Renal Replacement Treatment for End Stage Renal Failure: The Ideal Scenario

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128

ABSTRACT

The treatment of end-stage renal failure (ESRF) with dialysis and transplantation has been very successful. Although the incidence and causes of ESRF in India are likely to be similar to those in the rest of the world, economic barriers result in only a very limited number of patients receiving renal replacement therapy.

The choice of renal replacement therapy must be evidence-based. There are an increasing number of options for dialysis and well established protocols for deceased and living donor transplantation.

The following factors are important in ensuring the best outcomes for patients in haemodialysis: durable vascular access, preferably a native arteriovenous fistula; avoidance of the use of central venous catheters for dialysis; adequate duration and frequency of dialysis; correction and prevention of salt and water overload, and hence hypertension; correction of anaemia; and maintenance of optimal nutrition.

The resurgence of interest in increased frequency haemodialysis provides greater treatment flexibility and improved outcomes for patients. Barriers to daily dialysis are logistic, economic and technical.

The "ideal scenario" for dialysis in the 21st Century is optimal, rather than barely adequate, dialysis. This will involve more frequent dialysis with simpler technology allowing an increase in home dialysis.

INTRODUCTION

The choice of any renal replacement therapy must be evidence-based. When patients and nephrologists decide on treatment options the factors that are known to influence outcome must be considered; even when it is not always possible to provide the ideal because of lack of resources. My purpose is to discuss the "ideal scenario", with predominant emphasis on haemodialysis.

INCIDENCE AND PREVALENCE OF END-STAGE RENAL FAILURE (ESRF)

In the developed world, the treatment of end-stage renal failure (ESRF) with dialysis, whilst costly, has been remarkably successful. A brief history of the major landmarks in the development of treatments for ESRF is shown in Table 1. Since the 1980s there has been a marked increase in the incidence of treated ESRD with projections from the USA suggesting that the incidence will continue to rise at the rate of 6-7% annually, at least until 2010.[1]

There is little information on the incidence and prevalence of ESRF in India. The causes of ESRF in India are probably similar to those in countries with reliable renal disease registries (see Table 2) and so it is likely that the rates of ESRF will be similar to those in the rest of the world (Table 3).[2-4]

TREATMENT OPTIONS FOR END-STAGE RENAL FAILURE

The options available for treatment of ESRF are shown in Table 4. These treatments may be facility or home-based. Home-based treatments are the cheapest. Physician and patient preference, the local health system and the funding options for dialysis will influence the choice of treatment.

Renal transplantation

Compared with chronic dialysis, renal transplantation generally provides improved survival, improved quality of life, and is cheaper in the long term. There is a global shortage of kidney donors and for most patients with ESRF dialysis is the only treatment option. There are about 45 major centres performing transplants in India.[4] In India, 80-90% of transplanted kidneys are from living donors. The outcomes of kidney transplantation have shown a steady improvement in the last 10 years. One-year unadjusted survival for first deceased donor kidney transplants in the USA is 95% for patients and 89% for grafts. For first living donor transplants the figures are 98% and 94%, respectively.[5] Patients receiving a deceased donor kidney transplant in the USA during the period 1995-1999 had a graft survival half-life of 10.9 years.[6] After the first post-transplant year, the commonest causes

Table 1: Brief history of landmarks in renal replacement therapy

1861	Description of dialysis by Thomas Graham
1942	First successful haemodialysis by Willem Kolff
1954	First live donor transplant
1960	Quinton-Scribner arteriovenous shunt and first maintenance dialysis patient
1964	Arteriovenous fistula developed by Cimino and Brescia
1960s	Development of azathioprine
1980s	Development of venous cannulae for dialysis
1983	Introduction of cyclosporin
1989	Introduction of erythropoietin
1990s	Development of laparoscopic donor nephrectomy

of graft loss are chronic allograft nephropathy and patient death due to cardiovascular disease, infection or malignancy.

Barriers to transplantation include: the cost of immunosuppressive drugs (particularly in developing countries), the lack of donors, the impact of recipient co-morbidity on the feasibility and safety of transplantation, the deleterious effects of immunosuppression (infection, diabetes, malignancy or nephrotoxicity), and recurrence of the original renal disease in the graft. Renal transplant outcomes can be enhanced by using more living donors, carrying out transplantation before dialysis is needed, using younger donors, increasing the number of very well matched transplants and improving general medical care.

Dialysis treatment

In India, it is thought that only 5% of patients with ESRF are able to have a renal transplant and thus the options for the remainder are dialysis or palliative treatment, with certain death.[4] It has been estimated that there are about 400 dialysis units with 1000 dialysis stations in India. Until recently only a very small number of patients were treated with peritoneal dialysis.[4] Most dialysis is started in the expectation that the patient will receive a renal transplant in a short time. Economic considerations often result in patients receiving inadequate dialysis.

Determinants of outcome for dialysis patients

Worldwide the majority of patients with ESRF are treated with haemodialysis and most data on treatment outcomes are for this form of dialysis. About 35% of peritoneal dialysis patients switch permanently to haemodialysis in the first two years, while only 5% of haemodialysis patients switch to peritoneal dialysis.[7] The data available for patients treated with peritoneal dialysis suggest that residual renal function is the major treatment-related determinant of outcome. Haemodialysis is an efficient therapy for ESRF but the best clinical outcomes can only be achieved with adequate duration and frequency of dialysis sessions. These basic therapeutic principles are often not respected and, as a consequence, morbidity and mortality in maintenance haemodialysis patients have increased.

The Australia and New Zealand Dialysis and Transplant Registry reported an analysis of factors affecting the survival of 4,270 haemodialysis patients in Australia and New Zealand on dialysis for more than 90 days between March 1997 and September 2002.[8] The following factors were associated with

Table 2: Causes of end-stage renal failure (%) [2-4]

Cause	India	UK	New Zealand	USA	Japan
Glomerulonephritis	37	30	23	9	47
Diabetes	24	16	45	43	31
Hypertension	13	12	9	26	10
Chronic interstitial nephritis	14	8	5	2	2

Table 3: Incidence and prevalence of dialysis treatment for end-stage renal failure (pmp) [2-4]

	India	UK	Europe	New Zealand	USA	Japan
Incidence	Unknown	96	115	115	315	252
Prevalence	Unknown	528	659	403	1217	1624

pmp = patients permillion ppulai

reduced patient mortality: a native arteriovenous fistula with adequate blood flow, haemoglobin > 11 g/dl, adequate dose of dialysis as measured by urea removal, and treatment frequency of at least three times weekly with a treatment duration of at least 4.5 hours. Several other studies have shown that nutrition, adequacy of haemodialysis, blood pressure control and treatment time, anaemia and the use venous catheters, instead of native fistulae, affect patient survival.[9,10-14]

Achieving better outcomes for haemodialysis patients

The gold standard for survival for haemodialysis patients is the experience reported by Bernard Charra and colleagues from France for patients treated with long, slow dialysis.[15] They reported the 20-year actuarial survival of 445 unselected haemodialysis patients receiving 8 hours overnight dialysis, three times weekly. The survival rates were 87% at 5 years, 75% at 10 years and 43% at 20 years. This excellent patient survival was ascribed to adequate blood pressure control and a reduction in cardiovascular mortality. In contrast, in the USA annual mortality rates among haemodialysis patients are the highest in the industrialised world at 23% per year. Patients usually receive treatment three times weekly for 3-4 hours at a time. It has been estimated that one-sixth of these patients receive inadequate dialysis. Inadequate dialysis is related to poorer survival and increased hospital admissions and high inpatient costs. Barriers to adequate haemodialysis include dialysis under-prescription, the use of venous catheters, and shortened treatment time.[16]

The presence of diabetes and cardiovascular disease and old age understandably has an adverse effect on survival of dialysis patients.[17] Cardiovascular morbidity and mortality remain very high in haemodialysis.[18] This is due in great part to the insufficient control of extracellular volume and blood pressure. Long, slow dialysis controls (eight hours thrice weekly) blood pressure with only a minority of patients requiring anti-hypertensive drugs.[19,20] Anti-hypertensive medication is almost always necessary to control blood pressure if dialysis sessions are less than 5 hours.

Vascular access for haemodialysis

The arteriovenous fistula is the preferred form of vascular access for haemodialysis. Achieving a high prevalence of arteriovenous fistulae for haemodialysis patients requires a clear unit policy

Table 4: Treatment options for end-stage renal failure

Transplantation	Deceased donor		
	Living-related donor	Pre-emptive / After starting dialysis	
	Living-unrelated donor		
	Altruistic donor		
Haemodialysis	Conventional short hour thrice weekly	High flux dialyser / Low flux dialyser	Home / Satellite / Centre
	Long/slow thrice weekly		
	Daily short hour		
	Daily or alternate day nocturnal		
Peritoneal dialysis	Continuous ambulatory peritoneal dialysis (CAPD)		
	Automated peritoneal dialysis (APD)		
Palliative care	No renal replacement treatment		

Table 5: Comparative features of short daily and nocturnal haemodialysis.

Feature	Short daily haemodialysis	Nocturnal haemodialysis
Sleep	Undisturbed	Sleep possible Improved sleep apnoea
Arteriovenous fistula	Yes	Yes
Phosphate removal	Poor Phosphate binders needed	Excellent No dietary restriction
ß$_2$-microglobulin clearance (calculated)	10-15% greater than conventional dialysis	Four times that of conventional dialysis
Blood pressure medications	50% fewer than conventional dialysis	None
Treatment morbidity	Better	Excellent
Site	Home or centre	Home
Cost	Cheaper at home	Cheaper at home

Table 6: Benefits of increased frequency and duration of dialysis

Provides more dialysis with less morbidity
Improved middle molecule (β2-microglobulin) clearance
Fewer post-dialysis symptoms
Better BP control with fewer (or no) drugs
Regresssion of left ventricular hypertrophy
Improved appetite, fewer dietary restrictions and improved nutrition
Improved control of calcium/phospate metabolism
Higher haemoglobin with lower dose of erythropoietin
Improved sleep - less sleep apnoea
Improved neurocognitive function
Improved quality of life and rehabilition
Reduced hospitalisation
Improved survival

and the joint involvement in the planning of all vascular access procedures of surgeons, dialysis clinicians and nephrologists. Such planning should be individualised and favour permanency, not expediency, to reduce early failure rates. Prolonged patency rates are dependent on skilled initial use of AV fistulae by dialysis staff.[21,22]

Increased frequency dialysis

Despite refinements over the past 20 years, conventional haemodialysis remains a morbid, "unphysiologic" experience for many patients. Its intermittent nature, which is a compromise between patient acceptance, economics and dialysis adequacy, makes it a far from ideal therapy. Patients experience massive fluid shifts and metabolic alterations during 3 times weekly (conventional, short hours) haemodialysis, and intolerable symptoms such as severe hypotension, headaches, muscle cramps, restless leg syndrome, insomnia and pruritus. A small, but growing, experience with increased frequency dialysis (Table 4) suggests that daily dialysis is associated with a reduced mortality and improve quality of life in comparison to conventional dialysis.[23] The features of short dialysis and nocturnal daily dialysis are shown in Table 5. Daily haemodialysis has considerable potential to improve quality of life and reduce morbidity in patients with ESRD (Table 6). Barriers to its implementation are logistic, economic and technological. Home or community-based care and the development of a haemodialysis machine utilising reuse and automated cleaning and set-up can overcome these barriers.

SUMMARY

The ideal scenario for dialysis treatment in the 21st Century is optimal, rather than just adequate, dialysis. This will involve longer duration and more frequent dialysis utilising dialysis machines that are essentially automatic and require little, or no, preparation or maintenance by patients or staff.

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Useful websites

www.anzdata.org.au
www.usrds.org