



# *Benefits of every other day dialysis (EODD) on dialysis patients with symptomatic cardiovascular disease*

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## SUMMARY

*With the purpose to improve the clinical situation of nine hemodialysis patients who suffer from severe cardiovascular disease and are highly symptomatic after weekends without dialysis because of fluid overload, their dialysis schedule was changed from 5 hours in 3 sessions per week to 4 hours every other day sessions (EODD), avoiding 72 hours of interdialytic weeked period.*

*In each patient, during 38 sessions previous to starting the EODD (stage 1: 3 months) and the 38 sessions in EODD, which followed the first month of this dialysis regime (stage 2), the frequency of the next incidences was registered (ratio in 348 sessions, in every stage, of this patients group): presence of dysnea and/or hypertension pre dialysis session, pre or intra dialysis angor, emergency sessions with hypotension and sessions without achieving predetermined dry-weight.*

*During the EODD stage, sessions, with disena, hypertension and pre or intra dialysis angor were reduced in 80% ( $p < 0.001$ ); the incidence of sessions with hypotensive episode or sessions without achieving dry-weight decreased in a third.*

*All patients experimented a considerable improvement in their clinical situation. In addition, the whole group reduced dry-weight and later regained it without presenting symptoms which had motivated EODD schedule.*

*EODD schedule improves the clinical situation in patients with cardiopathy who would not do so when following previous schedule (which includes 48 hours without dialysis).*

**Key words:** *Every other day hemodialysis, EODD, cardiovascular disease, dysnea in hemodialysis.*

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## BENEFICIOS DE LA HEMODIÁLISIS EN DÍAS ALTERNOS SIN DESCANSO DE 72 HORAS (EODD: EVERY OTHER DAY DIALYSIS) EN PACIENTES CON ENFERMEDAD CARDIOVASCULAR SINTOMÁTICA

### RESUMEN

*Con el objetivo de mejorar la situación clínica de un grupo de nueve pacientes en hemodiálisis con patología cardiovascular severa, que mantenía síntomas causados por expansión de volumen con mala tolerancia al fin de semana sin diálisis, cambiamos la pauta de tres sesiones semanales de 5 horas con descanso de fin de semana por el régimen de hemodiálisis en días alternos con sesiones de 4 horas sin descanso de 72 horas en el fin de semana.*

*En cada paciente, durante las 38 sesiones del esquema primitivo previas al inicio de la diálisis alterna (fase 1: 3 meses) y en las 38 sesiones del esquema alterno (fase 2) que siguieron al primer mes de su inicio se registraron las frecuencias por sesión de las incidencias siguientes: presencia de disnea y/o hipertensión arterial antes de la sesión, angor pre o intradiálisis, sesiones urgentes no programadas, sesiones con hipotensión y sesiones sin lograr el peso seco.*

*Los resultados se expresan en porcentaje de incidencias en 348 sesiones del grupo de pacientes en cada fase de los dos esquemas de diálisis.*

*En la fase de hemodiálisis en días alternos las sesiones del grupo con disnea, hipertensión o angor se redujo en un 80% ( $p < 0,001$ ); las sesiones con al menos una hipotensión y aquellas en las que no se alcanzó el peso seco disminuyeron en un tercio.*

*Todos los pacientes experimentaron una mejoría clínica importante y bajaron el peso seco para recuperarlo posteriormente sin reaparición de los síntomas que motivaron el cambio de esquema.*

*La hemodiálisis en días alternos es un sistema que mejora la clínica de los pacientes con patología cardiovascular respecto al esquema de 5 horas en 3 sesiones semanales con dos días sin diálisis.*

**Palabras clave:** *Hemodiálisis en días alternos, diálisis alterna, enfermedad cardiovascular, disnea en hemodiálisis.*

### INTRODUCTION

Cardiovascular (CV) diseases represent the major mortality cause in the hemodialyzed population in western countries. Besides, patients that have access to this treatment are increasingly older and have a clinical history of risk factors for these pathologies. In this population, it is critical to control the extracellular volume (ECV) expansion in the inter-dialysis time and to maintain hemodynamic tolerance to hemodialysis (HD)<sup>1</sup>.

For that purpose, HD regimens have been developed in which increasing time and frequency of sessions has reduced patients' morbidity and mortality<sup>2-3</sup>. However, some of these regimens encounter implementation difficulties in many HD units due to logistic, resources or geographic scattering problems, among others.

Since 2002, in our unit we have increased dialysis time by 20%, changing from four to five hours

in the classic schedule of 3 days per week, in order to improve the tolerance to volume loss. In this way we obtained a general decrease in inter-dialysis events and of arterial hypertension (AHT) frequency, with a better control of lean weight.

However, the weekend interval without hemodialysis still interferes negatively in patients with CV disease who have difficulties in achieving their lean weight after this volume expansion period.

In order to improve this situation, during 2003 we adopted an every other day hemodialysis (EODD) regimen, without the 2 days off dialysis, based on Lecce's group experience<sup>4</sup>, in patients that remained symptomatic after the dialysis-free weekend.

### PATIENTS AND METHODS

Follow-up was done in 9 patients, five men and four women, with a mean age of 72 years (SD  $\pm$  9.3;

**Table I.** Clinical history of cardiovascular disease in the group

Patient	1	2	3	4	5	6	7	8	9	(%)
AMI		X							X	22
Angina	X	X	X		X		X		X	67
LVH	X	X	X	X	X	X	X	X	X	100
CV	X	X	X			X	X	X		67
↓EF	X	X	X				X	X	X	67
APE	X	X	X	X	X	X	X	X	X	100
Arrhythmia	X	X	X			X	X			56
AHT	X		X						X	33
Diabetes	X		X		X				X	33

AMI: acute myocardial infarction; LVH: left ventricular hypertrophy; CV: cardiac valvulopathy; ↓EF: decreased left ventricular ejection fraction (<50%); APE: acute pulmonary edema; AHT: arterial hypertension.

range: 56-80), a mean HD treatment of 75.5 months (SD ± 71.5, range: 19.3-249.4), a medical history of CV disease (table I) and that shared in common the presence of heart failure symptoms and events related to poor tolerance during the dialysis procedure on a 5-hour, 3 times per week (5h × 3/W) regimen.

The 9 patients that previously were on a 5h × 3/W HD dialysis-free weekend regimen (Phase 1) (13 sessions, 65 HD hours/month) shifted to an EODD regimen (Phase 2) with four-hour sessions, without weekend break-off (15 sessions, 60 HD hours/month). Days sequence on EODD regimen was: monday-wednesday-friday-sunday-tuesday-thursday-saturday-monday, etc.).

In both regimens, each patient remained with the same prescription for dialyzer (high-permeability synthetic membrane: AN69 or polyamide; surface area 1.6 or 2.1 m<sup>2</sup>) with Qb: 350 mL/min, Qd: 500 mL/min, and constant bicarbonate concentrate and sodium profile at 140 mEq/L, with ultrafiltration (UF) control monitors.

Monthly protocols for laboratory analysis and dialysis quality controls were maintained at the second HD session the first week of each month.

As a general criterion, the total UF limit was 3% of the total weight, although individual adjustments were made according to each patient condition.

Lean weight adjustment was done weekly according to clinical data, the course and events on previous sessions, and in each session as necessary.

Criteria for including patients in EODD were one or more of the following: presence of pre-HD resting dyspnea with pulmonary crackles and/or hypertension (BP > 160/90) and/or angina; poor tolerance to UF with events of hypotension and/or angina during the sessions, and lack of lean weight control during the week.

During the 38 HD sessions (3 months) of phase 1 immediately previous to phase 2, and during the 38 sessions (2.5 months) of phase 2 done 1 month apart from the HD regimen shifting, the following percentages of events were analyzed in each patient:

a) sessions with resting dyspnea at the beginning of the session; b) hypertension at the beginning of the session; c) emergency sessions; d) sessions with presence of pre-HD or intra-HD angina; e) sessions with symptomatic hypotension (one or more hypotension episodes that required volume replacement to control them); f) sessions in which the lean weight goal set was not reached at the end of the sessions, with a positive margin of +0.2 kg.

Lean weight at the end of phase 1 (weight 1), the least lean weight obtained in phase 2 (weight 2), and set up lean weight within 6 months of EODD onset (weight 3) were recorded.

Descriptive statistics were performed, using arithmetic means, standard deviation (SD) and medians for quantitative parameters; for qualitative variables, frequency distribution was used. For inferential statistics Student's t test and chi-squared test were used for association of quantitative and qualitative variables, respectively. The p significance degree selected, independently of the analysis and type of variable analyzed, was the one that corresponds to a high level of significance (p < 0.05). When this level has not been reached it has been referred as not significant (NS).

## RESULTS

Results are expressed (Table II) as the percentage of HD sessions in which events were recorded in the group of patients, out of a total of 342 sessions in each of both phases (9 patients × 38 HD sessions = 342 sessions for the group in each phase).

All patients experienced a dramatic reduction in the percentage of sessions with initial presence of dyspnea, angina, AHT and emergency sessions (p < 0.001) during the EODD phase. Percentage of ses-

**Table II.** Percentage of eventful sessions in the group

	Phase 1: HD 342 Mean (SD)	Phase 2: HD 342 Mean (SD)	Dif %	p
Dyspnea	15.2 (12.5)	2.3 (2.4)	-84.8	0.001
AHT	23.4 (33.3)	4.7 (5.7)	-79.9	0.001
Emergency HD	7.6 (6.8)	0.9 (1.8)	-89.4	0.005
Angina	4.1 (7.4)	0 (0)	-100	0.001
Hypotension	47.4 (22.8)	31.5 (21.7)	-33.5	NS
Not lean weight	38.1 (17.2)	25.1 (19.9)	-34.1	NS

**Table III.** Lean weight course

Pt. #	Weight 1	Weight 2	Dif (P1-P2)	%	Weight 3	Dif (P3-P2)	%
1	67.5	63.5	-4	-5.9	62.5	-1	-1.5
2	58	55	-3	-5.1	56.5	+1.5	+2.7
3	83	81	-2	-2.4	85	+4	+4.9
4	56.5	54	-2,5	-4.4	57	+3	+5.5
5	101.5	99.5	-2	-1.9	100	+0.5	+0.5
6	61	58.5	-2,5	-4.1	61.5	+3	+5.1
7	70	69	-1	-1.4	75	+6	+8.6
8	73.5	73	-0,5	-0.6	73.5	+0.5	+0.6
9	69.5	67.5	-2	-2.8	70.5	+3	+4.4
Mean	71.1	69	-2.1	-3.2	81.2	+2.2	+3.4
SD	14	14.3	-1.0	-1.7	14.2	+2.1	+3.1

Weight 1: lean weight (kg) at the end of phase 1. Weight 2: least lean weight (kg) achieved during phase 2. Weight 3: lean weight (kg) within 3 months of phase 2.

sions with hypotension and of sessions in which the lean weight set up at the onset of each session was reduced in one third as compared to phase 1, but not reaching statistical significance ( $p = \text{NS}$ ).

In two of the three patients that had pre-HD AHT with an anti-hypertension drugs prescription, normalization of blood pressure levels was achieved during the EODD phase, withdrawing the medication.

All patients improved their tolerance to UF while on EODD and a reduction of lean weight, as compared to the one they had at the end of phase 1, was achieved.

Within 3 months of initiation of EODD phase, one patient kept his weight lower than the one on phase 1, but he had gained 1 kg in relation to the initial loss; 4 patients had gained between 0.5 and 1.5 kg as compared to the intermediate loss, and the remaining increased their lean weight above 2 kg, without presenting the symptoms they had on phase 1. Although mean  $Kt/v$  (Dauguidas 2<sup>nd</sup> g) of the group per session was reduced in phase 2 in relation to time, from 1.58 to 1.42, the hemodialysis product (HDP)<sup>5</sup> increased from 45 to 49.

## DISCUSSION

The more recent data of the DOPPS study<sup>6</sup> indicate that only 30% of the greater death risk that present HD patients in the USA, as compared with those in Japan or Europe, may be explained by a greater influence of co-morbidity factors in that population. This fact supports the hypothesis that the methodology in the HD procedure may be one of the survival determinant factors together with others such as the features of the systems for the procedure provision<sup>7</sup>.

In all HD populations, CV risk is directly related to mortality<sup>8</sup>, being the most frequent death cause<sup>9</sup> and its incidence is maximal on Mondays or Tuesdays, after the 72-hour interval without HD, a situation that does not occur in peritoneally dialyzed patients<sup>10</sup>.

Maintenance of an ECV expansion without reaching the lean weight at the end of HD sessions<sup>11</sup> leads to an overload situation that directly influences on patients symptoms and exacerbates during the 72-hour periods without HD<sup>12</sup>.

Age and CV conditions (arteriosclerosis, ischemic heart disease, cardiomyopathy) that elderly patients on HD present make that compensating mechanisms of UF (cardiac output, peripheral resistances, vascular repletion capability from the interstitium) may not be able to stand the UF rates that until recently were reasonable: it is difficult for these patients to tolerate hourly volume losses higher than 1% of body weight<sup>13</sup> without experiencing hypotension that, in turn, requires fluid reposition and lowering of UF, closing the loop of volume lack of control. In order to prevent it, critical prediction profiles have not been found<sup>14</sup>. Besides, HD hypotension itself is a risk factor associated to greater CV morbidity and mortality<sup>15</sup>.

As in most of the HD units, our incident population is old (40% of patients are older than 70) with high numbers of co-morbidities, most of which CV, and has difficulties for reaching lean weight with the classical 4-hour 3-sessions per week regimen.

For this reason, since the year 2000, we increased sessions time from 4 to 5 hours, in three sessions per week to augment depuration and tolerance to UF, trying to improve morbidity and survival<sup>16</sup>.

However, this group of nine patients with severe CV disease kept an unstable clinical situation with frequent unbalances, specially after the HD-free weekend; moreover, they remained symptomatic during the week with a poor response to UF profiles that exceeded an hourly rate of 0.5% of weight.

With the goal of improving their clinical situation, their HD prescription was shifted to the 4-hour every other day sessions regimen without breaking off on weekends, a scheme that Lecce and coworkers assigned to their series patients with lower body surface area and weight; patients weighting more than 60 kg had four sessions per week but did not strictly follow the every other day dialysis. Because of organization criteria and for not reducing our attendance capability we chose the EODD.

So that the needed readjustments in organization, sanitary transport, shift and patients changes of the Unit would not interfere with the study, events recording was done, in each patient, during the last

38 sessions of phase 1, leaving a one-month interval with EODD sessions, and recording again the course during the following 38 sessions.

During the EODD phase, an improvement in the patients clinical situation was observed: the frequency of pre-HD dyspnea and extraordinary sessions was reduced over 80%, angina episodes during the sessions cleared out, AHT frequency at the beginning of the sessions was reduced by 80%, tolerance to UF improved, and sessions with hypotension and those in which set up lean weight was not reached were reduced one third.

Although total number of dialysis hours per month and per patient was reduced in five hours, and the mean weekly Kt/V of the group lowered from 4.74 to 4.26 (-10%), all patients maintained our minimal weekly Kt/V goal of 3.9; The Hemodialysis Product (HDP)<sup>5</sup> (# hours) × (# sessions/week)<sup>2</sup> changed from 45 to 49, reflecting a good adequacy of the procedure by increasing sessions frequency, already described<sup>17,18</sup>.

The determinant factor of this course has been avoiding volume overload that accumulates during the two days without HD, and that conditioned the later course of UF intolerance during the week, a fact already described by Mastrangelo et al.<sup>4</sup>, and explaining the good outcomes in CV morbidity and mortality and AHT reduction in Lecce's patients.

Although hypotension appearance during EODD has been reduced one third, a better outcome could have been expected according to previous results: in Lecce's data, hypotension occurred in 8.7% of sessions, in 1998, much lower than the one we obtained during the EODD phase, although mean age in our patients was much higher (72 vs 48 years) and they had greater CV morbidity. Besides, it is likely that a confounding factor may have occurred due to caution excess during the first sessions of phase 2 while we increasingly adjusted lean weight according to medical history of patients<sup>19</sup>; a more comprehensive assessment of the final weight to be reached seems necessary before each session.

After educing lean weight during EODD, we have recorded a progressive increase greater than 1.5 kg in six patients, without reoccurrence of ECV expansion symptoms, associated with a better appetite; this fact, already described<sup>20</sup>, goes along with BP normalization some time after ECV control (lag phenomenon), as it occurred in two of our three patients with AHT that could withdraw hypertension medication.

By avoiding the two-days break-off from HD, EODD adapts better to the patients clinical situation<sup>21</sup> and has allowed, in our case, to maintain an hourly UF at recommended levels, which range from

0.5% to 1.5% of weight loss per hour<sup>13</sup>, with a total weight loss per session that must be kept under 3% of body weight since by trespassing this «security zone» the incidence of hypotension rises and the vicious circle of ECV expansion is maintained<sup>22</sup>.

There exist several experiences that demonstrate survival and morbidity improvements by increasing the time and/or the frequency of dialysis sessions, as it is the case with daily HD (DHD)<sup>23-24</sup>. However, universal implementation of DHD may be complicated, as it is our case, if there exist a wide geographic scattering of population centers from the hospital which limits access to daily treatment, together with the costs increase in disposable material caused by the sessions frequency.

On the other hand, EODD also represents a reasonable alternative to long dialysis regimens of three or more sessions per week because with a monthly increase of just two sessions per patient it allows keeping the design of three patient shifts per day for each HD slot: good clinical outcomes are maintained with a minimal increase in human (Sundays coverage), disposable and transport resources, without reducing the offer of HD slots, an inconvenience that does happen with longer duration sessions since EODD compensates time reduction with an increase in frequency. Besides, we should consider costs savings by means of reduction in hospital admissions, emergency HD sessions for pulmonary edema among other complications that occur after the 72-hour period without HD and that EODD avoids<sup>25</sup>.

In conclusion, EODD has already demonstrated excellent outcomes in Europe<sup>4</sup> and the USA<sup>25</sup> and is a valid alternative that has improved our patients' situation with high CV risk, with a small increase in costs; therefore, we are offering this regimen to all of our patients, independently of their age and CV risk.

We emphasize the importance of assuming strategic changes giving precedence to frequency and time of sessions<sup>26-27-28</sup> for improving the procedure tolerance and the survival of HD patients that show clinical situations different from the past and require different solutions to their treatment.

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