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How can symptomatic hypotension be improved in hemodialysis patients: cold dialysis vs *isothermal dialysis*

R. Ramos[1], C. Soto[1], R. Mestres[1], J. Jara[1], H. Zequera[2], J. I. Merello[2] and F. Moreso[1]

[1]Hemodialysis Unit. Serveis d'Ajut. Hospital St. Antoni Abat. Vilanova i la Geltrú. Barcelona.
[2]Fresenius Medical Care. Madrid.

SUMMARY

Background: *Symptomatic hypotension is the most frequent acute complication affecting patients during chronic hemodialysis treatment sessions. Many reports have demonstrated that the use of cool dialysate has a protective effect on blood pressure during hemodialysis treatments. In the present study, we investigated whether preventing the hyperthermic response had favourable effects on hemodynamic stability during the hemodialysis procedure while affording good tolerance to patients.* ***Methods:*** *We investigated the effect of thermal control of dialysate on hemodynamic stability in hypotension-prone patients in our center. Patients were eligible for the study if they had symptomatic hypotensive episodes (> 3/12 session/month) during the* screening *phase. The study was designed with two phases for the same selected patients and two treatment arms, each phase lasting 4 weeks. In the first phase, we adjusted dialysate temperature on 36 ºC for 12 sessions (cold dialysis) and in the second phase we used a device allowing the regulation of thermal balance (Blood Temperature Monitor; Fresenius Medical Care, Bad Homberg, Germany), that keep body temperature unchanged (isothermic dialysis).* ***Results:*** *Nine HD patients were enrolled and completed the study. During the* screening *1% of dry weight, and blood pressure ± phase the mean ultrafiltration was 4 16 mmHg (p ± 16 to 80 ± decreased from 99 < 1.7 sessions of 12 ± 0.001). In 5.0 treatments were complicated by hypotension. In the first and second phase we observed a decrease of complicated treatments with symptomatic hypotension 1.7; p ± 1.6 y 2.8 ± 1.7* versus *2.7 ± (5.0 < 0.01). Both procedures: Cold dialysis and Isothermic dialysis was well tolerated by patients.* ***Conclusion:*** *Results show that active control of body temperature can significantly improve intradialytic tolerance in hypotension-prone patients.*

Key words: ***Hemodialysis. Hypotension. Blood temperature monitoring. Dialysate temperature.***

CÓMO MEJORAR LA HIPOTENSIÓN SINTOMÁTICA EN HEMODIÁLISIS: DIÁLISIS FRÍA *VS* DIÁLISIS ISOTÉRMICA

RESUMEN

Introducción: *La hipotensión sintomática es la complicación aguda más frecuente que afecta a los pacientes durante las sesiones de hemodiálisis. Varios trabajos han demostrado que el uso de baja temperatura en el baño de diálisis protege de esta hipo-*

Correspondence to: Dra. Rosa Ramos Sánchez
Ciutat Sanitaria i Universitaria de Bellvitge
C/ Feixa Llarga, s/n
08907 L'Hospitalet del Llobregat (Barcelona). Spain
E-mail: 30965rrs@comb.es

tensión en pacientes susceptibles de ella. En nuestro estudio, analizamos si la prevención de la reacción hipertérmica de la sesión de hemodiálisis tendría una respuesta favorable en la estabilidad hemodinámica de los pacientes permitiéndoles una buena tolerancia. ***Métodos:*** *Analizamos el efecto del control de temperatura del dializado en la estabilidad hemodinámica de pacientes predispuestos a hipotensión sintomática en nuestro centro. En la fase de* screening *seleccionamos aquellos pacientes que tuvieron más de tres episodios hipotensivos en las 12 sesiones del mes. Posteriormente los mismos pacientes pasaron a las siguientes dos fases de 4 semanas cada una. En la fase 1, ajustamos la temperatura del baño a 36º C de forma constante para las 12 sesiones (diálisis fría) y en la segunda fase, utilizamos un (Blood Temperature Monitor; Fresenius Medical Care, Bad Homberg, Germany), que permite mantener constante la temperatura corporal (diálisis isotérmica).* ***Resultados:*** *Nueve pacientes fueron incluidos y finalizaron el estudio. Durante la fase de* screening *la sustracción media fue del 4 ± 1% del 16 mmHg ± 16 a 80 ± peso seco, disminuyendo la tensión arterial media desde 99 (p < 1,7 sesiones de 12 ± 0,001) y presentando hipotensión sintomática en 5,0. Tanto en la fase 1 como en la 2 observamos un descenso de los tratamientos 1,7 ± 1,6 y 2,8 ± 1,7* versus *2,7 ± complicados con hipotensión sintomática (5,0 p < 0,01). Ambas técnicas: Diálisis fría tanto como diálisis isotérmica fueron bien toleradas por los pacientes.* ***Conclusión:*** *Los resultados muestran que un control activo de la temperatura corporal puede mejorar de forma significativa la tolerancia intradialítica en pacientes predispuestos a la hipotensión sintomática.*

Palabras clave: ***Hemodiálisis. Hipotensión. Diálisis isotérmica. Monitor de temperatura.***

INTRODUCTION

Symptomatic hypotension is the most common acute complication of hemodialysis patient. The origin is multifactorial. On the one hand, factors pertaining the patient his/herself such as cardiovascular condition, and on the other hand, factors related with the dialysis technique play a role. It is well known that one of these factors is the temperature of the dialysis fluid, inducing in the patient an increase or decrease in body temperature with the subsequent hemodynamic instability.

During the hemodialysis session there is an increase in energy production with increased heat. Rapid volume depletion and the release of inflammatory cytokines due to bioincompatibility phenomena produce this energy increase.[1,2] On the other hand, there is sympathetic response manifested as peripheral vasoconstriction, preventing energy loss through the skin.[3] These events, together with heat transference by irradiation from the extracorporeal circuit to the environment and energy release from the volume of ultrafiltered body fluid,[4] are an important cause of increased body heat.

As a consequence of the vasodilation reflex that abrogates the vasoconstrictive response to ultrafiltration, this increase in central body temperature may cause hemodynamic instability, promoting the occurrence of hypotension episodes, especially in susceptible patients.[5]

Studies done in the 1980s confirmed that low temperature of the dialysis fluid (34º-35.4º C) improved hemodynamic and cardiovascular tolerance to hemodialysis session (cold dialysis) as compared with those patients in whom the temperature of the dialysis fluid was increased to 37º C or higher.[6-11] Other authors showed that the use of high-temperature dialysis fluid was accompanied by symptomatic hypotensive episodes in susceptible patients.[12-16]

Therefore, lower temperatures are recommended to improve the tolerability to the dialysis session. It is necessary to decrease the temperature of the dialysis fluid and the temperature of the returning fluid to improve heat loss during dialysis and to keep constant the body temperature. However, the greatest drawback of this «cold dialysis» is the patient intolerance to temperature loss.[9,17] It has recently been proposed that isothermal dialysis performed with a non-invasive temperature-monitoring device of the dialysis fluid improves the treatment tolerance since it prevents the temperature increase that occurs with hemodialysis at constant temperature.[5,18] Besides, with this procedure the body temperature would remain stable while preserving the benefits of cold dialysis but without the side effects of hypothermia. The theoretical advances are evident, although there are no comparative studies between one technique and another showing cardiovascular stability in the patient.

We present the following study in which we compared the tolerability to the dialysis session using isothermal dialysis and a temperature-monitoring device with standard dialysis decreasing the temperature of the dialysis bath.

PATIENTS AND METHODS

The objectives of the present study were:

1. To compare whether the method of keeping the patient isothermal by means of the BTM module (blood temperature monitor, Fresenius 4008H/S) is superior to the simpler method of adjusting constant the dialysis fluid temperature at 36º C at the beginning of the dialysis session.
2. To identify the type of target patients that may benefit from the BTM module in reducing the number of symptomatic hypotension episodes.
3. To determine the impact of the methods applied on nursing intervention times required to treat hypotension and on the reduction of fluids and plasma expanding solutions required during hypotension episodes.

The efficacy variable was symptomatic hypotension defined as the decrease in systolic blood pressure higher than 20 mm Hg as compared to baseline, associated to at least one of the following: nausea, vomiting, cramps, or dizziness, requiring medical intervention such as stopping UF, postural measures, administration of more than 200 mL of saline solution. Other variables considered were: predialysis systolic blood pressure (SBP), predialysis diastolic blood pressure (DBP), SBP at 1st hour, DBP at 1st hour, SBP at 2d hour, DBP at 2d hour, SBP at 3d hour, DBP at 3d hour, SBP at 4th hour, DBP at 4th hour, post-dialysis SBP, post-dialysis DBP, minimal SBP during hypotension (HS), number of monthly HS, hour of occurrence of HS, volume of saline during HS, volume of colloidal solutions during HS, pre-dialysis weight, post-dialysis weight, total UF, effective time on dialysis, initial temperature of the dialysis fluid, final temperature of the dialysis fluid, presence of predialysis fever, presence of intra-dialysis fever.

Study design

A prospective study was undertaken at our Unit. The inclusion and exclusion criteria, as well as the criteria for withdrawing from the study are shown in table I. The patients were submitted to conventional dialysis according to the usual regimen. The study was carried out in three phases, each one of them with 12 sessions:

1. *Screening phase*. Patients were recruited among those presenting a number of dialysis sessions complicated with symptomatic hypotension > 3/12. The criteria defining «symptomatic hypotension» have been previously described. The presence of severe anemia or cardiac complication justifying this complication was ruled out. Profiles: Na+ profiles were discontinued in those patients receiving them. Patients having prescribed some type of UF profile were switched to profile #1 (profile of decreasing UF). The temperature of the dialysis fluid was 37º C (predetermined by the machine). Food intake was allowed.
2. *Phase 1. Manual adjustment:* during the 12 following sessions, the temperature of the dialysis fluid was set constant at 36º C. The temperature from the patient's armpit opposite to the arm carrying the fistula was taken. Other dialysis parameters, such as blood flow, dialysis duration, or ultrafiltration profile, were not modified in relation to the screening phase.
3. *Phase 2. BTM:* for the next 12 sessions, dialysis sessions were carried out with the temperature control function of the BTM module. In order to rule out the influence of a high temperature of the dialysis

Table I. Inclusion, exclusion and withdraw criteria

Inclusion criteria

1. Patients on chronic hemodialysis for longer than 3 months.
2. Patients carrying a functioning arterial-venous fistula.
3. Dialysis regimen of 3 weekly sessions, of at least 180-minutes duration each.
4. Presenting during the *screening* phase > 3/12 dialysis sessions complicated with symptomatic hypotension.
5. Written consent from the patient (legal issue).
6. Patients >18 years.

Exclusion criteria

1. Patients with severe cardiac failure (grades III-IV NYHA).
2. Patints with ejection fraction by echocardiogram < 40%.
3. Patients with severe anemia (hematocrit < 30% and/or hemoglobin < 10 g/dL).
4. Patients eith difficulties with the arterial-venous fistula and/or requiring a central catheter for dialysis and/or uni-puncture.
5. Participation in other studies.
6. Pregnancy, breastfeeding.
7. Some psychological condition interfering with the patient's ability to adhere to the study protocol.

Criteria for withdrawing from the study

1. Patient's decision.
2. Investigator's decision to discontinue a patient from the study for medical reasons.
3. Occurrence of one of the exclusion criteria.
4. The patient's does not adhere to the study protocol.
5. End of HD (e. g., transplantation, change of technique).

Table II. Number of hypotension episode per patient and phase HS = Hypotension

	Mean UF (L/Session)	Screening Phase # HS	Phase 1 # HS	Phase 2 # HS
Case 1	2.3	5	4	3
Case 2	3	5	4	3
Case 3	1,8	4	3	6
Case 4	2.1	8	0	2
Case 5	2.3	6	4	3
Case 6	2.6	3	1	0
Case 7	1.5	3	1	1
Case 8	2.6	7	4	4
Case 9	3.1	4	3	3
Mean		5	2.7	2.8
SD		1.7	1.6	1.7
		P < 0.001	P < 0.01	P < 0.01

HS = Hypotension.

fluid, the latter was adjusted at the beginning of the session the closest possible at 0.5 º C intervals to the pre-dialysis temperature of the patient. The device kept this temperature constant until the BTM module started automatic control approximately within 20-20 minutes. The temperature was measured at the armpit opposite to the arm carrying the fistula. Other dialysis parameters, such as blood flow, dialysis duration, or ultrafiltration profile, were not modified in relation to the *screening* phase.

The study was carried out simultaneously in all patients. The *screening* phase started on January of 2005, and the other two phases were consecutive.

The results are expressed as mean ± standard deviation. The comparison between the groups was done by the Student's t test.

RESULTS

The study was started in the year 2005 and 9 (4 men and 5 women) out of the 95 patients attending the Unit at that time met the inclusion criteria. Mean age was 64 ± 14 years, with a mean time on hemodialysis of 35 ± 30 months. Five out of nine included patients were diabetic (3 women and 2 men). Dialysis duration was 225 ± 26 minutes per session. During the screening phase, mean substraction was 4 ± 1% of dry weight, and mean arterial blood pressure decreased from 99 ± 16 to 80 ± 16 mm Hg ($p < 0.001$), presenting symptomatic hypotension in 5.0 ± 1.7 out of 12 sessions. The temperature of the dialysis fluid during this phase was 37º C (the standard temperature prescribed by default by the dialysis machine: Fresenius 4008S). Table 2 shows the number of hypotension episodes per patient and phase. In phase 1 (constant fluid temperature at 36º C), mean body temperature at the end of the dialysis session was 36.3 ± 0.5, and the difference with regards to body temperature measured in the patients at the beginning of the session was not significant. During this phase, a reduction in the number of sessions complicated with symptomatic hypotension was observed (5.0 ± 1.7 versus 2.7 ± 1.6; $p < 0.01$). During the next phase (phase 2, with BTM), a reduction in the number of hypotension episodes was also observed (5.0 ± 1.7 versus 2.8 ± 1.7; $p < 0.01$). There were no differences in cardiac rhythm between both phases, or in mean ultrafiltration required by each patient. Both total proteins and hematocrit remained stable throughout the study in all patients.

Recirculation of the vascular access was also analyzed using the same monitoring device, being 10.6 ± 1.8%.

DISCUSSION

It is well known that the option of lowering the dialysis bath temperature to a constant temperature may be an unreliable practice since there are substantial variations in body temperature from one patient to another that may reach up to 2º C. In our study, the results obtained by using one technique or the other were similar, and both options are valid for achieving better hemodynamic stability. It is likely that the small sample size and the strict limitations in inclusion and exclusion criteria did not allow us appreciating the inter-patient thermal differences.

The initial temperature during the screening phase was the standard one, at 37º C, assuming that it is the physiological body temperature. However, this an incorrect assumption since, on the one hand, the inter-subject temperature varies, and on the other hand, predialysis temperature o the patients tends to be low, around 36º-36.5º C.[19]

In previous studies, one of the problems with cold dialysis was the poor tolerance experienced by the patients.[9] All of our patients tolerated well the temperature decrease to 36º C during phase 1. We assume that this good tolerance was due to the use of a temperature of the dialysis bath not as low as that used in other studies (35-35.5º C).[20] Minimal differences in body temperature of only 0.3-0.8º C are perceived as different by the different patients.[21] Although we should take into account that «cold dialysis» may have harmful effects, especially in those patients with poor myocardial function,[22-23] only small differences in body temperatures of our patients, produced by lowering the temperature of the dialysis fluid, are able of inducing beneficial effects over the harmful effects of hypothermia.[24] This shows the need for being very accurate when measuring body temperature and individualizing the temperature of the dialysis fluid prescribed.

In order to avoid changes in body temperature related with the dialysis circuit itself, the blood should be in the return line at least at the same temperature than that at the arterial or outflow line. In their study, Maggiore *et al*.[25] used a feedback system that allowed getting rid of body heat accumulated during the dialysis session. This effect was achieved by using the Fresenius BTM, the same that we have used in phase 2, and which acts producing small changes in the dialysate temperature much more gradual than those obtained in previous studies, and that reaches it nadir temperature at the end of the dialysis session, when hypotension episodes are more frequent. Therefore, we believe that monitoring devices of arterial and venous temperature offer a good option for improving the quality of dialysis.

We may conclude stating that symptomatic hypotension of hemodialysis patients may be improved by varying the dialysate temperature. Both reduction of the fluid temperature to 36º C and the use of the BTM module have proven to be effective. Further studies with larger sample size would be required for a more in-depth review of the topic.

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