RENAL TRANSPLANTATION - AN EARLY EXPERIENCE

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ABSTRACT

Renal transplant (RT) is now a therapy of choice for end stage renal disease (ESRD). The Nephrology Unit, Asvini started functioning in Dec 90 and to date 1298 sittings of hemodialysis have been given to 45 patients. Of these, 35 were in ESRD and 11 patients underwent renal transplantation at this hospital during the period Jan 91 - Dec 93. One patient expired after 18 months of transplantation due to infection. Early experience in screening patients for RT, use of immunosuppression, management of rejection episodes and protocol are presented with special emphasis on its relevance to the Armed Forces.

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KEY WORDS : Transplantation; Renal Failure; Immunosuppression; Rejection.

Introduction

Renal transplant (RT) is now a well established modality for treating patients of end stage renal disease (ESRD) [1,2]. In India it is estimated that about 80,000 new cases develop ESRD every year. In the affluent countries maintenance dialysis (MD) and RT are two viable treatment options for ESRD. In India only a few patients can afford MD because of its exorbitant cost and RT is the only practical option for the vast majority. RT is being done in India since 1971 and about 3000 transplants are performed annually, accounting for about 3% of ESRD. The one year graft survival is now 85% and patient survival 94%. RT is not only cheaper than MD but the quality of life is also superior [3].

In the Armed Forces from 1975 to 1984 an average of 280 patients of ESRD were hospitalised per year, and these have increased in the last decade. It is estimated that of these more than 34 patients per year will require RT [4]. In Feb 91, INHS Asvini activated this RT programme and since then 11 successful RT have been carried out with live related donors (LRD).

Material and Methods

Since 1990, 35 patients of ESRD have been treated with hemodialysis at INHS Asvini. Of these, only 11 could get LRD and underwent RT between Jan 91 and Dec 93. These were 9 males and 2 females of ages varying from 24 yrs to 55 yrs. The donors were close relations (Table 1).

TABLE 1
Particulars of patients and donors

Initials	Patient		Donor		
	Age	Sex	Relationship	Age	Sex
CG	45	M	Cousin	25	M
BG	55	M	Cousin	27	M
DM	25	M	Father	55	M
SB	28	M	Mother	45	F
RS	24	M	Mother	55	F
CB	27	M	Father	58	M
PS	34	F	Cousin	27	M
NS	40	F	Sister	42	F
BK	37	M	Sister	40	F
HM	30	M	Sister	25	F
MR	44	M	Brother	46	M

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The cause of renal failure was chronic glomerulonephritis in seven cases, chronic interstitial nephritis, diabetic nephropathy, benign nephrosclerosis and reflux nephropathy in one case each.

All the donors were live related and underwent clinical examination and investigations to rule out any systemic disease or active infection. Their lower urinary tract, cardiopulmonary status and gastrointestinal systems were also evaluated. Selection was based on immunological criteria using ABO grouping, HLA-ABC & DR typing and tissue cross matching.

TABLE 2

Blood group and HLA match of patients and donors

Patient	Patient Blood Group	Donor Blood Group	HLA Match
CG	B+	B+	50%
BG	AB+	O+	50%
DM	O+	O+	50%
SB	AB+	A+	50%
RS	A+	A+	50%
CB	A+	A+	50%
PS	AB+	O+	50%
NS	O+	O+	100%
BK	O+	O+	25%
HM	A+	A+	50%
MR	A+	A+	50%

The recipients were adequately dialysed for 3-4 months and had been given 2-3 random blood transfusions during this period. In no case, donor specific transfusion was given.

The protocol followed by us during the pre-operative preparation of the recipient consisted of cross matching of donor cells and recipient serum on "Day Minus 2", when the recipient was also given oral cyclosporine (12 mg/kgbw) in two divided doses.

"On Day Minus 1" the patient was haemodialysed for 5 hours followed by Inj. cyclosporine (5 mg/kgbw max 250 mg) in 250 ml 5% dextrose over 4-6 hours, Inj methyl prednisolone (750 mg) in 5% dextrose over 4-6 hours, Inj. cefotaxime 1.0 gm and Inj. amikacin 500 mg (prophylactic antibiotics).

On "Day 0" (day of surgery), prophylactic antibiotics were continued and all baseline blood samples were taken.

The donor was prepared for nephrectomy as for any other surgical procedure, with special emphasis on adequate hydration on the night prior to surgery.

Surgery on the donor and recipient was performed simultaneously in adjacent theatres under GA. The recipient was operated extraperitoneally in the right iliac fossa and the vessels exposed. Donor nephrectomy was done and the kidney was perfused with cold Ringer's solution to which heparin 1000 units, lignocaine 5 ml and 7.5% bicarbonate 5 ml were added. The donor kidney after perfusion was kept under ice and taken to the recipient. The renal artery was anastomosed end to end with the internal iliac artery, the renal vein end to side with the external iliac vein, and the urinary tract continuity was established by ureteroneocystostomy.

The recipient was postoperatively managed by special renal trained nursing staff in a sterile room equipped with all cardiopulmonary support. The patient's hydration, electrolytes, bicarbonates, blood sugar, urea and creatinine were carefully monitored every 4 to 6 hours, since the patient goes into diuretic phase and passes 10-12 litres of urine per day in the immediate post operative period.

The initial immunosuppression was with parenteral cyclosporine (5 mg/kgbw) and dexamethasone (4 mg) and by 4th day oral fluids and oral immunosuppression was started. Cyclosporine 10 mg/kgbw was given on the 4th day and tapered to 5 mg/kgbw by 14th day. Later it was maintained at 2-3 mg/kgbw for 6-9 months, keeping the serum cyclosporine levels within the acceptable range. Prednisolone was started with 40 mg/day on 4th day and tapered to 20 mg/day by 28th day and thereafter tapered to 10 mg/day by 6 months and given in this dosage life long. Azathioprine (Imuran, Azoran, Imuzat) was added as the third immunosuppressive drug on the 4th day at 1 mg/kgbw

and increased to 2mg/kgbw by 28th day. Haematenics and calcium supplements were also given.

Post operatively the recipient and donor were given oral fluids on Day 3, light diet on Day 4 followed by removal of drain and mobilisation of patient. An ultrasound done on Day 10 was followed by removal of urinary catheter. Stitches were removed by Day 14. Subsequently the recipient was observed for a period of 3 months in hospital before being sent on leave for convalescence.

Results

The post transplant results are shown in Table 3. Of the 11 recipients the only mortality was one patient who expired after 18 months on account of opportunistic infections and tested HIV positive. Two patients are in chronic rejection but do not require dialysis. The remaining patients are doing well on therapy and are on regular follow up.

The post transplant complications in the recipients are enumerated in Table 4. Five patients had acute rejection and were treated with Inj methyl prednisolone 3.0 gm over 5 days. Two patients who had delay in diuresis recovered fully within a few hours. One of the donors had hypovolemic shock in the first hour after surgery on account of the ligature slipping at the renal vein anastomotic site,

however no fatality occurred. One recipient had shock because of oozing from the anastomotic site and a resurgery had to be done within 24 hours to secure haemostasis.

TABLE 4

Post transplant complications

Complications	No of Cases
Acute tubular necrosis	1
Cyclosporine toxicity	2
Acute rejection	5
Chronic rejection	2
Septicaemia	1 Expired
Persistent hypertension	2

Note : Some patients had more than one complication.

Discussion

Success in renal transplantation can be said to have become significant with the advent of HLA matching, and this was used for the first time in 1962 for selection of donor and recipient [5]. Another milestone was the first clinical use of cyclosporine in 1978 as immunosuppressant, which revolutionised the success of RT [6]. The graft survival in western countries at 1 and 5 years prior to use of cyclosporine was 78% and 47% and since its usage, it is 97% and 89% [7]. Initially the method used for immunosuppression was total body irradiation which was replaced by

TABLE 3

Graft survival at 1 & 2 years

Patient	Date of Transplant	Rejection Episode	Graft Survival		
			6 months	1yr	2yr
CG	11.2.91	01	+	+	CR
BG	15.4.91	01	+	+	CR
DG	19.7.91	02	+	+	Expired HIV +VE
SB	11.3.92	Nil	+	+	FU
RS	07.12.92	01	+	+	FU
CB	11.3.93	Nil	+	FU	FU
PS	19.4.93	01	+	FU	FU
NS	25.6.93	Nil	+	FU	FU
BK	12.7.93	Nil	+	FU	FU
HM	20.9.93	Nil	FU	FU	FU
MR	13.12.93	Nil	FU	FU	FU

Note : CR - Chronic Rejection, FU - under follow-up

azathioprine and steroids as a standard regime in 1963 [5]. However the prolonged use of this conventional therapy (AZT + PRED) in HLA identical sibling transplants resulted in loss of kidney due to chronic rejection after 3 years. With the availability of cyclosporine the renal function is not significantly worse after 3 years. Nevertheless since cyclosporine for prolonged periods can have nephrotoxicity, most centres are using azathioprine and low dose steroids in all cases after initial use of cyclosporine [8]. The same is followed at our centre.

All our transplant cases were given immunosuppression with 3 drugs (cyclosporine + azathioprine + prednisolone). No major untoward effects were detected clinically, biochemically and haematologically. Cyclosporine toxicity was suspected clinically in two cases and was confirmed by serum cyclosporine levels and they were managed by reducing the dose of cyclosporine. Liver function tests were regularly done since both cyclosporine and azathioprine are hepatotoxic and may have to be replaced by cyclophosphamide if indicated.

There are a number of factors influencing graft survival. The results of one haplotype identical living related transplants between siblings or between parent and child have improved dramatically in recent years. This is due first, to the use of donor specific transfusion (DST) with or without azathioprine cover and secondly to cyclosporine. The unresolved controversies at present are whether random transfusions are as effective as donor specific transfusions and whether the use of cyclosporine without transfusion is as effective as either DST or random transfusion [9]. We gave random transfusion with no deleterious side effects. For the moment, it seems wise to assume that pre-operative transfusions probably influence graft survival, but it must be said that there is increasing reluctance to give random transfusions before transplantation because of fear of transmitting human immunodeficiency virus (HIV).

Opler and Terasaki [10] first pointed out

that blood group "O" recipients have better graft survival than "Non O" recipients. However with the advent of cyclosporine this has little relevance. The protocol of blood grouping for RT between donor and recipient is in no way different from those used for blood transfusion. In three of our cases we have transplanted kidneys from O+ and A+ donors to an AB +ve recipient with no incompatibility or rejection.

In the pre cyclosporine era, graft survival was poorer in the elderly and older the age of the donor, poorer was the outcome. All our donors were in the age group of 26-58 yrs. The sex of donor and recipient also does not appear to influence the outcome. The other factors influencing graft survival are the initial functional status of the transplanted kidney as evident by immediate diuresis, number of rejection episodes and infection in the post operative period. Serum creatinine more than 2.5 mg% on the fifth post operative day also correlates with poor survival [7].

Dialysis and transplantation are costly treatments and in recent years every country has reflected on the cost effectiveness of these expensive therapies. Between the two, transplantation is the cheaper option as the patient can soon go to work and be a productive member of society. Also the patient survival rates after transplantation are better than on dialysis [10].

The problem in the Armed Forces was reviewed by a highly qualified panel in 1986 [4], and since 1988 the cost of RT in civil hospitals for entitled patients is reimbursed by the Government. RT programme was restarted in 1991. However some of the problems which have to be resolved in the Armed Forces are the duration of MD if no donor is available? In our centre we have given MD for a maximum duration of 21 months before the patient could be transplanted. Moreover in the absence of a live related donor (LRD), would philanthropic donor (unrelated) be acceptable, and could the wife be accepted as a donor? In chronic rejection cases, would retransplant be advocated? How long do we

manage patients with HIV and HBsAg positive status on dialysis. The provision of permanent trained nursing and paramedical personnel to run these specialised centres also needs to be considered. In our 35 cases of ESRD in three years, only 11 could bring forward LRD (33%) and were successfully transplanted. Another 8 expired, 10 are awaiting suitable donors, and the rest have been lost to follow up.

The availability of organs for transplant can be ensured by a legislation by the Central Government allowing use of cadaveric organs for transplant as is being done in the western countries. The flourishing illegal organ sale for RT will stop and this would result in benefit to the patients from poorer strata of life.

Patient and graft survival cannot be considered in isolation from the quality of life after transplantation. It is this potential not only to keep a patient alive but to restore them to a relatively normal existence which makes RT so attractive and the preferable form of treatment of ESRD.

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