

Continuous ambulatory peritoneal dialysis: perspectives on patient selection in low- to middle-income countries

Nicola Wearne¹
Kajiru Kilonzo²
Emmanuel Effa³
Bianca Davidson¹
Peter Nourse⁴
Udeme Ekrikpo^{1,5}
Ikechi G Okpechi¹

¹Division of Nephrology and Hypertension, University of Cape Town, Cape Town, South Africa;

²Department of Medicine, Kilimanjaro Christian Medical College, Moshi, Tanzania; ³Department of Medicine, University of Calabar, Calabar, Nigeria;

⁴Division of Paediatric Nephrology, Red Cross War Memorial Children's Hospital, Cape Town, South Africa;

⁵Department of Internal Medicine, University of Uyo, Uyo, Nigeria

Abstract: Chronic kidney disease is a major public health problem that continues to show an unrelenting global increase in prevalence. The prevalence of chronic kidney disease has been predicted to grow the fastest in low- to middle-income countries (LMICs). There is evidence that people living in LMICs have the highest need for renal replacement therapy (RRT) despite the lowest access to various modalities of treatment. As continuous ambulatory peritoneal dialysis (CAPD) does not require advanced technologies, much infrastructure, or need for dialysis staff support, it should be an ideal form of RRT in LMICs, particularly for those living in remote areas. However, CAPD is scarcely available in many LMICs, and even where available, there are several hurdles to be confronted regarding patient selection for this modality. High cost of CAPD due to unavailability of fluids, low patient education and motivation, low remuneration for nephrologists, lack of expertise/experience for catheter insertion and management of complications, presence of associated comorbid diseases, and various socio-demographic factors contribute significantly toward reduced patient selection for CAPD. Cost of CAPD fluids seems to be a major constraint given that many countries do not have the capacity to manufacture fluids but instead rely heavily on fluids imported from developed countries. There is need to invest in fluid manufacturing (either nationally or regionally) in LMICs to improve uptake of patients treated with CAPD. Workforce training and retraining will be necessary to ensure that there is coordination of CAPD programs and increase the use of protocols designed to improve CAPD outcomes such as insertion of catheters, treatment of peritonitis, and treatment of complications associated with CAPD. Training of nephrology workforce in CAPD will increase workforce experience and make CAPD a more acceptable RRT modality with improved outcomes.

Keywords: dialysis cost, dialysis fluid, peritoneal dialysis, peritonitis, nephrology workforce

Introduction

Chronic kidney disease (CKD) is a major burden on health care, with an estimated worldwide prevalence of 8%–16%, with growth predicted to become fastest in the poorest parts of the world.¹ CKD in Africa is 3–4 times more common than in developed countries¹ with the impact of rising rates of diabetes² and hypertension³ expected to contribute significantly to the CKD burden not only in Africa but also worldwide.⁴ Unfortunately, lack of availability of dialysis to accommodate the global CKD burden is alarming. In 2010, it was estimated that between 2 and 7 million people died prematurely due to lack of access to renal replacement therapies (RRTs).⁴

Continuous ambulatory peritoneal dialysis (CAPD) should be an ideal form of RRT in low- to middle-income countries (LMICs), particularly for those living in rural areas. Apart from fewer hospital visits, CAPD allows for greater flexibility with employment

Correspondence: Ikechi G Okpechi
E13 Renal Unit, Groote Schuur
Hospital and University of Cape
Town, Observatory, 7925 Cape
Town, South Africa
Tel +27 21 404 3321
Email Ikechi.okpechi@uct.ac.za

Table 1 Worldwide utilization of RRT (HD and PD only) in selected countries

Countries	Prevalent maintenance HD capacity (pmp)	Prevalent maintenance PD capacity (pmp)	% PD use among all dialysis patients
Developed countries ¹⁰⁻¹²			
USA	1,165	87.1	7.0
UK	365	61	17.0
Japan	2,148.4	71.9	3.3
Germany	768.1	38.8	4.8
Italy	738.8	78.3	9.6
Austria	449.7	43.3	8.8
Singapore	684	158	19
Developing countries ¹³⁻¹⁵			
South Africa	45	25	32
Sudan	46	85	3.5
Kenya	7.5	1.2	12
Egypt	421	0.3	0.0
Nigeria	8	0	0.0
Ghana	2	0	0.0
Senegal	4.1	1	18
Cameroon	5.9	0	0.0
Algeria	381	11.1	6.3
Nepal	10.1	1.5	13.5
India	18.0	5.8	24.5
Brazil	396.3	47	10.6

Note: Data from.¹⁰⁻¹⁵

Abbreviations: HD, hemodialysis; PD, peritoneal dialysis; pmp, per million population; RRT, renal replacement therapy.

and schooling. It is ideal for children and adolescents and those caring for others. It enables those living far from dialysis centers the convenience of home dialysis. Evidence also supports CAPD first policy prior to hemodialysis (HD) as there are known benefits for the preservation of residual renal function⁵ and protection of vascular access sites. Over the past two decades, the survival of patients treated with CAPD has steadily improved, both in absolute terms and in comparison to that of patients receiving HD.⁶⁻⁹ However, most studies showing survival benefit with CAPD have taken place in developed countries. Despite this, HD remains the most common RRT (Table 1)¹⁰⁻¹⁵ with most centers located in big cities and therefore inaccessible to vast numbers of the population living in remote areas. The aim of this review was to assess factors linked with patient selection, understand the reasons for poor utilization of CAPD in LMICs, especially in Africa, and suggest ways to improve CAPD use for end-stage renal disease (ESRD) treatment in developing countries.

Role of cost and availability of CAPD services

RRT represents an expensive form of health care technology. The cost of RRT consumes a significant proportion of

Table 2 Annual cost of HD and PD in selected developed and developing countries

Countries	Annual cost of HD (USD)	Annual cost of PD (USD)	HD/PD cost ratio	Year
Developed countries				
USA	68,253	56,807	1.2	2005
UK	42,679	26,389	1.6	2008
Sweden	70,796	46,018	1.5	2007
Canada	51,252	26,959	1.9	2002
Australia	21,633	36,140	0.6	2007
Developing countries				
Sudan	10,500	11,500	0.9	2010
India	8,160	4,800	1.7	2009
Malaysia	23,549	23,431	1.0	2005
South Africa	7,000	12,000	0.6	2010
Sri Lanka	3,888	9,600	0.4	2001
Namibia	24,500	24,500	1.0	2010
Kenya	16,000	12,000	1.3	2010

Note: Data from.¹⁷⁻²⁵

Abbreviations: HD, hemodialysis; PD, peritoneal dialysis.

health care budgets in developed countries, while the cost of care remains unattainable in most developing countries. Data from the United States Renal Data System (USRDS)¹⁶ show that Medicare expenditure for all CKD rose from \$41.2 billion in 2010 to \$50.4 billion in 2014 representing a 22.3% increase in cost. The total cost of care in the US in 2013 is in excess of the national budgets of many countries in sub-Saharan Africa, Latin America, and Central and East Asia. The cost ratio of HD to CAPD is much lower in LMICs (Table 2).¹⁷⁻²⁵ Also, dialysis availability in LMICs has thus been challenging given the double burden of communicable and noncommunicable diseases (NCDs) that many LMICs are faced with along with the added pressure to distribute health care resources to attend to all health challenges. The high cost of dialysis arises from the different components of service provision. It is generally agreed that CAPD is technologically less challenging than HD and hence provides an attractive strategy. Indeed, the governments of Thailand and Hong Kong have adopted a CAPD first policy to deal with its growing ESRD population.²⁶⁻²⁹

Cost comparison between CAPD and HD has been a subject of debate, even though CAPD is more affordable in most places.^{30,31} In places with developed CAPD services like South America, CAPD costs are lower compared to HD. As an example, the HD/CAPD ratio in Egypt is 0.22 compared to 1.5 in Mexico.³⁰ The difference in CAPD costs can be mainly explained by ability or otherwise of fluid manufacturing within a country and by government policies that support use of CAPD as a first option for RRT. In countries with CAPD first policy, cost and utilization have been noted to have improved.³² Similarly, countries that are able to manufacture

Table 3 Global health workforce for physicians, nephrologists, and nurses

World region	Number of physicians	Physician density*	Nurses density**	Nephrologists density***
WHO region				
Africa	33,183	2.7	1.16	1
America	1,981,621	21.5	3.05	22 (North America); 8 (South America)
Europe	2,356,671	32.1	8.19	31
South-East Asia	1,128,508	5.9	1.79	1
Western Pacific	2,435,023	14	4.74	9 (Australia and New Zealand)
Eastern Mediterranean	532,486	10	2.99	
Income group				
Low income	213,982	2.5	0.51	0.3
Lower middle income	1,991,612	7.9	1.08	1.6
Upper middle income	3,755,703	16.1	3.84	4.8
High income	3,186,223	28.7	–	–

Notes: *Reported as per 10,000 population. **The values obtained here are averages of the nurses/midwife density obtained from these regions (reported per 1,000 population). ***Reported as per 1,000,000 population. Data from.^{14,38–40}

Abbreviation: WHO, World Health Organization.

CAPD fluids are able to cut out cost of international transportation, various tariffs, and cost of storage, thus massively reducing the cost of CAPD.^{33,34} Unfortunately, due to the lack of infrastructure and appropriate technologies, most LMICs depend entirely on imported CAPD fluids which make the cost excessively high.

In Africa, the prevalence of CAPD varies from 0 to 45 per million population (pmp) compared with 90 pmp in the USA.³⁵ Limited CAPD utilization is also significantly related to the availability of adequately trained health care workers.³³ Human resource for health continues to be inadequate for primary health care in several LMICs where there has been a significant and demonstrable inequality in urban–rural distribution of health care workers, with the majority residing in urban settings^{36,37} (Table 3).^{14,38–40} Low workforce impacts on various aspects of CAPD usage including catheter insertion, management of catheter malfunction, treatment of peritonitis, and assessment of membrane function. Inadequate workforce may also influence the number of people available to provide the much required patient education for CAPD use.³²

Role of socio-demographic factors

The availability and/or utilization of CAPD in several LMICs is often dependent on prevailing socio-demographic factors, including level of education, availability of electricity and water supply, availability of an efficient sanitation system,

distance, and availability of transportation to the nephrology center. Often, CAPD provision may be accessible only through one provincial or regional hospital with several patients who need to access care dwelling very far away from such hospitals. In one study from South Africa, the mean distance patients needed to travel to the hospital was 122.9±78.2 km.⁴¹ In reality, this should be a reason to increase utilization of CAPD since patients will not have to travel frequently to hospital. However, the unavailability of other essential infrastructure (such as good road networks and adequate transport services – both of which are necessary for the delivery of CAPD consumables to patients and for patients to visit the hospital in emergencies) makes long distance from a dialysis center (or hospital) a negative factor when considering selection of patients for dialysis in LMICs.³⁵ One study from Canada found that, although remote-dwelling patients were more likely than urban dwellers to commence CAPD in distances ranging from 50 to >300 km than those residing within 50 km, the adjusted rates of death and the adjusted hazard ratio (HR) among patients initiating CAPD were significantly higher in those living further from nephrologists than those living within 50 km.⁴² Mortality and poor CAPD outcomes in LMICs could be much worse.

Availability of other social services such as housing, number of occupants at home, water supply, and availability of electricity often limits the use of CAPD due to associated high rates of peritonitis. Zent et al had questioned if CAPD should be used in the African context given that outcomes were poorer in communities where social services were unavailable. Their study investigated the relationship between episodes of peritonitis and exit site infection, and predetermined biomedical, socioeconomic, and psychosocial factors in 132 CAPD patients commencing the dialysis program in Cape Town, South Africa between 1987 and 1991.⁴³ They reported a strong association between high peritonitis rate and poor socioeconomic conditions when factors such as unemployment, low-level education, and informal housing with high occupant-to-bedroom ratio, no electricity or running tap water were considered.⁴³ In South Africa where dialysis rationing is still practiced,^{44,45} socio-demographic factors continue to play a role in determining modality selection for those patients lucky enough to be accepted.

Patients with poor health literacy often lack the knowledge needed to manage their treatment. A study from Taiwan used time-dependent statistical methods to retrospectively analyze factors related to peritonitis in 404 CAPD patients from a single center.⁴⁶ They reported that patients who had never received compulsory education showed a statistically higher incidence of CAPD-related peritonitis in the univariate

analysis ($p=0.04$) and a proportional hazards model identified education level (less than elementary school vs any higher education level) as having an independent association with CAPD-related peritonitis (HR: 1.45, 95% confidence interval [CI]: 1.01–2.06; $p=0.045$).⁴⁶ Low level of education often reduces the ability to assimilate health choices and negotiate access to appropriate providers. For instance, a patient on CAPD may not understand why they have to carry out multiple exchanges everyday while other ESRD patients on HD only need to go for dialysis 3 times a week or why they have to restrict fluid or diets high in potassium or phosphates. A study that examined self-reported adherence to therapeutic regimen for CAPD patients in Hong Kong found significant positive correlations between education level and non-adherence to dietary guidelines ($p=0.001$), fluid restriction ($p=0.001$), and dialysis regimen ($p=0.009$).⁴⁷ Other studies have shown an opposite trend in correlation.^{48,49} A low level of literacy and education in many LMICs may therefore contribute to reduced patient selection for this modality.

Other socio-demographic factors have also been reported to affect CAPD utilization in many countries. One study in Northern India showed that financial constraints (100%), lack of patient enthusiasm (100%), doubtful patient compliance (83.2%), and lack of an organized CAPD program (79.2%) were the main factors limiting more widespread use of CAPD.⁵⁰ It was also reported that none of the interviewed nephrologists as part of the study routinely discussed CAPD as a modality of therapy in their pre-dialysis care of CKD patients.⁵⁰ In many places, nephrologists perceive CAPD to be burdensome and not lucrative in terms of reimbursement given the fewer patient visits associated with care.^{35,51} In

Canada, following a change from a fee-for-service physician reimbursement system to a gross-revenue-neutral, modality-independent, weekly capitation fee, it was reported that new incentives caused by the altered physician reimbursement increased CAPD and nonhospital-based HD utilization.⁵²

In some centers, their experience with high peritonitis rates may discourage or limit further utilization of CAPD, especially if this is associated with increased mortality. Several LMICs have high peritonitis rates often leading to poor outcome (Figure 1A and B).^{41,53–71} Youmbissi et al⁷¹ concluded that high peritonitis rates will continue to limit the extension of CAPD in the developing world, particularly in tropical Africa, following their experience in Cameroon which showed that there were 40 episodes of peritonitis over 18 patient years, representing 2.2 episodes of peritonitis every patient year. However, other centers have not increased the use of CAPD despite seeing a reduction in peritonitis rates over time due to other factors.^{33,43}

Role of comorbid diseases

ESRD patients initiating RRT usually have preexisting comorbidities which increase the risk for poor outcomes.^{72,73} The presence of single or multiple comorbid conditions makes the option of CAPD difficult against the backdrop of increased cost to their care in addition to an increased risk of mortality.⁷⁴ Estimates show that the prevalence of NCDs such as diabetes, hypertension, coronary artery disease, heart failure, obesity, chronic respiratory diseases, and various cancers continues to increase globally. The increase has been projected to be higher in LMICs where NCDs will account for 69% of disease burden in 2020, up from 47% in 1990.⁷⁵

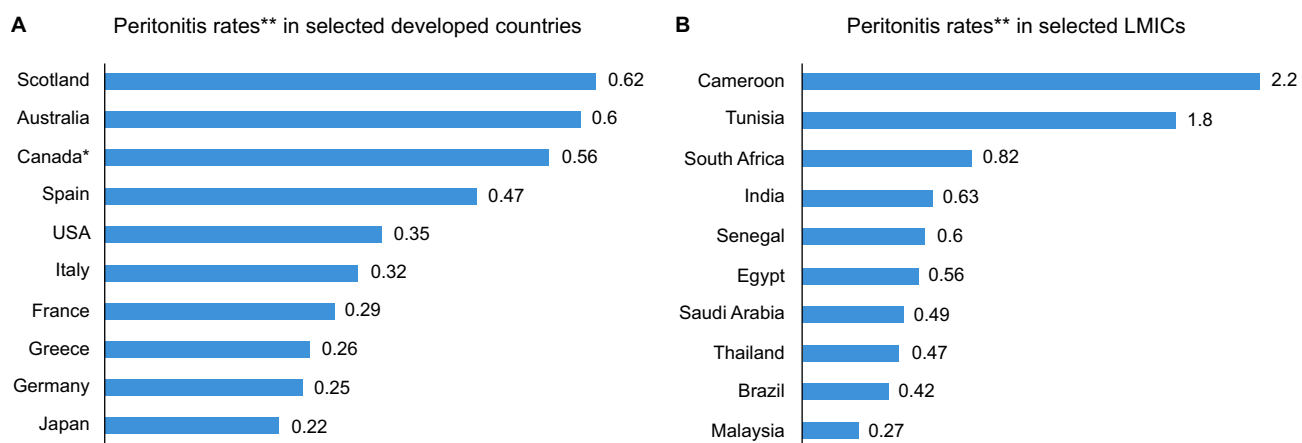


Figure 1 Peritonitis rates in selected developed (A)^{53–62} and developing (B)^{41,63–71} countries.

Notes: *Canadian data mainly from population of First Nations people. **Peritonitis rates expressed as episodes/patient years.

Abbreviation: LMICs, low- to middle-income countries.

Close to 1 billion people were estimated to be malnourished in 2000–2002 with >90% living in LMICs.⁷⁶ Nutritional indices have been shown to significantly predict the outcomes in CAPD,⁷⁷ and malnutrition has been reported to be present in up to 72% of prevalent CAPD patients in India assessed by the subjective global assessment (SGA).⁷⁸ In one study, various nutritional indices were found to be predictive of peritonitis in CAPD patients including SGA ($p=0.009$), serum albumin level ($p=0.005$), and calorie intake ($p=0.006$).⁷⁹

Coexistence of diabetes mellitus has been shown to be a negative prognostic factor for patient and technique survival in CAPD.^{41,80,81} Glucose control often becomes erratic after initiation of CAPD necessitating increased dosing of antidiabetic agents and increasing cost of care for patients paying out of pocket. In a study of 373 CAPD patients with 197 diabetic patients comparing patient survival between diabetic and nondiabetic patients, the relative risk (RR) of mortality in nondiabetics was less than that in diabetic patients (odds ratio [OR]: 0.43, 95% CI: 0.26–0.68; $p=0.001$) and diabetes was a strong predictor of mortality in multivariate analysis (OR: 1.95, 95% CI: 1.23–3.07; $p=0.004$).⁸⁰ Our study from rural Limpopo in South Africa has shown that mortality risk according to dialysis modality was significantly modified by diabetes mellitus status in both univariate and multivariable analyses as mortality risk was ~5 times higher among diabetics on CAPD relative to nondiabetics on HD (HR: 4.99, CI: 2.13–11.71).⁸¹

For ESRD patients with concomitant heart failure, CAPD has been reported to be associated with better outcomes than HD, especially for those with contraindications for a heart transplant.^{82–84} However, patients with significant cardiac disease will be deemed ineligible for chronic RRT in places where dialysis is rationed^{44,45} and access to treatment for heart failure and other cardiovascular disease may already be proving difficult.⁸⁵ Nonetheless, CAPD has been shown to be associated with fluid and sodium removal through the peritoneal membrane, and this leads to a significant plasma volume reduction, normalization of serum sodium, and restoration of diuretic responsiveness, as well as an improvement in New York Heart Association (NYHA) functional class, and reduction of hospitalization and readmission rates in patients with heart failure.^{82–84} In a single center, prospective, nonrandomized study involving patients showing symptoms and signs of congestive heart failure refractory to maximum tolerable drug treatment, CAPD treatment was associated with improved NYHA functional class ($p<0.001$), raised life expectancy after 12 months, and a better perception of the state of health.⁸³

Obesity has been demonstrated in several studies in both high-income countries and LMICs to confer a survival advantage on patients who are on CAPD.^{86–88} Despite this, physicians are less likely to prescribe CAPD for obese patients owing to concerns about inadequate ultrafiltration, solute clearance, exit site infections, and peritonitis.⁸⁹ In LMICs, obese people are likely to be excluded from publicly funded programs mainly due to the policy of rationing and also due to the bias for several complications and poor outcome of kidney transplantation of obese patients (reviewed extensively in Tran et al).⁹⁰ Well-motivated, appropriately pre-dialysis educated and trained patients may be offered the choice of CAPD.

Effect of transitioning of children and adolescents into adulthood

Worldwide, an increasing number of adolescent and young patients need to be transitioned from pediatric service or present directly to an adult nephrology service. Adolescents and young adults have been recognized to have an increased risk of non-adherence at the time of transfer to adult care.^{91–93} Thus, kidney outcomes have been shown to be reduced in adolescents compared with other age groups and transitioning from pediatric to adult nephrology services has been identified to be problematic and sometimes traumatic.^{93,94} The reasons for the adherence issues and poor outcomes observed in adolescents/young adults making transitions to adult care are multifactorial. For many adolescents, leaving the care of their pediatrician may be viewed as a passage from security to uncertainty and many have been known to return to their pediatric caregivers. Also, although the most frequent etiology of adolescent-onset CKD is glomerular diseases, congenital diseases such as renal dysplasia and other hereditary conditions leading to CKD are much more prevalent in younger children and adult nephrologists may be unfamiliar with the treatment of such conditions.⁹³ Finally, the management of chronic diseases in adolescents/young adults alongside other psychological, physical, developmental, and sexual changes associated with this age group can be challenging for patients.

The process of transitioning young adults, as outlined by the International Society of Nephrology and International Pediatric Nephrology Association consensus statement,⁹⁵ requires the availability of health care professionals working collaboratively in a coordinated health care system. Several LMICs lack the workforce, coordination, and necessary structures to allow for an effective transitioning program and thus adolescents/young adults in these countries often

enter adult renal service unprepared for the challenges often leading to poor outcomes. The challenges of treating this group are compounded by the fact that there is paucity of data comparing dialysis outcomes in this specific age group, especially from LMICs.

CAPD should, however, be the ideal form of RRT in adolescents/young adults given that, in the short term, CAPD outcomes have been reported to be better than HD,^{6,96} allows for preservation of vascular access (important for young patients facing a lifetime of RRT),⁹⁷ preserves residual renal function,^{5,98} may have a lower cumulative risk of coronary calcifications than HD,⁹⁹ and allows children to attend school (if they perform night time CAPD or automated CAPD). One Australian study found school attendance to be significantly higher in adolescents on peritoneal dialysis (PD) than those on HD ($p=0.001$) and did not report any association between modality and dialysis outcomes.¹⁰⁰ In Cape Town, because of the high proportion of young patients in our CAPD service, policies have been implemented which aim to assist with treatment and outcomes. First, all those <25 years old receive automated PD. CAPD enables young adults to achieve greater normalcy in their lives, including the freedom to complete school and studies. This method avoids the need for bag exchanges at school/college. It not only increases the patients comfort with the modality but also facilitates parent involvement and supervision at night. However, it has been noted that adolescents may find the prolonged nocturnal PD treatment to be too intrusive into their social time, leading to skipped or shortened treatments and poor outcome from non-adherence.¹⁰¹ Moreover, the resources and home setting to support CAPD may be unavailable for those from very poor communities without adequate amenities.

PD first policy: is this feasible in LMICs?

PD is an important but underutilized RRT modality for ESRD patients initiating dialysis worldwide (Table 1). It has been suggested that underutilization of CAPD may be related to lack of expertise and absence of pragmatic strategies¹⁰² as well as with government policy, economics, provider or health care professional education, and patient-related factors.¹⁰³ USRDS data show that 93% of all incident dialysis patients start in-center HD even though there is lack of evidence for the discrepancy.¹⁰⁴ CAPD has been shown to improve patient survival,⁶⁻⁹ retain residual kidney function,^{5,98} as well as reduce the financial burden of RRT.¹⁰⁵ These should be reasons to embrace CAPD as the initial RRT modality of choice in many LMICs although this is not the case. Liu et al have shown that a CAPD first policy is

practiced only in Hong Kong and Thailand, whereas Mexico, Guatemala, USA, Canada, India, China, and Spain have a CAPD-favored policy.¹⁰³ The advantage of patient survival in CAPD has often been reported within the first few years of RRT initiation. Studies that have not shown superior benefit have reported comparable outcomes between CAPD and HD. Unfortunately, data on improved survival benefit of CAPD are lacking from LMICs, especially from Africa. The Dialysis Outcomes in Colombia showed that there was a higher adjusted mortality risk (12.7%) associated with HD when compared to CAPD, despite CAPD patients being poorer, more likely to be diabetic, and having higher comorbidity scores than HD patients.¹⁰⁶ The only available published study in Africa comparing the outcomes of adult patients treated with HD and CAPD, however, reported an increased RR of death in patients receiving CAPD compared to HD.⁸¹

Also, a CAPD first policy should be attractive for patients initiating RRT given that CAPD preserves residual renal function and observational studies have reported an association between residual renal function and improved patient survival and quality of life.¹⁰⁷ The CANUSA study demonstrated that every 250 mL increment in urine volume in CAPD patients was associated with a 36% decrease in the RR of death (RR: 0.64, 95% CI: 0.51–0.80),⁵ and other studies have now shown that CAPD protects residual function longer than HD, and it can be preserved for up to 3 years on CAPD.⁹⁷

Despite the advantages of a CAPD first policy, this initiative can only be possible in an environment with accumulated CAPD experience, government support, and locally produced PD fluid. Li and Chow have suggested that in order to achieve a successful CAPD first policy, inherent patient factors, patient selection strategies, and improving technique-related factors (such as training of physicians, nurses, patients, and caregivers) need to be given careful consideration.¹⁰² The presence of several of these factors already creates a barrier to successful implementation of CAPD first policies in several LMICs. If these barriers could be overcome, then CAPD first should be the correct patient choice; however, there is insufficient data to support this approach from LMICs.

Conclusion and future perspectives

There are no easy solutions for improving CAPD uptake as a modality of RRT in LMICs given the enormous health challenges that several of these countries continue to experience. Fundamentally, the cost of CAPD fluids and lack of trained workforce and necessary expertise in carrying out CAPD may underscore the real reasons why CAPD is underutilized. New ideas for making CAPD fluids available should be looked for including ways to commence local (or regional) production of

fluids. This is likely to reduce the cost of CAPD and improve utilization. There is also need for training of nephrology workforce in LMICs to improve their uptake and increase their experience in CAPD use. Workforce training and retraining will be necessary to ensure that there is coordination of CAPD programs and increase the use of protocols designed to improve CAPD outcomes such as insertion (and removal) of catheters, treatment of peritonitis, treatment of anemia and bone disease, and timing of transfer to HD. Training of workforce will also improve the quality of patient education through their involvement in the process of care as well as improving patient understanding of various aspects of CAPD.

Disclosure

The authors report no conflicts of interest in this work.

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