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CLINICAL STUDY

Intradialytic hypotension is associated with dialytic age in patients on chronic hemodialysis

Maurizio Bossola[1], Alice Laudisio[2], Manuela Antocicco[3], Nicola Panocchia[1], Luigi Tazza[1], Giuseppe Colloca[3], Matteo Tosato[3], and Giuseppe Zuccalà[3,4]

[1]*Hemodialysis Service, Department of Surgery, Catholic University of the Sacred Heart, Rome, Italy,* [2]*Department of Geriatrics, Campus Bio-Medico University, Rome, Italy,* [3]*Department of Gerontology, Geriatrics and Psychiatry Catholic University of the Sacred Heart, Rome, Italy, and* [4]*Emergency Department, Catholic University of the Sacred Heart, Rome, Italy*

Abstract

Objective: Intradialytic hypotension (IDH) is common in patients on chronic hemodialysis, but knowledge on determinants is still unclear. The present study aims at evaluating the association between IDH and dialytic age (DA) in patients on chronic hemodialysis. *Methods*: Between January 2012 and January 2013, 82 patients on chronic hemodialysis for at least 1 year were screened for inclusion in the present study. Of these, 14 were excluded because of advanced heart failure (n.9), history of alcohol/substance abuse (n.1), diagnosis of dementia (n.2), actual instability of clinical conditions requiring hospitalization (n.2). IDH was defined as a decrease in systolic blood pressure ≥20 mmHg or a decrease in mean arterial pressure (MAP) by 10 mmHg associated with clinical events and need for nursing interventions. The number of IDH episodes in 10 consecutive hemodialysis sessions was recorded for each patient. Linear and logistic regressions were adopted to assess the adjusted association between IDH and DA. *Results*: The mean DA was 92 ± 81. Eleven patients (16%) experienced IDH. DA was associated with IDH (OR = 1.01; 95% CI = 1.01–1.02; $p = 0.048$), after adjusting for potential confounders. DA was associated with the numbers of IDH events in the unadjusted model ($B = 0.02$; 95% CI = 0.01–0.03; $p = 0.042$), after adjusting for age and sex ($B = 0.01$; 95% CI = 0.01–0.03; $p = 0.042$) as well as in the multivariable model ($B = 0.02$; 95% CI = 0.01–0.05; $p = 0.045$). *Conclusion*: DA is associated with an increased probability of IDH and with increased number of IHD events. Studies are needed to understand the underlying factors of such an association.

Keywords

Dialytic age, hemodialysis, hypotension, intradialytic

History

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Introduction

Symptomatic intradialytic hypotension (IDH) continues to be a major problem in end-stage renal disease patients on chronic hemodialysis.[1,2] The incidence of IDH has not decreased despite considerable technical progress in hemodialysis during the last years.[2,3] Data from the 1426 patients derived from the hemodialysis (HEMO) study show that a median of 12.5% of dialysis sessions were complicated by IDH requiring saline infusion, and lowering of the ultrafiltration rate or reduced blood flow.[3]

IDH is not well tolerated by patients because of the occurrence of gastrointestinal, muscular and neurological symptoms. In addition, IDH may cause organ hypoperfusion resulting in cardiac, neurologic, vascular, and gastrointestinal complications.[4–8] Overall, IDH causes discomfort, and reduces treatment efficacy, thus increases morbidity. In addition, IDH contributes to increased monitoring and workload of nurses and physicians, thereby increasing treatment costs.[4–8]

Several factors contribute to IDH, such as the compromised autonomic nervous system, hormonal response, and cardiovascular compensatory mechanisms, including vascular compliance, venous capacity, and cardiac function. In addition, during hemodialysis treatment, fast removal of intravascular fluid, slow refilling rates, increases in body temperature, components of the dialysis fluid (buffer, water and electrolytes), etc. may cause hemodynamic instability.[5–9]

However, the main factor causing an acute decrease in blood pressure during HD treatment is hypovolemia due to inadequate ultrafiltration.[10] It is well known that healthy subjects can tolerate a decline in circulating blood volume up to 20% before hypotension occurs, but in patients on chronic hemodialysis hypotension may occur with a significant smaller decline in blood volume.[6]

Recently, Flythe et al.[11] have demonstrated that systolic blood pressure variability in patients on chronic hemodialysis is associated with greater dialytic fluid removal and rate as well as with older age and dialytic age (DA).

Address correspondence to Maurizio Bossola, Istituto di Clinica Chirurgica, Università Cattolica del Sacro Cuore, Largo A. Gemelli, 8 – 00168 Roma, Italy. Tel: +39 06 30155485; Fax: +39 06 30155491; E-mail: maubosso@tin.it

The present study aims at evaluating the association between IDH and DA in prevalent patients on chronic hemodialysis.

Methods

Participants

Between January 2012 and January 2013, 82 patients affected by end-stage renal failure who had received three times weekly hemodialysis for at least 1 year at the Hemodialysis Unit of the Catholic University, Rome, Italy, were screened for inclusion in the present study. Exclusion criteria were as follows: advanced heart failure (according to the criteria of the European Society of Cardiology),[12] diagnosis of dementia based on DSM-IV criteria,[13] history of alcohol or substance abuse, previous diagnosis of psychotic disorders, clinical instability requiring hospital admission. We excluded 14 patients because of advanced heart failure (9 patients), history of alcohol or substance abuse (1 patient), diagnosis of dementia based on DSM-IV criteria (2 patients), and actual instability of clinical conditions requiring hospitalization (2 patients). Therefore, data were available for 68 participants.

The study protocol was approved by the local ethic committee, and all participants provided written informed consent.

Intradialytic hypotension

The number of episodes of IDH in 10 consecutive hemodialysis sessions was recorded for each patient. According to EBPG guideline on hemodynamic instability,[6] IDH was defined as a decrease in systolic blood pressure $\geq$20 mmHg or a decrease in mean arterial pressure (MAP) by 10 mmHg associated with clinical events and need for nursing interventions.

Covariates

All patients received 4-h bicarbonate hemodialysis three times a week. The blood flow ranged from 250 to 300 mL/min, with a dialysis rate flow of 500 mL/min. All patients were treated with high-permeability membranes. Membranes were not reused. Comorbidity was quantified using the Charlson comorbidity score index.[14] Diagnoses were coded according to the International Classification of Diseases, ninth edition, and Clinical Modification codes.[15] All drugs assumed by participants were coded according to the Anatomical, Therapeutic, and Chemical codes.[16]

Interdialytic weight gain (IDWG) and predialysis systolic blood pressure of 10 consecutive hemodialysis sessions (the same used to record IDH) were recorded and mean and median values were calculated. Blood samples were obtained after overnight fasting from patients through the arteriovenous fistula or the central venous catheter immediately before their scheduled hemodialysis session at the beginning of the week. Plasma was separated within 30 min, and samples were stored at $-70\,^{\circ}C$ at the Department of Laboratory Medicine, Catholic University, Rome, and were not thawed until analyzed.

Statistical analyses

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS for Mac version 20.0, 2011, SPSS Inc., Chicago, IL); differences were considered significant at the $p<0.050$ level. Data of continuous variables are presented as mean values $\pm$ SD. Analysis of variance for normally distributed variables according to the occurrence of IDH was performed by ANOVA comparisons; otherwise, the nonparametric Kruskal–Wallis H test was adopted. Chi-squared analysis was used for dichotomous variables.

Multivariable logistic regression analysis was adopted to estimate the association of IDH with age, sex, and variables of interest, including DA. All the covariates were introduced simultaneously into the regression models. Also, multivariable linear regression analysis was used to assess the association of intradialytic hypotensive events with age, sex, and variables of interest, including DA. All the covariates were introduced simultaneously into the regression models.

Results

The mean DA was 92 ± 71 months. The presence of IDH was detected in 11/68 (11.2%) patients. The mean number of intradialytic hypotensive events was 0.8 ± 0.2. The main characteristics of participants are depicted in Table 1. Patients with IDH showed a higher DA, as compared with subjects without IDH (141 ± 113 months vs. 82 ± 68 months; $p=0.025$). There was a positive correlation between IDH events and DA ($r_s=0.24$; $p=0.042$).

Multivariable analysis

According to logistic regression, DA was associated with IDH in the unadjusted model (OR = 1.01; 95% CI = 1.01–1.02; $p=0.026$), after adjusting for age and sex (OR = 1.01; 95% CI = 1.01–1.03; $p=0.035$), and in the multivariable model (OR = 1.01; 95% CI = 1.01–1.02; $p=0.048$, Table 2).

According to linear regression, DA was associated with the numbers of IDH events in the unadjusted model ($B=0.02$; 95% CI = 0.01–0.03; $p=0.042$), after adjusting for age and sex ($B=0.01$; 95% CI = 0.01–0.03; $p=0.042$), as well as in the multivariable model ($B=0.02$; 95% CI = 0.01–0.05; $p=0.045$, Table 3). Also, systolic blood pressure was

Table 1. Characteristics of the participants according to the presence of IDH in 10 consecutive hemodialysis sessions.

	Patients with IDH ($n=11$) n (%) or mean $\pm$ SD	Patients without IDH ($n=57$) n (%) or mean $\pm$ SD	p
Age (years)	60 ± 18	62 ± 14	0.742
Sex (female)	5 (45%)	20 (35%)	0.517
Charlson comorbidity index score	4 ± 3	3 ± 2	0.296
Hemoglobin (g/dL)	11.8 ± 0.9	11.3 ± 1	0.133
Serum creatinine (mg/dL)	10.1 ± 3.2	10.5 ± 3.2	0.713
Serum albumin (g/dL)	3.8 ± 0.2	3.9 ± 0.3	0.301
Dialysate sodium concentration (mEq/L)	140 ± 2	139 ± 2	0.089
Blood flow (mL/min)	268 ± 41	278 ± 26	0.281
Interdialytic weight gain (%)[a]	4.2 ± 1.3	3.5 ± 1.2	0.126
Use of ACE-Inhibitors or Sartans	6 (54%)	28 (49%)	0.998
Predialysis systolic blood pressure (mmHg)	128 ± 14	128 ± 13	0.905
Dialytic age (months)	141 ± 113	82 ± 68	0.025

[a]Expressed as percentage of the dry weight.

Table 2. Association (odds ratios, OR, and 95% confidence intervals, CI) of IDH with the variables of interest in the multivariable regression model. All the covariates were entered simultaneously into the regression model.

	OR	95% CI	*p*
Age (years)	0.94	0.87–1.03	0.198
Sex (female)	0.74	0.10–5.12	0.747
Charlson comorbidity index score	1.08	0.65–1.80	0.767
Hemoglobin (g/dL)	2.01	0.79–5.16	0.144
Serum creatinine (mg/dL)	0.88	0.60–1.29	0.513
Serum albumin (g/dL)	0.11	0.01–2.68	0.176
Dialysate sodium concentration (mEq/L)	1.39	0.90–2.14	0.138
Blood flow (mL/min)	0.97	0.94–1.01	0.165
Interdialytic weight gain (%)[a]	1.59	0.78–3.23	0.200
Use of ACE-Inhibitors or Sartans	2.92	0.71–11.66	0.129
Predialysis systolic blood pressure (mmHg)	1.07	0.98–1.16	0.152
Dialytic age (months)	1.01	1.01–1.02	0.048

[a]Expressed as percentage of the dry weight.

Table 3. Association (B coefficients, and 95% confidence intervals, CI) of intradialytic hypotensive events with the variables of interest in the multivariable regression model. All the covariates were entered simultaneously into the regression model.

	B	95% CI	*p*
Age (years)	−0.01	−0.02–0.01	0.566
Sex (female)	−0.12	−0.56–0.33	0.598
Charlson comorbidity index score	0.01	−0.08–0.11	0.780
Hemoglobin (g/dL)	0.22	0.03–0.40	0.021
Serum creatinine (mg/dL)	−0.02	−0.10–0.06	0.545
Serum albumin (g/dL)	−0.68	−1.47–0.11	0.092
Dialysate sodium concentration (mEq/L)	0.04	−0.05–0.13	0.399
Blood flow (mL/min)	−0.01	−0.01–0.01	0.211
Interdialytic weight gain (%)[a]	0.19	0.03–0.36	0.024
Use of ACE-Inhibitors or Sartans	0.24	−0.06–0.55	0.116
Predialysis systolic blood pressure (mmHg)	0.02	0.01–0.03	0.047
Dialytic age (months)	0.02	0.01–0.05	0.045

[a]Expressed as percentage of the dry weight.

positively associated with IDH ($B = 0.02$; 95% CI = 0.01–0.03; $p = 0.047$), as well as hemoglobin levels ($B = 0.22$; 95% CI = 0.03–0.40; $p = 0.021$). Eventually, interdialytic weight gain was positively associated with IDH ($B = 0.19$; 95% CI = 0.03–0.36; $p = 0.024$).

Discussion

The results of the present study indicate that, in patients on chronic hemodialysis, DA is associated with increased probability of IDH and with the number of intradialytic hypotensive events.

Despite continuous progress in the dialysis technologies, IDH remains a common complication of hemodialysis[3] that contributes to reducing the tolerability of dialysis and is associated with morbidity and mortality.[3,4] IDH causes a drop in cardiac output, which may lead to multiorgan dysfunction with an increased risk of myocardial infarction, heart failure, and neurologic complications.[4–8]

Several factors might account for the association of IDH with DA.[5–10] It has been reported that endothelial dysfunction is associated with IDH due to the effect of dialysis on several serum mediators of the endothelial function.[17] Accordingly, DA might be associated with endothelial dysfunction. Also, vascular calcification, which increases with the duration of dialysis,[18] might be responsible for the impairment of vasoconstriction and for arterial stiffness resulting in IDH. Finally, the observation that in the present study the IDWG was significantly correlated with DA may also contribute to explain the association of IDH with DA. It remains to be determined if other factors, which may contribute to IDH such as impaired baroreflex sensitivity, reaction of resistance and capitance vessels and autonomic dysfunction[6,19–22] are associated with DA in patients on chronic hemodialysis.

The percent IDWG also was correlated with IDH. High IDWG may be the result of consumption of beverages with high caloric values and/or solid food or, alternatively, it may represent excessive intake of water and/or salt.[1] Our results are in agreement with those of Takeda et al.[23] who demonstrated that excessive interdialytic weight gain was one of the independent risk factors for IDH in a cohort of 111 patients on chronic hemodialysis. Similarly, Lindberg et al.[24] have shown, examining the records of 4498 patients of the Swedish Dialysis Database during 2002 to 2006, that patient characteristics associated with IDWG were younger age, lower body mass index, longer, and high blood pressure and DA. Interestingly, Lai et al.[25] have shown that both absolute IDWG and IDWG% were significantly correlated with IDH in men and heavy women and that absolute IDWG, rather than IDWG%, was an independent risk factor for IDH in heavy men and heavy women. It has also been reported that IDWG <1.5 kg/2 days is associated with fewer hyper- or hypotensive episodes.[26]

The observation that systolic blood pressure and hemoglobin levels were positively associated with IDH is difficult to explain Takeda et al.[23] have recently reported that no correlation was found between predialysis blood pressure values or addition of antihypertensive medications and the incidence of IDH. Possibly, higher hemoglobin levels may be expression of plasma concentration and relatively low blood volume. It is well known that these conditions may predispose to IDH.[1,6]

IDH was not correlated with age or with comorbidities. This in accordance with the study of Capuano et al. that showed that IDH was not more prevalent in elderly than in younger hemodialysis patients and in those with multiple comorbidities. This is an interesting result that suggests that frailty does not necessarily predispose to IDH in patients on chronic hemodialysis.[27]

The present study has some limitations. First, the cross-sectional design has not allowed establishing any cause-effect relationship. Second, the study lacks measurement of endothelial function and inflammatory markers. Third, due to its monocentric design, our study should be considered preliminary in nature.

However, as the number of subjects on chronic dialysis is rapidly growing, our results may be worthy of interest having in mind the improvement of care policy for patients on long-term dialysis.

In conclusion, DA is associated with an increased probability of IDH and with increased number of IHD events. Dedicated studies are needed to understand the underlying factors of such an association.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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