Intradialytic Hypertension in End Stage Renal Disease patient : Prevalence and clinical characteristic

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Abstract

Introduction : Intradialytic hypertension (IDH) is common and it increases the incidence of cardiovascular morbidity and mortality, however this is often ignored. The aim of this study is to identify the prevalence of IDH and compare the clinical characteristics of patients with and without IDH.

Methods : A cross sectional study was carried out in 3 hemodialysis clinics in Jakarta, Indonesia. We compared several clinical characteristics inpatients with IDH and control group without IDH. Nutritional status was also assessed using Subjective Global Assessment (SGA). IDH was defined as >10 mmHg increase in systolic blood pressure (BP) in at least four of six prior consecutive hemodialysis sessions. Student's T-test or Mann-Whitney test was used to compare the quantitative variables. Chi-Square or Fischer exact test was used to compare categorical variables.

Results : A total of 114 patients was included in this study. There were 86 (62.3%) male patients. IDH was present in 47 (34.1%) patients. The mean age in IDH and control group were 53.4 (±13.2) and 52.8 (±12.4) years respectively (*p*: 0.800). The mean BMI of IDH and control group were 21.8 (±3.7) and 24.0 (±4.4) kg/m^2 respectively (*p*: 0.031). The mean MAP during dialysis of IDH and control group were 108 (±13.1) and 98.6 (±23.2)mmHg respectively (*p*: 0.011). The median creatinine levels of IDH and control group were 8.1 (3.02-22.20)mg/dl and 10.8 (2.89-22.0)mg/dl respectively (*p:* 0.008). Interestingly, moderate to severe malnutrition status had significant association with IDH (OR: 2.31, p: 0.031). Patients who undergo dialysis thrice a week was associated with IDH rather than patients who undergo dialysis twice a week (OR: 2.27, *p*: 0.035).

Conclusion : The prevalence of IDH is higher than previously reported in other countries. The clinical characteristic of patients with IDH is lower BMI, higher MAP and lower creatinine levels than in patient without IDH. Moderate to severe malnutrition and frequency of dialysis per week had significant association with IDH.

Introduction

The phenomenon of blood pressure (BP) rise during or immediately after hemodialysis which result in post dialysis hypertension is recognized for several years but it often largely ignored. There are no accepted criteria to define intradialytic hypertension (IDH).[1] In some studies, intradialytic hypertension was defined as rise in mean arterial pressure >15 mm Hg within or immediately post dialysis.[2] In others, a lower threshold was applied (>10 mm Hg increase in systolic pressure)[3,3] and in some an inclusive definition was adopted (BP rise of any degree during the second or third intradialytic hour).[5] Other definitions include increasing intradialytic BP that remains unresponsive to volume withdrawal and worsening of pre-existing hypertension or new-onset hypertension after administration of erythropoietic-stimulating agents (ESAs)[6]

Intradialytic hypertension occurs more frequently in patients who are older, have lower dry weights, are prescribed more antihypertensive medications, and have lower serum creatinine. Being often ignored, intradialytic hypertension has

been reported associated with adverse outcomes. Recent studies have demonstrated intradialytic hypertension to be independently associated with higher hospitalization rates and decreased survival. In other report, intradialytic hypetension has been suggested to associated with vascular event and metabolic disorders such as inflammation and chronic uncorrected metabolic acidosis.[7]

Pathophysiology of intradialytic hypertension is uncertain, it is likely multifactorial and includes subclinical volume overload, sympathetic overactivity, activation of the renin angiotensin system, endothelial cell dysfunction, specific dialytic techniques, the use of erythropoietin stimulating agents, removal of antihypertension medication and vascular stiffness.[8]

In this study we examine the prevalence of intradialytic hypertension in end stage chronic disease population, for as far of our knowledge no research has been performing for evaluating this in Indonesia and we also assessing the clinical characteristic of patients with intradialytic hypertension and without intradialytic patient in end stage chronic kidney disease.

Method

This is a cross sectional study, carried out in 3 hemodialysis clinic in Jakarta. The inclusion criteria is hemodialysis patient on regular basis (2 or 3 session per week), at least 18 years old and
agreeing to participate in the study. We compared characteristic such as age, gender, MI duration of hemodilaysis, hemoglobin, hematocrit, ureum, creatinin, sodium, potassium, calcium, uric acid, ferritin, erythrocyte, iron, total cholesterol, MAP, dry body weight, frequency of dialysis per week, nutritional status and difference in pre-post dialysis weight in patient with IDH and control group without IDH.
The BP measurement of patients before the hemodialysis session were measured in the supine position after five minutes of rest, right before connecting the patient, and those of the end of session. BP was measured after the extracorporeal blood circuit was restored. The measurements were carried out by dialysis technicians or nurses, using an electronic BP machine of the OMRON® type.

We calculate the difference between pre-dialysis and post dialysis SBP, mean pre and post dialysis pulse, pre and post dialysis heart rate and IDWG. IDH was defined as >10 mmHg increase in systolic BP in at least four to six prior consecutive hemodialysis session. We also collect data the characteristic of the patient include age, gender, BMI, duration of hemodialysis, hemoglobin, hematocrit, ureum, creatinin, sodium, potassium, calcium, uric acid, ferritin, erythrocyte, iron, total cholesterol, MAP, dry body weight and frequency of dialysis per week. All these data was collected using direct anamnesis and medical record. The patient's nutritional status were assessed using Subjective Global Assesment (SGA).

Statistical analysis

We used T-test or Mann-Whitney test to compare the quantitative variables. Chi square or fischer exact test was used to compare categorical variables. The threshold of significance was for $p \leq 0.05$

Result

There was a total of 114 patients included in this study. IDH was present in 47 (34.1%) patients. The baseline characteristic of the patients are shown in table 1. The mean age of the patients was 52.8 years (±12.5) and male is 75.4%. The duration of hemodialysis was 38.6 (±36.2) months. The etiology of CKD is hypertension 59.6%, hypertension 59.8% and others 9.6%. The mean BMI was 22.9 (±4.4) kg/m2. Normal nutritional status according to SGA 48.6%, moderately malnourished 43.9% and severe malnourish 7.9%.

Table 1

Baseline characteristic	
Age (years) [mean SD]	52.8 (±12.5)
Duration of hemodialysis (months) [mean SD]	38.6 (±36.2)
BMI (kg/m2) [mean SD]	22.9 (±4,2)
Gender	
Male	86 (5.4%)
Etiology of CKD	
Diabetes	35 (30.7%)
Hypertension	68 (59.6%)
Others	11 (9.6%)
Diabetes	43 (37.7%)
Hypertension	88 (77.2%)
Subjective Global Assesment	
Normal	55 (48.2%)
Moderately Malnourished	50 (43.9%)
Severely Malnourished	9 (0.9%)

The comparison between IDH and non IDH group was seen in table 2. Patient who undergo dialysis thrice a week was associated with IDH rather than patient who undergo dialysis twice a week with OR 2.27 and p 0.035. And interestingly the nutrition status was associated with IDH when moderate to severe malnourished had OR 2.31 than normal nutrition with p 0.031. Patient with IDH had lower BMI and lower serum creatinin level compare to non IDH.

Table 2

Variable	IDH group	Control group	p
Age (Mean[SD])	54.4 (±13.2)	52.8 (±12.4)	0.800
BMI (Mean[SD])	21.8 (±3.7)	24 (±4.4)	0.031
Gender			
Male	29 (61.7%)	43 (62.4%)	
Female	18 (38.3)	24 (35.8%)	
Duration of HD (Median[Min-Max])	24 (2-192)	30 (6-96)	0.136
Frequency of HD			0.035
3 times/week	25 (53.2%)	22 (33.3%)	
2 times/week	22 (46.8%)	44 (66.7%)	
Hemoglobin (Mean[SD])	8.6 (±1.7)	8.3 (±1.5)	0.299
Hematocrit (Mean[SD])	26.5 (±5.6)	27.4 (±5.2)	0.380
Ureum (Mean[SD])	122.5 (±52.2)	146.1 (±135.4)	0.219
Creatinin (Median[Min-Max])	8.1 (3,0-22.2)	10.8 (2.9-22.6)	0.008
Potassium (Mean[SD])	7.3 (±11.9)	5.4 (±4.9)	0.355
Calcium (Mean[SD])	8.9 (1-13)	8.5 (0.9-11.1)	0.559
Uric acid (Mean[SD])	5.6 (±2.2)	11.1 (±21.4	0.184
Ferritin (Mean[SD])	314.2 (±462.3)	611.7 (±478.6)	0.111
Erythrocyte (Mean[SD])	1.29 (±1.65)	1.23 (±1.58)	0.834
Iron (Median[Min-Max])	43.5 (3.84-103)	66.0 (12-25.8)	0.160
Total cholesterol (Mean[SD])	194.0 (±86.6)	175.1 (±71.6)	0.578
Mean Arterial Pressure (Mean[SD])	108.3 (±13.1)	98.6 (±23.2)	0.011
Dry body weight (Mean[SD])	59.5 (±13.4)	61.7 (±14.5)	0.435
Subjective Global Assesment			0.031
Moderate to severe malnutrition	30 (63.8%)	29 (43.3%)	
Normal	17 (36.2%)	38 (56.7%)	

Table 2. Present the characteristic of patient with IDH and factor associated with IDH compare to control which is BMI, duration of hemodialysis, serum creatinin level and moderate to severe malnutrition.

Discussion

The prevalence of IDH in our study is 34.1%. It was higher than that of the CLIMB study [9] as well as the WAVE 2 study[10] , which reported respective prevalence rates of 13.2% and 12% The noted prevalence of IDH in our study was alarming, as it is currently considered a risk factor for cardiovascular mortality.[11] Inrig et al. noted an increased risk of hospitalization and death at 6 months in patients who had an increase in BP by 10 mmHg during the hemodialysis session as compared to the patients whose BP decreased during the hemodialysis session.[12]

Post-dialysis SBP was also more significantly correlated with the ambulatory inter dialytic BP than pre-dialysis.[13] Its management is necessary and can be facilitated through the adequate management of the blood volume with the estimate of an ideal weight, individualization of hemodialysis parameters, and use of modules for retro control of ultrafiltration. It is also necessary to identify such associated factors to support them optimally.

To obtain a good BP control in dialysis patients, we must define the correct dry weight and individualize the adequate sodium concentration in dialysate, thus to achieve a zero intradialytic sodium balance.[13] Elevated sodium removal may be due to our trying to reach a dry weight lower than the correct one, which may have, as a consequence, intradialytic hypotensive episodes and muscle cramps, which can lead to the need for an increase in dialysate sodium concentration, thirst, and eventually greater interdialytic weight gain causing as a final result an ECV increase and hypertension.[14] Such a phenomenon is particularly exciting when a lower urine volume is combined, such as in our subjects with intradialytic hypertension.

In our study, factors that could influence the increase in SBP during the hemodialysis session were BMI, duration of hemodialysis, serum creatinin level and moderate to severe malnutrition. Other studies have reported that intradialytic hypertensive patients were older and had lower values of serum creatinine and lower dry weight that similar to our result. That may be explained by our studies that these patients are more likely to be malnourished and generally consume more liquids. In addition to this assumption is the fact that intradialytic hypertensive patients have statistically significant lower values of serum sodium, and accordingly, larger and statistically significant gradient of sodium compared to the control group, leading to an increase in serum sodium during dialysis (positive sodium balance) which probably stores in the interstitium as osmotic inactive sodium, leading to salt–sensitive hypertension, which is confirmed by other studies. The positive sodium gradient increases thirst, leading to increased fluid intake and extracellular volume expansion and subsequent development of hypertension. The increase in the mean arterial pressure and systolic pressure during and after hemodialysis is probably associated with the impaired endothelial function and increased secretion of endothelin-1 and increased peripheral resistance, and can occur without significant changes in cardiac stroke volume. Clinical characteristics associated with intradialytic BP rise include lower body weight, lower serum creatinine. Lower creatinine levels may contribute to small reductions in osmolarity during dialysis and this prevents the blood pressure from falling.

Malnutrition has already been reported as specific cardiovascular risk factors for dialysis patients and each of the malnutrition, inflammation, and atherosclerosis (MIA syndrome) components worsens the survival of these patients. Malnutrition may be related to metabolic acidosis due to increased protein catabolism, decreased protein synthesis, endocrine abnormalities, and inflammation among dialysis patients. Metabolic acidosis defined by low serum bicarbonate (<22 mmol/L) is a common condition in end stage renal disease patients resulting in inflammatory stimulation, lipids oxidation, and oxidative stress. Maintenance dialysis therapies are often unable to completely correct the base deficit. Previously, the association of uremic acidosis with arterial pressure has been reported in hypertensive patients.

The limitation of this study: Small number of participants, no assessment of intradialytic sodium balance, and the blood pressure is not measured during the interdialytic period by 24-hour ABPM

Conclusion

The prevalence of IDH is higher than previously reported in other countries. The clinical characteristic of patients with IDH is lower BMI, higher MAP and lower creatinine levels than in patient without IDH. Moderate to severe malnutrition and frequency of dialysis per week had significant association with IDH.

Disclaimer

The abstract of this study has been presented in 55th ERA EDTA congress in Copenhagen Denmark on May, 2018.

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