Alternative hemodialysis regimens

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Abstract

The mortality rate among patients on hemodialysis (HD) is extremely high. Remaining life expectancy for a patient initiating HD is only approximately one quarter of that of the general population at the same age bracket. The conventional HD regimen based on four-hour sessions three times a week was empirically established nearly four decades ago and needs to be revisited. Since the failure of the HEMO Study to demonstrate the clinical benefits of higher urea Kt/V for patients on conventional HD, an increasing interest for alternative HD regimens has emerged aiming at providing a treatment for improving survival rates. Short daily HD and long nocturnal HD stand out as the most promising alternative regimens. Economical obstacles which could hinder the clinical application of emerging knowledge in the field should be overcome.

Keywords: dialysis, survival, chronic kidney failure.

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Introduction

Despite all technological advances incorporated to treatment, the mortality rate among patients on hemodialysis (HD) remains extremely high.[1] As evidenced in the HEMO Study [2], the lack of clinical benefits deriving from the increase in the dose of dialysis in patients maintained on the conventional regimen of three sessions a week suggests that more innovative therapeutic approaches should be considered to effectively increase the life expectancy of that population.

In addition to the traditional regimen of four-hour sessions three times a week, here denominated conventional hemodialysis (CHD), there are several alternative proposals regarding the length and frequency of HD sessions. Due to the lack of a universal nomenclature, the alternatives of treatment were divided into short daily hemodialysis and long nocturnal hemodialysis. The latter was divided into every night nocturnal (actually, five to seven nights per week) or nocturnal three times a week. The type of treatment can also be classified according to the place where it is performed, that is, home or dialysis center. Home HD is considered a safe form of treatment that provides great comfort to the patient and can help to increase room availability in dialysis centers. Because home HD has not been implemented in Brazil due to logistic reasons and legal restrictions, we will emphasize the treatment performed at dialysis centers.

Conventional hemodialysis

Establishing conventional hemodialysis

The clinical use of HD began more than 60 years ago. Initially, HD was indicated

only for the treatment of acute kidney failure, aiming at maintaining the patient alive long enough for renal function recovery. Hemodialysis as an option of treatment for chronic uremia has spread since the 1960s, changing the natural course of the then inexorably fatal disease.[3]

From 1960 onwards, the first patients with chronic kidney disease undergoing maintenance HD initially had 20- to 24-hour sessions at five- to seven-day intervals (a regimen similar to that used for treating acute kidney failure at the time). With that regimen the patients still remained very symptomatic, with nauseas and vomiting, lethargy, peripheral neuropathy, hyperpotassemia, and signs of hypervolemia, mainly a few days after the procedure. Thus, the frequency of the sessions was increased to twice a week. However, with the twice-a-week frequency, the patients ended up developing peripheral neuropathy and severe joint calcifications, which were attenuated when, around 1964, the frequency of dialysis was increased to three times a week, with a session length of approximately ten hours.[3]

In 1972, when the congress of the USA approved the universal access to HD for its citizens, three sessions a week were established as sufficient to provide dialysis adequacy and, at the same time, to serve a large number of patients within a limited budget. Then, to accommodate an exponential increase in the number of patients, the session length was rapidly reduced so that a larger number of patients could be dialyzed per machine at the same day, creating the concept of dialysis shift. This regimen accommodates a large number of patients, distributed over morning, afternoon and night, part of them undergoing dialysis on Mondays, Wednesdays, and Fridays, while others undergo dialysis on Tuesdays, Thursdays, and Saturdays. The constant pressure for room optimization and functionality of the dialysis centers ended up perpetuating that HD regimen.

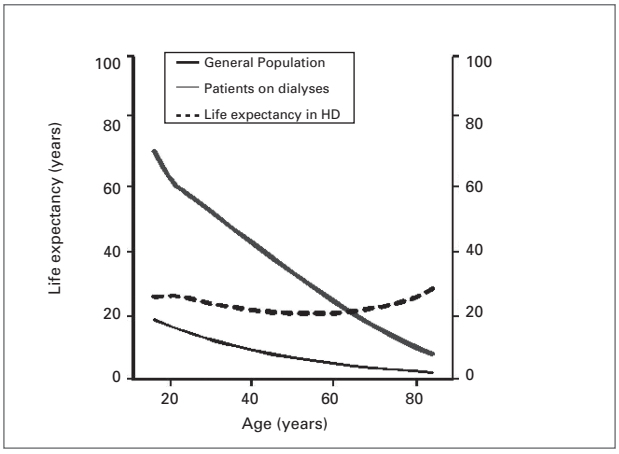
In short, the traditional HD regimen of three sessions a week with an approximate length of four hours each was established empirically almost four decades ago.

Limitations of the conventional regimen

Considering that the ideal treatment should be able to restore the life expectancy of a patient to a value close to that of the general population at the same age bracket, it is evident that the conventional regimen of four-hour sessions three times a week does not meet that objective. According to the United States Renal Data System (USRDS),[1] regardless of the age bracket, the remaining life expectancy of a patient at the beginning of the substitutive renal therapy through dialysis is only one fourth of that of the same age general population (Figure 1). For example, individuals aged 25 to 29 years have a remaining life expectancy of approximately 52 years, while patients beginning dialysis at that same age bracket have a remaining life expectancy of approximately 13 years. On the other hand, those beginning dialysis between 65 and 69 years have a remaining life expectancy of approximately four years, while the remaining life expectancy of the same age general population is approximately 17 years.

Establishing three HD sessions per week is particularly appealing as it increases the capacity of the dialysis centers to serve patients and allows for rest on Sundays. However, it does not seem reasonable that the frequency of treatment and the asymmetrical distribution of interdialytic intervals be based on social or work aspects. That regimen implies long periods without dialysis (two days during the week and three days on the weekends) and abrupt correction of the alterations at each dialysis, leading to great oscillations of blood volume and biochemistry over the week. Those characteristics of CHD justify the asymmetrical distribution of sudden death observed in that population, more frequent at the beginning of the week (after a long period without HD) and during HD, or in the following hours.[4]

Figure 1. Remaining life expectancy of the general population and the population on dialysis in the USA, according to the age bracket and percentage of remaining life expectancy of patients on dialysis as compared with the general population (%)..



Treatment per se, in this CHD regimen, would be a cause of heart damage. In a recent study, Burton *et al.*[5] assessed 70 patients on dialysis through echocardiography performed before, during, and after a conventional HD session. Forty-five patients (64%) had a transient regional alteration of left ventricular wall mobility, denominated "stunned" myocardium, induced by conventional HD. "Stunned" myocardium is considered a subclinical sign of ischemia and a cause of myocardial fibrosis. Those patients with "stunned" myocardium have a greater risk of worsening their ventricular ejection fraction and of death in the following 12 months. "Stunned" myocardium has been associated with an eight-fold increase in the risk of death, mainly that of cardiovascular causes. Many patients who had no "stunned" myocardium on their first assessment ended up developing that ventricular wall motility alteration in a new assessment one year later. The main variables associated with the risk of developing "stunned" myocardium are the great ultrafiltration volume and the decrease in the intradialytic blood pressure, even to non-hypotensive levels. But those are common, if not inherent, factors of conventional HD, due to the need to ultrafiltrate in a short period of treatment all the volume accumulated during the long interdialytic interval.

In the HEMO Study [2], a large prospective randomized clinical trial, in which 1846 patients on regular HD were randomized to have an eKt/V of approximately 1.05 or of 1.45 or greater, no benefits were found with intensification of dialysis. There are several hypotheses to explain the lack of benefit with the increase in urea clearance in CHD. That regimen of dialysis can neither normalize blood pressure nor control phosphatemia without the use of chelating agents in most patients. To achieve such objectives, a reduction in blood volume and the loss of phosphorus in three HD sessions equivalent to that absorbed from the diet over an entire week would be necessary. Thus, the transference of water and phosphorus from the intra- to the extracellular space at a velocity lower than their removal through dialysis poses a great limitation to CHD efficacy. Such objectives are more easily achieved in longer and/or more frequent dialysis regimens.[6-10]

There is evidence that the longer treatment, even in CHD, is associated with a smaller risk of death, regardless of the Kt/V achieved. Japan, where patients frequently undergo dialysis for four to five hours per session, has the lowest HD mortality rate in the world. On the other hand, the risk of death of patients on HD in the United States, where most of them undergo dialysis for less than four hours per session, is almost four times greater than that in Japan.[1]1

Long nocturnal hemodialysis

Long nocturnal hemodialysis (NHD) was described by Shaldon more than 40 years ago as an option of home treatment with excellent clinical results.[12]

The lowest mortality rate in dialysis has been reported in Tassin, France, where, four decades ago, a dialysis program of three sessions per week lasting up to eight hours each session, but usually during the day, was started. Survival after 10 and 20 years among those patients is approximately 70% and 50%, respectively.[6] Based on that long and favorable experience, many dialysis units in several countries have recently undergone adaptations to provide, during the night, a program similar to that initially established in Tassin. In a study recently carried out in Turkey, 224 patients migrated from CHD to NHD of eight hours, three times a week, and were compared with 224 other patients who continued on CHD, paired by age, sex, diabetes, and HD time. After a mean one-year follow-up, the following were observed: a 78%-reduction in the risk of death; a 74%-decrease in the number of hospitalization days; a 79%-reduction in the episodes of hypotension during HD; an increase in serum albumin; a reduction in phosphorus; and the need for much lower doses of erythropoietin, phosphorus chelating agents, and antihypertensives.[13] A great advantage of the NHD regimen performed at the dialysis center is that it uses a ready and available structure, without competing for room (on the contrary, more patients can be cared at dialysis centers during a formerly inactive period).

Another variant of long NHD was conceived by Pierratos[14] in Toronto, Canada, in 1994. That method of HD encompasses three benefits: home dialysis, every day dialysis, and long-length dialysis. Patients are dialyzed five to seven times a week for up to eight hours per night. Blood and dialysis solution flows are lower than those in CHD. In that dialysis method, patients have excellent control of blood pressure, with normalization of the left ventricular mass, improvement of anemia, and correction of the serum levels of phosphorus,

which sometimes requires the addition of phosphate to the dialysis solution.[15]

Short daily hemodialysis

One alternative proposed to CHD is daily hemodialysis (DHD) of short duration, idealized by Buoncristiani in Perugia, Italy.[16] It is simple and of relatively easy implantation, and can be performed at both dialysis centers and home.

Even if patients on DHD undergo a total dialysis time per week close to that of patients on CHD, the overall removal of solutes is greater in DHD because of the higher concentration gradient existing between plasma and the dialysis solution at the beginning of the session.[17] A way of comparing the dialysis dose of patients undergoing HD with different frequencies of treatment per week is the conversion to weekly standard Kt/V (std Kt/V) [18] (Figure 2). For example, a patient with equilibrated Kt/V (eKt/V) of 1.2 per session, three times a week, will have a std Kt/V of approximately 2.15; if that same patient had an eKt/V of 0.6 per session and was dialyzed six times a week, his std Kt/V would be approximately 2.75, which is almost 30% greater.

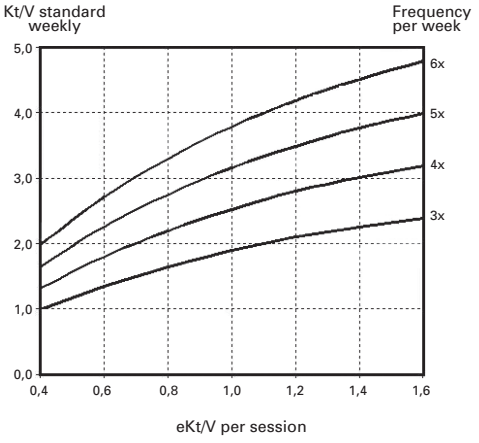
Even though patients undergo twice the number of sessions, they do not have a significant increase in the complications associated with vascular access.[19,20] A strategy to minimize the inconvenience of the increase in the number of punctures in DHD is the adoption of the arteriovenous fistula puncture according to the buttonhole technique, which is the repetitive use of the same puncture site with noncutting needles. This puncture technique causes less pain and is associated with fewer local complications, such as hematomas and aneurysmatic formations.[21]

In that modality of treatment, patients usually undergo six sessions a week, except for Sundays, with a session length of two to three hours. Patients on DHD show a significant improvement in several clinical, laboratory, and echocardiographic parameters.[9,10,20,22] Patients also improve their quality of life.[23]

As previously mentioned, patients on CHD have only approximately 25% of remaining life expectancy when beginning dialysis as compared with the general population. According to a large prospective observational multicenter study, short DHD provides an estimated increase in survival of 9 to 15 years for patients aged 20 to 65 years.[24] Reports of improvement in clinical findings and quality of life spread from patient to patient have boosted the growth of that type of treatment. Only in 2007, more than one thousand new patients started short daily home HD in the USA.[25]

In view of the growing evidence of the benefits of more frequent and/or longer HD, based only on observational or randomized studies with a limited number of patients, the National Institutes of Health of the USA decided to sponsor two large multicenter studies, the Frequent Hemodialysis Network: Daily Dialysis and the Frequent Hemodialysis Network: Nocturnal Dialysis, which started in 2006.[26] After the conclusion of those studies, new patterns of maintenance HD prescription are expected to consolidate.

Figure 2. Estimation of weekly standard Kt/V (ordinate) based on known values of eKt/V per session (abscissa) and the frequency of dialysis per week. Graph elaborated based on the equation described in reference 18.



Indications for more frequent and/or longer HD

There is no contraindication for the more frequent and/or longer dialysis regimen. However, because of the shortage of room availability and economic impact, those options could be offered preferentially in some clinical situations, such as the following: in the presence of hemodynamic instability, with intolerance to removal of enough

fluid for maintaining blood volume under control; hypertension refractory to other clinical measures; hyperphosphatemia refractory to the use of chelating agents and diet; worsening of the nutritional status due to no other cause than uremia; intolerance to the conventional dialysis regimen, with recurring symptoms at the end of the session, such as headache, nausea, and intense and prolonged fatigue; and for pregnant women already on dialysis (in this situation, increase the frequency, without reducing time).

Conclusions

The high mortality rate associated with the conventional hemodialysis regimen emphasizes the need for urgent changes in the strategy of application of renal function substitution methods. Hemodialysis should be predominantly performed in a more frequent and/or longer regimen. It is worth emphasizing that the economic limitations of the application of emerging knowledge in the area should be overcome. The use of home dialysis is expected to substantially increase based on the principle that medical procedures should offer the greatest safety and comfort possible to patients.

References

1. United States Renal Data System. Annual Report 2009.
2. Eknoyan G, Beck GJ, Cheung AK *et al*. Hemodialysis (HEMO) Study Group. Effect of dialysis dose and membrane flux in maintenance hemodialysis. N Engl J Med 2002; 347:2010-9.
3. Blagg CR. The early history of dialysis for chronic renal failure in the United States: a view from Seattle. Am J Kidney Dis 2007; 49:482-96.
4. Bleyer AJ, Hartman J, Reeves-Daniel A, Satko SG, Russell G. Characteristics of sudden death in hemodialysis patients. Kidney Int 2006; 69:2268-73.
5. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. Clin J Am Soc Nephrol 2009; 4:914-20.
6. Innes A, Charra B, Burden RP, Morgan AG, Laurent G. The effect of long, slow haemodialysis on patient survival. Nephrol Dial Transplant. 1999; 14:919-22.
7. Culleton BF, Walsh M, Klarenbach SW *et al*. Effect of frequent nocturnal hemodialysis vs conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial. JAMA 2007; 298:1291-9.
8. Ayus JC, Achinger SG, Mizani MR *et al*. Phosphorus balance and mineral metabolism with 3 h daily hemodialysis. Kidney Int 2007; 71:336-42
9. André MB, Rembold SM, Pereira CM, Lugon JR. Prospective evaluation of an in-center daily hemodialysis program: results of two years of treatment. Am J Nephrol 2002; 22:473-9.
10. Ayus JC, Mizani MR, Achinger SG, Thadhani R, Go AS, Lee S. Effects of short daily versus conventional hemodialysis on left ventricular hypertrophy and inflammatory markers: a prospective, controlled study. J Am Soc Nephrol 2005; 16:2778-88.
11. Saran R, Bragg-Gresham JL, Levin NW *et al*. Longer treatment time and slower ultrafiltration in hemodialysis: associations with reduced mortality in the DOPPS. Kidney Int 2006; 69:1222-8.
12. Shaldon S. Independence in maintenance haemodialysis. Lancet 1968; 1:520.
13. Ok E, Duman S, Asci G *et al*. Eight-Hour Nocturnal In-Center Hemodialysis Provides Survival Benefit over Four-Hour Conventional Hemodialysis. J Am Soc Nephrol 2008; 19:70A-71A.
14. Pierratos A, Ouwendyk M, Francoeur R *et al*. Nocturnal hemodialysis: three-year experience. J Am Soc Nephrol 1998; 9:859-68.
15. Pierratos A. Daily (quotidian) nocturnal home hemodialysis: Nine years later. Hemodial Int 2004; 8:45-50.
16. Buoncristiani U. Fifteen years of clinical experience with daily haemodialysis. Nephrol Dial Transplant 1998; 13 (Suppl 6):148-51.
17. Greene T, Daugirdas JT, Depner TA, Gotch F, Kuhlman M. Solute clearances and fluid removal in the frequent hemodialysis network trials. Am J Kidney Dis 2009; 53:835-44.
18. Leypoldt JK. Urea standard Kt/V for assessing dialysis treatment adequacy. Hemodial Int 2004; 8:193-7.
19. Quintaliani G, Buoncristiani U, Fagugli R *et al*. Survival of vascular access during daily and three times a week hemodialysis. Clin Nephrol 2000; 53:372-7.
20. Martins-Castro MC, Luders C, Elias RM, Abensur H, Romao JE Jr. High-efficiency short daily haemodialysis- morbidity and mortality rate in a long-term study. Nephrol Dial Transplant 2006; 21:2232-8.
21. van Loon MM, Goovaerts T, Kessels AG, van der Sande FM, Tordoir JH. Buttonhole needling of haemodialysis arteriovenous fistulae results in less complications and interventions compared to the rope-ladder technique. Nephrol Dial Transplant 2009 (in press).
22. Fagugli RM, Reboldi G, Quintaliani G *et al*. Short daily hemodialysis: blood pressure control and left ventricular mass reduction in hypertensive hemodialysis patients. Am J Kidney Dis 2001; 38:371-6.
23. Puñal Rioboó J, Sánchez-Iriso E, Ruano-Ravina A *et al*. Short daily versus conventional hemodialysis quality of life: a cross-sectional multicentric study in Spain. Blood Purif 2009; 28:159-64.
24. Kjellstrand CM, Buoncristiani U, Ting G *et al*. Short daily haemodialysis: survival in 415 patients treated for 1006 patient-years. Nephrol Dial Transplant 2008; 23:3283-9.

25. Lockridge RS Jr, Pipkin M. Short and long nightly hemodialysis in the United States. Hemodial Int 2008; 12(Suppl1):48-50.

26. Suri RS, Garg AX, Chertow GM *et al*. Frequent Hemodialysis Network (FHN) randomized trials: study design. Kidney Int 2007; 71:349-59.