Manual Individualization of the Dialysate Flow According to Blood Flow: Effects on the Hemodialysis Dose Delivered and on Dialysate Consumption

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ABSTRACT

Background: The objective of this study was to assess the impact of the decreasing dialysate flow rate (Qd) on the dialysis dose delivered (spKt/V) and to estimate the resulting water saving. Methods: It was a prospective 4-week-period study that included chronic hemodialysis patients with clinical and hemodynamic stability. Patients successively was dialysated with a Qd of 500 mL/min (Qd500), at 1 (mean Qd1 = 310 mL/min), 1.2 (mean Qd1.2 = 368 mL/min) and 1.5 (mean Qd1.5 = 464 mL/min) times the blood flow rate. Each dialysate flow rate was applied for one week. During these 4 weeks, the following parameters were constant: duration of dialysis, blood flow rate, anticoagulation, membrane nature and surface. Results: Forty-five chronic hemodialysis patients were included with a mean age of 48.4 ± 12.07 years. The weekly mean spKt/V was statistically higher with a Qd1.5 compared to the Qd500 (p = 0.001). The proportion of patients achieving a standardized dialysis dose ≥ 1.4 was statistically higher with Qd500 (64.4%) compared to Qd1 and Qd1.2 which were 57.8% and 55.6%, respectively. It was statistically higher with a Qd1.5 (93.3%) compared to Qd500 (p = 0.036). The dialysate volume used with a Qd500 was higher compared to the other Qd (p = 0.0001). Conclusion: An adequate dialysis dose could be achieved with a Qd1.5, allowing to significantly reducing amount of water.

Key words: Hemodialysis; Dialysis dose; Dialysate flow rate; Dakar.

Background

The delivered dialysis dose is an important morbidity and mortality predictor on chronic hemodialysis patients [1,2]. A minimum of Kt/V balanced in urea (eKt/V) of 1.2 is recommended thrice per week and without residual renal function [3]. This delivered dialysis dose depends on the dialyzer used, dialysis time and its conditions of use (blood flow rate or Qb, dialysate flow rate or Qd, blood connection and dialysate to dialyser and ultrafiltration) [4]. In the 1960s, the optimal Qd considering the conformation of the dialyzers in use was 500 mL/min [4]. However, increasing the Qd from 500 to 800 mL/min for a constant Qb to 450 mL/min with the same dialyzer increased dialysis dose by 14% [5]. In conventional dialysis systems, the total dialysate volume required for each treatment is determined by the Qd and the duration of the treatment. A Qd of 500 mL/min (Qd500) will therefore require 500 mL x 60 min = 30L/h. Thus, the higher the Qd, the more water the system uses. A compromise between a Qd, a dose of dialysis delivered and the cost of water must therefore be found. To that extent, the new AutoFlow (AF) function of some dialysis machines, automatically adjusts the Qd according to the Qb of the individual patient. The consequence of this approach is a significant economy of the dialysis fluid consumption [6,7]. A Moroccan team compared the dialysis dose with 3 flow rates (Qd500, Qd700 and an average Qd of 404 ± 29 mL/min) suggested no interest in increasing Qd beyond 500 mL/min to obtain a target dialysis dose with a significant economy in the dialysate used [4]. Kult et al. also noted in a clinical trial that the Qd/Qb ratio must be greater than 1.2 in order to optimize the dialysis dose [6]. A ratio less than 1.2 (eg 1.0) could be an option to reduce the dialysate consumption [8]. We therefore asked ourselves this research question: is the Qd reduction effective to reach a spKt/V ≥1.4. The aims of this study were to (i) evaluate the impact to decrease the Qd on the dialysis dose delivered to chronic hemodialysis patients and to (ii) estimate the possible water saving in conventional hemodialysis.

METHODS

Study population

Chronic hemodialysis patients of nephrology, dialysis and renal transplant department on Aristide le Dantec University Hospital (HALD) in Dakar were targeted. For inclusion in the study, patients were required to be older than 18 years, stable clinical and hemodynamic course, with arteriovenous fistulas for vascular access, dialysated regularly thrice weekly and were consenting. Patients with a serious cardiovascular event (myocardial infarction, heart failure with or without left ventricular ejection function alteration) in the past 3 months or with diabetes were not included. Patients who had: dysfunction of the arteriovenous fistula (AVF), a change in certain hemodialysis parameters (time, anticoagulation, Qb), hospitalization during study period and those who decided to withdraw from the study were excluded. All included patients were dialyzed with Nipro® machine (SURDIAL 55 PLUS model). The dialysate were composed of sodium 140 mmol/L, chlorine 109 mmol/L, calcium 1.50 mmol/L, bicarbonate 34 mmol/L, magnesium 0.5 mmol/L, potassium 2 mmol/L and glucose at 1 g/L.

Study design

It was a monocentric prospective study conducted during 4 week (October 28, 2019 to November 23, 2019). Included patient were exposed to 4 types of Qd. They were dialysated as follows:

Week 1 Qd500: 3 sessions with Qd = 500 mL/min;

Week 2 Qd1: 3 sessions with Qd = 1.0 x Qb mL/min;

Week 3 Qd1,2: 3 sessions with Qd = 1.2 x Qb mL/min;

Week 4 Qd1.5: 3 sessions with Qd = 1.5 x Qb mL/min.

Data collected

During these sessions Qb and spKt/V were collected directly from the dialysis machine screen. Mean weekly spKt/V was calculated at the end of each week and was the outcome. From the Qd and the duration of the session (ds), DIALYSATE VOLUME (DV) WAS CALCULATED ACCORDING TO THE FORMULA: DV = QD X DS.

The other parameters were collected: epidemiological parameters (age, gender), clinical parameters (initial nephropathy, duration of dialysis (months), characteristics of the dialyser (nature of the membrane, exchange surface), medical history, comorbidities and anthropometric parameters (dry weight (kg), height (cm), Body Mass Index (BMI) (kg / m2)). Low Qd hemodialysis was defined by any session in which the Qd was less than 500 mL/min. The normalized target dialysis dose was reached if the value of the weekly spKt/V was greater or equal to 1.4 [9].

Statistics

The data were entered through Sphinx software version 5.1.0.2 (Parc Altais, 27 rue Cassiopée, 74650 Chavanod, France). Data analysis was carried out with SPSS (Statistical Package for Sciences Socials) software version 18 (IBM®, Endicott, United States). The analytical study was made from cross tables. To compare frequencies, the Pearson chi-square test or Fisher's bilateral exact test were used depending on their applicability. The average comparison was performed with the analysis of variance test (ANOVA) for the dependent (linked) samples. The test was significant for a p-value <0.05. The Odds Ratio with Confidence Interval was used as the association measure.

RESULTS

Forty-five (45) patients were included. The flow graph is presented in **Figure 1**. The mean age was 48.4 ± 12.07 years with a sex ratio (M / F) of 2. Hypertensive nephropathy was noted in 17 patients (37.78%), chronic glomerulonephritis in 9 patients (20%). The mean hemodialysis duration was 92.28 ± 44.54 months. The mean baseline weight and mean inter-dialytic weight gain were 64.03 ± 13.27 kg and 1.68 ± 0.75 kg respectively. The mean BMI was 21.45 ± 3.79 kg/m2. 17.8% of patients were lean (BMI <18.5 kg/m2) and
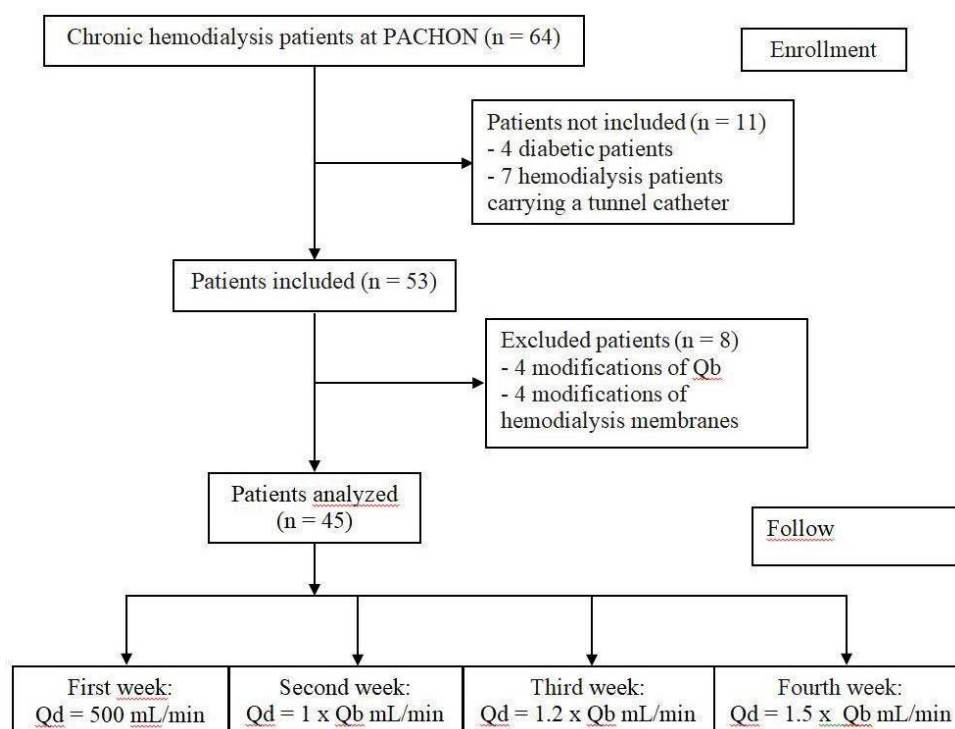
Figure 1: study design. Qd = dialysate flow rate. Qb = blood flow rate. n = number.

15.5% obese (BMI> 30 kg/m2). All patients were dialysated four (4) hours, 3 times per week. The hemodialysis membranes were synthetic with a mean exchange area of 1.86 ± 0.15 m2. The mean Qb was 310 ± 20.22 mL/min. The mean weekly Qd was 500 mL/min in the first week (Qd500), 310 ± 20.22 mL/min in the second week (Qd1), 368 ± 29 mL/min in the third week (Qd1.2) and 464 ± 29 mL/min at the fourth week (Qd1.5).

The mean weekly spKt/V was 1.43 ± 0.19 with a Qd500, 1.42 ± 0.15 with a Qd1, 1.40 ± 0.12 with a Qd1.2 and 1.53 ± 0.13 with a Qd1.5 (**Figure 2**). The mean weekly spKt/V obtained with a Qd1.5 was statistically higher than those obtained with a Qd500 (p = 0.001).

The spKt/V obtained with Qd1 and Qd1.2 were not different from that obtained with Qd500 (p = 0.663 and 0.231 respectively). The proportion of patients who reached a spKt/V ≥ 1.4 according to the Qd is shown in **Table 1**. The proportion of patients achieving a spKt/V ≥ 1.4 was statistically higher with a Qd500 compared to Qd1 and Qd1.2 (OR of 5.77; 95% CI [1.5-21.9] and 4.89; 95%

CI [1.31-18.26] respectively). The proportion of patients achieving spKt/V ≥ 1.4 was statistically higher with Qd1.5 compared to Qd500 (p = 0.036). The mean weekly DV with a Qd500 was 120L. The other DV according to Qd are given in **Table 2**.

DISCUSSION

Dialysate flow rate and normalized dialysis dose (spKt/V)

In the 1960s, the optimal Qd was 500 mL/min and the increase in Qd was associated with an increased dialysis dose [2]. The influence of Qd on the purification of small molecules is more important as the hydraulic permeability of the membrane [10]. The improvements in modern dialyzers, including changes in the packing density of the fibers and the conical design, the waving of the fibers and the addition of spacer yarns in the fiber bundle, allow for better distribution of the dialysate flow through the dialysate compartment [11, 12]. Thus, they theoretically reduce the need for a high Qd to obtain adequate dialysis. The adaptation of the Qd can be done automatically from the Qb depending to the generator
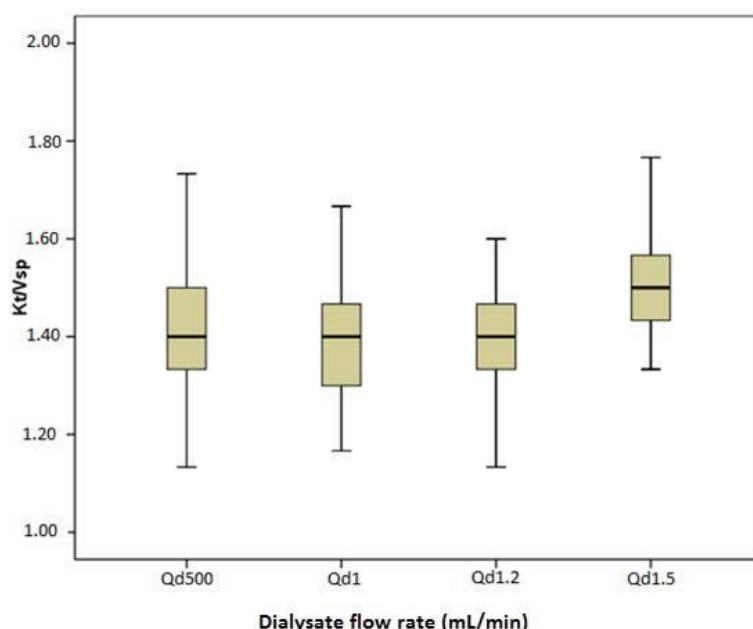
Figure 2: Effect of the 4 different types of dialysate flow on the mean weekly (spKt/V). The box plot shows that the dialysate flow rate at 1.5 times the blood flow rate was higher than the other dialysate flows rate. Qd500 = dialysate flow rate at 500 mL/min. Qd1 = dialysate flow rate at one time blood flow rate. Qd1.2 = dialysate flow rate at 1.2 times the blood flow rate. Qd1.5 = dialysate flow rate at 1.5 times the blood flow rate.

Table 1: Distribution of chronic hemodialysis patients according to the achievement of the normalized target dialysis dose and to the different dialysate flow rates.

	Qd500 (%)	Qd1 (%) ✓	Qd1.2 (%) ✓✓	Qd1.5 (%) ✓✓✓
spKt/V<1.4	16(35.6)	19(42.2)	20(44.4)	03(06.7)
spKt/V≥1.4	29(64.4)	26(57.8)	25(55.6)	42(93.3)
All	45(100)	45(100)	45(100)	45(100)

Qd = dialysate flow rate. SpKt/V=single pool normalized target dialysis dose. ✓ HR 5.77; CI 95% [1.5-21.9] for Qd1
Versus Qd500. ✓✓ HR 4.89 ; CI 95% [1.31-18.26] for Qd1.2 versus Qd500. ✓✓✓ p=0.036 for Qd1.2 versus Qd500.

Table 2: Variations in dialysate volumes (DV) according to the dialysate flow rates.

	Mean (L)	Standard deviation	p
DV Qd500 (reference)	120	0	
DV Q1	74.4	4.85	< 0.001
DV Q1.2	88.63	5.59	< 0.001
DV Q1.5	111.47	7.06	< 0.001

used in order to optimize the purification while minimizing the consumption of dialysate and therefore the cost [4]. A randomized crossover study in patients with body weight <65 kg reported that reducing Qd from 500 mL/min to 400 mL/min had no impact on Kt/V, interdialytic weight gain, blood pressure or electrolyte disturbances. Conversely, it reduced the consumption of dialysate from 120L to 96L [13]. These results suggest that there is no major interest in increasing the Qd beyond 500 mL/min for obtain the target Kt/V, which allows a significant saving in the dialysate used. Mesic and al. had also noted that a Qd/Qb ratio could be less than 1.2 which would allow a reduction in dialysate consumption [9]. In our framework, we do not have generators capable of automating Qd from an AF factor in all our centers. Thus, this study made it possible to assess the possibility of manually adjusting the Qd as a function of an AF factor (1; 1.2; 1.5). We found that these AF factors made it possible to obtain Qd lower than 500 mL/min thus ensuring a lower water consumption. The main question was whether these low Qd would allow a sufficient dose of dialysis to be administered to our patients while consuming less dialysate.

Thus dialysis with Qd1.5 was a low Qd dialysis which made it possible to administer a sufficient dose of dialysis while saving dialysate consumption. A study, using Qb from 150 to 200 mL/min found that reducing Qd from 500 mL/min to 400 mL/min reduced urea, creatinine and phosphate clearance when the Qb/Qd fell below 1.2 [14]. The low Qd observed with AF reduced the use of dialysate and acid concentrate by 20% and the use of bicarbonate powder by 23% [14]. With an AF factor of 1.5, the mean Qd in our study was 464 ± 29 mL/min, lower than Qd500. The superiority of Qd1.5 compared to Qd500 needs to be confirmed by other studies.

Dialysate volume and water saving

In conventional dialysis systems, the total VD required for each treatment is determined by the Qd and the duration of the treatment. Higher the Qd is, the more the system use dialysate. Assuming a Qd of 500 mL/min, a patient is exposed to at least 120 L of dialysate during hemodialysis session of 4 hours. Annual consumption of dialysate for operation of single hemodialysis generator at the rate of 12 hours per day (3 connections) and 6 days per week is estimated at 112 m3, without considering water which is rejected by the filters at carbon and reverse osmosis membranes before use in dialysis. A study conducted by Jabrane et al. at Mohamed VI Teaching Hospital, showed an approximate mean annual estimation of water consumption for hemodialysis of 1216.8 m3 at the rate of 3 daily connections for 13 hemodialysis generators [15]. In our series, we noted a lower VD (111L) with a Qd1.5 (statistically significant difference) compared to Qd500 (120L). This result suggests a dialysate savings of around 9L per 4-hour hemodialysis session, or 1,296 L per patient per year, while achieving an adequate dialysis dose. About 100 patients are hemodialysed in the 2 units of the HALD, thus 129,600 L of dialysate could be saved per year, or 129.6 m3 of dialysate. This can have a significant ecological impact. Dialysis consumables such as acid bath and bicarbonate concentrate can also be streamlined. Health care is a major contributor to resource depletion and greenhouse gas emissions. The environmental impact of hemodialysis appears to be particularly high, suggesting that the nephrology community has an important role to play in exploring environmentally friendly healthcare practices.

Opportunities to reduce the environmental impact of hemodialysis include capture and reuse of water discharged by reverse osmosis, the use of renewable energy, improved waste management and the potential reduction of Qd [16]. Our study outlined that reducing Qd would reduce the environmental impact of hemodialysis. These results require further work for confirmation. Nevertheless, we can conclude that Qd1.5 is at least as effective as Qd500 with a gain on the consumption of dialysate.

Potential Benefits of Reducing Dialysate Flow Rate in Patients

All chronic hemodialysis patients included in this study had a high flux synthetic dialysis membrane based on polyether sulfone. These membranes can lead to increase bio-incompatibility phenomena as well as micro-inflammation in these patients due to retro filtration and no ultrapure dialysate. The decrease in Qd and consequently in consumption of dialysate can lead to a decrease in the amount of back-filtered dialysate. The NECOSAD-2 study had shown that for the same Kt/V urea, patient survival was better if residual renal function (RRF) persisted [17]. The role of ultrapure water seems essential. In a pilot study by Schiffl et al. an ultrapure dialysate was associated with better preservation of the RRF compared to the conventional dialysate (p <0.05) [18]. A conventional (pure) dialysate, used in our hemodialysis center, can be harmful on the RRF [18]. By reducing Qd, the RRF could be better protected. A study is needed to assess the impact of Qd reduction on the preservation of the RRF. Malnutrition-Inflammation-Atherosclerosis syndrome is common in hemodialysis patients [19] and the use of a conventional dialysate could play a role in micro-inflammation of patients due to retro-filtration of endotoxins especially if membranes high-flux are used [20]. Reducing Qd and thus consuming dialysate could reduce this chronic micro-inflammation.

CONCLUSION

An adequate Kt/V could be reached with a Qd1.5 thus allowing a significant water saving. Hemodialysis centers must be equipped with generators having Qd-independent modules based on Qb. Otherwise, manual autonomy can allow better respect for the environment while achieving an adequate Kt/V.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

LIST OF ABBREVIATIONS

AF: auto flow

AVF: Arteriovenous fistula

BMI: Body Mass Index

CER: research ethics committee

ds: duration of session

DV: Dialysate Volume

HALD: Aristide le Dantec University Hospital

Qb: blood flow rate

Qd: dialysate flow rate

Qd1.2: dialysate flow rate at 1.2 time the blood flow rate

Qd1.5: dialysate flow rate at 1.5 times the blood flow rate

Qd1: dialysate flow rate at 1time the blood flow rate

Qd500: dialysate flow rate of 500 ml / min

RRF: Residuel Renal Function

UCAD: Université Cheikh Anta Diop

DECLARATIONS

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