



The Effect of Interdialytic Weight Gain on Blood Pressure in a Population of Chronic Hemodialysis Patients

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Abstract

Introduction: Hypertension, often associated with hypervolemia, is common in chronic hemodialysis patients. However, the relationship between interdialytic weight gain (IDWG) and blood pressure (BP) is incompletely characterized. Our study seeks to appreciate the relationship between IDWG and BP in a cohort of chronic hemodialysis patients. **Patients and Methods:** It is a prospective study involving 52 chronic hemodialysis patients and 528 dialysis sessions following a hemodialysis program of 3 times a week, where BP and IDWG were measured before the session. The dialysis sessions occurred over a period of 30 days from January 02 to 30, 2019 in the Hemodialysis unit of Mohammed V Military Training Hospital. Demographic data and dialytic parameters were collected over a 30-day period then analyzed using the following statistical tools: correlation coefficient r , simple linear regression (univariate analysis) and multiple linear regression (multivariate analysis). **Results:** Mean age was 55 ± 12 years, 48% were men, 32.7% were diabetic and 61.5% were on antihypertensive therapy. In univariate analysis, each 1 kg increase in IDWG was associated with an increase of 3.3 mmHg in systolic BP ($p = 0.01$) and 2.7 mmHg in diastolic BP ($p = 0.006$). In multivariate analysis, after adjusting for confounding factors, an increase of 1 kg of IDWG was associated with an increase of 1.7 mmHg of systolic BP ($p = 0.05$) and 1.8 mmHg of diastolic BP ($p = 0.05$). **Conclusion:** Our results show that there is a significant association between IDWG and BP, however, its modest magnitude can't explain alone the variations of BP in the chronic hemodialysis patients.

Subject Areas

Nephrology

Keywords

Interdialytic Weight Gain, Blood Pressure, Hemodialysis

1. Introduction

Hypertension (HTN) is common in patients with end stage renal disease (ESRD) including hemodialysis patients, with an estimated prevalence of 25% to 80% [1]

The cause of HTN, although multifactorial [2], is mainly attributed to the loss of renal regulation of water and salt excretion, resulting in extracellular volume (ECV) overload and adverse cardiac remodeling [3] [4].

Management of HTN may be difficult in this particular population, that's why the widely adopted approach is using a combination of ultrafiltration during dialysis and antihypertensive medications to assure an optimal control of blood pressure (BP).

However, HTN of the dialysis patient is not solely due to overload, other factors such as arterial stiffness, inappropriate stimulation of the renin-angiotensin system and the osmotic effects of sodium and glucose contribute through a complex role play [1].

The interdialytic weight gain (IDWG) is defined by [predialytic weight of the current session-postdialytic weight of the prior session], primarily reflects the intake of water and salt between 2 dialysis sessions. The IDWG is commonly used as one of main means to appreciate the hydration state of the ECV, and since the hydration state of ECV is a fundamental determinant of BP, this implies a direct relationship between IDWG and BP.

To better understand the relationship between interdialytic weight gain (IDWG) and systolic and diastolic BP, we performed a prospective study that analyzed the data of a cohort of stable hemodialysis patients.

In fact, the relationship between interdialytic weight gain (IDWG) and systolic and diastolic BP have thoroughly been studied by numerous authors, most of whom found a significant positive correlation between IDWG and both SBP and DBP such as Inrig, J.K., *et al.* [5], Lopez-Gomez, *et al.* [6], Chen-Huan, *et al.* [7] and Rahman, M., *et al.* [8]; which we'll detail their results in the discussion section.

2. Purpose of the Study

To study the association between IDWG and systolic and diastolic predialytic BP, check its independence relative to various demographic and dialytic characteristics that are suspected to affect BP, and check the scope of this association.

3. Patients and Methods

This is a prospective study that took place in the Hemodialysis unit of Mo-

ammed V Military Training Hospital in which we have selected 52 stable chronic hemodialysis patients, and we've studied the dialysis sessions they received over a period of 30 days from January 02 to 30, 2019, *i.e.* 528 sessions, predialytic systolic BP (SBP) and diastolic BP (DBP) blood pressure were measured in a sitting position by a nurse on the arm devoid of vascular access, after 10 min of rest.

The IDWG corresponds to: [predialytic weight of the current session-postdialytic weight of the prior session], the rest of the variables identified were: age, gender, dry weight (DW), ultrafiltration volume (UF), predialytic plasma Na, presence or absence of diabetes, presence or absence of antihypertensive treatment.

The data was collected manually (age, gender, presence or absence of diabetes, presence or absence of antihypertensive treatment) using specific charts and by exploiting the data provided by fresenius dialysis machines software.

The exclusion criteria were: subjects undergoing hemodialysis for acute renal failure, patients who had an uncontrolled hypertension (SBP > 220 mmHg, DBP > 130 mmHg), extreme age (<18, >85 years), ESRD patients on conventional hemodialysis for less than 3 months.

Statistical Analysis

The variable of interest that we seek to explain is predialytic BP (SBP then DBP respectively), thanks to one or more explanatory variables identified.

The association between IDWG and BP parameters was estimated using regression models:

Initially, univariate linear regression analysis was performed to independently obtain a crude association between IDWG (or other explanatory variables) and BP. Then the variables that are significant in the univariate analysis with a $p < 5\%$ or that are considered clinically relevant, are inserted in the multivariate analysis model. This multivariate linear regression allows us to assess the association between IDWG and BP by adjusting for potential confounding factors such as: age, sex (male = 0, female = 1), predialytic plasma Na, diabetes (no = 0, yes = 1), antihypertensive therapy (no = 0, yes = 1).

Statistical significance is defined as $p < 0.05$. All analyzes were performed with SPSS software version 20.

4. Results

A total of 52 patients who received 528 dialysis sessions were included in our study. Overall, participants had an average age of 55 years, 48% were men, 32.7% were diabetic and 61.5% were taking antihypertensive medication (**Table 1**).

The correlation study has shown a significant positive correlation between IDWG and each of predialytic SBP ($r = 0.18$, $p = 0.01$) and predialytic DBP ($r = 0.2$, $p = 0.006$); pearson correlation coefficient r was used given that IDWG, SBP and DBP were quantitative variables and had a Gaussian distribution.

Table 1. Characteristics of participants.

Characteristics	
Age (years)	55 ± 12
Gender	
Male (%)	25 (48%)
Female (%)	27 (52%)
Predialytic BP (mmHg)	
Systolic: SBP	142 ± 22
Diastolic: DBP	70 ± 16
IDWG (Kg)	
Dry weight (Kg)	71 ± 13
UF volume (ml)	1374 ± 924
Diabetes	
no (%)	35 (67.3%)
yes (%)	17 (32.7%)
anti-HTN therapy	
no (%)	20 (38.5%)
yes (%)	32 (61.5%)
Predialytic plasmatic Na (mmol/l)	136 ± 1

BP: blood pressure, IDWG: interdialytic weight gain, UF: ultrafiltration. Quantitative variables are expressed as mean ± standard deviation and qualitative variables are expressed in number and percentage (%).

Univariate analysis has shown that IDWG was significantly associated with both predialytic SBP and predialytic DBP. In fact, an increase of 1 kg of IDWG was associated with an increase of 3.3 mmHg in SBP ($p = 0.01$) and 2.7 mmHg in DBP ($p = 0.006$).

In multivariate analysis, these associations were still significant after adjusting for the following confounding factors: age, gender, diabetes, antihypertensive therapy, and plasmatic Na.

Dry weight and UF volume were excluded from multivariate analysis because of their non-significance in univariate analysis.

However, adjusting for these confounding factors resulted in a change in the estimate of BP increase per 1 kg of IDWG from 3.3 to 1.7 mmHg for SBP and from 2.7 to 1.8 mmHg for DBP, a change revised downwards.

In other words, taking into account the confounding factors, an increase of 1 kg of IDWG was associated with an increase of 1.7 mmHg of SBP ($p = 0.05$) and 1.8 mmHg of DBP ($p = 0.05$) (**Table 2** and **Table 3**).

In the multiple regression model, gender and diabetes were also independently associated with both SBP and DBP, yet, taking antihypertensive therapy was significantly associated with SBP alone.

Table 2. Simple (univariate) and then multiple (multivariate) linear regression using predialytic SBP as the dependent variable and the following variables as independent variables.

	Univariate			Multivariate		
	Regression Coefficient	IC 95%	p	Regression coefficient	IC 95%	p
Age* (years)	0.001	(-0.26, 0.26)	0.9			
Gender* female	-15	(-21.9, -9.1)	<0.001	-12	(-19.3, -5.8)	<0.001
IDWG (Kg)	3.3	(0.6, 6)	0.01	1.7	(1.2, 4.3)	0.05
Dry weight (Kg)	0.05	(-0.2, 0.3)	0.7			
UF volume (ml)	-0.001	(-0.004, 0.003)	0.8			
Diabetic*	9	(1.9, 16)	0.01	7	(0.06, 14.5)	0.04
presence of anti-HTN therapy*	-6.9	(-13.7, -0.04)	0.05	-8	(-14.5, -1.4)	0.01
Predialytic plasmatique Na (mmol/l)	-1.3	(-3.4, 0.7)	0.2	-0.5	(-2.5, 1.5)	0.6

IDWG: interdialytic weight gain, UF: ultrafiltration, *qualitatives catégorical variables (male gender, absence of diabetes, absence of antiHTN therapy: are considered as reference categories). This multivariate model explains 17% predialytic SBP variations (Determination coefficient: R2 = 17%).

Table 3. Simple (univariate) and then multiple (multivariate) linear regression using predialytic DBP as the dependant variable and the following variables as independent variables.

	Univariate			Multivariate		
	Regression coefficient	IC 95%	p	Regression coefficient	IC 95%	P
Age* (years)	-0.2	(-0.4, -0.06)	0.008	-0.2	(-0.4, 0.01)	0.06
Gender* female	-8	(-12.8, -3.3)	0.001	-10	(-15, -5)	<0.001
IDWG (Kg)	2.7	(0.8, 4.7)	0.006	1.8	(1.1, 3.6)	0.05
Dry weight (Kg)	-0.01	(-0.2, 0.2)	0.8			
UF volume (ml)	0.001	(-0.002, 0.003)	0.8			
Diabetic*	-9	(-14.4, -4.3)	<0.001	-8.7	(-14, -3.4)	0.001
Presence of antiHTN therapy*	-7	(-12, -2)	0.005	-3.3	(-8.2, 1.6)	0.2
Predialytic plasmatic Na (mmol/l)	0.2	(-1.3, -1.7)	0.7			

IDWG: interdialytic weight gain, UF: ultrafiltration, *qualitatives catégorical variables (male gender, absence of diabetes, absence of antiHTN therapy: are considered as reference categories). This multivariate model explains 22% of predialytic DBP variations (Determination coefficient: R2 = 22%).

Thereby, female subjects had lower SBP and DBP compared to male subjects, diabetics had higher SBP and lower DBP compared to non-diabetics, and patients who were on antihypertensive therapy had a slightly lower SBP compared to those who were not on treatment (**Table 2** and **Table 3**).

5. Discussion

The IDWG of a given dialysis unit can vary considerably, since most patients

have between 2 and 3.5 kg of IDWG (<5% of the dry weight) [9].

IDWG should be less than 4% to 4.5% of dry weight (KDOQI 2006 recommendations).

Our study found a significant association between IDWG and both predialytic systolic BP ($r = 0.18$, $p = 0.01$) and predialytic diastolic BP ($r = 0.2$, $p = 0.006$). After adjusting for confounding factors, an increase of 1 kg of IDWG was related to an increase in SBP/DBP of 1.7/1.8 mmHg.

Our results are in agreement with those observed in several other studies reported in the literature.

In fact, Inrig, J.K., *et al.* [5] reported in a study of 442 subjects that has analyzed 32,295 dialysis sessions, a significant relationship between IDWG and systolic BP outlining that an increase in IDWG of 1% of dry weight was associated with an increase of 1 mmHg of systolic BP ($p < 0.001$).

The work of Lopez-Gomez, *et al.* [6] demonstrated that IDWG was correlated with systolic BP ($r = 0.31$, $p < 0.001$), diastolic BP ($r = 0.31$, $p < 0.001$) and with nutritional parameters (nPCR, BMI, serum albumin)

Similarly, Chen-Huan, *et al.* [7], found a significant correlation between IDWG and SBP ($r = 0.31$, $p < 0.001$), MAP: mean arterial pressure ($r = 0.31$, $p < 0.001$) and DBP ($r = 0.31$, $p < 0.001$)

Finally, Rahman, M., *et al.* [8], found a significant association between IDWG and BP only in stage 3 hypertensive patients, this association was not found in normotensive patients or patients with moderate hypertension.

However, some publications report the lack of relationship between IDWG and BP [10] [11] [12] [13], among which we can mention:

Testa, *et al.* [10], who conducted a one-year prospective study to identify the determinants of IDWG, have found a significant association between IDWG and nPCR (normalized protein catabolic rate) suggesting that IDWG may be used as a potential nutritional marker; however, they found no correlation between IDWG and BP.

Salem, *et al.* [11], also, found no influence of IDWG on BP, even after 1 year of dialysis.

Our results show a low correlation, although statistically significant, between IDWG and both SBP and DBP ($r = 0.18$ and $r = 0.2$ respectively), that's why IDWG variations are accompanied by only a modest increase in BP (1.7/1.8 mmHg for each 1 kg of IDWG)

This low magnitude of BP variation was also found in the above-mentioned studies, that showed either a low or moderate correlation between IDWG and BP (correlation coefficient $r < 0.5$ in all positive studies).

This finding suggests that variations in BP, although correlated with IDWG, cannot be explained solely by the latter, which highlights the importance of other additional factors in the control of BP in dialysis-treated ESRD patients.

In fact, the pathophysiological mechanism of hypertension in dialysis is multifactorial; the main factors responsible for it, are summarized in **Table 4**.

Table 4. Factors responsible for hypertension in hemodialysis patients.

Reasons for Hypertension in Hemodialysis patients
Extracellular volume excess/volume overload
Derangements of renin-angiotensin system
Sympathetic overactivity
Impaired endothelium-dependant vasodilatation
Uremic toxins (ADMA, homocysteine)
Genetic factors
Geographic factors influence of climate
Correction of renal anemia by rHuEPO
Secondary hyperparathyroidism
Sodium intake/dialysate sodium concentration
Hemodialysis regimen

ADMA: asymmetric dimethylarginine; rHuEPO: Recombinant Human Erythropoietin; Matthias P. Horl, Hemodialysis-Associated Hypertension: Pathophysiology and Therapy AJKD February 2002.

This pathophysiological foundation encourages us to adopt a more holistic approach towards hypertension in dialysis patients, that's why in addition to ultrafiltration (guided by IDWG), it would be wise to:

- **Control sodium intake:** by adopting a diet that is restricted to salt [14], we recommend a salt intake ≤ 5 to 6 gram/day, *i.e.* ≤ 75 mg/kg of patient weight.
- **Reduce the sodium concentration of the dialysate:** has the benefit of reducing thirst sensation at the end of the dialysis session and reducing the predialytic MAP, which will allow in certain cases to reduce or even discontinue the antihypertensive therapy [15], however this reduction must be done gradually over several weeks.
- **Control blood sugar:** similarly to salt, high blood sugar levels increase thirst sensation due to the osmotic effect of glucose, which explains the interest of satisfactory glycemic control in dialysis patients.
- **Control the volemia:** dialysis patients should drink to their thirst, taking into account their residual diuresis; hence, the water intake recommended is estimated at 500 to 1000 ml/day + residual diuresis.
- **Personalize Dialysis Prescription:** patients who skip or shorten one or more dialysis sessions are more likely to experience hypertension than adherent patients [16], so in some cases prolonging sessions or increasing their frequency has shown effectiveness in better BP control [17] [18] [19] [20]
- **Personalize antihypertensive therapy:** by adapting the dosage and the time of administration to each patient profile. For this purpose ABPM (Ambulatory Blood Pressure Measurement) can be very interesting because not only it is more accurate than BP measurements in a dialysis center but it also pro-

vides information on BP variations during nycthemeron guiding antihypertensive drugs prescription.

Otherwise, our results did not find a significant association between predialytic plasma Na and BP. This negative result challenged us, given the well-established role of Na in BP regulation, and the fact that a steady sodium balance is known to be the cornerstone of good interdialytic BP control [21], which is corroborated by abundant literature [22] [23] [24] [25]. This discrepancy can be explained by:

- The fact that no instructions were given to patients to change their eating habits, so there may be a bias in patients who have eaten a meal high in salt shortly before their blood sample, since it has been shown that a meal containing salt had an immediate and significant effect on plasma sodium [26].
- The number of measurements of plasma Na per patient: the patients subject to the 3rd dialysis session of the day had less available plasma Na numbers (and thus more missing data) than those of the 1st and 2nd session because of the non-availability of the laboratory, which creates a selection bias.
- The plasma Na measurement technique: could lack precision (possible calibration error...)

6. Strengths and Limitations

Our study presents several strengths in particular: the prospective nature of the study allowing a considerable reduction of the information bias, as well as a sufficient number of patients' observations allowing a statistical analysis of quality.

However, it also has some limitations:

- Presence of other potential confounding factors unmeasured in our study and therefore not taken into account during the analysis, such as: glycemia, inter-dialytic salt intake, nutritional status (albuminemia), residual diuresis, etc.
- BPs measured in the hemodialysis center may still be inaccurate, despite the fact that we insisted to follow a standardized measurement protocol.
- Even if our study shows a positive correlation between IDWG and predialytic BP, a causal link between these two variables cannot be retained, because the study responds to an observational design not an interventional one.

7. Conclusions

In conclusion, our study demonstrates that IDWG is significantly associated with predialytic systolic and diastolic BP in hemodialysis patients.

However, although the relationship between IDWG and BP is statistically significant, the magnitude of the relationship remains modest, suggesting the interaction of several factors, in addition to IDWG, in BP control in the dialysis patient.

Broader cohorts are needed to deepen the understanding of IDWG role in BP regulation in dialysis patients.

Ethical Consent

The ethical consent has been provided by the ethical committee of Rabat Faculty of Medicine and Pharmacy.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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