Renal Replacement Therapy Preferences Survey: Is Allo-Hemodialysis an Acceptable Option for Patient Caregivers and Health Care Professionals?

Israel Campos^{a, b} Jesus Arellano^a Victor Gomez^a Jorge Quiroz^{a, b}
Luis Alfonso Mariscal^{a, b}

^aDepartment of Nephrology, Hospital General “Dr. Miguel Silva”, Morelia, Mexico; ^bDepartment of Research and Educational, NausLife Hemodialysis Clinics, Morelia, Mexico

Keywords

Renal replacement therapy · Allo-hemodialysis · Survey

Abstract

End-stage kidney disease (ESKD) is a worldwide unsolved problem. Access to renal replacement therapies (RRT) is still a challenge in some developed countries and even more so in developing countries. Allo-hemodialysis (alloHD) is a recently proposed, still hypothetical, alternative RRT where the blood of a healthy subject (“buddy”) flows countercurrent to the patient’s blood through the dialyzer. Solutes and fluid are transferred to the buddy and then cleared by his/her healthy kidneys, making alloHD essentially a procedure where the buddy “donates” kidney function intermittently to the patient. Its drastically reduced complexity makes alloHD particularly attractive for low-resource settings. The acceptance of alloHD by patients, caregivers, and health care professionals (HCP) is unknown. In this cross-sectional study, we surveyed the preferences and acceptance of alloHD in 3 groups: caregivers related to ESKD patients, nonrelated caregivers (nrCG), and HCP. Four areas were explored: RRT preferences, kidney organ donation for transplant acceptance, alloHD acceptance as a potential RRT, and alloHD technique acceptance. Hemodialysis was the preferred form of RRT. Kidney donation acceptance was similar in all groups. Inter-

mittent kidney function donation (i.e., alloHD) was mainly accepted by related and nrCG but less accepted by HCP (87, 90, and 60% respectively, $p < 0.01$). New RRT alternatives such as alloHD are expected to be better received and accepted once animal, and clinical studies have demonstrated their feasibility, safety, and benefits. New RRT strategies are required primarily in most vulnerable populations and should be explored.

© 2019 S. Karger AG, Basel

Introduction

Currently, end-stage kidney disease (ESKD) is overwhelming health care systems in many countries worldwide [1, 2]. Renal replacement therapies (RRT) currently available are unequally distributed [3]. Hemodialysis (HD) is the most prevalent type of RRT around the world [4]. Although any RRT type is available in most countries, it is limited to specific subgroups of the population and frequently the most vulnerable populations have no access to treatment or even diagnostic tests [5]. Premature death was reported worldwide in up to 7 million people annually due to lack of RRT access [3]. Since the inception of HD, peritoneal dialysis (PD), and kidney transplant (KT) in the last century [6, 7], no new RRT strategies have been explored.

Allo-HD (alloHD), a new and innovative dialytic RRT, has been proposed recently [8]. In alloHD, the kidney patient's blood flows inside the dialyzer countercurrent to blood from a healthy subject ("buddy"). Dialysis' physical principles apply in this model, allowing the transfer of fluid and solutes between the patient and the buddy. Solutes and fluid transferred into the buddy are then cleared by his/her healthy kidneys, making alloHD essentially a procedure where the buddy "donates" kidney function intermittently to the patient. This drastically reduced complexity makes alloHD particularly attractive for low-resource settings.

AlloHD involves risks, for example, the need of a vascular access in the buddy, the unknown effects of intermittent solute and fluid transfer through a dialyzer membrane to the buddy, and infection risks in the event of dialyzer blood leaks. Mathematical models and ex vivo experiments have demonstrated efficacy of alloHD to remove uremic solutes, such as urea, creatinine, and other uremic toxins [8]. Although this new technique demonstrates theoretical and ex vivo efficacy, patients, caregivers, and health care professionals (HCP) will be challenged to accept a completely novel RRT, especially because it involves a healthy subject as a potentially new patient to care for.

The acceptance of new paradigm-breaking treatments always travels in parallel with ethical and medical concerns for the prescriber as well as the patient, even more if this new treatment implies a substantial change in the standard treatment. Historical examples are first organ transplantation [9], assisted human reproductive techniques [10], and others. The objective of this study was to explore the preference of RRT type and acceptance of alloHD treatment across kidney patient's caregivers and nephrology HCP based on the up-to-date information about this new RRT technique.

Methods

We conducted a cross-sectional survey in 3 groups: caregivers related to kidney patients-related caregivers (rCG), non-rCG (nrCG), and nephrology HCP. The survey took place from March to June 2019 at the NausLife HD Clinics and Hospital General "Dr. Miguel Silva" in Morelia, Mexico.

Before asking survey questions, we briefly explained the current RRT modalities, including KT. We then explained alloHD. A short slide presentation on an electronic tablet accompanied this explanation. The survey comprised 4 questions and was administered following the explanation of RRT modalities. The participants responded anonymously to the following 4 questions:

For caregivers:

Question 1: If you would require RRT, which type of therapy would you prefer?

Question 2: Would you donate a kidney to the person you care for?

Question 3: Would you donate the function of your kidney intermittently (i.e., serve as an alloHD buddy) to the person you care for?

Question 4: Do you agree with the alloHD procedure?

For HCP:

Question 1: If you would require RRT, which type of therapy would you prefer?

Question 2: Would you donate a kidney?

Question 3: Would you donate the function of your kidney intermittently (i.e., serve as an alloHD buddy)

Question 4: Do you agree with the alloHD procedure?

A dichotomic response was the only option for all questions ("HD or PD" for question 1, "Yes" or "No" for questions 2, 3, and 4).

We collected the frequency of responses and assessed the differences between groups by chi-square test or one-way ANOVA test with Bonferroni correction. A *p* value <0.05 was considered statistically significant.

Results

We approached 139 subjects. A total of 125 participants (54% females) completed the survey, 33 rCG, 42 nrCG, and 50 HCP. Their mean age was 41.9 ± 17 years. By group, the mean age was for rCG 50.9 ± 15.3 years, for nrCG 44.9 ± 16.2 years, and for HCP 33.4 ± 15 years, respectively ($p < 0.001$).

HD (67%) was the most frequent RRT modality in patients who were taken care of by the respective caregivers, followed by PD (13%); 20% did not receive any form of RRT. Among the HCP, 78% were physicians and 22% non-physicians (nutritionist, nurses, and technicians).

Out of all 125 participants, 85.6% preferred HD as RRT (Q1), 94.4% accepted kidney donation (Q2), 60% accepted alloHD (Q3), and 79% accepted the alloHD procedure (Q4). Stratified by group, the responses were as follows: Q1: rCG (79%), nrCG (83%), and HCP (94%) preferred HD ($\chi^2 = 4.26$, $p = 0.11$); Q2: rCG (94%), nrCG (91%), and HCP (98%) accepted kidney donation ($\chi^2 = 2.4$, $p = 0.29$); Q3: rCG (76%) and nrCG (67%) accepted alloHD more frequently compared to HCP (44%; $\chi^2 = 9.5$, $p = 0.009$) and; Q4: rCG (88%) and nrCG (91%) accepted the alloHD procedure more frequently compared to HCP (64%; $\chi^2 = 11.7$, $p = 0.003$; Fig. 1).

Finally, we analyzed the responses by gender and age. For Q1, 40% males vs. 47% females ($\chi^2 = 0.009$, $p = 0.92$) preferred HD; for Q2, 41% males vs. 54% females ($\chi^2 = 4.81$, $p = 0.02$) accepted to donate a kidney; for Q3, 26%

Fig. 1. Survey response frequencies. Question 1: * rCG vs. HCP, $p < 0.05$. Question 3: * cCG vs. HCP, $p < 0.01$, ** non-rCG vs. HCP, $p < 0.05$. Question 4: * rCG vs. HCP, $p < 0.05$, ** non-rCG vs. HCP, $p < 0.01$. The figure describes ** value as $p < 0.05$ in question 3, and $p < 0.01$ in question 4. Those are the values represented by **. rCG, related caregivers; nrCG, nonrelated caregivers; HCP, health care professionals; HD, hemodialysis; RRT, renal replacement therapies; alloHD, Allo-hemodialysis.

males vs. 34% females ($\chi^2 = 0.19, p = 0.66$) accepted alloHD; and for Q4, 36% males vs. 43% females ($\chi^2 = 0.004, p = 0.94$) accepted the alloHD technique.

Response type by age differed only regarding Q4, where mean age in the group who accept the alloHD technique vs. nonaccepted was 44 ± 16.2 vs. 34 ± 17.9 years, respectively ($p = 0.007$).

Discussion

This is the first ever analysis exploring alloHD acceptance by ESKD patient caregivers and HCP, respectively. Current access to RRT is limited especially in vulnerable populations, with low economic resources being in most cases the main barrier [3, 11, 12]. The gap between estimated incidence and prevalence of ESKD and access to RRT was described by Anand et al. [13]. Even in developed countries, disparities have been demonstrated regarding access to KT in vulnerable populations [14]. In this scenario, many people die prematurely because a lack of access to affordable RRT. New RRT methods must be explored to reduce this gap. AlloHD is a new RRT technique that has the potential to decrease economic burden to patients, their families, and the health care system, especially in low- and low-middle income countries. While still in a predevelopment stage, alloHD has shown promising *in silico* and *ex vivo* results [8]. Clearly, successful animal studies are necessary before alloHD can be considered for humans. There are several open questions, mainly related to the technical proce-

dures of the treatment per se, safety, feasibility, ethical aspects, beside others.

We were interested to explore if alloHD would be a RRT modality potentially accepted by kidney patient's caregivers and renal HCP, respectively. To that end, we created a cross-sectional questionnaire. In our study, most patients who needed a caregiver were on HD (66%). This proportion is higher compared to other data reported from Mexico in previous studies (40%), but closer to the proportion in Latin America (75%) [15]. Frequently HD is offered as a first RRT choice due to the clinical conditions of our patients at dialysis initiation (usually symptoms such as acute pulmonary edema, seizures, vomiting, arrhythmia due to hyperkalemia, requiring urgent dialysis initiation). These circumstances could explain the lower proportion of PD patients in our cohort. The HCP group comprised of physicians and non-physicians, most of the subjects included in this survey where physicians (80%), including interns, residents and nephrology fellows from 2 different centers. The HCP were younger compare to patient caregivers.

When we analyzed the preferred RRT (Question 1), no differences were detected between groups, most of the subjects preferred HD compared to PD. While we are not aware of studies in our country to compare our results to, they are opposite to those reported by Morton et al. [16], who found in a sample of pre-dialysis patients and caregivers that the 66% preferred "home based" (PD or home HD) RRT modalities over "in-center" HD. Patients' age could be a factor that influences RRT choice, in addition

to factors such as life expectancy, autonomy in daily live, financial burden, and others [17, 18]. Due to the small sample size, we did not explored these variables in our population. A recent German study explored the patients perspectives on RRT choices, since sometimes patients felt not being involved in the decision-making process [19].

No differences were found in kidney donation acceptance between groups (Question 2). The same high acceptance of kidney donation (>90%) was reported in a study including health care workers in Mexico, Cuba, and Spain [20], and comparable results are seen in the largest Mexican KT center, where 89% of transplanted kidneys come from living donors [21].

We found marked group differences with respect to Questions 3 and 4, respectively. These questions probed into the acceptance of intermittent kidney function donation (i.e., alloHD) and the alloHD technique, respectively. Most of those participants who accepted alloHD (donation and technique) were patient caregivers. In contrast, HCP showed a more guarded attitude. Due to absent animal and clinical studies, we did expect that concerns would be voiced by HCP, who are medically more knowledgeable and have first-hand experience with various RRT modalities.

Altruistic kidney donation has been explored in many ways, including psychosocial impact on donors, non-altruistic and coerced solid organ transplantation [22], economic burden and impact on organ donors [23] and, even more, the impact of kidney donation on the health status of kidney donors, especially their risk to develop ESKD themselves [24].

To date no study has explored the acceptance of “intermittent kidney function donation” (i.e., alloHD). Ethical concerns may lead the list of inquiries in alloHD, a review on a massive altruistic kidney donation by a religious community to nonrelated kidney disease patients [25] highlighted a myriad of pros and cons around community kidney donation. Eventually, the ethical aspects where addressed by understanding the real motivation and absence of coercion, with a clear understanding of benefits and risk to donors. Currently, in our country, a public health care coverage for RRT does not exist for more than half of the population. These circumstances force kidney patients to eventually spend all their financial resources on medical care and finally stop RRT (HD or PD). Even worse, a substantial number of ESKD patients do not even initiate RRT due to the lack of insurance and financial means. We think that there exists an ethical mandate to explore alternative RRT modalities

that have the potential to provide affordable RRT to underserved kidney patients. AlloHD may provide such an alternative RRT modality and therefore there is a need to explore its acceptance especially in the most vulnerable patients.

Conclusions

Current RRT modalities are well accepted by caregivers and health care providers, the preferred RRT is HD compared to PD. Most survey participants accepted to donate a kidney. Absent animal and clinical studies, intermittent kidney function donation (i.e., alloHD) is mainly accepted by caregivers (the potential “buddies”), and to a lesser extent by HCP. New treatment alternatives could be better received and accepted once clinical studies demonstrate their feasibility, safety, and benefits. New RRT strategies such as alloHD are required mainly for the most vulnerable populations and should be explored.

Acknowledgments

We acknowledge the support during survey conduction to Enrique Lopez, MD and Marco Paniagua, MD.

Statement of Ethics

The present survey study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Disclosure Statement

The author has no conflicts of interest to declare.

Financial Support

None to declare.

Author Contributions

I.C., J.A., V.G., J.Q., and L.A.M.: survey development and preparation. I.C.: survey conduction. I.C. and L.A.M.: statistical analysis. I.C.: manuscript writing. J.A., V.G., J.Q., and L.A.M.: manuscript review and final preparation.

References

- 1 Lv JC, Zhang LX. Prevalence and Disease Burden of Chronic Kidney Disease. *Adv Exp Med Biol*. 2019;1165:3–15.
- 2 Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives. *Lancet*. 2013 Jul;382(9888):260–72.
- 3 Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. *Lancet*. 2015 May;385(9981):1975–82.
- 4 Qarni B, Osman MA, Levin A, Feehally J, Harris D, Jindal K, et al. Kidney care in low- and middle-income countries. *Clin Nephrol*. 2019, Epub ahead of print.
- 5 Htay H, Alrukhaimi M, Ashuntantang GE, Bello AK, Bellorin-Font E, Benghanem Gharbi M, et al. Global access of patients with kidney disease to health technologies and medications: findings from the Global Kidney Health Atlas project. *Kidney Int Suppl* (2011). 2018 Feb;8(2):64–73.
- 6 van Gijn J, Gijssels JP, Nurmohamed SA. [Kolff and the artificial kidney]. *Ned Tijdschr Geneesk*. 2013;157(16):A5711.
- 7 Timsit MO, Kleinclauss F, Thuret R. [History of kidney transplantation surgery]. *Prog Urol*. 2016 Nov;26(15):874–81.
- 8 Kotanko P, Maheshwari V, Thijssen S. FP536 Allo-Hemodialysis as a Novel Renal Replacement Modality: Urea Kinetics in A Pediatric Use Case. *Nephrol Dial Transplant*. 2019 Jun;34(suppl 1):gfz106.
- 9 Gracia D. [Organ transplantations: half a century of ethical pondering]. *Nefrologia*. 2001; 21 Suppl 4:13–29.
- 10 Rao RA. Assisted human reproductive techniques—emerging ethical and legal implications. *Med Law*. 2001;20(2):295–9.
- 11 Crews DC, Bello AK, Saadi G; for the World Kidney Day Steering Committee. Burden, Access, and Disparities in Kidney Disease. *Am J Nephrol*. 2019;49(3):254–62.
- 12 Robinson BM, Akizawa T, Jager KJ, Kerr PG, Saran R, Pisoni RL. Factors affecting outcomes in patients reaching end-stage kidney disease worldwide: differences in access to renal replacement therapy, modality use, and haemodialysis practices. *Lancet*. 2016 Jul;388(10041):294–306.
- 13 Anand S, Bitton A, Gaziano T. The gap between estimated incidence of end-stage renal disease and use of therapy. *PLoS One*. 2013 Aug;8(8):e72860.
- 14 Keddiss MT, Sharma A, Ilyas M, Zhang N, Khamash H, Leischow SJ, et al. Transplant center assessment of the inequity in the kidney transplant process and outcomes for the Indigenous American patients. *PLoS One*. 2018 Nov;13(11):e0207819.
- 15 Pecoits-Filho R, Rosa-Diez G, Gonzalez-Bedat M, Marinovich S, Fernandez S, Lugon J, et al. Renal replacement therapy in CKD: an update from the Latin American Registry of Dialysis and Transplantation. *J Bras Nefrol*. 2015 Jan-Mar;37(1):9–13.
- 16 Morton RL, Snelling P, Webster AC, Rose J, Masterson R, Johnson DW, et al. Dialysis modality preference of patients with CKD and family caregivers: a discrete-choice study. *Am J Kidney Dis*. 2012 Jul;60(1):102–11.
- 17 Han E, Haldane V, Koh JJ, Quek RY, Ozdemir S, Finkelstein EA, et al. Perspectives on decision making amongst older people with end-stage renal disease and caregivers in Singapore: A qualitative study. *Health Expect*. 2019 Oct;22(5):1100–10.
- 18 Walker RC, Morton RL, Palmer SC, Marshall MR, Tong A, Howard K. A Discrete Choice Study of Patient Preferences for Dialysis Modalities. *Clin J Am Soc Nephrol*. 2018 Jan;13(1):100–8.
- 19 Balzer MS, Clajus C, Eden G, Euteneuer F, Haller H, Martin H, et al. Patient Perspectives on Renal Replacement Therapy Modality Choice: A Multicenter Questionnaire Study on Bioethical Dimensions. *Perit Dial Int*. 2019, Epub ahead of print.
- 20 Ríos A, López-Navas A, Ayala-García MA, Sebastián MJ, Abdo-Cuza A, Martínez-Alarcón L, et al. The attitude toward living kidney donation among personnel from units related to donation and transplantation in Spain, Mexico and Cuba. *Ren Fail*. 2014 May;36(4):489–94.
- 21 Solis-Vargas E, Evangelista-Carrillo LA, Puente-Camacho A, Rojas-Campos E, Andrade-Sierra J, Cerrillos-Gutiérrez JI, et al. Epidemiological Characteristics of the Largest Kidney Transplant Program in Mexico: Western National Medical Center, Mexican Institute of Social Security. *Transplant Proc*. 2016 Jul-Aug;48(6):1999–2005.
- 22 Jowsey SG, Schneekloth TD. Psychosocial factors in living organ donation: clinical and ethical challenges. *Transplant Rev (Orlando)*. 2008 Jul;22(3):192–5.
- 23 Jacobs C, Thomas C. Financial considerations in living organ donation. *Prog Transplant*. 2003 Jun;13(2):130–6.
- 24 Li SS, Huang YM, Wang M, Shen J, Lin BJ, Sui Y, et al. A meta-analysis of renal outcomes in living kidney donors. *Medicine (Baltimore)*. 2016 Jun;95(24):e3847.
- 25 Mueller PS, Case EJ, Hook CC. Responding to offers of altruistic living unrelated kidney donation by group associations: an ethical analysis. *Transplant Rev (Orlando)*. 2008 Jul;22(3):200–5.