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Peritoneal dialysis after failed kidney transplantation; a case series with review of the literature

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ABSTRACT

Kidney transplantation is a definite treatment for end-stage renal disease (ESRD). However, management of allograft dysfunction has remained a major challenge and some patients return to dialysis after renal transplantation. Studies showed that peritoneal dialysis (PD) results in a higher chance of survival and a lower risk of delayed allograft dysfunction compared to hemodialysis (HD). For this reason, this study explored the initiation of PD in six patients with renal allograft dysfunction in Tabriz Imam Reza hospital (referral PD center). This case reported the results of PD and incremental PD among these patients with failed kidney transplantation. Creatinine and hemoglobin levels, duration of starting PD, PD exchange, PD modality, immunosuppressive drugs mortality rate and urine volume were evaluated during the study. In conclusion, although re-transplantation is a gold standard therapy in failed kidney transplant patients, PD or incremental PD could be a suitable and home-based modality for preserving renal function and urine output in these patients.

Case Series

Implication for health policy/practice/research/medical education:
Although renal transplantation is a definite therapy for end-stage renal disease (ESRD), the management of allograft dysfunction has remained a major challenge. Our study showed that peritoneal dialysis (PD) or incremental PD is a bridge-like treatment and could be a good option for preserving residual renal function and maintaining urine volume until successful kidney re-transplantation.

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Introduction

Although kidney transplantation is proved as a definite treatment for end-stage renal disease (ESRD), management of allograft dysfunction remains a major challenge among nephrologists. Patients with a failed kidney allograft (FKA) represent a distinctive and growing chronic kidney disease (CKD) population that are at higher risk for unpleasant events (1). Evidence from the UK Renal Registry in 2015 found that 13% of adult kidney transplanted people have a glomerular filtration rate (GFR) of less than 30 mL/min/1.73 m^2. Nevertheless, the increasing number of patients with FKA, a strategy of the timing of renal replacement therapy and a kind of treatment, are different and only a few of these CKD patients undergo peritoneal dialysis (PD) (2). A recent meta-analysis showed that pre-transplant CKD patients that have undergone PD for renal replacement therapy have a higher chance of survival and lower risk of delayed allograft dysfunction compared to the patients who were on hemodialysis (HD) (3). There is scanty research on the role of PD in the post-transplant period and its application in FKA. For this reason, we decided to discuss the initiation of PD as renal replacement therapy in patients with declining renal allograft, especially those who have some residual allograft function. Finally, six renal allograft dysfunction patients were introduced who were recently (about 12 months ago) placed on a PD procedure in Tabriz Imam Reza hospital (referral PD center).

Definition, epidemiology, and patient outcomes after graft failure

Recently, several reasons are demonstrated for kidney allograft failure, including recurrence of past glomerular disease, drug toxicity of calcineurin inhibitors, BK virus nephropathy, and chronic allograft nephropathy (CAN). CAN refers to the dysfunction of kidney allograft at least one year after transplantation due to immunological processes that are divided into cell-mediated or humoral

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immune responses (4). During the recent decades, the number of patients with an established diagnosis of FKA has increased. Graft loss is correlated with a higher weight of psychological and medical morbidity in CKD patients (5). In terms of survival, several studies demonstrated that patients losing functional kidney allografts and returning to dialysis had worse outcomes compared to the ESRD patients with no history of transplantation. However, analysis of the Renal Epidemiology and Information Network (REIN) registry showed similar survival outcomes between patients with FKA diagnosis aged below 65 years and other ESRD patients (6).

The importance of residual renal function in patients with FKA

Patients with FKA, especially in the first months of starting dialysis, have a significantly higher mortality risk than ESRD patients without transplantation history (7). Some studies showed that when FKA patients have a GFR of below 45%, maintaining each 5 mL/min/1.73 m^2 of GFR is associated with a 15% lower risk of both cardiovascular events and death (8). Preserving residual renal function is a dominant prognostic factor in both HD and PD patients. The survival benefit of preserving kidney function is attributed to better volume control, higher clearance of middle-size molecules that are not harvested easily by usual dialysis methods, and decreased systemic inflammation (9). Although several studies showed that preserving residual renal function could be managed by multiple protective strategies including the use of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, avoiding nephrotoxic drugs and utilizing biocompatible membrane fluid, PD and incremental PD have still more important benefits in preserving renal function and could improve life quality in ESRD patients.

Time of institution of renal replacement therapy in FKA

In contrast to the CKD population, only limited data are available for the appropriate onset of dialysis in FKA patients. It should be noted that these patients have a worse outcome in comparison to CKD patients due to comorbidities and earlier consumption of immunosuppressant drugs that pose them with a higher risk of infection and cardiovascular events (10). Studies showed that there was no survival benefit in earlier prescribing dialysis in any group of FKA, especially among healthier and younger individuals (11).

Choice of dialysis in FKA patients

Patients with FKA would be placed on dialysis therapy until finding a suitable donor that is similar to the other ESRD population. Studies in the Asian countries, such as Honk Kong and Thailand, that choose PD as the first option for ESRD patients showed that PD is not inferior to HD, and it acts as a bridge-like treatment until organ transplantation (12). PD is accepted rigorously and efficiently in these patients, while one study showed a slight degree of peritonitis. Another Belgian study showed that FKA patients that undergo PD have better survival outcomes and a lower incidence of peritonitis comparable to the patients who had no history of kidney transplantation. Preliminary reports recommended that the risk of PD-related infectious complications does not increase in FKA patients (13). A large-scale study of patients who started dialysis after the established kidney transplant failure showed that the option of dialysis modality (HD or PD) did not affect patient survival in general (14). Finally, a meta-analysis study in 2020, which evaluates the survival rate of failed kidney transplant patients undergoing PD, showed that these patients do not have worse outcomes than the other ESRD patients. In this study, similar mortality, technique survival and peritoneal infection rates were observed between the two patients (15). Another larger cohort study with 328 involved patients who started PD after their first kidney transplant failure demonstrates the same rate of peritonitis and survival rate as patients who did not have transplanted kidneys (16). Finally, many studies established that the outcome of patients starting PD after kidney transplant failure was similar to the patients who choose HD. Therefore, PD can be regarded to be a good treatment choice for patients returning to the dialysis center after kidney transplant failure (1).

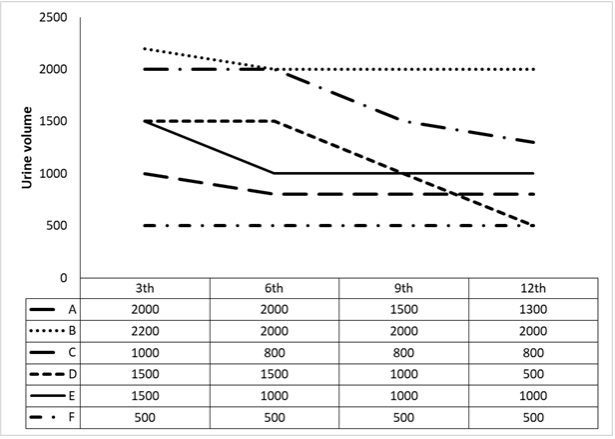
Incremental PD

Incremental PD is a PD procedure that is lower than the typical "full dose" of PD described for CKD patients. In this regard, the fusion of residual kidney function (RKF) and peritoneal clearance would be adequate to perform kidney clearance but the order could be augmentable, if (and when) RKF decreased (17). Incremental PD has several advantages including of lower chance of peritonitis, milder exposure to dialysate fluid glucose, the slighter chance of the formation of advanced glycated products, more patient acceptance and lower technical failure and finally being inexpensive (18). In terms of hospitalization and mortality, studies showed that incremental PD has a favorable effect on diabetic patients with acceptable residual renal function (19).

Case Series

PD and especially incremental PD began in six patients with failed kidney transplant recipients. In addition, 66.7% of patients were female (n= 4) and 33.3% of patients were male (n= 2). The mean age and weight of all patients were 45.33±11.32 years and 66.33±9.56 kg, respectively. The median creatinine (Cr) level was 5.1 (4.72-6.4) and the mean hemoglobin level was 10.43±2.03. The median duration of starting PD to kidney failure was 11.83±1.6. Three patients had one PD exchange per day (50%) and the others had two, three, or four PD exchanges per day. PD modality in all patients was continuous ambulatory peritoneal dialysis (CAPD). Moreover, all patients

consumed cyclosporine as a immunosuppressive drug twice a day with different dosage including 50/50 (n= 3, 50%), 25/25 (n=1, 16.7%), 25/50 (n=1, 16.7%), and 50/75 (n=1, 16.7%). In addition, five patients survived and only one patient died because of the COVID-19 (Table 1). Urine volume was evaluated among PD patients after failed renal transplantation at the 3rd, 6th, 9th, and 12th months. It was revealed that the median urine volume of PD patients increased at the 6th [1500 (875-2050) versus 1750 (875-3500)] but the process decreased at the 9th [1000 (725-1625)] and 12th [900 (500-1475)] (Figure 1).



	3th	6th	9th	12th
A	2000	2000	1500	1300
B	2200	2000	2000	2000
C	1000	800	800	800
D	1500	1500	1000	500
E	1500	1000	1000	1000
F	500	500	500	500

Figure 1. Urine volume of all peritoneal dialysis patients after failed kidney transplantation.

Discussion

Kidney transplantation is the gold standard treatment for all patients with native or transplanted kidney failure. However, limited access to a suitable donor especially in second transplantation requires that many patients with FKA receive prolonged renal replacement therapy. Among ESRD patients undergoing HD or PD, preserving the urine volume is an important prognostic marker that is accomplished with decreased cardiovascular events and mortality. Proposed mechanisms responsible for these effects include better controlling of water and solutes, Effective clearance of middleweight molecules, and decrease of inflammation (9). A strategy in this field is starting peritoneal dialysis. Overall, ESRD patients who have started PD especially incremental PD with icodextrin and biocompatible solutions have better preservation of residual urine volume to HD (20). A recent comprehensive systematic review revealed that incremental PD could preserve residual renal function and urine volume, especially in the first year of treatment (21). It is found in current studies that starting PD in patients waiting for a kidney transplant can be more beneficial or at least equally important compared to HD. Even so, patients placed on PD are healthier than the non-PD group (22).

Although Urine output alone should not be used for the detection of residual kidney function, studies showed that this parameter has a good correlation with patient outcomes undergoing renal replacement therapy. ESRD patients with urine volume greater than 500 mL/d have significant residual kidney function for controlling adverse effects, such as pulmonary edema and hyperkalemia (23). A study in ESRD patients on HD showed that even patients with greater than 100 mL/d of urine had a 65% lower risk for cardiovascular-related death (24). A large-scale multicenter study on 670 hemodialysis patients on self-report urine output every 6 months demonstrated that residual urine output (UOP) is associated with better survival and quality of life in dialysis patients, and significant correlations exist between lower urine output and higher mortality. Therefore, having a baseline UOP of >250 mL/d and maintaining UOP within 1 year had a significantly lower risk of mortality (25). All of the patients in our study had at least 500 ml/day of urine output at end of one year after the onset of PD. On the other hand, our study showed that starting PD in FKA can also preserve urine output until one year of starting PD.

Conclusion

While re-transplant could be a gold standard for declining renal allograft dysfunction, PD or incremental PD would be a bridge-like treatment and a good option for preserving

Table 1. Clinical information of PD patients after failed kidney transplantation

Patient	Age	Gender	Time of allograft failure	HGB	Weight	PD modality	Frequency of PD exchange/day	PD dialysate type	Cr on initiation PD	IS drugs and outcome	Outcome
A	55	Female	12 months ago	11.9	68	CAPD	One Exchange/day	2	5.5	Cyc 50/25	Alive
B	47	Female	13	9	81	CAPD	One	1 or 2	5	Cyc 50/50	Alive
C	38	Female	12	9.5	52	CAPD	3 Exchange/day	1 and 2	5.2	Cyc 50/50	Alive
D	53	Male	10	10	65	CAPD	2	1 and 2	5	Cyc 75/50	Alive
E	53	Male	10	8.4	62	CAPD	1 Exchange/day	1	3.9	Cyc 50/50	Death due to COVID-19
F	26	Female	14	13.8	70	CAPD	4 Exchange/day	1 and 2	9.1	Cyc 25/25	Alive

CAPD: continuous ambulatory peritoneal dialysis, Cr: creatinine, Cyc: cyclosporine, HGB: hemoglobin, IS: immunosuppressive, PD: peritoneal.

residual renal function and maintaining urine volume until successful kidney transplantation. This inexpensive home-based modality can be used more extensively for other conditions similar to FKA.

Authors' contribution

MA and FF were the principal investigators of the study. MA and FF were included in preparing the concept and design. MA, FF, KB and SMH revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical approval

This case series was conducted in accord with the World Medical Association Declaration of Helsinki. Patients has given us their written informed consent for publication as a case series article. This study was approved by the ethics committee (Ethical code: IR.TBZMED.REC.1401.115) of Tabriz University of Medical Sciences. This study was extracted from a research project at the Kidney Research Center at this university (Grant# 69738). Additionally, the authors completely have observed the ethical issues including data fabrication, falsification, plagiarism, double publication misconduct, or submission and redundancy.

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