Middle Articles

HOSPITAL TOPICS

Integrated Regional Haemodialysis and Renal Transplantation Centre

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Summary: During the first year of an integrated hospital haemodialysis/home dialysis/renal transplantation service 56 patients with chronic renal failure were accepted for treatment. Twenty-five of these have had a cadaveric renal transplant, seven are established on home dialysis, and 18 are still receiving maintenance dialysis in the 10-bedded hospital unit. The overall survival rate is 66%. The rate of referral from the immediate vicinity of the unit of patients suitable for treatment by these methods was about 25-30 per million per year.

Introduction

It is now well established that useful life may be prolonged in patients with chronic renal failure by maintenance haemodialysis and renal transplantation (Advisory Committee of Human Kidney Transplant Registry, 1968; Drukker *et al.*, 1968; Parsons and Clark, 1968). It is also apparent that these methods of treatment are closely interdependent and that neither alone can meet the demand. Ideally, therefore, centres providing a service for the treatment of such patients should develop facilities for hospital dialysis, a home dialysis training programme, and renal transplantation, and all these aspects of management should be closely integrated.

We report here the experience obtained in such a centre during the first year after the opening of a maintenance haemodialysis unit. The purpose of the paper is to outline some of the problems involved in organizing an integrated hospital maintenance dialysis/home dialysis/cadaveric transplantation service.

Patients

Patients with "end-stage" chronic renal failure referred to the renal unit were first admitted to a general medical ward for detailed assessment. Most patients aged between 15 and 55 years were accepted for treatment in a new 10-bed maintenance haemodialysis unit which opened on 1 April 1968, but a few were rejected on psychiatric grounds or because of extensive arterial disease. Two patients who were considered suitable died before treatment could be started. Fifty-six

patients were accepted during the first year; six of these had already been on maintenance haemodialysis for 3 to 15 months in a small "pilot" unit. All had had to give up their work despite conventional conservative treatment. The age and sex distribution of the patients is shown in Table I. The presumptive cause of the renal failure was: chronic glomerulonephritis

TABLE I.—Age and Sex Distribution

	Age:	10-19	20-29	30-39	40-49	50-59	Total
Males	..	0	14	12	14	1	41
Females	..	2	5	4	4	0	15

38, chronic pyelonephritis 8, cystinuria and chronic pyelonephritis 1, malignant hypertension 6, polycystic kidneys 1, post-partum renal cortical necrosis 1, systemic lupus erythematosus 1.

Maintenance Haemodialysis

All patients were treated initially by hospital dialysis (Fig. 1), and, so far, patients awaiting renal transplantation have

FIG. 1.—General scheme of management of patients with severe chronic renal failure.

remained on hospital dialysis. Those living within reasonable distances of the centre lived at home during this period, but

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patients from afar have had to be housed either in "convalescent" beds or in approved lodgings.

Most patients destined for home dialysis were dialysed during the daytime (Wednesday and Saturday) and attended for home dialysis training during the other weekdays. Very ill patients were also dialysed during these two daytime shifts whenever possible. The remainder were dialysed on four overnight shifts. Each patient received two 14-hour dialyses per week. Warm, single-pass, two-layer Kiil haemodialysers and automated individual-patient proportioners (Lucas or Dylade B) were used for both hospital and home dialysis. All the patients described here had external arteriovenous shunts.

Transplantation

All transplanted kidneys were of cadaveric origin. Of the 56 patients under review one had already had an unsuccessful transplant removed before April 1968 and a further 25 patients received transplants between 1 April 1968 and 1 July 1969. No patient has had more than one transplant.

Removal of the recipient's own kidneys was not routinely performed, but two patients required bilateral nephrectomy before transplantation because of impending blindness due to uncontrolled hypertension; a third patient had bilateral nephrectomy four months after transplantation because of persistent hypertension.

Cadaver Kidneys

Cadaveric kidneys were obtained from patients aged between 22 and 60 years who had suffered irreversible brain damage due to intracranial haemorrhage, trauma, or primary cerebral tumour. Kidneys were removed after the heart beat had stopped and after death had been confirmed by a doctor who had cared for the patient during life and by another member of the hospital staff not connected with the transplant team. The permission of the dead patient's relatives was always obtained, either by one of the surgeons or by a hospital chaplain. Donor and recipient were compatible with regard to major blood groups; leucocyte typing was not used in selection during this period. Potential donors were excluded if there was any evidence of renal disease, systemic infection, or malignant disease other than primary cerebral tumour. On five occasions both donor kidneys were transplanted simultaneously into two separate recipients.

After post-mortem bilateral nephrectomy the kidneys were perfused with cold (0–4°C.) heparinized Hartmann's solution and temporarily stored in vacuum flasks containing iced water. The mean ischaemic time of all donor kidneys was 130 minutes, including 65 minutes' "warm ischaemia." Six donor kidneys were removed in other hospitals (up to 40 miles (64 km.) away); in these the mean total and warm ischaemic times were 190 and 85 minutes respectively.

General Postoperative Care

Postoperatively, patients were barrier-nursed in single cubicles, but because of a shortage of suitable cubicles they often had to be moved to a general ward within three weeks of operation. Routine prophylactic antibacterial therapy was not given. The patients were seen daily by a member of both the surgical and the medical teams together; a bacteriologist also attended, organized the collection of specimens, and advised on the treatment of infections. Patients were discharged from hospital or transferred to a convalescent hospital as soon as they were reasonably well, the renal function was improving satisfactorily (creatinine clearance about 30 ml./min.), and a stable maintenance dose of immunosuppressive drugs had been achieved. They rarely left hospital less than four weeks after operation, but the period varied considerably according to the feasibility of frequent outpatient surveillance.

After discharge they were at first seen at least twice weekly for estimation of plasma urea and creatinine and white cell count. Subsequent follow-up of patients living a long way from the centre has been undertaken, in part, by their local referring hospital.

Immunosuppressive Therapy

Immunosuppressive therapy was started at or just before transplantation. With minor modifications, the following regimen was adopted.

Azathioprine.—The standard dose of 3.5 mg./kg. by mouth was reduced to 1.0–1.5 mg./kg. during periods of impaired renal function (urine volume <1 litre/24 hours, creatinine clearance <10 ml./min.) or when the W.B.C. count fell below 4,000/cu.mm.

Prednisone.—A dose of 100 mg./day was given for the first two days and then reduced by 10 mg./day until the seventh day. A dose of 40 mg./day was continued until the thirtieth day and then reduced to 30 mg./day. This dose was slowly reduced during the following three months to 10 mg./day if there was no evidence of rejection, on generally accepted criteria (Chisholm *et al.*, 1969). During rejection episodes the dose was increased to 100 mg. six-hourly for 48 hours and then reduced over three or four days to the previous dose or to 30mg./day, whichever was the greater.

Actinomycin C.—This was given only when the rejection process failed to respond to other measures and when there was no leucopenia or thrombocytopenia. In these circumstances 100 µg./day was given intravenously for up to three successive days.

Local External Irradiation.—Four doses of 150 r. were given on alternate days, starting as soon as practicable during the post-operative period. During graft rejection, further irradiation was given in divided doses to a total dose of 1,200 r.

Results

Patient Survival

Thirty-seven (66%) of the 56 patients accepted for treatment during the period 1 April, 1968 to 1 April, 1969 were alive on 1 July, 1969 (Fig. 2). Seven were established on

FIG. 2.—Fate on 1 July 1969 of 56 patients with "end-stage" chronic renal failure accepted during the period 1 April 1968 to 1 April 1969.

maintenance haemodialysis in the home (mean survival 19 months, including six months at home) and 12 had good renal function after transplantation (mean survival nine months). Eighteen of the 56 patients were still receiving maintenance haemodialysis in the hospital unit (mean survival five months). Of these, 14 had expressed a preference for renal transplantation and the remaining four were being trained for home dialysis. Three of the 14 patients awaiting renal transplantation had already had one unsuccessful transplant; 10 were considered to be fit for operation.

The relative contribution of hospital dialysis, home dialysis, and renal transplantation in the management of these patients

up to July 1969 is summarized in Fig. 3. For the 25 patients who had received a cadaveric kidney by 1 July 1969 the mean waiting period on maintenance haemodialysis was 10 weeks (range 1 to 40 weeks).

FIG. 3.—Role of hospital dialysis, home dialysis, and cadaveric renal transplantation in the management of 56 patients with “end-stage” chronic renal failure. A new maintenance dialysis unit opened on 1 April 1968 (indicated by dotted line).

Morbidity

Transplantation.—Many of the well-recognized complications of renal transplantation have been encountered, including urinary fistulae 3, iliac artery haemorrhage 2, gastroduodenal bleeding 1, wound haemorrhage associated with postoperative haemodialysis 3, and hypercalcaemia 1. Cushingoid facies are evident in most survivors and the blood pressure is slightly high in all but one.

Maintenance Haemodialysis.—The main problems were undoubtedly related to the external arteriovenous shunts, which frequently clotted or became infected and had to be replaced. Pyrexia and rigors during dialysis, presumably due to bacterial pyrogens, have proved troublesome from time to time. Intercurrent infections, including septicaemia and bacterial endocarditis, have also occurred. Hypertension was sometimes difficult to control, and fluid overload was a problem in a few patients. Three patients developed cardiac tamponade due to haemopericardium and required a partial pericardiectomy, and three developed disabling peripheral neuropathy. Clinical evidence of bone disease and hepatitis has not yet been observed.

The follow-up period is short (3 to 14 months), but in the 12 patients who still retain transplanted kidneys the mean blood urea is 52 mg./100 ml. (range 39-73 mg./100 ml.) and the mean serum creatinine 1.5 mg./100 ml. (range 1.2-2.1 mg./100 ml.). All 12 patients have returned to some form of

useful employment or are about to do so. Similarly, the seven patients on home dialysis are fit enough to work, but 6 of the 18 patients still on hospital dialysis are not.

Mortality

Nineteen patients (34%) have died; 9 had received haemodialysis only and 10 had also had a renal transplant. The mean survival of this group of patients was 5.8 months (range 0.3 to 20 months). Ten patients died within three months of starting maintenance haemodialysis. Death was often due to a combination of factors; the predominant causes in four main groups of patients are shown in Table II.

TABLE II.—Causes of Death in Patients with Terminal Uraemia Accepted for treatment between 1 April 1968 and 1 April 1969

Never fit enough for renal transplantation or home dialysis (five patients)	
Cerebrovascular disease; hypertension; shunt problems	1
Cerebrovascular disease; cardiac failure	1
Cardiac arrest during nephrectomy; hypertension; hyperkalaemia	1
Systemic lupus erythematosus; purulent peritonitis	1
Sudden death at home; cause unknown	1
Became fit enough for renal transplantation but died while waiting (four patients)	
Cerebrovascular accident	2
Cardiac failure; hypertension	1
Staphylococcal septicaemia; acute bacterial endocarditis	1
Died following renal transplantation without the need for further haemodialysis (four patients)	
Ureteric leak; septicaemia; pulmonary embolus	2
Intra-abdominal abscess; bleeding duodenal ulcer	1
Chest infection; epileptic fits	1
Died after returning to regular haemodialysis after removal of an unsuccessful renal transplant (six patients)	
Cardiac failure	2
Lobar pneumonia	1
Bacterial endocarditis; septicaemia; shunt problems	1
Septicaemia; marrow hypoplasia	1
Died during anaesthesia for reinsertion of arteriovenous shunts; hypertensive heart disease; hyperkalaemia	1

Discussion

An important consideration with any form of treatment is the extent to which it can be made available to those who require it. Up to now only a small proportion of the patients who might benefit have been treated by maintenance haemodialysis or renal transplantation. The precise demand for these facilities is still not known with certainty; estimates have varied between 18 and 75 per million per year (Alwall, 1966; de Wardener, 1966; Thaysen, 1966; Lipworth, 1968). Because of the exceptional circumstances of starting with a large empty unit we were able during the first year to accept practically all suitable patients referred. Moreover, the criteria of suitability were broad because in such circumstances it is difficult to refuse treatment to any patient. The population density in the region is greatest close to the dialysis unit, and the number of patients accepted from the two adjacent counties were at the rate of 34 (Monmouthshire) and 23 (Glamorganshire) per million per year. If the higher rate is assumed to be representative of the true incidence, the annual demand in Wales (population 2,600,000) would be about 90 patients per year. It is clear that neither renal transplantation nor home dialysis alone can cope with this demand, especially since, in addition to new patients, the number of patients requiring second and third transplants will increase.

The only logical approach to the problem is an integrated hospital dialysis/home dialysis/transplantation service, with free movement from one form of treatment to another as necessary. Clearly, in order to achieve a continuous turnover in the hospital unit every attempt must be made to avoid accepting patients who are not suitable for either home dialysis or renal transplantation. In practice, however, it is often very difficult to assess patients who are severely uraemic; early referral with regular follow-up by the renal unit is probably the most reliable method of selection.

One of the problems with an integrated service is deciding what proportion of the hospital dialysis facilities should be kept in reserve to cope with failed transplants and temporary

difficulties with home dialysis. We have arbitrarily reserved 20% of the facilities for this purpose, and so far this has proved adequate. Other problems encountered with various aspects of the service are best discussed separately.

Hospital Maintenance Haemodialysis

The main problem has been infection and clotting of external arteriovenous shunts. The decision to incorporate in the dialysis unit a small operating-theatre where shunt surgery can be performed has certainly been justified. There were considerable difficulties at first in building up a team of trained nursing staff and technicians. At present the nursing staff consists of two full-time sisters and 3 full-time staff nurses. There are also 18 part-time nurses who each work 8 to 32 hours per week. The remaining ancillary staff include one senior technician, two trainee technicians, and three male orderlies. There has been no difficulty in obtaining junior medical staff, but this can be attributed to the close relation between the maintenance dialysis unit and the professorial medical unit. Maintenance haemodialysis commitments are therefore shared by several of the junior medical staff.

Haemodialysis in the Home

Our experience of home dialysis is limited, but the problems encountered have been fewer than expected, possibly because the first patients to be established on home dialysis were carefully selected. The training of patients has been undertaken almost entirely by the nursing staff and technicians, and the medical staff have had to devote little time to it. Similarly, local authority adaptations to patients' homes have been arranged almost entirely by a non-medical home dialysis administrator. Undue delays have occurred in some instances, but local authorities are now completing the adaptations more quickly. The patients are in better health than when on hospital dialysis, but temporary hospital dialysis has been necessary on several occasions, confirming the need to reserve hospital facilities for this purpose. Geographical factors are likely to prove troublesome, since some parts of the region are 200 miles (320 km.) away from the renal unit. One patient lives at a distance of 160 miles (257 km.), but additional smaller units will probably be needed to support an increasing number of patients of this kind.

Cadaveric Renal Transplantation

The shortage of healthy cadaveric kidneys is probably the most serious impediment to the efficient use of the hospital dialysis unit. To what extent this shortage is the result of poor co-operation and communication with medical staff in other hospitals is not known. Eight potentially suitable donors were not used, because of refusal of consent by surviving relatives in five and failure to contact relatives when death occurred in three. Simple methods of isolated kidney preservation have proved reliable, and transport of kidneys from other hospitals and between neighbouring transplantation units (Birmingham and Bristol) has not been difficult to arrange. The full implications of prospective tissue typing and inter-unit collaboration are not yet clear, either in terms of the results to be expected in individual patients or in relation to logistics, but it seems likely that the cadaveric kidneys avail-

able could be used more effectively (Terasaki *et al.*, 1967; van Rood, 1969).

Mortality

Although the mortality rate in this series is similar to the average mortality for all European dialysis centres (Drukker *et al.*, 1968), it is much higher than the mortality in some dialysis units (Comty *et al.*, 1966; Scribner, 1967). This is accounted for by several factors. Patient selection was not as rigid as it might have been and some deaths were possibly avoidable. Closer supervision and more intensive haemodialysis might have prevented deaths due to hyperkalaemia and cardiac failure from fluid overload. If a great deal of attention is devoted to a small number of carefully selected patients excellent results are to be expected, but if an attempt is made to treat as large a number of patients as possible it is difficult to provide the same degree of attention to each individual patient and results may well be less satisfactory.

Comparison of the mortality rates of maintenance haemodialysis and transplantation can be misleading in an integrated service, since the relative mortality rates will depend on the policy of the unit. Thus if all patients who are not rehabilitated by haemodialysis receive a renal transplant the results of transplantation will be prejudiced. If, on the other hand, only young and good surgical-risk patients are selected for renal transplantation the dialysis programme will contain only the older age groups and a higher incidence of cardiovascular and other complications will result (Rubini *et al.*, 1968). Perhaps the most valid assessment of the success or otherwise of a regional centre is the overall survival rate, based on the number of patients *needing* treatment rather than on the number who actually received it.

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