Incremental versus Conventional Hemodialysis: Which is Better for Prevalent Hemodialysis Patients?

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ABSTRACT

Background: Incremental hemodialysis is based on the simple idea of adjusting its dose according to the metrics of residual kidney function. Indeed, most patients initiating dialysis have some degree of residual kidney function. Incremental dialysis may preserve residual renal function and improve survival in comparison with full-dose dialysis.
Objective: To compare the intervention arm (incremental hemodialysis) with the control arm (standard 3 hemodialysis sessions/week).
Patients and Methods: A prospective cohort study was conducted, recruiting 50 patients from multiple hemodialysis units, over six months. The prevalent patients were divided randomly into equal two treated groups. The outcomes compared adequacy of hemodialysis and detection of hazards as well as complications, including vascular access failure and associated interventions, cardiovascular events and hospital admissions, and mortality in both groups.
Results: Regarding the occurrence of cardiovascular events, chest pain, there were no significant differences between both groups. Arrhythmia was not recorded in the incremental group, while in the conventional group it was recorded in 2 patients, and there was no significant difference between both groups. Regarding the need for hospital admission, there was no significant difference between both groups. As regards the occurrence of vascular access failure, it was recorded in 2 patients in the incremental group, compared to 4 patients in the conventional group, with no significant difference between both groups. Adequacy of hemodialysis (in the form of urea reduction ratio and KT/V) was better in the incremental group.
Conclusion: Incremental hemodialysis was superior to the conventional one regarding the adequacy of dialysis, with monthly follow-up till 6 months. There were no significant differences between both groups regarding cardiovascular events, vascular access failure, and hospitalization.
Keywords: Incremental hemodialysis, Conventional hemodialysis, Cairo.

INTRODUCTION

The majority of hemodialysis (HD) patients initiate dialysis with a relatively intense thrice-weekly HD sessions /week regimen of 3–4 hours per session, with little individualization of prescription based on residual kidney function (RKF) or other patient factors [1]. Incredibly, the 3 HD sessions/week schedule has been widely accepted worldwide without ever undergoing any randomized controlled trial (RCT) to examine whether less frequent HD treatments would be inadequate or harmful [2]. It is plausible that the routine practice of fixed-dose 3 HD sessions/ week in patients with substantial RKF may be harmful, contributing to an accelerated loss of RKF [3]. The Kidney Diseases Outcomes Quality Initiative (KDOQI) suggests that minimum targets of the adequacy of the dialysis dose (Kt/V) may be reduced in those with residual renal urea clearance (Kru) <2mL/min/1.73 m² [2].

The European Best Practice Guidelines (EBPG) recommend measuring RKF in HD patients using the mean of urea and creatinine clearances. The commencement of HD is associated with increased levels of mortality, particularly in the elderly [4]. This early period is associated with frequent episodes of hypotension even in units undertaking longer hours and using slower ultrafiltration rates [5]. Intradialytic

episodes of hypotension appear to have deleterious effects on both cardiac and cerebral function [6].

The other organ susceptible to hypotension and often overlooked is the kidney; repeated episodes of intradialytic hypotension are implicated in the loss of RKF, which in turn has a negative impact on UOP and greater ultrafiltration requirements, leading to a vicious cycle with progressive renal injury [7]. Aside from end-organ effects, the Dialysis Outcomes and Practice Patterns Study (DOPPS) has highlighted the wide variation in time to recovery. Ten percent of all patients took longer than 12 hours to recover from an HD session, with an increased recovery time associated with age and comorbidity [8].

Incremental HD has a lower burden of treatment. There appear to be no adverse clinical effects during the first years of incremental HD and when there is significant RKF [9]. The advantages of incremental HD might be particularly important for elderly patients with short life expectancy, where transplantation is not an option [10].

RKF may confer many benefits to patients with end-stage renal disease (ESRD) on maintenance HD including associations with better patient survival and health-related quality of life [1]. RKF in dialysis patients plays an important role in fluid and salt removal, effective phosphorus excretion, middle molecule clearance, and endogenous vitamin D and

erythropoietin production [11]. Loss of RKF is linked to decreased survival likely from poorer uraemic solute clearance, volume and blood pressure control, higher erythropoietin requirement, more inflammation, and higher left ventricular mass [12]. Finally, the available literature suggests greater preservation of RKF with infrequent dialysis [13]. The regular monitoring of RKF by periodic urine collections is required to ensure that RKF is being maintained [14]. If the potential benefits of incremental HD will be confirmed by RCTs, then starting dialysis at a full dose will be subjecting patients to unnecessarily long or more frequent treatments for an unnecessarily long time, and at a higher cost [15].

Criteria for candidates that may benefit from incremental hemodialysis (IHD); Good RKF with UOP > 0.5 L/d (or KRU>3 ml/min). Limited fluid retention between two conservative HD treatments with fluid gain < 2.5 kg (or < 5% of ideal dry weight) without HD for 3-4 days. Limited or readily manageable cardiovascular or pulmonary symptoms without clinically significant fluid overload. Suitable body size relative to RKF. Hyperkalemia (K, >5.5 mEq/L) is infrequent or readily manageable. Hyperphosphatemia (P> 5.5 mEq/L) is infrequent or readily manageable. Good nutritional status without the florid hypercatabolic state. Lack of profound anemia (Hb>8 g/dL) and appropriate responsiveness to anemia therapy. Infrequent hospitalizations and easily manageable comorbid conditions. Satisfactory health-related quality of life. Use of the criteria on 2x/week HD therapy patients should be re-evaluated once a month [10].

The present study aimed to compare the intervention arm (incremental HD) with the control arm (standard 3 HD sessions /week). Prevalent patients were randomized to one of the two treatment groups in equal proportion. The primary outcome was comparing the adequacy of HD between both groups. Secondary outcomes were detecting all-cause mortality and significant events, including vascular access failure and associated interventions, cardiovascular events, and hospital admissions.

PATIENTS AND METHODS
This was a prospective cohort study conducted on 50 patients divided into two groups; 25 patients on HD with 2 sessions weekly (Incremental HD), and 25 patients on HD with 3 sessions weekly (Standard HD). Patients were selected from different Cairo governorate HD units.
Inclusion Criteria: Patients included were 18 years old or more, and HD sessions were either two or three sessions weekly, four hours for each session using the same bicarbonate dialysate concentration, and heparin as an anticoagulant, blood pump was 250- 300 ml/min for all patients.
Exclusion Criteria: Change in dialysis modality during the study period.

Sample Size: Fifty patients on maintenance HD from different HD units, divided into 2 groups (each group included 25 patients): **Group 1:** patients on HD twice-weekly (Incremental HD) and **Group 2:** patients on HD with three sessions weekly (Standard HD).

Ethical Considerations:
The study had been approved by the local ethical committee of Ain Shams University. Informed consent had been obtained from all patients before enrolment in the study after explaining the study purpose, methods, risks, and benefits to them. The individuals involved in the research had the right to withdraw from the study at any time without jeopardizing their right to receive medical care. This work has been carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All patients were subjected to the following:
History taking with a detailed history including (age, etiology of ESRD, duration of HD, type of vascular access) and complete clinical examination.
Laboratory Investigations: had been done at the start of the study, monthly and at the end of the study (after 6 months): Hemoglobin level, serum creatinine, blood urea, serum albumin, calcium and phosphorus (monthly), and serum PTH / 3 months.

Adequacy of dialysis: had been estimated at the start, monthly, and at the end of the study period by:
- Calculated Kt/V using **Kt/V Daugirdas Formula**: Kt/V Daugirdas = -ln((BUNPost / BUNPre) - (0.008 * Hours)) + ((4 - (3.5 * BUNPost / BUNPre)) * UFVol / Weight Post) [16].
- Calculated Urea reduction ratio (URR): Had been estimated at the start, monthly and at the end of the study period URR=100% × (predialysis BUN−post-dialysis BUN)/predialysis BUN [17].

Interdialytic weight gain (IDWG): had been estimated at the start, monthly, and at the end of the study period: IDWG (Kg): pre-dialysis weight – Post-dialysis weight [18].
Ultrafiltration rate (UFR): had been estimated at the start, monthly, and at the end of the study period.
The ultrafiltration volume was calculated as the change in body weight (BW) throughout dialysis (ie, predialysis BW–post-dialysis BW). The ultrafiltration rate (UFR) was expressed in mL/hour/kg by dividing the ultrafiltration volume by the dialysis session duration and target dry BW [19].

The comparison between the 2 groups regards the following items: Episodes of hospitalization. Vascular access failure and associated interventions. Cardiovascular events (arrhythmia – hypotension – hypertension (HTN) – chest pain). Episodes of Intra-dialytic hypotension. Ultrafiltration requirements. Kt/V, urea reduction ratio. Bone mineral biochemistry

(calcium, phosphorus, and PTH). Hemoglobin level, and serum albumin.

Imaging: Echocardiography.

Statistical methods

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013. Quantitative normally distributed data described as mean±SD (standard deviation) after testing for normality using the Shapiro-Wilk test, then compared using the independent t-test (two independent groups) and paired t-test (paired data). Qualitative data were described as numbers and percentages and compared using the Chi-square test and Fisher's Exact test for variables with small expected numbers. The level of significance was taken at P-value < 0.050 was significant, otherwise was non-significant.

RESULTS

Table 1 showed there were no significant differences between both groups regarding age, gender, weight, height, or BMI. The mean age of the patients was 43.4±8.5 in the incremental group and 44.3±8.7 in the conventional group.

Table (1): Baseline demographic characteristics of the studied groups:

Variables		Incremental (N=25)	Conventional (N=25)	P-value
Age (years)	Mean±SD	43.4±8.5	44.3±8.7	^0.719
	Range	26.0–58.0	26.0–58.0	
Gender	Male	11 (44.0%)	12 (48.0%)	#0.777
	Female	14 (56.0%)	13 (52.0%)	
Weight (kg)	Mean±SD	73.9±10.3	73.7±10.9	^0.958
	Range	55.0–90.0	58.0–96.0	
Height (m)	Mean±SD	1.68±0.06	1.69±0.04	^0.331
	Range	1.59–1.78	1.61–1.78	
BMI (kg/m^2)	Mean±SD	26.3±3.9	25.7±4.1	^0.638
	Range	17.8–32.7	20.5–37.0	

BMI: Body mass index. ^Independent t-test. #Chi-square test.

Table 2 showed there were significant differences between both groups at each follow-up, with superiority of the incremental arm at each follow-up visit (higher URR).

Table (2): URR among the studied groups

Month	Measures	Incremental (N=25)	Conventional (N=25)	P-value
Baseline	Mean±SD	37.7±13.9	29.8±10.6	0.029*
	Range	3.1–59.8	10.6–43.4	
Month-1	Mean±SD	33.7±10.0	26.7±10.9	0.021*
	Range	16.5–52.9	5.8–39.6	
Month-2	Mean±SD	27.7±11.0	21.9±8.2	0.040*
	Range	12.3–46.3	6.5–36.8	
Month-3	Mean±SD	23.7±8.7	18.7±7.1	<0.001*
	Range	12.0–41.6	7.0–31.9	
Month-4	Mean±SD	20.2±8.7	11.3±4.8	<0.001*
	Range	7.1–41.8	4.8–24.3	
Month-5	Mean±SD	16.8±11.1	7.8±3.8	<0.001*
	Range	2.2–51.7	1.3–16.5	
Month-6	Mean±SD	16.4±7.7	7.1±4.5	<0.001*
	Range	1.2–30.7	0.7–16.5	
#P-value		<0.001*	<0.001*	

^Independent t-test (Comparison between groups) #Paired t-test (Comparison between month-1 and month-6). **URR:** urea reduction ratio

Table 3 showed there was no significant difference between both groups regarding vascular access failure.

Table (3): Vascular access failure among the studied groups

Status	Incremental (N=25)	Conventional (N=25)	P-value
Failure	2 (8.0%)	4 (16.0%)	
No failure	23 (92.0%)	21 (84.0%)	0.667

Fisher's Exact test

Table 4 showed there was no significant difference between both groups regarding episodes of hospitalization.

Table (4): Hospital admission among the studied groups

Status	Incremental (N=25)	Conventional (N=25)	P-value
Admission	2 (8.0%)	5 (20.0%)	
No admission	23 (92.0%)	20 (80.0%)	0.417

Fisher's Exact test

Figure 1 showed that the incremental group had significantly higher URR values than the conventional group.
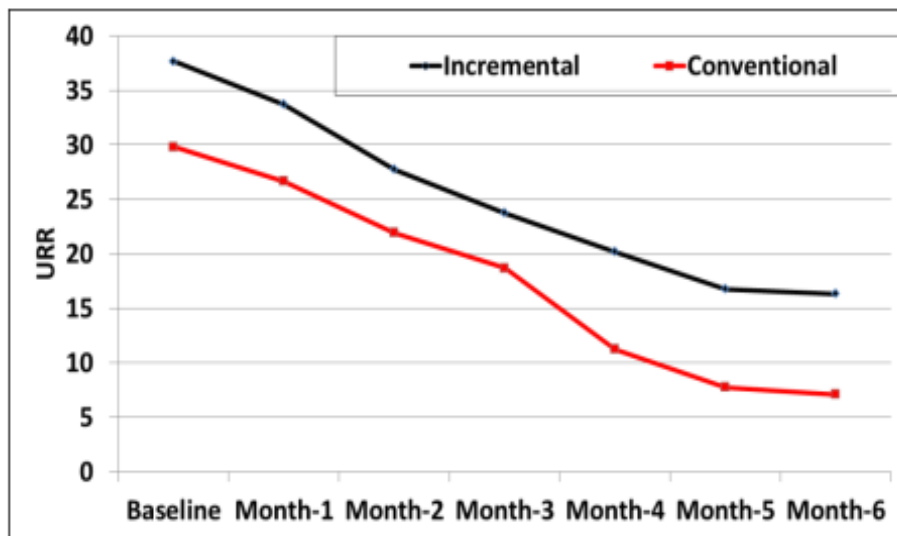

Figure (1): URR among both groups.

Figure 2 showed that the incremental group had significantly higher KT/V values than the conventional group with P-values of 0.033, 0.029, at baseline and one month, respectively, P-values of <0.001 at two, three, four, and five months and a P-value of 0.004 at six months.
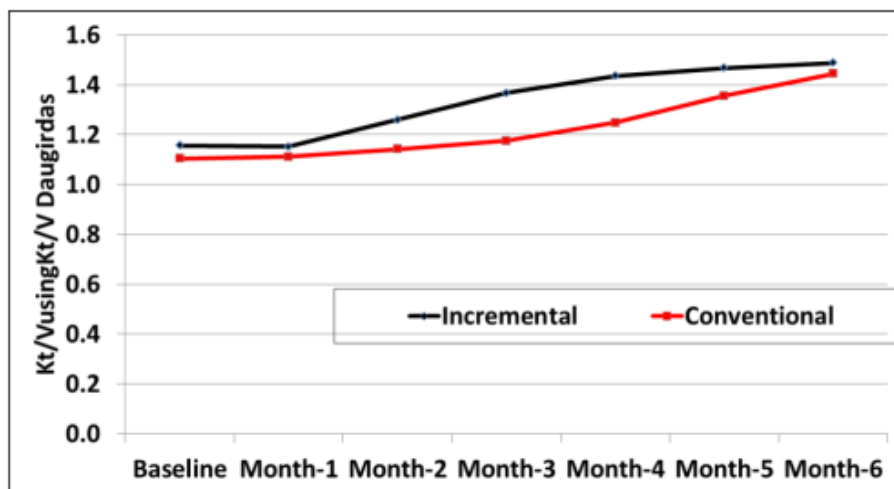

Figure (2): KT/V among both groups.

Figure 3 showed there were no significant differences between both groups regarding cardiovascular events.
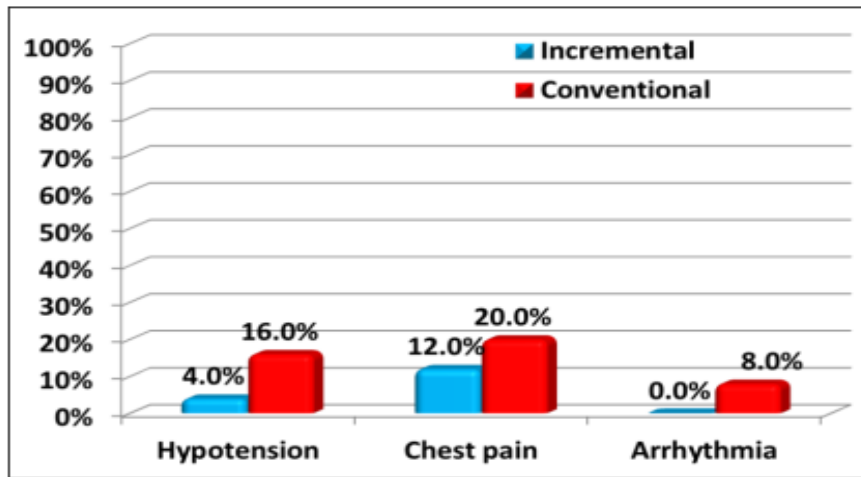
Figure (3): Cardiovascular events among both groups.

DISCUSSION

Regarding the baseline demographic data, there were no significant differences between both groups regarding age, gender, weight, height, or BMI with P-values of 0.719, 0.777, 0.958, 0.331, and 0.638, respectively.

There were no significant differences in any of the lipid profile parameters between the two groups.

As regards the difference in the serum albumin level as an indication of the nutritional status in each group separately at each visit, there were no significant differences. Comparing both groups at each follow-up, there were no significant differences as well. Regarding Patients' ESR as an indicator of inflammation, there were no significant differences between both groups.

In a study by **Zhang and colleagues**[20]**,** which will be mentioned in detail later, the main biochemical and clinical measures such as serum albumin, total cholesterol, BMI, showed no significant differences between the two groups at baseline. This was consistent with our findings.

Regarding patients' hemoglobin levels over the study follow-up period in the incremental group, it had a non-significant P-value of 0.509, while in the conventional group it had a highly significant **P-value of <0.001.**

These results were partly consistent with the results collected from a cohort study by **Zhang and colleagues** [20]**,** were in the first part of the study, they examined a total of 168 ESRD patients over ten years were screened and divided into two groups based on the initial six-month HD frequency: Group A included 58 patients who received twice-weekly HD for at least 6 months and did not switch to the thrice-weekly HD pattern during this period. Group B included 110 HD patients who started HD treatment thrice weekly and maintained this regimen so consistently until the end of the cohort. In this part of the study, there was no significant difference between the two groups regarding the hemoglobin levels, suggesting that twice-weekly treatment can achieve comparable HD adequacy.

In our study, while the follow-up hemoglobin levels from baseline to the fourth month showed no significant differences between both groups, the follow-ups at five and six months showed a significant difference, suggesting a protective effect of the twice-weekly compared to the thrice-weekly regimen. A study with a longer follow-up period can add evidence to whether this finding is consistent and persistent over time or it was a temporary finding. A factor that can be implicated in explaining this finding is the blood loss associated with a more frequent regimen.

However, in the study by **Obi and colleagues** [21]**,** it was reported that patients treated with the incremental regimen had lower concentrations of hemoglobin and other differences at baseline, but these differences were attenuated over time. This was inconsistent with our study, where the difference had a build-up pattern across visits.

However, in the study by **Obi and colleagues**[21], there was a significant difference, which remained significant across the following quarters irrespective of adjustment models. Also, patients treated with the incremental regimen had less dialysis frequency, shorter dialysis time, lower concentrations of hemoglobin and serum corrected calcium, and higher serum ferritin concentrations at baseline, but these differences were attenuated over time.

Regarding PTH levels in each group separately, at follow-up visits, there were no significant differences. Also, comparing the two groups at each follow-up, there were no significant differences.

In the study mentioned before by **Zhang and colleagues**[20]**,** iPTH showed no difference between the two groups at baseline, as did our study.

As regards to CRP level in the incremental group at each visit, there was no significant difference. In the conventional group at each visit, there was no significant difference also. Comparing the two groups at each follow-up, there were also no significant differences.

In the study mentioned before by **Obi and colleagues** [21]**,** when they matched all 351 patients in the incremental regimen group to 8,068 out of 23,294 patients in the conventional regimen group, and despite that the differences in baseline characteristics between the two groups were largely attenuated by this matching procedure, variables that are potentially associated with

treatment regimen including nPCR were not attenuated. This was inconsistent with the findings in our study.

As regarding the difference in the serum calcium level in the incremental group at each visit, in the incremental group, and the conventional group, separately, there were no significant differences in both groups. Also, when comparing the two groups, at each follow-up visit, there were no significant differences.

In the study done by **Obi and colleagues** [21], patients treated with the incremental regimen had lower concentrations of serum corrected calcium at baseline, but these differences were attenuated over time. This was consistent with our study.

Serum phosphorus levels, at each visit, in the incremental group and the conventional group, separately, showed no significant differences in both groups. Also, there were no significant differences between both groups, at each follow-up.

In the study mentioned before by **Zhang and colleagues** [20], slightly lower serum phosphorus was observed in patients on an incremental regimen at baseline, this perhaps is due to the higher proportion of patients with adequate RKF in this group, which might lead to the excretion of phosphorous in the urine. This might refer to a selection bias in the study that needs to be adjusted for. This was inconsistent with our study where we detected no significant differences between the two groups.

In a single-center retrospective study by **Kaja and colleagues** [22], conducted over 20 years, patients who had twice-weekly sessions for 3 months during the 12 months following initiation of twice-weekly HD were identified for comparison with patients who dialyzed thrice-weekly. It was found that there were no significant differences between both groups in phosphorus levels. This was in concordance with the findings in our study, but it's worth mentioning that this study considered patients in the twice-weekly group if they continued for at least three months on the twice-weekly regimen in the first year after starting the regimen, while in our study patients were chosen if they continued for at least six months. This adds more weight to our study, even though the number of patients was much lesser in our study.

A prospective cohort study by **Hwang and colleagues** [23], was conducted on 685 regular ESRD cohorts above 18 years old receiving HD for at least 3 months. Patients were divided into 3 groups; twice-weekly HD with RKF, thrice-weekly HD with RKF, and thrice-weekly HD without RKF, with RKF was defined as the production of more than 100 mL/day of urine [24]. In this study, the hemoglobin level and serum level of albumin showed no significant differences during the entire follow-up, which was consistent with our study.

Regarding the UFR in the incremental group at each visit, there was a highly significant difference (**P-value of <0.001**). The same occurred in the conventional group (**P-value of <0.001.**

In the study mentioned before by **Zhang and colleagues** [21], they reported that the average UFR per HD session was similar between both groups. This was inconsistent with our study; where a significant difference was reported at all follow-up visits between the two groups, as well as in each group separately.

Again, in the above-mentioned study by **Kaja and colleagues** [22], there was a significant difference between twice-weekly HD and thrice-weekly HD groups regarding UFR (lower in the twice-weekly group). This was inconsistent with our findings. This inconsistency between the two studies can be explained by the difference in the size of the study population and the selection criteria for the twice-weekly group.

In the study mentioned before by **Hwang and colleagues** [23], UFR was significantly lower during the entire follow-up in patients with RKF undergoing twice-weekly HD. This was consistent with our study.

Regarding the differences in the inter-dialysis weight gain at each visit, it showed a highly significant difference, in each group separately, **P-value of <0.001.** Comparing the two groups at each follow-up, there was no significant difference at baseline with a P-value of 0.910, while there were significant differences at the following visits.

In the study mentioned before by **Obi and colleagues** [21], they established that the incremental regimen was associated with a less weekly cumulative percentage IDWG. The study reported a significant trend towards better survival in patients with the incremental regimen observed across higher increments of KRU and lower increments of weekly IDWG.

The same finding was confirmed in the study by **Lin and colleagues** [13], which was conducted on 74 patients (23 on twice-weekly HD and 51 on thrice-weekly HD), they found that the thrice-weekly group had higher IDWG compared to the twice-weekly group. Both studies were consistent with our study regarding the IDWG.

While HD patients receiving infrequent HD treatment are thought to be at risk of high IDWG and hypervolemic status [11], in the study by **Hwang and colleagues** [23], they found that the dry weight of the 3 patients' groups did not differ, and the net fluid balance was lower in patients with RKF receiving twice-weekly HD; a finding that is consistent with our findings.

As regards serum creatinine level, before dialysis, at each visit, there was a highly significant difference in each group separately with a P-value of <0.001. As regards the differences between the two groups at each follow-up, there were no significant differences at baseline and one month, while there was a significant difference at all next visits, with a P-value of <0.001. Serum creatinine level, after dialysis, at each visit, showed a significant difference in each group separately with a P-value of <0.001. Regarding the differences between both groups at each follow-up, there were significant differences at all visits.

Regarding serum urea level, before dialysis, at each visit, there was a significant difference in each group separately with a P-value of <0.001. Regarding serum urea level, after dialysis, at each visit, there was a significant difference in each group separately with a P-value of <0.001. Also, there were significant differences between both groups at all visits.

URR at each visit, in the incremental group and the conventional group, separately, showed highly significant differences in both groups. As regards the differences between both groups at each follow-up, there were significant differences, with the superiority of the incremental arm.

Regarding Kt/V as an indicator of dialysis adequacy using the Kt/V Daugirdas calculator in the incremental group, at each visit, there was a highly significant difference; the same as in the conventional group. When comparing the two groups at each follow-up, there were also significant differences, again with the superiority of the incremental arm.

In the study mentioned before by **Zhang and colleagues[20],** they found that both weekly Kt/V and URR were not significantly different between the incremental and conventional groups, suggesting that twice-weekly treatment can achieve comparable HD adequacy rather than superior it. They reported that the average UFR per HD session was similar between both groups.

In the study by **Hwang and colleagues [23],** dialysis adequacy was assessed as renal Kt/V at all follow-up points and was significantly greater in patients with RKF receiving twice-weekly HD than in patients with or without RKF receiving thrice-weekly HD. These findings suggest that twice-weekly HD treatment can achieve a sufficient dialysis dose, similar to that of thrice-weekly HD treatment if RKF is appropriately preserved. This, also, was consistent with the findings of our study.

Regarding the differences in the UOP at each visit, there was a highly significant difference with a P-value of <0.001 in each group separately. Comparing the two groups at each follow-up, there was no significant difference at baseline, while there were significant differences at all the follow-up visits.

In a large retrospective longitudinal cohort by **Obi and colleagues[21],** 23,645 patients on maintenance HD with available RKF data during the first 91 days (or quarter) of dialysis, and who survived the first year after dialysis, whereas 8,068 patients with conventional HD regimen were matched and compared to 351 patients with the incremental regimen. In this matched cohort, both KRU and urine volume (UV) showed a significantly slower decline over time in the incremental versus conventional regimens (P-values of <0.001 for both). This was consistent with the findings in our study, where a significant difference was recorded at each visit after the baseline session.

Again, in the study mentioned before by **Lin and colleagues[13],** the twice-weekly group had higher residual UOP, higher residual GFR, and higher weekly renal Kt/V, while the thrice-weekly group experienced a faster decline in UOP and renal creatinine clearance/month. This was consistent with our study.

In the study by **Hwang and colleagues [23],** they presumed that a greater total fluid removal in patients with RKF undergoing thrice-weekly HD was associated with a greater intake of caloric and protein foods, which led to better nutritional status. These findings support the assumption at hand, that a twice-weekly regimen is adequate for preserving the RKF.

In our study, regarding the occurrence of cardiovascular events, there were no significant differences between the two groups. Arrhythmia was not recorded in the incremental group, while in the conventional group it was recorded in 2 patients, and there was no significant difference between both groups. As regards the need for hospital admission, there was also no significant difference between both groups. Regarding the occurrence of vascular access failure, it was recorded in 2 patients in the incremental group, compared to 4 patients in the conventional group, with no significant difference between both groups.

In the previously mentioned study by **Zhang and colleagues [20],** the prevalence of CVD and hospitalization rate in the previous year was also similar in both groups at baseline.

However, in the study mentioned before by **Lin and colleagues [13],** the twice-weekly HD suffered from significantly fewer intradialytic hypotensive episodes. There was no difference between the two groups in the incidence of AVF dysfunction. More thrice-weekly HD patients were hospitalized due to infections from any cause. While our study showed the same finding in part, the difference was not statistically significant.

To elaborate more on the relationship between less frequent dialysis and reduced events of chest pain, **McIntyre and colleagues[25]** suggest that there may be a direct effect of reduced ultrafiltration on limiting dialysis-induced myocardial damage.

In conclusion, patients undergoing twice-weekly HD had non-inferior outcomes for dialysis adequacy and CVE hospitalization compared with patients undergoing thrice-weekly HD. We suggest that decisions about infrequent HD should be made carefully based on RKF, patients' nutritional status, and other suggested risk factors.

Limitations of the study: The study had a small sample size with a relatively short follow-up period.

CONCLUSION

Incremental HD was superior to the conventional one regarding the adequacy of dialysis, with monthly follow-up till 6 months. There were no significant differences between both groups regarding cardiovascular events, vascular access failure, and hospitalization.

Regarding HD, RCTs are lacking and are urgently needed. If the potential benefits of incremental HD will be confirmed by RCTs, then starting dialysis at a full dose will be subjecting patients to unnecessarily long or more frequent treatments for an unnecessarily long time, and at a higher cost.

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