2018

Measuring the prevalence of intradialytic hypotension in a satellite dialysis clinic: Are we too complacent?

Ulrich Steinwandel
Edith Cowan University

Nick Gibson
Edith Cowan University

Mandy Towell-Barnard
Edith Cowan University

Richard Parsons

James J. R. Rippey

See next page for additional authors

10.1111/jocn.14309
This is an author's manuscript of:
Steinwandel, U., Gibson, N., Towell-Barnard, M., Parsons, R., Rippey, J. J. R., & Rosman, J. (2018). Measuring the prevalence of intradialytic hypotension in a satellite dialysis clinic: Are we too complacent?. *Journal of Clinical Nursing, 27*, e1561-e1570. doi:10.1111/jocn.14309
Available here.

This is the peer reviewed version of the following article: Steinwandel, U., Gibson, N., Towell-Barnard, M., Parsons, R., Rippey, J. J. R., & Rosman, J. (2018). Measuring the prevalence of intradialytic hypotension in a satellite dialysis clinic: Are we too complacent?. Journal of Clinical Nursing*, 27, e1561-e1570. doi:10.1111/jocn.14309. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions.*

MEASURING THE PREVALENCE OF INTRADIALYTIC HYPOTENSION IN A SATELLITE DIALYSIS CLINIC: ARE WE TOO COMPLACENT?

Abstract

Aims and objectives

Measuring the prevalence of symptomatic (S-IDH) and asymptomatic intradialytic hypotension (A-IDH) or post-dialysis overhydration in a satellite haemodialysis clinic in Western Australia.

Background

Intradialytic hypotension is one of the most common side-effects of haemodialysis caused by ultrafiltration provoking a temporary volume depletion. The prevalence of asymptomatic hypotension during dialysis has been rarely reported, but is considered to have the same negative consequences as symptomatic hypotension on various end organs like the brain and the gastro-intestinal tract.

Design

Observational study on a retrospective 3-month period of nurse - recorded fluid related adverse events.

Methods

Data collection on the occurrence of S-IDH and A-IDH during a total of 2357 haemodialysis treatments in 64 patients. Body weight of patients at the time of cessation of treatment was recorded, and patients whose weight exceeded their ideal body weight by at least 0.5 kg, were classified as overhydrated.
Data analysis was performed using SPSS version 24 software.

Results

Symptomatic intradialytic hypotension was the most common adverse event measured in this cohort, and occurred during 221 (9.4%) of all treatments, whereas asymptomatic intradialytic hypotension occurred in 88 (3.7%) of all treatments. Total occurrence of intradialytic hypotension was 13.1% and symptomatic was observed in 30 patients, implying that nearly every second patient had at least one symptomatic episode within three months. Overhydration occurred in a total of 103 (4.4%) of all treatments, and involved 17 patients.

Conclusions

Symptomatic and asymptomatic intradialytic hypotension were the most commonly observed adverse events in this cohort, overhydration occurrence was considerably less common.

Keywords

Symptomatic intradialytic hypotension, asymptomatic intradialytic hypotension, haemodialysis, overhydration, fluid overload, satellite dialysis, renal nurses

Introduction

Despite numerous technical improvements, intradialytic hypotension (IDH) is still a classical problem in satellite dialysis clinics. Previous literature has reported very divergent rates of occurrence, ranging from 20-60%(Rocha, Sousa, Teles, Coelho, & Xavier, 2015; Schiller, Arramreddy, & Hussein, 2015). There is more evidence emerging about the damaging effects of IDH (Chao, Huang, & Yen, 2015; McIntyre, 2010) causing morbidity and increased mortality rates in haemodialysis patients(Flythe, Xue, Lynch, Curhan, & Brunelli, 2015). Therefore, awareness of IDH warrants the attention of all renal healthcare professionals involved in direct patient care (Ghaffar & Easom, 2015).
Primarily, each IDH event has a critical impact on the quality of life of haemodialysis patients and is responsible for significant patient symptoms like cramps, fatigue, nausea and vomiting, dizziness and loss of consciousness (S-IDH). Asymptomatic IDH (A-IDH) has been defined as a systolic blood pressure (SBP) drop of 20 mmHg or more according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines(National Kidney Foundation Inc., 2005), but

without any clinical symptoms. Multiple definitions for IDH exist, ranging from intradialytic SBP drop combined with nursing interventions like saline bolus administration and pausing of ultrafiltration. (Flythe et al., 2015). Other IDH definitions focus solely on intradialytic SBP assessment with the precondition of a SBP drop of 20-40 mmHg or nadir SBP of 90-100 mmHg (Dheenan & Henrich, 2001; Flythe et al., 2015). However, the combination of SBP fall with SBP nadir of less than 110 mmHg has also been commonly accepted as IDH definition (Flythe et al., 2015; Imai et al., 2006). IDH also has damaging effects on a variety of organ systems. There is sufficient evidence that any event of an IDH, either symptomatic or asymptomatic, qualifies as an ischemic insult (Bradshaw & Bennett, 2015; Daugirdas, 2015; Davenport, 2015). It has been reported that it adversely affects end organs including the brain, gastrointestinal tract and the heart, and causes deterioration of residual kidney function, as well as cardiac stunning and ischemic brain injury (McIntyre & Goldsmith, 2015). It has also been linked to vascular access thrombosis (VAT), insufficient dialysis dose and mortality (Flythe et al., 2015). In conclusion, IDH is harmful and every effort must be undertaken to avoid its occurrence. Daugirdas (2015) suggested that by measuring the incidence of IDH, the quality of care could be improved, as it would then come to the attention of renal healthcare providers who could evaluate their existing IDH preventive methods. This measure could prompt quality improvement measurements for the improved awareness, identification and prospective treatment of IDH. It could also lead to important changes in policy and practice to reduce IDH prevalence.
As we try to achieve euvolemia during haemodialysis, using ultrafiltration, sometimes this goal cannot be achieved for multiple reasons. This can result in post-treatment overhydration (OH), in some way converse to IDH, and has been described as strongly linked to left ventricular hypertrophy (LVH) and increased morbidity and mortality (Huang, Filler, Lindsay, & McIntyre, 2015).

Materials and Methods

Study design

Retrospective observational study of 64 patients over a period of 3 consecutive months from June to August 2015. A total of 2357 dialysis treatments were investigated for the occurrence of S-IDH, A-IDH and OH.

Setting, sample and data collection

A regional satellite haemodialysis unit in Western Australia (WA) was selected for this observational study. Ethics approval was obtained by the South Metropolitan Health Service Human Research Ethics Committee, the Human Research Ethics Committee of Edith Cowan University and the Western Australian Aboriginal Health Ethics Committee prior to this project. Renal nurses in this unit are required to create a patient progress report after each haemodialysis treatment. This report contains information about transcribed pre- and post-treatment weight, ideal body weight (IBW), ultrafiltration (UF) goal and multiple blood pressure recordings over the course of the haemodialysis treatment. Any significant clinical events which were considered to be treatment related or indicative of the current clinical condition, are also routinely recorded. Each patient progress report summarized the course of the treatment. Events of S-IDH were documented, following the definition of the K/DOQI guidelines (National Kidney Foundation Inc., 2005), as a fall in systolic blood pressure of at least 20 mm Hg together with at least two of the symptoms including abdominal discomfort, yawning, sighing, nausea, vomiting, muscle cramps, restlessness, dizziness or fainting and anxiety. A-IDH was recorded where the systolic blood pressure fell at least 20 mmHg, but with no further recorded clinical symptoms in the patient progress report. Patients were classified to be OH, when their post-treatment weight exceeded at least 0.5 kg of their IBW.

Study population

Patients with chronic kidney disease attended maintenance haemodialysis three times per week, one group of patients attended the clinic for haemodialysis on Monday, Wednesday and Friday (MWF) and the other group attended on Tuesday, Thursday and Saturday (TTS). Demographic data were recorded for each participant, and included: gender, age, ethnicity (self-declared), cause of kidney disease and socio-economic status (SES). The definition of SES was taken from the “Postal Area (POA) Index of Relative Socio-economic Advantage and Disadvantage, 2011” released by the Australian Bureau of Statistics under the Socio-economic Indexes for Areas (SEIFA). Patients were coded according to the SEIFA index corresponding to their residential postcode and classified as belonging to either “lower”, “lower-medium”, “upper-medium” or “high” socio-economic status. Comparison of the groups (MWF and TTS) with respect to their demographic data was performed

using the Chi-square test or t-test as appropriate. Occurrence of outcomes (SIDH, AIDH, and OH) following each treatment were analyzed using a generalized estimating equation (GEE). This model was used so that correlations between outcomes for treatments belonging to the same patient could be taken into account. Similarly, to a logistic regression, the results of the GEE model were expressed as odds ratios, their 95% confidence intervals and p-values. The GEE model was used to assess possible relationships between the independent variables (demographic variables as well as month, day of treatment, day number of treatment, duration of treatment) and the occurrence of any IDH (S-IDH or A-IDH), and OH. Data analyses were conducted using the SPSS version 24 statistical software, and, following convention, a p-value<0.05 was taken to indicate a statistically significant association in all tests.

Results

There were 64 patients included for study: 45 (70.3%) male and 19 females (29.7%). Patients were predominantly Caucasian (61%) or Indigenous Australian (IA) (20%). There were 34 patients treated on MWF, and 30 on TTS, and these 2 groups were found to be similar for all baseline characteristics (Table 1). Mean age overall was 63.0 years (SD 15.8), with most ages ranging from 48 to 72 years except for some skewness towards the older age groups (two patients were older than 88 years).

Table1. Baseline demographics of MWF and TTS group (person-based)

	MWF group	TTS group	Total	
	(n= 34)	(n=30)	(n=64)	*p* Value
Male, *n* (%)	25 (73.5)	20 (66.7)	45 (70.3)	0.55
Female, *n* (%)	9 (26.5)	10 (33.3)	19 (29.7)	
Age, (yr)				
Mean (SD)	62.6 (16.5)	63.3 (15.3)	63 (15.8)	0.86*
Race, *n* (%)				0.3
Caucasian	18 (52.9)	21 (70)	39 (60.9)	
Australian Aboriginal	6 (17.6)	7 (23.3)	13 (20.3)	
Asian	6 (17.6)	2 (6.7)	8 (12.5)	
Indonesian	2 (5.9)	0	2 (3.1)	
Indian	1 (2.9)	0	1 (1.6)	
Tongan	1 (2.9)	0	1 (1.6)	
Cause of ESRD, *n* (%)				0.73
Diabetes mellitus	11 (32.4)	7 (23.3)	18 (28.1)	
Glomerulonephritis	9 (26.5)	7 (23.3)	16 (25)	
Hypertension	3 (8.8)	5 (16.7)	8 (12.5)	
Reflux nephropathy	3 (8.8)	4 (13.3)	7 (10.9)	
Polycystic kidney disease	2 (5.9)	3 (10)	5 (7.8)	
Alport syndrome	2 (5.9)	0	2 (3.1)	
FSGS	1 (2.9)	1 (3.3)	2 (3.1)	
Nephropathy unknown gen.	1 (2.9)	1 (3.3)	2 (3.1)	
Ischemic nephropathy post AAA repair	1 (2.9)	0	1 (1.6)	
Renal cell ca	1 (2.9)	0	1 (1.6)	
Vasculitis	0	1 (3.3)	1 (1.6)	
Pyelonephritis	0	1 (3.3)	1 (1.6)	
Treatment Duration, *n* (%)				0.88
3 hr	1 (2.9)	1 (3.3)	2 (3.2)	
3.5 hr	1 (2.9)	2 (6.7)	3 (4.8)	
4 hr	24 (70.6)	20 (66.7)	43 (68.3)	
4.5 hr	4 (11.8)	2 (6.7)	6 (9.5)	
5 hr	4 (11.8)	5 (16.7)	9 (14.3)	

Baseline demographics were similar in both patient cohorts with a similar distribution of the causes of end-stage renal disease (ESRD). The most common causes of ESRD were diabetes mellitus, glomerulonephritis and hypertension, followed by reflux nephropathy and polycystic kidney disease. No significant difference was observed between groups for cause of renal failure ($\chi^2 = 7.76$, df = 11, p = 0.73). Most patients received 4 h haemodiafiltration (HDF) per treatment, while significantly less attended 4.5 or 5 h treatment. Only five patients were on a schedule of 3.5 h or less. Again, there was no significant difference between the groups when observing for treatment duration ($\chi^2 = 1.18$, df = 4, p = 0.88). (Table1)

S-IDH occurred during 221 treatments and A-IDH was observed during 88 treatments, resulting in a total of 309 (13.1%) treatments with any form of IDH. OH developed less frequently, in only 103 of all treatments (4.4%) and only in 17 patients, but interestingly 11 of the OH patients also had IDH episodes on different days. 6 patients had repeated OH episodes. More than half of all patients had at least one episode of IDH during the observation period, while a third had at least two or more IDH episodes. With increasing duration of the dialysis session, a higher frequency of IDH events was observed. The highest incidence of S-IDH or A-IDH was 23.6%, observed in the patient group receiving 4.5 h treatment, followed by the 5 h treatment group with an incident rate of 22.3% of all treatments. Shorter treatments of 3 to 4 h had significantly fewer IDH episodes. There was a significant difference between various treatment durations for the occurrence of any IDH ($\chi^2 = 65.35$, df = 4, p <0.001). In contrast, the shorter the treatment, the more OH events occurred, peaking at 18.6% OH in the 3 h group, also demonstrating a significant difference between treatment durations ($\chi^2 = 53.03$, df = 4, p <0.001). Females had a higher rate of IDH than male patients ($\chi^2 = 6.45$, df = 1, p = 0.01). At the time of leaving the dialysis unit, females also had slightly more episodes (5.1%) of overhydration than males (4.1%), but with no statistically significant difference.

Most episodes of IDH developed in patients with diabetes and hypertension, followed by those with glomerulonephritis and reflux nephropathy ($X^2 = 15.25$, df = 4, p = 0.04). Polycystic kidney disease, focal segmental glomerulosclerosis (FSGS) ranked much lower with only 2 to 8 % of all treatments. Interestingly, two patients with Alport syndrome had the highest occurrence of OH, followed by patients with hypertension and diabetes mellitus ($X^2 = 51.06$, df = 11, p <0.001).

With regard to ethnicity, it was observed that IAs experienced the highest occurrence of IDH events. Caucasian patients had slightly fewer IDH events, but without a significant difference between these groups. However, patients of Asian origin showed an event rate of IDH which was significantly lower than both IAs and Caucasians ($X^2 = 14.28$, df = 2, p= 0.001). Asian patients also had the lowest event rate of OH compared to all other ethnicities. In contrast, most OH events occurred in IAs followed by Caucasians ($X^2 = 25.8$, df = 2, p<0.001).

There were only marginal differences in events across months. August had a slightly higher event rate of IDH than June and July. This was similar for OH. The highest occurrence of IDH was noted on a Friday, followed by Monday and Saturday. (Table2)

Table2. Occurrence of S-IDH, A-IDH, any IDH and OL (treatment-based)

	N	S-IDH	A-IDH	Any IDH	OH
Treatments, *n (%)*	2357 (100)	221 (9.4)	88 (3.7)	309 (13.1)	103 (4.4)
Female, *n* (%)	680 (28.9)	75 (11)	33 (4.9)	108 (15.9)	35 (5.1)
Male, *n* (%)	1677 (71.1)	146 (8.7)	55 (3.3)	201 (12)	68 (4.1)
Duration, *n* (%)					
3 h	86 (3.6)	7 (8.1)	2 (2.3)	9 (10.4)	16 (18.6)
3.5 h	114 (4.8)	10 (8.8)	3 (2.6)	13 (11.4)	1 (0.9)
4 h	1564 (66.4)	126 (8.1)	26 (1.7)	152 (9.8)	53 (3.4)
4.5 h	238 (10.1)	33 (13.9)	23 (9.7)	56 (23.6)	17 (7.1)
5 h	355 (15.1)	45 (12.7)	34 (9.6)	79 (22.3)	16 (4.5)
Cause of ESRD, *n* (%)					
Diabetes mellitus	658 (27.9)	78 (11.9)	33 (5)	111 (16.9)	40 (6.1)
Hypertension	278 (11.8)	30 (10.8)	10 (3.6)	40 (14.4)	21 (7.6)
Glomerulonephritis	606 (25.7)	47 (7.8)	28 (4.6)	75 (12.4)	12 (2)

Reflux nephropathy	271 (11.5)	26 (9.6)	4 (1.5)	30 (11.1)	9 (3.3)
Polycystic kidney disease	170 (7.2)	7 (4.1)	2 (1.2)	9 (5.3)	2 (1.2)
FSGS	79 (3.4)	3 (3.8)	3 (3.8)	6 (7.6)	0
Alport syndrome	77 (3.3)	2 (2.6)	0	2 (2.6)	11 (14.3)
Nephropathy unknown gen	218 (9.2)	0	0	0	4 (5.7)
Ethnicity, *n* (%)					
Caucasian	1416 (60.1)	141 (10)	47 (3.3)	188 (13.3)	52 (3.7)
Indigenous Australian	492 (20.9)	57 (10.8)	30 (5.7)	87 (16.5)	43 (8.2)
Asian	449 (19)	23 (5.5)	11 (2.7)	34 (8.2)	8 (1.9)
Month of year, *n* (%)					
June	798 (33.9)	58 (7.7)	29 (3.9)	87 (11.6)	34 (4.5)
July	809 (34.3)	69 (8.5)	25 (3.1)	94 (11.6)	30 (3.7)
August	750 (31.8)	94 (11.8)	34 (4.3)	128 (16.1)	39 (4.9)
Day of week, *n* (%)					
Monday	407 (17.3)	45 (10.3)	20 (4.6)	65 (14.9)	37 (8.5)
Tuesday	373 (15.8)	33 (8.8)	11 (2.9)	44 (11.8)	26 (7)
Wednesday	397 (16.8)	31 (7.8)	15 (3.8)	46 (11.6)	16 (4)
Thursday	366 (15.5)	32 (8.7)	10 (2.7)	42 (11.5)	8 (2.2)
Friday	405 (17.2)	38 (9.4)	23 (5.7)	61 (15.1)	10 (2.5)
Saturday	409 (17.4)	42 (11.1)	9 (2.4)	51 (13.5)	6 (1.6)

Monday and Tuesday had the highest occurrence rates for any IDH with 14.0%, followed by Friday (MWF) and Saturday (TTS) (13.8% combined). The midweek-day had the least occurrence of IDH in both groups with 11.5%, demonstrating significant difference. There was a series of treatments which were scheduled for a Sunday. These showed an unusual level of increase in IDH events. As this was not part of the normal process of regular dialysis treatments, we removed them from data analysis. OH was most frequent on Mondays in the MWF group and Tuesdays in the TTS group (Table3).

Table3. Occurrence of S-IDH, A-IDH, any IDH and OL in the combined MWF and TTS groups (treatment-based)

	Treatments	S-IDH	A-IDH	Any IDH	OH
Events during treatments per Days of week, *n* (%)					
Monday and Tuesday	780 (33.1)	78 (10.0)	31 (4.0)	109 (14.0)	63 (8.1)
Wednesday and Thursday	763 (32.3)	63 (8.3)	25 (3.3)	88 (11.5)	24 (3.2)
Friday and Saturday	814 (34.6)	80 (9.8)	32 (3.9)	112 (13.8)	16 (2.0)

A Generalized Estimating Equation (GEE) was performed to assess the impact of several factors on the likelihood of the event of any form of IDH. The model initially contained 10 independent variables (gender, age, ethnicity, cause, duration of treatment, month of year, day of treatment, day of treatment, socio-economic status and group). An exchangeable variance structure was used to model the intra-patient correlations, and the method of backward elimination was used to exclude non-significant results. The final model to investigate the occurrence of any form of IDH contained the predictors gender, age, cause, month of year, day of treatment and duration (Table4).

Table4. *Generalized Estimating Equation (GEE) model predicting likelihood of any IDH events by gender, age, ethnicity, cause, group, day of week, month, day of treatment, duration and socio-economic status*

Predictor	Number (%) of any IDH events N(%)	Odds Ratio (OR)	95% C.I. Lower	95% C.I. Upper	p-value
Patient's Gender					
Female	108 (15.9)	1.71	1.001	2.92	0.050
*Male	201 (12)	1 (reference)	.	.	.

Patient's Age					
24 -90 years	309 (13.1)	1.02	1.001	1.04	0.038
Cause					0.004
Glomerulonephritis	75 (12.4)	0.44	1.22	2.88	0.020
Hypertension	40 (14.4)	0.84	0.34	2.04	0.693
Reflux Nephropathy	30 (11.1)	1.21	0.51	2.89	0.662
Other	17 (8.3)	0.58	0.27	1.26	0.166
*Diabetes	111 (16.9)	1 (reference)	.	.	.
Month					0.033
*June	87 (11.6)	1 (reference)	.	.	.
July	94 (11.6)	1.002	0.75	1.38	0.992
August	128 (16.1)	1.54	1.05	2.26	0.027
Day of treatment					0.371
*Monday or Tuesday	109 (13.4)	1 (reference)	.	.	.
Wednesday or Thursday	88 (11.6)	0.84	0.62	1.14	0.266
Friday or Saturday	112 (14.3)	1.06	0.76	1.46	0.739
Duration					<0.001
3 h/ 3.5 h	22 (10.9)	1.1	1.08	1.36	0.032
*4 h	152 (9.8)	1 (reference)	.	.	.
4.5 h	56 (23.6)	3.08	1.47	6.45	0.003
5 h	79 (22.3)	3.6	1.82	7.12	<0.001

*Note: * variable used as the reference variable.*

The results of this model showed that females had almost twice the odds of experiencing any form of IDH in comparison to males. Patients with glomerulonephritis had significantly lower odds of an IDH event when compared to those with diabetes. There was also a much higher likelihood of IDH in August than in June or July. While no statistical significance was found for the day of treatment, treatment duration had an important impact on predicting IDH. Longer treatment hours had a threefold higher chance of IDH in the 4.5 h group and 3.6-fold higher in the 5 h group respectively, in comparison to the 4 h patient group. Patients receiving 3 h treatment had 10% higher chance of experiencing IDH. There was no statistical significance when observing for day of treatment, ethnicity, group or socio-economic status.

A GEE model was also applied to predict the probability of postdialytic overhydration (OH) initially using the same independent variables as in the previous model for IDH. By eliminating the non-significant results the final model contained the variables age, duration, day of treatment and cause (Table5).

Table5.*Generalized Estimating Equation (GEE) model predicting likelihood of overhydration (OH) events by gender, age, ethnicity, cause, group, day of week, month, day of treatment, duration and socio-economic status*

Predictor	Number (%) of OH events N(%)	Odds Ratio (OR)	95% C.I.		p-value
			Lower	Upper	
Patient's Age					
24 -90 years	103 (14.4)	1.06	1.03	1.09	<0.001
Day of treatment					
Monday or Tuesday	63 (7.7)	5.65	2.14	14.93	<0.001
Wednesday or Thursday	24 (3.1)	1.38	0.57	3.34	0.476
*Friday or Saturday	16 (4.1)	1 (reference)	.	.	.
Ethnicity					
Caucasian	52 (3.7)	1 (reference)	.	.	.

Indigenous Australian	43 (8.2)	1.94	1.46	11.97	0.008
Other	8 (1.9)	0.47	0.83	5.54	0.113
Duration					
3 h / 3.5 h	17 (18.9)	0.05	1.32	2.89	<0.001
4 h	53 (3.4)	0.53	0.23	1.20	0.129
4.5 h	17 (7.1)	0.14	1.57	3.88	<0.001
*5 h	16 (4.5)	1 (reference)	.	.	.
Cause					
Diabetes mellitus	40 (6.1)	0.35	0.12	1.01	0.051
Hypertension	21 (7.6)	0.15	1.34	3.63	0.010
Glomerulonephritis	12 (2)	1.12	0.22	5.62	0.892
Reflux Nephropathy	9 (3.3)	0.83	0.25	2.77	0.763
*Other	17 (7)	1 (reference)	.	.	.

*Note: * variable used as the reference variable.*

Interestingly, this model revealed that patients had a more than 5 times higher chance to be overhydrated after the dialysis treatment on the first day of the week (Monday or Tuesday) than on a Friday or a Saturday). Patients receiving 3 h treatment had only a small, but statistically significant chance for the occurrence of postdialytic OH in comparison to patients receiving 5h treatment. Similarly, patients receiving 4.5 h treatment had a 14% higher likelihood of experiencing OH after their treatment. Diabetics and hypertensive patients had a higher risk of experiencing OH, compared to other causes. IA had almost double the risk than Caucasians to experience OH.

Discussion

This is the first study investigating the prevalence of S-IDH, OH and particularly A-IDH in a patient cohort over three months. As A-IDH has detrimental effects on various organ systems similarly to S-IDH, we considered it important to also investigate its occurrence. Combining the prevalence of A-IDH (3.7%) and S-IDH (9.4%) resulted in a total IDH prevalence of 13.1%, significantly greater than the occurrence of OH (4.4%). This highlights the magnitude of the IDH problem. Current National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines (National Kidney Foundation Inc., 2005) contain only recommendations for goals of pre- or postdialysis blood pressures, but do not recommend any frequency for monitoring intradialytic blood pressure measurements. When intradialytic blood pressure measurements are not performed routinely and continuously by nurses as standard practice, and if patients do not display any symptoms, A-IDH might occur frequently and yet remain undetected (Horkan, 2013). Moreover, some authors recommend intervening in the event of A-IDH as a pre-emptive method to improve long-term outcomes for patients and to decrease morbidity and mortality (Bradshaw & Bennett, 2015). Some authors have posited "…that the dialysis community has tacitly accepted that IDH is an innate feature of the HD treatment "(Schiller et al., 2015, p. 233) and is therefore not focused on its prevention and early identification. This highlights the need to also capture A-IDH events when analyzing IDH.

The study cohort of 64 patients included a relatively small number of female patients (n=19), but our results showed a higher percentage of IDH events amongst females than males. This is congruent with previous research where most IDH events occurred in older, female and diabetic patients (Sands et al., 2014). Our GEE model also confirmed this trend, where females had almost double the risk of experiencing an IDH compared to males (OR=1.71, 95% CI:1.001-2.92, p=0.05). As the reference group in the model, diabetics had not only the highest number of IDH events, but they also had the highest risk of suffering from IDH than any other disease group.

S-IDH peaked in the 4.5 h group and A-IDH peaked in the 5 h group. These findings were also confirmed by the GEE model. Patients receiving 3 h treatment had only a 35% reduced chance of any form of IDH (OR=0.65, 95% CI:0.44-0.96, p=0.03). In contrast, an individual with the maximum of 5 h treatment duration had more than 3.5 times the chance of experiencing IDH (OR=3.6, 95% CI:1.82-7.12, p<0.01). These findings stand in stark contrast with some authors who suggest, that an

expansion of treatment time, generally or on an individual basis, should reduce the incidence rate of IDH (Agar, 2016; Hossli, 2005) as this should reduce the ultrafiltration rate per hour. The higher occurrence of IDH episodes may be explained by large interdialytic weight gains (IDWG) resulting in higher ultrafiltration rates in some of the patients in our study. This assumption correlates with the findings of Schulz et al. (2007), where fewer episodes of IDH in patients with IDWG <1.5kg/2days were described. This is consistent with the findings of Santos, Peixoto, and Perazella (2012) where excessive IDWG was associated with more events of IDH. However, it is not unlikely that other additional factors, like intradialytic food intake, especially during increased treatment times or incorrect IBW might have contributed to a higher prevalence.

The policy of the dialysis unit in our study allowed for a maximum ultrafiltration rate (UFR) of 1000ml/h for each patient within the cohort, regardless of their individual IBW. While this might work for some patients well, it might be difficult for others, especially if their IBW is much lower than 100kg. Where UF removes too much intravascular plasma water, or removes it too rapidly, intravascular hypovolaemia may result (Caplin, Kumar, & Davenport, 2011). IDH is thought to be a direct consequence of this imbalance between excessive intravascular fluid removal and inadequate passive plasma refilling (Davenport, 2006). This is confirmed by Agar (2016) who has argued that extending treatment time would allow for additional time to remove fluid safely, especially for patients with larger IDWG. Agar (2016) also stresses the importance of an individual fluid removal (UFR) rate of only ≤10 ml/kg/hour as beyond that value morbidity, including hypotension, increases significantly. He further proposed a rather individualized treatment duration approach to minimize the risk of hypoperfusion of end organs. This recent and individualized approach is supported by several other authors (Flythe & Brunelli, 2011; Huang et al., 2015; Ludvigsen, Hermansen, & Lindberg, 2015). It is possible that in this study, some of the IDH events may have been caused by an unnecessarily high UFR. An individually tailored UFR approach could potentially mean fewer IDH events in the future for patients with extended treatment hours.

The comparatively low occurrence rate of OH post treatment demonstrates that most patients left the dialysis unit more often “dry” than “wet”. This trend is also confirmed by the lowest OH occurrence on the last day of the week in both groups (MWF=2.5% and TTS=1.6%) compared to Monday (MWF=8.5%) and Tuesday (TTS=7%). This is, on the one hand, a result of everyone’s efforts to achieve a maximum fluid removal per treatment by the end of the week, so it should be considered the most desirable outcome. On the other hand, seeing this in the light of the high number of events of IDH, it could reflect a poor outcome with an initially “good” treatment intention. The high risk of OH (OR5.65, 95%CI:2.14-14.93, $p<0.01$) on the first day of the week, seen in our results, could have several causes. Firstly, during the longer interval of the weekend, patients with little to no residual output function have simply more time to accumulate excess fluid. Secondly, as a precaution, nurses might not want to achieve exact IBW readings post-treatment already on the first day of the week, when a patient initially does not show any significant clinical signs of OH. Therefore, a nurse could then allow for a reduced or moderate UF goal, as the next treatment will follow after a relatively short time interval.

The highest frequency (16.5%) of any IDH episodes was noted amongst IAs. There are several factors that could influence this. It was noted that some patients in this group had repeatedly missed their regular scheduled treatment. For this reason, on the subsequent scheduled treatment they had more fluid to be removed to regain euvolemia, but concurrently had a higher risk of experiencing IDH with this temporarily larger IDWG. Considering that, of all ethnic groups, they also had the highest incidence rate of OH post treatment, it may have been the case that this patient group encountered more difficulty in adhering to fluid restriction and avoiding excessive oral fluid intake. Confirming this, the model revealed that IAs had nearly twice the risk compared to Caucasians of finishing their first treatment of the week overhydrated. Another reason for this fact could be a miscommunication between the nurses and IA when overhydration occurs. Cass et al. (2002) reported that miscommunication is common between non-indigenous health care professionals and Indigenous patients in haemodialysis units. Their study highlighted that this communication needs to improve for patients to better understand and adhere to treatment goals and that “fundamental change is required for Aboriginal patients to have significant input into the management of their illness” (Cass et al., 2002).

Excess fluid volume has been previously described as being directly associated with hypertension (Çelik, Kara, Yilmaz, & Apiliogullari, 2011) and an increased post dialytic blood pressure has been

correlated with elevated hydration status (Nongnuch et al., 2015). Conversely, Takeda, Toda, Fujii, Sasaki, and Matsui (2006) reported that additional antihypertensive medications, decreasing pre- and intradialytic blood pressures, was not associated with an increase in the frequency of IDH. These authors concluded that there is no correlation between predialytic and intradialytic blood pressure and the incidence of IDH. Interestingly we found in our study a high number (14.4%) of IDH events in patients with hypertension. This could be possibly caused by the nurses' assumption of hypertension being caused by excess fluid. Consequently, overestimating ultrafiltration goals and concurrently unaware of the genuine intravascular volume status of a patient, which could not have been validated as there were no tools for its specific measurement on hand. As *sometimes* excess fluid shows in some patients as a symptom of hypertension, some renal nurses may tend to assume that hypertension may *always* be a sign of hypervolemia. As then there are no other objective parameters available to assess intravascular volume, they may then tend to challenge the patients' dry weight, subsequently trying to remove more fluid, ultimately with the result of an IDH event. Additionally, the majority (65%) of the 17 overhydrated patients also had episodes of IDH during other treatments. This may either be due to unsuccessful attempts to remove excess fluid, or incorrectly assessed IBW.

Limitations

As an observational study, patients in this study were not randomized to their treatment days so the findings are not generalizable to the broader population. This study did not collect any data concerning the dialytic age, antihypertensive medication and the residual urine output from the patients. IBW assessments and adjustments during the study period were based only on clinical findings (the nurse's clinical assessment and BP measurements) therefore OH findings could not be validated with bioimpedance method.

Conclusion

IDH remains one the foremost adverse events for patients receiving haemodialysis. Adding the events of A-IDH, which may be generally underreported, to S-IDH, emphasizes the issue of IDH. Our study has confirmed that the problem of IDH is not only common, but even greater when A-IDH is included, increasing the total number of IDH episodes by almost a third. Modelling revealed that females had almost twice the risk of an IDH event, and patients with 4.5 h or more treatment time had more than three times the risk of an IDH event. It may be that this increased risk correlates with the general maximum UFR of 1000ml/h for every patient in our study unit, irrespective of their IBW. This undifferentiated approach has been associated with detrimental effects in previous studies. OH was significantly less frequently observed than IDH. Further, due to the lack of accurate and objective parameters for volume assessment, renal nurses can sometimes only roughly estimate how much UF could be too much for the patient they treat. Future research on the prevalence of IDH will need to include residual output of the participants as this may have a direct effect on the definition of UF goals which will subsequently affect the likelihood of IDH events. Dialysis units need more preventive strategies in place to reduce the prevalence of IDH and to improve health outcomes for patients.

Anecdotally, unit specific policies for IBW adjustment, maximum UFR and intervention protocols on symptomatic and asymptomatic IDH seem to vary greatly between dialysis units worldwide, but probably have a significant influence on the incidence of IDH. Most importantly, renal nurses and other healthcare providers in haemodialysis must be made aware of the existence of A-IDH and S-IDH and their adverse effects. Knowledge about the frequency of these events and patients most at risk can potentially increase their understanding of the "bigger picture" and long-term effects of the treatment they provide. Drawing their attention to this obvious problem could be one of the key features of future efforts to improve outcomes for patients. As renal nurses initiate treatments, decide on UF goals, UFR and constantly observe patients during haemodialysis, they need to be better equipped with knowledge about fluid shifts and the negative impact of IDH, whether combined with symptoms or not. Realizing and acknowledging the limitations of maximum UFR for each patient could potentially lead to beneficial changes in how renal nurses decide each day on treatment goals. Furthermore, use of existing and new objective fluid assessment tools like bioimpedance measurements (Body Composition Monitor – BCM Fresenius) or ultrasound of the inferior vena cava on a broader scale by more nurses could possibly result in better health outcomes. In summary, this has potential to increase the discussion amongst nurses and their patients at handover treatments

and upon treatment initiation. Therefore, all relevant aspects of the decision-making process by nurses upon treatment initiation should be a most important subject for future research studies.

The results of this observational study highlight the unacceptably high prevalence of IDH on a day-to-day basis and that renal nurses need more objective parameters to measure and assess information prior to and during haemodialysis treatments to evaluate the intravascular volume status.

Relevance to clinical practice

The high occurrence of hypotension related events demonstrates that ultrafiltration treatment goals in satellite dialysis clinics are sometimes overestimated, resulting in regular significant symptomatic episodes for the patient. Raising the awareness on the prevalence of IDH amongst renal nurses could be an essential initial step before collectively preventative strategies in haemodialysis satellite units are implemented.

Conflict of interest

The authors declare that there is no conflict of interest.

References

Agar, J. W. (2016). Personal viewpoint: Limiting maximum ultrafiltration rate as a potential new measure of dialysis adequacy. *Hemodial Int, 20*(1), 15-21. doi: 10.1111/hdi.12288

Bradshaw, W., & Bennett, P. N. (2015). Asymptomatic Intradialytic Hypotension: The Need for Pre-Emptive Intervention. *Nephrology nursing journal : journal of the American Nephrology Nurses' Association, 42*(5), 479-485; quiz 486.

Caplin, B., Kumar, S., & Davenport, A. (2011). Patients' perspective of haemodialysis-associated symptoms. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 26*(8), 2656-2663. doi: 10.1093/ndt/gfq763

Cass, A., Lowell, A., Christie, M., Snelling, P. L., Flack, M., Marrnganyin, B., & Brown, I. (2002). Sharing the true stories: improving communication between Aboriginal patients and healthcare workers. *The Medical journal of Australia, 176*(10), 466-470.

Çelik, G., Kara, I., Yilmaz, M., & Apiliogullari, S. (2011). The Relationship between Bioimpedance Analysis, Haemodynamic Parameters of Haemodialysis, Biochemical Parameters and Dry Weight. *Journal of International Medical Research, 39*(6), 2421-2428. doi: 10.1177/147323001103900643

Chao, C.-T., Huang, J.-W., & Yen, C.-J. (2015). Intradialytic hypotension and cardiac remodeling: a vicious cycle. *BioMed research international, 2015*, 724147. doi: 10.1155/2015/724147

Daugirdas, J. T. (2015). Measuring intradialytic hypotension to improve quality of care. *J Am Soc Nephrol, 26*(3), 512-514. doi: 10.1681/ASN.2014090860

Davenport, A. (2006). Intradialytic complications during hemodialysis. *Hemodialysis International, 10*(2), 162-167. doi: 10.1111/j.1542-4758.2006.00088.x

Davenport, A. (2015). Will Incremental Hemodialysis Preserve Residual Function and Improve Patient Survival? *Seminars in dialysis, 28*(1), 16-19. doi: 10.1111/sdi.12320

Dheenan, S., & Henrich, W. L. (2001). Preventing dialysis hypotension: A comparison of usual protective maneuvers. *Kidney international, 59*(3), 1175-1181. doi: 10.1046/j.1523-1755.2001.0590031175.x

Flythe, J. E., & Brunelli, S. M. (2011). The Risks of High Ultrafiltration Rate in Chronic Hemodialysis: Implications for Patient Care. *Seminars in Dialysis, 24*(3), 259-265. doi: 10.1111/j.1525-139X.2011.00854.x

Flythe, J. E., Xue, H., Lynch, K. E., Curhan, G. C., & Brunelli, S. M. (2015). Association of mortality risk with various definitions of intradialytic hypotension. *Journal of the American Society of Nephrology : JASN, 26*(3), 724-734.

Ghaffar, U., & Easom, A. K. (2015). A quality improvement project: Strategies to reduce intradialytic hypotension in hemodialysis patients. *Nephrology news & issues, 29*(5)

Horkan, A. (2013). Fifteen-Minute versus Thirty-Minute Blood Pressure Evaluation During Chronic Hemodialysis. *Nephrology Nursing Journal, 40*(3), 255-258. doi: 10.1111/j.1525- 139X.2009.00643.x

10.1053/ j.ackd.2012.03.003

Hossli, S. M. (2005). Clinical management of intradialytic hypotension: survey results. *Nephrology nursing journal : journal of the American Nephrology Nurses' Association, 32*(3), 287.

Huang, S.-H. S., Filler, G., Lindsay, R., & McIntyre, C. W. (2015). Euvolemia in hemodialysis patients: a potentially dangerous goal? *Seminars in Dialysis, 28*(1), 1-5. doi: 10.1111/sdi.12317

Imai, E., Fujii, M., Kohno, Y., Kageyama, H., Nakahara, K., Hori, M., & Tsubakihara, Y. (2006). Adenosine A1 receptor antagonist improves intradialytic hypotension. *Kidney Int, 69*(5), 877-883. doi: 10.1038/sj.ki.5000088

Ludvigsen, M. S., Hermansen, H. M., & Lindberg, M. (2015). The quality of nursing care during intradialytic fluid removal in haemodialysis: time to change practice? *Journal of Clinical Nursing, 24*(11-12), 1733-1736. doi: 10.1111/jocn.12735

McIntyre, C. W. (2010). Recurrent circulatory stress: the dark side of dialysis. *Seminars in Dialysis, 23*(5), 449-451. doi: 10.1111/j.1525-139X.2010.00782.x

McIntyre, C. W., & Goldsmith, D. J. (2015). Ischemic brain injury in hemodialysis patients: which is more dangerous, hypertension or intradialytic hypotension? *Kidney International, 87*(6), 1109-1115. doi: 10.1038/ki.2015.62

National Kidney Foundation Inc. (2005). K/DOQI Clinical Practice Guidelines for Cardiovascular Disease in Dialysis Patients. *American Journal of Kidney Diseases, 45*, 16-153. doi: 10.1053/j.ajkd.2005.01.019

Nongnuch, A., Campbell, N., Stern, E., El-Kateb, S., Fuentes, L., & Davenport, A. (2015). Increased postdialysis systolic blood pressure is associated with extracellular overhydration in hemodialysis outpatients. *Kidney International, 87*(2), 452-457. doi: 10.1038/ki.2014.276

Rocha, A., Sousa, C., Teles, P., Coelho, A., & Xavier, E. (2015). Frequency of intradialytic hypotensive episodes: Old problem, new insights. *Journal of the American Society of Hypertension,* doi: 10.1016/j.jash.2015.07.007

Sands, J. J., Usvyat, L. A., Sullivan, T., Segal, J. H., Zabetakis, P., Kotanko, P., . . . Diaz-Buxo, J. A. (2014). Intradialytic hypotension: Frequency, sources of variation and correlation with clinical outcome. *Hemodialysis International, 18*(2), 415-422. doi: 10.1111/hdi.12138

Santos, S. F. F., Peixoto, A. J., & Perazella, M. A. (2012). How Should We Manage Adverse Intradialytic Blood Pressure Changes? *Advances in Chronic Kidney Disease, 19*(3), 158-165. doi: 10.1053/j.ackd.2012.03.003

Schiller, B., Arramreddy, R., & Hussein, W. (2015). INTRA-DIALYTIC HYPOTENSION IN CONVENTIONAL HEMODIALYSIS Intra-dialytic Hypotension in Conventional Hemodialysis: Unavoidable in Some, but Preventable in Most. *Seminars in Dialysis, 28*(3), 233-235. doi: 10.1111/sdi.12356

Schulz, E. G., Wagner, F., Fischer, N., Wolf, A., Korth, U., & Weber, M. H. (2007). Body weight telemetry in patients with endstage renal failure on hemodialysis: preliminary data. *Deutsche medizinische Wochenschrift., 132*(9), 423.

Takeda, A., Toda, T., Fujii, T., Sasaki, S., & Matsui, N. (2006). Can predialysis hypertension prevent intradialytic hypotension in hemodialysis patients? *Nephron Clin Pract, 103*(4), c137-143. doi: 10.1159/000092910