that long term haemodialysis is an acceptable mode of treatment for renal failure due to diabetes mellitus [1,2]. To evaluate this claim we reviewed our experience of the treatment of 27 diabetic patients with end-stage renal failure.

Patients and methods

From 1971 to 31 December 1981, 27 diabetic patients (19 males, 7 females) with end-stage renal failure were treated by haemodialysis and transplantation.
Observations were extended to 31 July 1982. At the initiation of substitutive therapy, age of the patients averaged 35 years (range 17–51), and duration of diabetes ranged from 7 to 37 years (mean: 20).

None of the patients accepted for haemodialysis, apart from one, had any contraindication to transplantation.

Actuarial survival rates were calculated [3]. Overall patient survival irrespective of the method of treatment was calculated from the initiation of therapy onwards. Separate survival curves for haemodialysis (HD) and transplantation (TP) were calculated, the follow-up being interrupted when the patient was switched from one method of treatment to another.

Results

Four patients were transplanted without prior haemodialysis (TP₁). Twenty-three were haemodialysed (HD₁), 16 of whom were subsequently transplanted (TP₁). Nine transplanted patients returned to haemodialysis (HD₂) and/or underwent a second transplantation (TP₂). Overall survival of the 27 patients irrespective of the treatment method was 73.8 per cent at one year and 43.1 per cent at five years (Table I). Follow-up averaged 37.1 months (range 0.5–109). Patient survival according to the method of treatment is also given in Table I.

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<th>TABLE I. Patient and graft survival</th>
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Per cent graft survival

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TP₁ + TP₂

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(n) Number of patients or grafts at risk
HD₁ Haemodialysis prior to transplantation
TP₁ First graft
TP₂ Second graft
It is identical (73.3%) at 24 months for haemodialysis (HD\textsubscript{1}) and for transplanted subjects (TP\textsubscript{1}).

First graft survival (TP\textsubscript{1}) is 55 per cent at one year and 34 per cent at five years. Of 20 first grafts (19 cadaver, one mother donor) 14 were lost: eight from rejection (acute five, chronic three), five as a result of patient death (functioning graft) and one from technical failure. Actuarial graft survival of first and second transplant are not very different (Table I).

The evolution of cardiovascular and neurological complications in patients with at least six months follow-up either after transplantation (TP\textsubscript{1}) or on haemodialysis (HD\textsubscript{1}) is described in Table II. Both groups had a virtually identical prevalence of changes in ECG (rhythm or conduction disturbances, Q waves), worsening of ocular lesions (loss of sight of one eye or reduction of visual acuity by 50 per cent at least), vascular disease leading to distal amputation and, finally, significant reduction of nerve conduction velocity. However, it should be noted that follow-up after transplantation was for approximately three times longer than that on haemodialysis.

Pathological examination of eight graft samples was performed. In three instances biopsy obtained within three months after transplantation revealed either acute rejection or acute tubular necrosis. Three more biopsies taken between 11 and 66 months after transplantation to elucidate the reason of deteriorating graft function showed lesions of chronic rejection with, in two cases, superimposed signs of acute rejection. The two last samples came from necropsy material, 16 and 65 months after transplantation. Besides signs of chronic rejection the first graft had glomerular lesions compatible with incipient diabetic glomerulosclerosis whereas the other graft had typical lesions of nodular diabetic glomerulosclerosis.

Eleven of the 27 patients are presently alive. Three patients on haemodialysis (follow-up 9 to 57 months) are completely rehabilitated. Out of eight transplanted patients (follow-up 20 to 109 months) seven have a very gratifying rehabilitation. In six of them serum creatinine is below 2mg/dl and four have no proteinuria.

| TABLE II. Evolution of cardiovascular and neurological complications in diabetic patients treated by HD\textsubscript{1} (n=10) or TP\textsubscript{1} (n=11) for more than six months |
|-----------------|----------------|----------------|----------------|----------------|
|                 | Follow-up duration (months) | Worsening ECG (n) | Worsening vis acuity (n) | Distal amputations (n) | Shortening VNC (n) |
| HD\textsubscript{1} | 6.5–57 (m : 13.4) | 0/8 | 2/7 | 1/10 | 0/4 |
| TP\textsubscript{1} | 14–105 (m : 46.5) | 3/11 | 3/11 | 3/11 | 0/4 |

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Discussion

Global survival of our patients is 43 per cent at five years. This encouraging result justifies the pursuit of substitutive therapy in diabetic patients with end-stage renal failure.

On the basis of our data we have tried to evaluate the respective advantages of transplantation and haemodialysis. Our 73 per cent one year survival on haemodialysis is comparable to the results of other groups [4–6]. By contrast, our two year graft survival for first and second transplants is only 37 per cent. It reflects mainly poor graft tolerance. Nevertheless, patient survival after transplantation is satisfactory: 82 per cent at one and 73 per cent at two years. These results are within the range reported in the literature with a two year survival ranging from 45 per cent in a Scandinavian series [7] to 68 per cent in Najarian’s group [8]. Comparison, however, is difficult insofar that the selection criteria vary from one group to the other.

Do these results confirm our attitude of accepting patients only if they are suitable candidates for transplantation?

Patient survival at one year is almost the same with dialysis and transplantation. This observation is even more striking if one considers that transplantation is performed after a waiting time on haemodialysis averaging six months. Three out of five deaths on haemodialysis occurred within this interval, suggesting that the waiting period acts as a filter before transplantation. Among the other reasons invoked in favour of transplantation is the hope of a more favourable evolution of extra renal complications of diabetes [9,10]. This is not confirmed in our series. However, we should remember the difference in mean follow-up between the two therapeutic modalities.

Transplantation carries its own risks. Amputation is frequent after transplantation [8,9,11,12]. Indeed three transplanted patients of our series underwent five amputations. Recurrence of diabetic nephropathy in the graft is also a hazard. In two grafts recurrence was documented, mild incipient glomerulosclerosis in one and severe typical nodular glomerulosclerosis in the other. Similar recurrences have been documented by Mauer in 1976 [13]. Up to now, however, recurrence of diabetic nephropathy does not seem to have clinical consequences [14].

Thus overall the poor prognosis attributed to haemodialysis in diabetic patients [15] is not confirmed in our series. Survival on haemodialysis may be quite adequate provided that therapy is initiated early and that blood pressure is rigorously controlled [6]. It does not seem justified therefore to refuse substitutive therapy to diabetic patients who cannot be transplanted. A similar shift of opinion has become manifest recently on both sides of the Atlantic [6,16] even in centres which initially preferred transplantation [8]. In our opinion, transplantation remains, whenever possible, the best therapy both for clinical and economical reasons [17]. However, when the risk is prohibitive or when the patient is reluctant to undergo surgery, haemodialysis remains a suitable alternative.

Much progress remains to be made: whatever the mode of therapy, patient survival is lower in diabetic than in non-diabetic subjects. In our centre global
five years' survival reaches 78 per cent in non-diabetics compared with 43 per cent in diabetics of similar age. The main cause of death is cardiovascular complications in haemodialysis and infection after transplantation [18]. It is too early to evaluate the results of continuous ambulatory peritoneal dialysis in diabetics and to identify its place in the treatment of diabetic end-stage renal failure. Early results, however, are promising [19]. This would further our conclusion that other than transplantation, adequate substitutive therapy can be offered to uraemic patients.

References

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Open Discussion

NICHOLLS (Sheffield) Can I ask you what population you have been drawing your patients from because 27 patients over 10 years suggests a fair degree of selection which could of course have a crucial bearing on the outcome. Obviously to quote patient survival in hospital does not tell us anything about the community mortality of diabetic renal failure.

VANDENBROUCKE All our patients except one have been selected for treatment with a view to transplantation. The criteria for inclusion are diabetic patients with long-standing insulin dependence with proteinuria and retinal microaneurysms. In two patients with no microaneurysms we have a biopsy. We have excluded patients that cannot be transplanted.
NICHOLLS  I am sorry you misunderstood me. What I wished to know was the size of the population from which your patients are drawn.

VAN YPERSELE (Brussels) Maybe I can answer that question in so far as in our country each hospital does not care for a specific population. Our unit has a large number of referrals. We thus cannot evaluate the population of diabetics from which our sample is taken. However, it is a small sample of carefully selected patients younger than 45 years, not blind, and without severe peripheral vascular disease. These criteria are meant to select appropriate candidates for transplantation.

MUTS-HOMSMA (Leiden) How were your matching criteria for HLA- A, B and DR especially for those patients who were transplanted without prior dialysis in comparison with non-diabetics; in cases of poor graft survival?

VANDENBROUCKE HLA- A and B matching were the same as those of our other transplant patients.

MUTS-HOMSMA Did you make a further selection with respect to age in your patients?

VANDENBROUCKE Yes, we have selected patients under the age of 45.

MUTS-HOMSMA Was there a difference in patient survival, especially in the younger patients?

VANDENBROUCKE No, no difference.

WALDEK (Salford) What percentage of diabetics in renal failure does your population represent? Secondly how do you assess ocular deterioration in these patients assuming that all the patients you have taken on can see at the onset of treatment, and thirdly in your dialysis treatment what type of dialysis regime do you carry out with particular reference to the dosage of heparin?

VANDENBROUCKE For the first question on the incidence of diabetic nephropathy I have no information, but the group was carefully selected. As for your second question ocular deterioration was assessed by regular fundoscopic examination and arteriography. For the third question regarding the dialysis treatment of diabetic patients we do not make any differences from other patients except for a frequent check of blood glucose. For all patients we use minimal heparinisation.

WALDEK I would like to suggest that if a larger population of diabetics on haemodialysis were studied you would find that there would be a high incidence of ocular complications as we have found in our population.

VANDENBROUCKE Our purpose was not to evaluate the extent of the deterioration of extrarenal involvement in dialysed diabetics. We just wanted to show
that in diabetic patients selected for transplantation, long term dialysis was an acceptable alternative to transplantation. Thus when these patients are reluctant to undergo transplantation our motivation to change their opinion should not be excessive.