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Original Article

Daily Hemodialysis: Short Term Clinical Evaluation

Hussein Chahine, Tarek Elbaz and Abdallah Abdallah

Department of Internal Medicine, Faculty of Medicine, Al Azhar University, Egypt.

ABSTRACT

Background: The clinical outcome of hemodialysis can be improved when frequency increases. Daily hemodialysis, with short dialytic sessions and reduction of interdialytic interval, may increase the depurative efficiency and optimize the physiology of dialytic treatment.

Objectives: Our aim was to evaluate the feasibility of daily hemodialysis in routine clinical practice & its effect on some aspect of uremic pathology.

Methods: We studied, prospectively, 10 patients (6 M, 4 F), aged 37.4 ± 9.57 yrs, treated for at least 3 months with daily hemodialysis. A standard cumulative weekly time (12-15 hrs) with session length (120-150 min) for 6 sessions a week and a delivered calculated Kt/V ranging 3.24-3.93 per week was achieved. Patients were allowed free diet and selection of their preferable time for the session. All patients were switched from standard HD (4 hrs 3 times weekly) for a period of 35 ± 15.2 months, due to patient preference (3 patients) or because they could not be managed satisfactorily on standard schedule (4 patients due to fluid overload &/or severe hypertension, 3 patients due to extreme cardiovascular instability). Diabetics were excluded, as well as, patients having problems with their vascular access or with poor clinical metabolic conditions.

Results: There was a significant increase in the mean (SD) dry body weight (Kg) from 65.2 ± 13.01 to 66.07 ± 13.56 ($p < 0.01$) & a decline in mean arterial BP (mmHg) from a mean (SD) of 101.0 ± 7.81 to 96.53 ± 3.4 at the beginning & end of the study respectively. A significant rise in Hb (gm/dl) from 7.52 ± 1.7 to 8.37 ± 1.84 & Htc % from 24.05 ± 5.67 to 27.33 ± 6.30. The serum PO4 (mg/dl) declined from 5.37 ± 0.6 to 4.7 ± 0.35 with elevation of HCO3 (mEq/L) from 20.04 ± 0.74 to 23.02 ± 0.48 at the beginning & the end of the study respectively. The mean (SD) of the Serum albumin, cholesterol & triglyceride in mg/dl at the entry & end were respectively, 4.09 ± 0.23 & 4.23 ± 0.24, 171.5 ± 12.24 & 195.5 ± 8.93, 151 ± 11.3 & 154.3 ± 10.52. Echocardiographic assessment at the entry & end of the study revealed a significant decrease in LVTDD (56.53 ± 3.90 to 52.31 ± 3.90), IVS (13.16 ± 1.57 to 11.97 ± 1.43), LVPW (11.36 ± 1.76 to 10.51 ± 1.53) ($p < 0.01$) in mm.

Conclusions: We conclude from our study that the protocol of daily hemodialysis is feasible in routine clinical practice, is well tolerated by patients and has a low incidence of complications. The clinical results are better than those obtained with standard dialysis, leading to a better correction of some uremia-induced pathology (anemia, malnutrition, acid-base balance, hemodynamic instabilities, and cardiac hypertrophy).

INTRODUCTION

"Short dialysis schedule" (4 hrs three times a week), remained over the last 20 years, the gold standard dialysis time schedule all over the world[1]. This dialysis schedule results in important fluctuations of body fluid volume and solutes. A higher dialysis frequency, resulting in lower peaks and smaller amplitudes of fluctuations, will diminish the so-called "unphysiology of dialysis"[2]. During the interdialytic interval, there is alteration in the homeostasis of body fluids, accumulation of hydrogen ions, alteration in the intracellular/extracellular gradient, and accumulation of water. So, a reduction in the interdialytic interval, as short as 24 hrs, certainly will have a favorable effect on cell metabolism and

cardiac hemodynamics by reducing the water overload[3]. In daily HD the weekly fluid overload is spread over six sessions. In each session, the degree of hypovolemia will be lower and so the post-dialysis hypovolemic state will last for less time and the blood volume rebound will be less pronounced, and this should be reflected in the patient's well-being observed in daily HD[4]. Many workers during the last decades showed a marked improvement of several clinical items, including metabolic control, volume and blood pressure regulation, erythropoiesis, cardiac function, working capacity, and quality of life when patients were treated on short daily basis[5]. The hemodynamic changes were more pronounced, blood pressure normalized in the hypertensive patients, and antihypertensive medication had to be reduced to prevent hypotension, while the more frequent ultrafiltration of lower volumes resulted in more stable dialysis sessions, which may have been important to achieve an accurate dry weight with the disappearance of dialysis induced hypotensive episodes and muscle cramps[6]. Another aspect concerning the correction of events connected with uremia is the improvement in anemia. Patients treated with daily HD during the pre-erythropoeitin era had significantly higher hemoglobin and hematocrit[7]. Recently it was shown that higher hemoglobin and hematocrit, and a reduced use of erythropoeitin, in terms of both the incidence of use and dosage, as well as, improved nutritional status occurred. The plasma albumin, prealbumin, transferrin, the plasma cholesterol and triglycerides were within the normal range in the majority of patients[3]. A more frequent dialysis treatment schedule might give some further advantage to phosphate removal, taking advantage of the greater removal rate in the first 2 hrs[8]. In addition the frequency of treatment exerts a strong influence on acid base fluctuations and consequently daily HD should improve the acid-base status, since high frequency treatments better approximate the physiological functions[9].

It was shown definitely that daily hemodialysis induces an impressive improvement of the most important parameters of left ventricular hypertrophy, with a clear tendency towards regression with time[10]. Moreover patients with dialysis-resistant signs and symptoms, namely, severe anemia, uncontrolled hypertension, pericarditis, cardiac failure, uremic osteodystrophy, peripheral neuropathy, pruritis, insomnia, may improve after daily dialysis[11].

AIM OF THE WORK

The study had the aim of acquiring some data for the purpose of evaluating the feasibility of the protocol in routine clinical practice, its real usefulness regarding its effect on survival and its effects on some aspects of the uremic pathology not well corrected by standard dialysis (control of arterial hypertension, correction of anemia, the acid-base balance, the nutritional status, and left ventricular hypertrophy).

SUBJECTS AND METHODS

A total of 10 patients, 6 males & 4 females with an age range 23-49 years (mean 37.4 ± 9.57) [Table 1] were switched

to daily hemodialysis (DHD) for a period of at least 3 months, from the 1st of September 1998 to the 30th of November 1998, at Al Hussein University Hospital dialysis unit. All patients were on standard hemodialysis schedule (4 hours, three times weekly) for a period ranging from 18 to 60 months (mean 35.0 ± 15.2). Patients were switched to DHD according to their personal preference (n = 3), or due to unsatisfactory management on the standard schedule (n = 7) [Table 1]. Diabetics were excluded, as well as patients having problems with their vascular access and patients with poor clinical or metabolic conditions (liver cirrhosis, cerebrovascular stroke). The etiology of ESRD was chronic GN (n = 4), chronic pyelonephritis (n = 2), hypertensive nephrosclerosis (n = 2), and unsettled in 2 patients.

Six of the patients were hypertensive, and poorly controlled by antihypertensive medications (ACEi, ß blockers, and Ca channel antagonist) [Table 2].

All patients had native AV fistula. Their clinical status was optimized 2 months prior to enrolment in the study by conventional schedule, using volumetric machines on bicarbonate dialysis & Hemophan dialysers according to surface area. Dialysate flow rate was 500 ml/min & blood flow rate range was 250 – 300 ml/min for a total dialytic time of 12-15 hrs per week, utilizing systemic heparinization, using the standard two 15-16 gauge needles All patients were treated on an outpatient basis.

Daily dialysis schedule

We used the same machines, bicarbonate dialysis, as well as the same membranes, blood & dialysate flow, for a cumulative weekly time (12-15 hrs) with a session length (120-150 min) for 6 sessions a week. With a delivered Kt/V ranging 1.08-1.31 per session (3.24-3.93 per week), patients were allowed free diet & selection of their preferable time for session.

Antihypertensive medication was recorded. Anemia was treated by IV iron at the end of dialysis session according to serum ferritin, and the phosphate binder Ca carbonate was given at 2-3 gm/day.

Intradialytic vascular stability was evaluated by identifying & recording hypotensive episodes defined by the following criteria: symptoms (nausea, vomiting and symptomatic hypotension), a drop in mean arterial BP by 20 mmHg or below 80, and recording any therapeutic intervention (saline or plasma expander).

Dialytic efficiency was controlled by monthly evaluation of Kt/V utilizing the modified formula of Daugirdas.

Periodic monthly controls were urea, creatinine, uric acid, electrolytes, Hb & Htc, PO 2, P CO2, HCO3 and ECG.

At the beginning & end of the study determination of serum albumin, total cholesterol & triglyceride level was done, as well as echocardiographic evaluation of left ventricular end diastolic dimension (LVTDD), interventricular septum (IVS) and left ventricular posterior wall thickness (LVPW).

Table 1: Patient data.

N	Gender	Age (yr)	Body weight (kg)	Duration of dialysis (m)	Etiology of ESRD	Reason for switch to DHD
1	M	49	79	60	HTN nephrosclerosis	Patient's preference
2	F	43	53	30	Chronic pyelonephritis	Cardiovascular instability
3	M	23	59	24	Chronic GN	Fluid overload &/or HTN
4	F	38	67	18	Chronic GN	Fluid overload &/or HTN
5	M	44	89	18	Chronic pyelonephritis	Patient's preference
6	M	46	63	48	Unknown	Patient's preference
7	F	24	39	36	Chronic GN	Cardiovascular instability
8	M	48	69	48	HTN nephrosclerosis	Fluid overload &/or HTN
9	M	26	69	48	Chronic GN	Fluid overload &/or HTN
10	F	42	65	20	Unknown	Cardiovascular instability

Table 2: Antihypertensive regimens.

N	Mean BP (mmHg)	Antihypertensive medication
1	110	CCA
3	108.66	ACEi, CCA, ß blocker
4	111.6	ACEi
5	103	ACEi
8	105	CCA, ACEi, ß blocker
9	108	ACEi

RESULTS

In our studied patients, at entry and during the run-on period (3 months), there was a significant reduction of the ultrafiltration volume per session (UF/L per session), from a mean of 2.29 ± 0.42/L to 1.39 ± 0.18/L (t 11.12, $p < 0.01$), [Table 3].

A mean weekly Kt/V of 3.56 ± 0.2 and 3.58 ± 0.2 at the entry & end of the study respectively (t 0.36, $p < 0.05$) was reached.

There was a significant increase in mean body weight in kg from 65.2 ± 13.61 at the entry to 66.07 ± 13.56 at the end of the study (t 18.40, $p < 0.01$) shown in Fig 1.

A decline in arterial blood pressure was noticed, where the mean diastolic BP was 88.0 ± 7.05 and 82.7 ± 3.56 mmHg at the entry and end of the study respectively (t 3.04, $p < 0.05$), [Fig. 2] and for the systolic BP 132 ± 11.11 and 124.0 ± 4.11 mmHg (t 3.5, $p < 0.01$) [Fig. 3] and the mean arterial blood pressure 101.0 ± 7.81 and 96.53 ± 3.4 mmHg (t 3.61, $p < 0.01$) at entry and end respectively.

Results for the serum phosphate were 5.37 ± 0.6 and 4.7 ± 0.35 mg/dl at the entry and at the end respectively (t 3.11, $p < 0.05$) shown in Table 4.

The mean & SD for hemoglobin were 7.52 ± 1.7 and 8.37 ± 1.84 gm/dl (t 8.12, $p < 0.01$), [Fig 4] and for the hematocrit percent were 24.05 ± 5.67 and 27.33 ± 6.30 % (t 6.7, $p < 0.01$) at the entry & the end of the study respectively, [Fig. 5].

There was a significant increase in the mean serum level of albumin, cholesterol and triglyceride, 4.09 ± 0.23 and 4.23 ± 0.24 (t 6.33, $p < 0.01$) [Fig. 6] 171.5 ± 12.24 and 195.5 ± 8.93 (t 7.16, $p < 0.01$) [Fig. 7] 151 ± 11.3 and 154.3 ± 10.52 (t 3.80, $p < 0.01$) [Fig. 8] mg/dl at the entry and the end of the study respectively.

A significant increase in the mean serum bicarbonate from 20.04 ± 0.74 to 23.02 ± 0.48 mEq/L (t 10.0, $p < 0.01$) at the entry and the end of the study respectively, [Fig. 9].

Echocardiographic assessment at the entry and end of the study revealed a significant decrease in left ventricular end diastolic dimension (LVTDD), interventricular septum (IVS), and left ventricular posterior wall thickness (LVPW) in mm, as shown in Table 5.

Table 3: Ultrafiltration volume per liter per session at entry and during run-on period of the study.

UF/L per session		Mean ± SD	Minimum	Maximum
	Entry o M	2.29 ± 0.42	1.30	2.7
	1 M	1.39 ± 0.18	1.0	1.5
	2 M	1.39 ± 0.18	1.0	1.5
	End 3 M	1.39 ± 0.18	1.0	1.5

Table 4: Serum phosphate levels.

PO4		Mean ± SD	Minimum	Maximum
	Entry o M	5.37 ± 0.6	4.5	6.1
	1 M	5.02 ± 0.32	4.4	5.5
	2 M	4.71 ± 0.44	4.1	5.3
	3 M	4.7 ± 0.35	4.1	5.1

Table 5: Echocardiographic assessment.

In mm		Mean ± SD	Maximum	Minimum	t
LVTDD	Entry o M	56.53 ± 3.90	63.0	51.2	14.78 $p < 0.01$
	End 3 M	52.31 ± 3.90	59.0	47.0	
IVS	Entry o M	13.16 ± 1.57	15.0	10.0	6.85 $p < 0.01$
	End 3 M	11.97 ± 1.43	13.9	9.6	
LVPW	Entry o M	11.36 ± 1.76	14.0	9.0	5.40 $p < 0.01$
	End 3 M	10.51 ± 1.53	13.0	8.7	

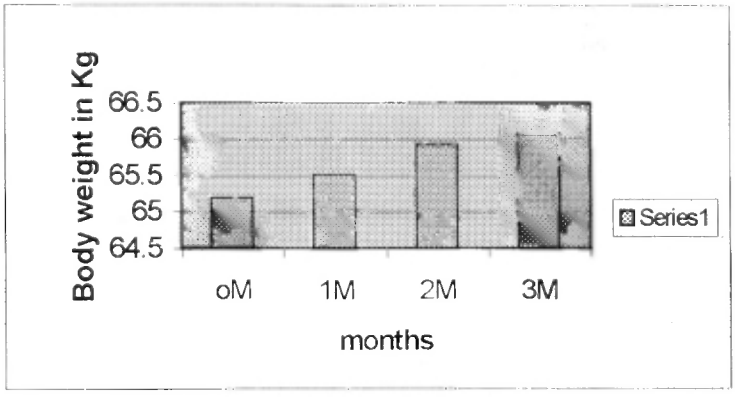

Fig. 1: Mean body weight in kg at the entry & during run-on period of the study (3 months).

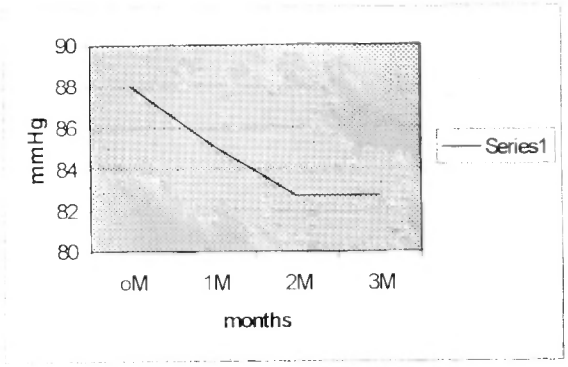

Fig. 2: Mean Diastolic BP mmHg at entry & during run-on period (3 months).

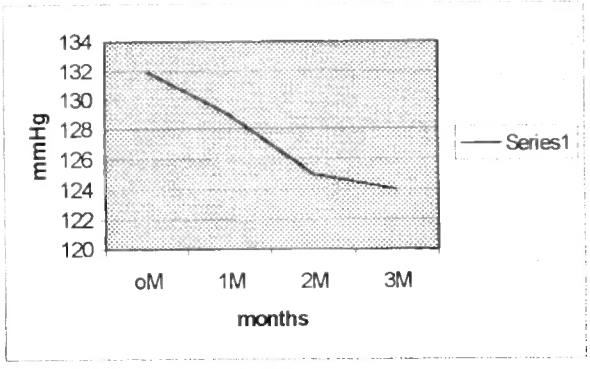

Fig. 3: Mean systolic BP mmHg at the entry & during run-on period (3 months).

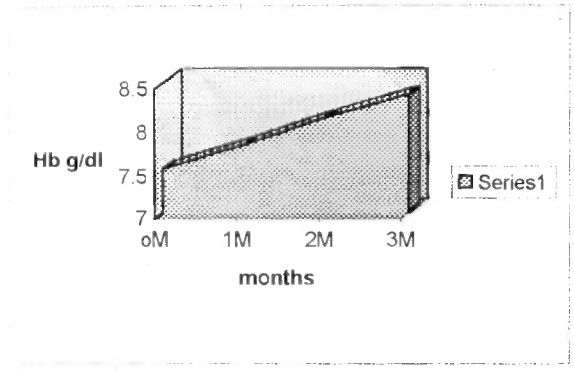

Fig. 4: Hemoglobin in g/dl at entry & during run-on period of the study (3 months).

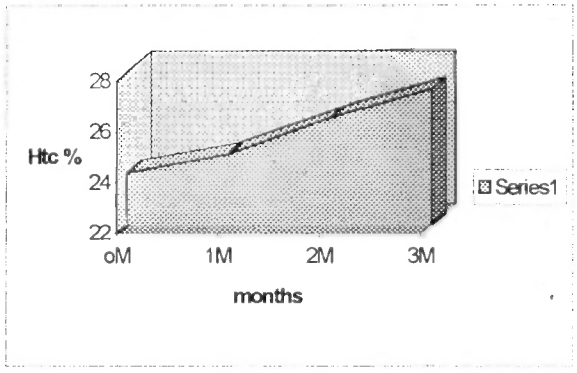

Fig. 5: Mean Hematocrit % at the entry & during the run-on period of the study (3 months).

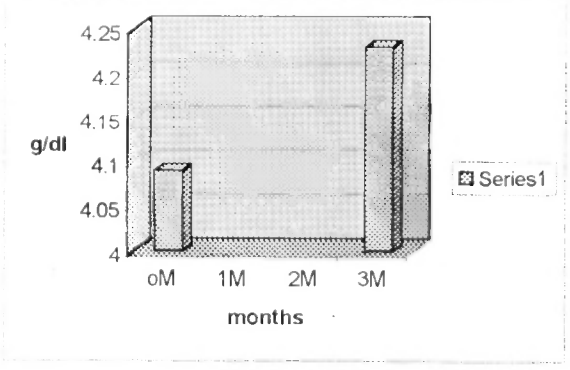

Fig. 6: Mean serum albumin g/dl at the entry & the end of the study.

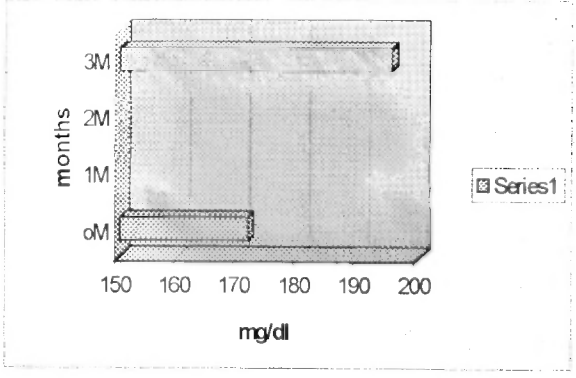

Fig. 7: Mean serum cholesterol mg/dl at the entry & the end of the study.

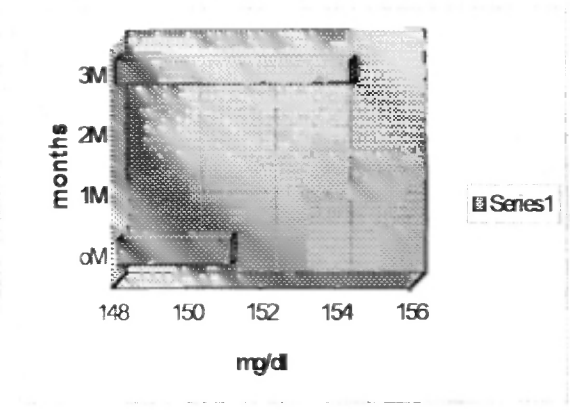

Fig. 8: Mean serum triglyceride mg/dl at the entry & end of the study.

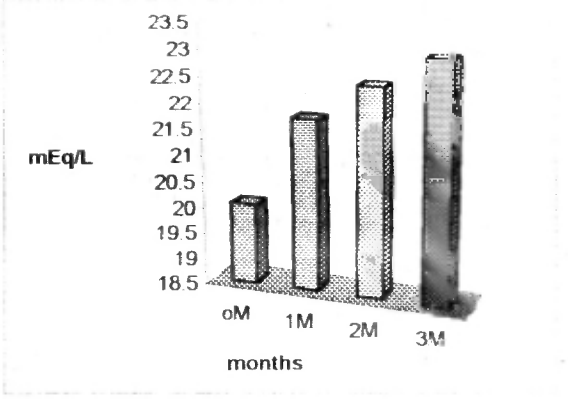

Fig. 9: Mean serum HCO3 mEq/L at the entry & during run-on period (3 months).

DISCUSSION

Our daily hemodialysis protocol had two objectives: (i) a stable level of depurative efficiency even though the sessions were short; and (ii) a reduction in the interdialytic interval.

It was possible to obtain the compliance of the patients, who were convinced by the level of well-being achieved. All patients stated improvement with daily hemodialysis schedule as regards a better physical performance. Several subjective symptoms disappeared or improved; patients noticed less thirst, insomnia, prurigo, and asthenia, with an improvement in appetite and well being. Whether the improvement in physical condition is related to an improvement in hemodynamic control, less fluctuations of body fluid volume, lower peak concentrations of toxins, less fluctuations of solute concentrations, a more liberal life style; is at the moment a matter of speculation. It was predicted that the rate of removal of low molecular weight solute is a function of the solute's plasma concentration which decreases rapidly in an exponential fashion after the start of dialysis. In order to increase the mass of solute removed per week, it is more efficient to increase the frequency of sessions than to prolong the duration of sessions[12].

No hospitalization was necessary in our patients during the study period, and no serious concomitant disease occurred. The arterio-venous fistula was not affected by the more frequent puncture. No thrombosis or prolonged bleeding occurred and it was shown that the frequent use of the vascular access did not result in a higher incidence of those complications. The acceptance of the patient was good: neither the pain of frequent puncture, nor the daily connection to the machine have ever been problems with a more positive attitude towards the treatment due to the dramatic improvement in clinical conditions and somehow, also by the shortness of the session.

The hemodynamic changes were pronounced; the blood pressure normalized in hypertensive patients and the antihypertensive medications had to be considerably reduced. The optimal control of hypertension is probably due to the better achievement and maintenance of the true

dry-weight with only minor interdialytic oscillations and to a better control of sodium balance, as well as, due to more frequent ultrafiltration of lower volumes resulting in more stable dialysis sessions. The lower fluctuations of body fluid volume were correlated with the disappearance of dialysis induced hypovolemic symptoms, namely hypotension and cramps. Both extremes of fluid state have to be compensated by the cardiovascular system of the patients, which frequently is in an abnormal state. A pathological cardiovascular system responds differently to the stress of fluid fluctuation. Whether dysvolemia is an independent risk factor in the prognosis of dialysis patients still awaits further elucidation. The dysvolemic puzzle of prevention of dialysis hypotension and simultaneous prevention of interdialysis hypertension can only be solved by a change in dialysis schedule, which might attenuate the extremes of the volume cycle[13]. Thus the effect of a daily dialysis rhythm on blood volume variations is different from what is obtained with the traditional thrice-weekly regimen, if we consider that in six weekly treatments the weekly fluid overload is spread over six session[14].

There was a decrease in serum phosphorus, to the extent of reducing the phosphate binding agents as phosphate removal is high in the first hour of dialysis and then rapidly declines[15].

In our study, there was stability of the patient's acid-base status and a significant rise in the plasma bicarbonate level. In standard thrice-weekly intermittent therapies, the task of counter-balancing a 48 hrs metabolic acid production during the interdialytic period should be accomplished during few hours of dialysis. Consequently, the acid-base status fluctuates from a post-dialytic alkalosis to a pre-dialytic acidosis. Acidosis and possibly alkalosis have a clinical relevance in dialysis patients even if they are mild and transient[16,17]. In daily treatments, less fluctuation could occur.

The data of the present study show a higher hemoglobin and hematocrit, that seems to be related to the dialysis protocol, and were rapid within the first three months. The favorable effect of the protocol on anemia may be attributed to its effect on acid-base equilibrium, its known that the disappearance of acidosis limits the Bohr effect and reduces its effect on erythrocyte DPG[7]. The protocol by its greater depurative capacity may have a beneficial effect by intervening at the level of dialysable anemia-inducing factors, because it is known that dialysis can act on some erythropoiesis inhibitors (ribonucleases, medium-sized molecules), remove some hemolysing substances[7] or may partially modify peripheral resistance to erythropoietin.

Nevertheless, a decrement in serum ferritin should be expected possibly as a result of increased iron losses. More iron supplementation is necessary in daily HD patients.

An increase in serum triglyceride, total cholesterol, as well as, serum albumin, are regarded as another advantage of the schedule. A higher intake of proteins and calories presumably to dietary freedom, was made possible by the less discontinuous nature of the depuration. Other studies that

used low molecular weight heparin, which is not associated with higher serum cholesterol concentration[6], negated frequent heparinization as a cause of rise in serum cholesterol.

The dialytic efficiency of our protocol has been confirmed by calculation of Kt/V. The cumulative weekly Kt/V remained constant, exceeding 3, with no change between daily and standard dialysis. The daily HD schedule ensures the stable delivery of a constant dialytic dose (Kt/V) with reduction in the interdialytic interval.

In our study a reduction in cardiac hypertrophy was evident by reduction in echocardiographic parameters: the left ventricular end diastolic dimension, the interventricular septum, and the left ventricular posterior wall thickness. This positive effect could be ascribed to the fact that daily HD, with its more frequent and physiological schedule, acts favorably on all etiological factors of left ventricular hypertrophy in uremics, namely the arterial hypertension, the increase in cardiac output associated with the anemia, the more intense cyclic water overload that takes place in schedules with long interdialytic interval and which is responsible for dilative cardiomyopathy, dialytic hypotension and hypoxia, which aggravate arterial desaturation and endocardial oxygenation, cardiomyopathy due to protein deficiency; and uremic toxins. Our dialytic protocol may influence most of these factors.

In conclusion, our protocol was not used for a sufficient length of time (3 months) and involved only a minority of patient population (10 patients), not enabling us to make a valid judgment, but we can speculate.

The protocol of daily hemodialysis is feasible in routine hospital practice, is well tolerated by patients and has a low incidence of complications.

This type of schedule is efficient because it ensures the stable delivery of a dialytic dose (Kt/V) and reduces the interdialytic interval.

The clinical results are better than those obtained with standard dialysis, leading to a better correction of some uremia-induced pathology (anemia, malnutrition, acid-base balance, hemodynamic instabilities, and cardiac hypertrophy).

At present, daily dialysis seems indicated for the relief of some apparently dialysis-resistant signs & symptoms and possibly to prevent some dialysis-induced complications which may take place in long term intermittent schedules.

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