Options of Renal Replacement Therapy in CKDu

Abstract
Patients with advanced Chronic Kidney Disease of Unknown origin (CKDu) need to plan for renal replacement therapy. The patients usually affected are probably best served with living-related renal transplantation. Potential donors from the same area are possibly at risk for developing CKDu and need close monitoring post kidney donation. Peritoneal dialysis (PD) is probably a better option as hemodialysis (HD) centers are located in urban areas only and patients have the convenience of receiving therapy at home. The “PD first” pilot project of Sri Lanka is a unique initiative that trains community physicians to offer PD to patients with advanced CKDu. In Telengana and Andhra Pradesh, the Aarogyasri insurance scheme provides for poor patients to avail of free HD and transplantation in government and private hospitals. Much more needs to be done to care for all those who are affected. A public–private partnership model for providing comprehensive care to patients with advanced CKDu can be undertaken in all areas affected by CKDu that makes renal replacement therapy (RRT) available and accessible, irrespective of financial and social limitations.

Keywords: Hemodialysis, insurance, PD first, peritoneal dialysis, transplantation

Introduction
The principal objectives of CKDu management are identifying the etiology of CKDu for prevention of onset of disease and screening for early detection to retard progression. The unfortunate reality is early stages of illness being clinically silent; one is forced to plan for renal replacement therapy (RRT) in this group of patients as the disease progresses.

Available options of renal replacement therapy
RRT modalities of hemodialysis (HD), transplantation, and peritoneal dialysis (PD) can theoretically be offered to all patients of advanced CKDu. There are unfortunately several important pragmatic considerations that go beyond medical reasons toward the choice of RRT modality.

Transplantation
Most patients are young or middle aged, that is, between the ages 30 and 60 years.[1] Overall, transplantation is the best and most cost-effective RRT modality and is offered to all advanced CKD patients, unless there are medical contraindications. The Transplantation of Human Tissues Act in Sri Lanka and the Transplantation of Human Organs Act in India have diminished commercial transplantation. Similar to other patients with advanced CKD, transplantation may be offered for those CKDu patients with healthy voluntary related kidney donors. If the potential donor is living in the same area where CKDu is prevalent, it may be argued that this noble gesture is fraught with unquantified risk of developing CKDu in the future.[2] Such a donor needs close monitoring and nephrology follow-up. If such a suitable living donor is unavailable in the immediate family, the option of waiting for a deceased donor kidney transplantation must be discussed and patient listed for the same.

Dialysis
In most parts of the world (except countries that have adopted the “Peritoneal Dialysis first” policy), HD is the default RRT modality. However, the population where CKDu is prevalent is predominantly nonurban in nature and those affected live in areas far afield of HD units. In one of the affected areas in Sri Lanka, patients need to travel distances of 20 km or more for HD.[2] There is also a paucity of availability of HD stations to offer RRT to all affected.

In this context, use of PD as the RRT modality of first choice suggests itself. There are several advantages for CKDu patients.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Access this article online
Website: www.indianjnephrol.org
DOI: 10.4103/ijn.IJN_396_19

How to cite this article: Varughese S, Agarwal SK, Raju TR, Khanna T. Options of renal replacement therapy in CKDu. Indian J Nephrol 2020;30:261-3.
affected individuals. Convenience of home-based therapy and freedom from twice- or thrice-weekly visits to a HD unit are the most compelling. Patients with CKDu are often the breadwinners of their families and visits to a HD unit robs them of their livelihood because of the time lost in travel and therapy. Added to this is better initial survival with PD and slower decrease in residual renal function in comparison with HD.

Over the last two and a half years, the Sri Lankan government has undertaken a new initiative that is slowly bearing fruit now. PD is offered in CKDu-affected areas as part of a pilot “PD first” policy unique in South Asia. This approach makes RRT easily accessible to patients living in rural areas, and cost-effective strategies including local manufacturing of fluid have been attempted successfully. Especially in regions where health care is at least partially provided in the public sector, the cost of fluid is often offset by the money saved. The high costs of HD machines and consumables, valuable hospital space required to host the dialysis unit, other infrastructure, and personnel, the last being the most burdensome are areas where PD is seen to be superior. In addition, in patients who are newly initiated on dialysis without time for adequate preparation for RRT, the risk of catheter-related bacteremia and other infections far outweighs the risk of peritonitis.

Community physicians, nurses, and other staff are trained in the science of PD. Each local PD clinic has a doctor, a nurse, and five assistants to train all the patients in the area and oversee their dialysis regularly. Prior to initiating PD, patients’ homes are suitably modified (e.g., by installing hand washing sink) to enable them to perform PD easily within their homes. In parts of India, where clean running water is unavailable, patients are encouraged to use diluted potassium permanganate solution to wash hands before doing exchanges.

The Teaching Hospital at Kandy, Sri Lanka, sends nephrologists to supervise patient care only at initiation of PD and when there are major complications. The major teething trouble in implementation of this project has been acceptance by the community. Only 10% of those initially advised PD were willing for the therapy. The start of a “pre-end stage renal disease” clinic has helped patients to be more receptive to being initiated on PD.

The support provided by the international fraternity of nephrologists to this venture has been commendable. The International Society of Nephrology Sister Center partnership of the Teaching Hospital at Kandy and Stanford University Division of Nephrology is addressing the challenges encountered by this project, especially the high peritonitis rates. The quality improvement initiative endeavors to reduce peritonitis rates and hospitalizations by close monitoring of clinical events and initiating teaching interventions.

The International Society of Nephrology is attempting several strategies to detect CKDu. Of these, the passive detection approaches include looking at registry data like mortality registry as well as dialysis and transplant registry. Using the dialysis and transplant registries in United States Renal Data System (USRDS), European Renal Association-European Dialysis and Transplant Association (ERA EDTA) and Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) it is planned to look at both incident and prevalent end stage kidney disease (ESKD) of unknown etiology. This approach holds promise as an efficient system of identifying hot spots. Age-standardized and region-specific estimates can also be obtained. The validity of this approach is questionable as there are many patients with untreated ESKD in low and middle income countries (including hotspots of CKDu). Also, many cases may be wrongly attributed to CKDu where both known causes (presenting extremely late in the illness when the etiology is not obvious) and CKDu may coexist.

**Financial implications and palliative care**

It is a reasonable assumption that the majority of advanced CKDu that are lost to follow up die due to inability to initiate or sustain RRT. In addition to the non-availability of related kidney donors is the requirement of monetary resources for the same. CKDu devastates the entire family. Often children are forced to drop out of school to work and earn a living in place of the sick, dying, or dead breadwinner of the family.

Simultaneous with the attempts at treating all patients with advanced CKDu, there is an increased recognition for the need for palliative care for patients with CKDu. Inability to have a kidney transplantation and inadequate facilities for dialysis necessitate make palliative care for these patients necessary. Both in India and Sri Lanka, renal palliative care is rudimentary at best. Relief of symptoms in a dialysis patient also falls under the purview of this specialty. Presence of depression and other psychological challenges have not been studied in the CKDu population. Renal palliative workshops were held in Colombo and Anuradhapura under the aegis of the Society of Nephrologists in Sri Lanka. The recent efforts of Shanthi Foundation Australia, a charitable enterprise in developing palliative care unit and hospice for patients with CKDu, are noteworthy.

The governments of South Asian countries (barring Bhutan and Maldives) are unable to provide for complete coverage for all patients requiring transplantation. The Aarogyasri scheme is an insurance scheme of the states of Andhra Pradesh and Telengana that has been revolutionary. Poor patients (including those with advanced CKDu) may avail of free HD and transplantation services both in government and in private hospitals. CKDu patients in Sri Lanka are being taught different skills (e.g.,
beekeeping) that enable them to improve their financial position.[3]

Although much has been done, the job is yet unfinished. A model of public–private partnership must be undertaken that provides wholesome care of patients with advanced CKDu. For all who are eligible, living-related transplantation must be made available with financial support for surgery, costly immunosuppressive drugs, and follow-up. In all the others, dialysis must be made available at their doorstep. This, as discussed above, will be feasible only with a “PD first” policy such as being tried out in Sri Lanka. Those failing PD and those with contraindications should have facilities for HD as near their home as possible.

Conclusion

Patients with advanced CKDu need counseling to help them decide on the RRT modality that is most suitable to them. Risk of developing CKDu post kidney donation is unknown and must be explained to all potential donors and then closely monitored post donation. Those unable to proceed with living-related transplantation to be offered dialysis and PD may be the preferred RRT modality. This can be achieved by having small PD units in the community run by trained community physicians and nurses. The financial implications of RRT can be devastating to the patient and family and need intervention via a public–private partnership. Available resources such as the Aarogyasri scheme are a boon to the patients. Palliative care may be needed for those not able to receive RRT and also for symptom relief.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Chandrajith R, Nanayakkara S, Itai K, Aturaliya TN, Dissanayake CB, Abeysekera T, et al. Chronic kidney diseases of uncertain etiology (CKDu) in Sri Lanka: Geographical distribution and environmental implications. Environ Geochem Health 2011;33:267-78.
2. Nanayakkara N, Wazil AW, Gunerathne L, Dickowita S, Rope R, Ratnayake C, et al. Tackling the fallout from chronic kidney disease of unknown etiology: Why we need to focus on providing peritoneal dialysis in rural, low-resource settings. Kidney Int Rep 2016;2:1-4.
3. Abraham G, Varughese S, Mathew M, Vijayan M. A review of acute and chronic peritoneal dialysis in developing countries. Clin Kidney J 2015;8:310-7.
4. Termorshuizen F, Korevaar JC, Dekker FW, Van Manen JG, Boeschoten EW, Krediet RT, et al. Netherlands Cooperative Study on the Adequacy of Dialysis Study Group. Hemodialysis and peritoneal dialysis: Comparison of adjusted mortality rates according to the duration of dialysis: Analysis of The Netherlands cooperative study on the adequacy of dialysis. J Am Soc Nephrol 2003;14:2851-60.
5. Pike E, Hamidi V, Ringerike T, Wisloff T, Klemp M. More use of peritoneal dialysis gives significant savings: A systematic review and health economic decision model. J Clin Med Res 2017;9:104-16.
6. Liu FX, Gao X, Inglese G, Chuensaman P, Pecoits-Filho R, Yu A. A global overview of the impact of peritoneal dialysis first or favored policies: An opinion. Perit Dial Int 2015;35:406-20.
7. Reddy YN, Abraham G, Mathew M, Ravichandran R, Reddy YN. An Indian model for cost-effective CAPD with minimal man power and economic resources. Nephrol Dial Transplant 2011;26:3089-91.
8. Palmer D, Lawton WJ, Barrier Jr C, Fine Jr BD, Hemphill H, Nyah NN, et al. Peritoneal dialysis for AKI in Cameroon: Commercial vs locally-made solutions. Perit Dial Int 2018;38:246-50.
9. Khan IH, Catto GR, Edward N, MacLeod AM. Death during the first 90 days of dialysis: A case control study. Am J Kidney Dis 1995;25:276-80.
10. Varughese S, Abraham G. Chronic kidney disease in India. Clin J Am Soc Nephrol 2018;13:802-4.
11. Caplin B, Yang C-W, Anand S, Levin A, Madero M, Saran R, et al. on behalf of International society of nephrology’s international consortium of collaborators on chronic kidney disease of unknown etiology (i3C). The international society of nephrology’s international consortium of collaborators on chronic kidney disease of unknown etiology: Report of the working group on approaches to population-level detection strategies and recommendations for a minimum dataset. Kidney Int 2019;95:4-10.
12. Varughese S, John GT, Alexander S, Deborah MN, Nithya N, Ahamed I, et al. Pre-tertiary hospital care of patients with chronic kidney disease in India. Indian J Med Res 2007;126:28-33.
13. Kanathigoda S. Palliative care for Chronic Kidney Disease of unknown origin (CKDu) in Sri Lanka. Available from: http://www.shanthifoundation.org/2016/01/palliative-care-for-ckdu-of-unknown-origin-in-sri-lanka/. [Last accessed on 13 Jan 2016].
14. Rajiv Aarogyasri. [online]. Available from: http://www.ysraarogyasri.ap.gov.in/. [Last accessed on 2019 Sep 20]; https://aarogyasri.telangana.gov.in/. [Last accessed on 2020 Mar 21].