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Association Between Hypertension and Residual Renal Function in Hemodialysis Patients

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Abstract

Introduction. Cardiovascular diseases are the leading cause of death in hemodialysis patients. The decline of residual renal function increases the prevalence and severity of risk factors of cardiovascular morbidity and mortality in these patients. Hypertension is common in dialysis patients and represents an important independent factor of survival in these patients.

Methods. The study included 77 patients who are on chronic HD for longer than 3 months. Depending on the measured residual diuresis patients were divided into two groups. The study group consisted of patients with residual diuresis >250 ml/day, while patients from control group had residual diuresis <250 ml/day. All patients had their blood pressure measured before 10 consecutive hemodialysis treatments. Collected data were statistically analyzed using SPSS 16.0.

Results. The study included 77 hemodialysis patients, mean age of 56.56±14.6 years and mean duration of hemodialysis treatment of 24.0 months. Of the total number of patients, 39(50.6%) had preserved residual renal function. Hypertension was more common in the group of patients who did not have preserved residual renal function (68.4% vs 25.6%). There was statistically significant negative linear correlation between the volume of residual urine output and the residual clearance of urea and values of systolic blood pressure [(rho=-0.388; p<0.0001); (rho=-0.392; p<0.0005)], values of mean arterial pressure [(rho =-0.272; p<0.05); (rho=-0.261; p=0.023; p<0.05)] and values of pulse pressure in hemodialysis patients [(rho =-0.387; p<0.001); (rho=-0.400; p<0.0005)].

Conclusions. Residual renal function plays an important role in controlling blood pressure in patients on hemodialysis. More attention should be directed to preserve residual renal function, and after the start of hemodialysis by avoiding intensive ultrafiltration with optimal antihypertensive therapy.

Key words: hypertension, chronic renal failure, residual renal function

Introduction

Life expectancy among patients with chronic kidney disease (CKD), especially among those with end-stage renal disease (ESRD) has decreased, and is significantly lower than in the general population. The leading causes of morbidity and mortality among dialysis patients with ESRD are cardiovascular diseases (CVD), reported to be responsible for 50% mortality rate in these patients [1].

In 1995, Maiorca *et al*. were among the first to note an independent relationship between the presence of residual renal function and survival in patients on dialysis [2]. Residual renal function (RRF) is an important predictor of survival in peritoneal dialysis (PD) patients but its role in hemodialysis (HD) patients is less known. Loss of RRF is associated with higher arterial pressure, more severe anemia, greater degree of inflammation and malnutrition, and greater cardiac hypertrophy, all of which contribute to increased cardiovascular events in dialysis patients [3,7]. Thus, patients on hemodialysis (HD) had more rapid reductions in their RRF than those on peritoneal dialysis (PD) [4]. Hemodialysis seems to be worse than peritoneal dialysis (PD), probably because sudden drops in blood pressure are more likely in hemodialysis, since fluid is removed much more quickly during short hemodialysis sessions as compared to the longer treatment cycles in PD. A study conducted in the Netherlands showed an association between intradialytic hypotension/decrease in systolic blood pressure and decline of RRF [4,5]. These findings are corroborated by reported relations between diastolic blood pressure and decline of RRF [5,6]. A correlation between degree of volume expansion and urine output in a recent report has been used as the basis for suggesting that a certain degree of fluid overload may preserve RRF [7,14]. The CHOICE study provides evidence for several beneficial effects of RRF in HD patients. The study demonstrates a strong and independent relationship between a simply obtained urine output assess-

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ment and survival as well as improved QOL, lower inflammation and less EPO use in a national prospective cohort study of 734 incident HD patients [7].
RRF may be measured or estimated. The simplest measure of RRF is urine volume. Despite its shortcomings, urine volume has been correlated to GFR in studies, and most authors defined loss of RRF as estimated urine volume ≤ 200 mL/ 24 hour.
Aim of our stady was was the role of residual renal function in controlling blood pressure in patients with hemodialysis.

Material and methods

The study was conducted as intersection, prospective, clinical, comparative and descriptive study at the Clinic of Hemodialysis, Clinical Center of the University of Sarajevo. The study included 77 CKD patients.
Inclusion criteria: patients who received regular hemodialysis treatment three times a week, were age >18 and <75 years and agreed to participate in the study. The exclusion criteria were patients in hemodialysis treatment for less than three months and uncontrolled blood pressure. All patients provided informed consent for participation in the study. Depending on the measured residual diuresis patients were divided into two groups. The study group consisted of patients with residual diuresis >250 ml/day (n= 39), while patients from control group had residual diuresis <250 ml/day (n=38).
The following clinical and laboratory data of the groups were assessed: systolic blood pressure (SBP), diastolic blood pressure (DBP), length of hemodialysis treatment (LHT), urinary 24-hour volume (UV24hs), hemoglobin (Hb), serum calcium (Ca), serum phosphorus (P), parathormone (PTH), serum albumin (Alb).
All patients had their blood pressure measured before 10 consecutive hemodialysis treatments. The SBP and DBP were immediately obtained before the HD session using the arm opposite the AV fistula and represented the average of the last ten HD sessions. Mean arterial blood pressure (MAP) was calculated using the formula MAP= *(SBP-DBP)/3+DBP* and pulse pressure (PP) was calculated using the formula PP=*(SBP-DBP)*.
The residual urine output (UV) was collected during the interdialytic period. Interdialytic period is the time between two dialysis. (When postdialysis blood is collected for urea measurement, the patients empty their bladder. From this time, all urine collected and brought to dialysis unit when patient returns for the next dialysis).
In patients with residual diuresis residual clearance of urea was calculated using the following formula:

rCl U= (UV x UrU / ID Period) / Mean BUN

Mean BUN = (U1 + U2) / 2

UV -Urine Volume
ID -Interdialytic period
UrU -Urine Urea Concentation
U 2-the BUN just prior to the second dialysis of the week
U1-the BUN just after the first dialysis of the week

Interdialytic weight gain (iWG) represents the difference between body weight immediately after the HD session, and the weight obtained immediately before the next HD session. The iWG value was considered the arithmetic average of the last ten HD sessions. The assessment of adequacy of dialysis was done using the Kt/V index. Kt/V is defined as the dialyzer clearance of urea multiplied by the duration of the dialysis treatment divided by the volume of distribution of urea in the body.
Hypertension was determined according to the WHO criteria (office BP 140/90 and/or the use of antihypertensive therapy).

Blood analyses

All biochemical parameters were measured by commercial kits according to the manufacturer's instructions. Intact PTH was determined by immunoradiometrict assay on the gamma counter at the Institute of Nuclear Medicine, Clinical Center Sarajevo (reference range 10-65 pg/L, approximately three times the value of the upper limit of the reference interval is recommended for patients on dialysis). C-reactive protein CRP (reference range 0-5 mg/l) was measured by nephelometric method (quantitative measurement), and Hb-Hb (ref. range 138-175 g/L), serum calcium Ca (ref. 2 interval, 10 to 2.55 mmol/L, phosphorus P (ref. range 0.81 to 1.58 mmol/L) and serum albumin -Alba (ref. range from 35.0 to 50.0 g/L) were performed at the Institute of Clinical Chemistry and Biochemistry by standard laboratory procedures.

Statistical analysis

Measurements for normally distributed variables are reported as mean + standard error; median values and interquartile range are used to describe non-normaly distributed variables. Difference between the groups was assessed by the Student's t-test or Mann-Whitney U test. Values lower than 0.05 were considered significant. Spearman's correlation coefficient was used. Collected data were statistically analyzed using SPSS 16.0.

Results

The research involved 77(100%) hemodialysis patients, of whom 39(50.6%) had preserved residual renal function and residual diuresis >250 ml/24 hour.
The average diuresis of patients with preserved RRF was 1000.00 ml/24H (500.0-1300.00 ml/24H).
There was no evidence of a statistically significant difference in gender distribution of patients in comparison to other groups (p> 0.05).
The average age of patients in the study was 56.56±14.6 years. The average duration of hemodialysis treatment was 24.0 months (12.0 to 43.5 months). The average age

of patients with preserved RRF was less but not statistically significant compared to the average age of patients without preserved RRF. The median duration of hemodialysis treatment in the group of patients with preserved RRF was significantly lower than the mean value of the duration of hemodialysis treatment in the group of patients without preserved RRF. Average interdialytic weight gain in the group of patients with preserved RRF was also decreased significantly with respect to the average weight gain in the group of patients without preserved RRF (Table 1).

Primary renal diseases that led to the end-stage of renal failure in both groups were hypertension and diabetes mellitus, taking into concern that the group of patients without preserved RRF had more frequent hypertension, but not statistically significant (18 vs. 34%) (Table 1).

Table 1. Gender distribution, age, duration of hemodialysis treatment, interdialytic weight gain and primary renal disease in the observed group of patients

	With RRF		**Without RRF**		**p<**
	n	**%**	**n**	**%**	
Total	39	100	38	100	
Female/male?	25	64.1	28	73.3	ns
Female	14	35.9	10	26.3	ns
Age (years)	58.0		60.0		ns
Duration of HD (months)	16.0 (7.0-26.0)		38.0 (24.0-69.0)		0.0001
Interdialytic weight gain	2.4 (1.8 – 2.6)		3.5 (3.0 –4.0)		0.001
Hypertension	7	18	13	34	ns
Diabetes mellitus	9	23	8	22	ns
ADPKD	6	15	4	11	ns
GN chr	6	15	6	16	ns
Pn chr	6	15	3	8	ns
miscellaneous	4	10	3	8	ns
unknown	1	3	1	3	ns

Table 2 shows the value of clinical laboratory parameters in serum of hemodialysis patients with preserved and without residual renal function. C-reactive protein (CRP), phosphorus (P) and parathyroid hormone (PTH) levels in hemodialysis patients without preserved RRF were significantly higher compared to the same parameters in hemodialysis patients with preserved RRF. There were no significant differences in the concentrations of albumin, hemoglobin and calcium among patients with preserved RRF and those without preserved RRF.

Table 2. Clinical and laboratory parameters of groups

	With RRF (n=39)	**Without RRF (n=38)**	**p<**
C Reactive Protein (mg/L)	3.2 (1.7 – 7.1)	6.0 (4.1 – 10.3)	0.05
Albumin (g/L)	36.56 ± 0.62	36.03 ± 0.69	NS
Hemoglobin (g/L)	102.0 (98.0 – 112.0)	101.5 (96.5 – 107.0)	NS
Serum Phosphorus (mmol/L)	1.5 (1.2 – 1.9)	2.1 (1.6 – 2.3)	0.0001
Serum Calcium (mmol/L)	2.21 ± 0.03	2.25 ± 0.03	NS
PTH level (pmol/L)	226.24 ± 18.90	504.37 ± 46.01	0.0001

Table 3 presents difference in the prevalence of patients with hypertension and values of hemodynamic parameters in hemodialysis patients with and without preserved residual renal function. In the group of patients without preserved RRF hypertension was frequent (74.4% vs 25.6%) (χ^2*=14.149; p=0.0002; p<0.001).* The values of systolic blood pressure, mean arterial pressure and pulse pressure in hemodialysis patients without preserved RRF were significantly higher than those in the group of hemodialysis patients with preserved RRF. No significant differences in the values of diastolic blood pressure among patients with and without preserved RRF were found.

There was a statistically significant negative linear correlation between the volume of residual urine output and systolic blood pressure in hemodialysis patients (rho= -0.388; p<0.0001).

We also confirmed a statistically significant negative linear correlation between residual clearance of urea and systolic blood pressure in hemodialysis patients (rho=-0.392; p<0.0005).

Table 3. Presence of hypertension and hemodynamic parameters in the observed group

	With RRF (n=39)		Without RRF (n=38)		p<
	n	%	n	%	
With hypertension	10	25.6	26	68.4	
Without hypertension	29	74.4	12	31.6	
Systolic blood pressure BP (mmHg)	130.0(120.0-143.0)		150.0(140.0-160.0)		0.0001
Diastolic blood pressure DBP (mmHg)	80.0(70.0-80.0)		80.0(70.0-90.0)		NS
Mean arterial pressure MAP (mmHg)	95.5 ± 0.9		101.2 ± 2.1		0.05
Pulse pressure PP (mmHg)	57.0(40.0-65.0)		70.0(60.0-80.0)		0.0001

Volume of residual urine output and residual urea clearance did not correlate to the value of diastolic blood pressure in hemodialysis patients [(rho=-0.093; p=0.421) (rho=-0.078; p=0.502)]. In addition, there was a statistically significant negative linear correlation between the volume of residual urine output and the value of mean arterial pressure in hemodialysis patients (rho=-0.272; p<0.05). We also confirmed a statistically significant negative linear correlation between residual urea clearance and values of mean arterial pressure in hemodialysis patients (rho=-0.261; p=0.023; p<0.05).

A strong statistically significant negative linear correlation between the volume of residual urine output and the value of pulse pressure was observed in the analyzed groups (rho = -0.387; p <0.001) (Figure 1).

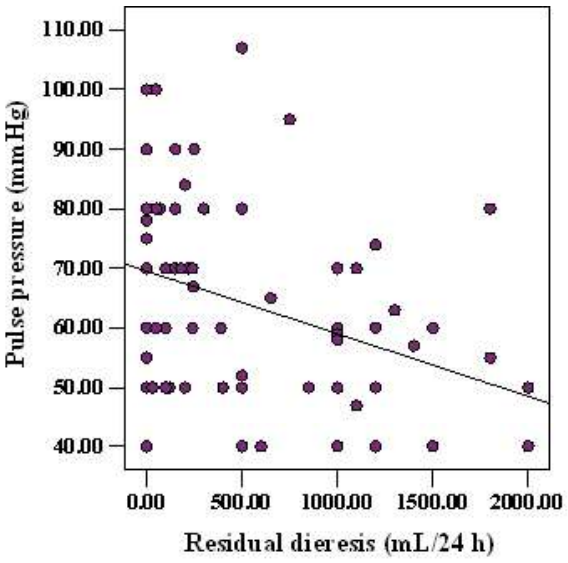

Fig. 1. Correlation between residual diuresis and pulse pressure rho= - 0.387, p<0.001

We also confirmed a strong statistically significant negative linear correlation between residual urea clearance and the value of pulse pressure in hemodialysis patients (rho=-0.400; p<0.0005) (Figure 2).

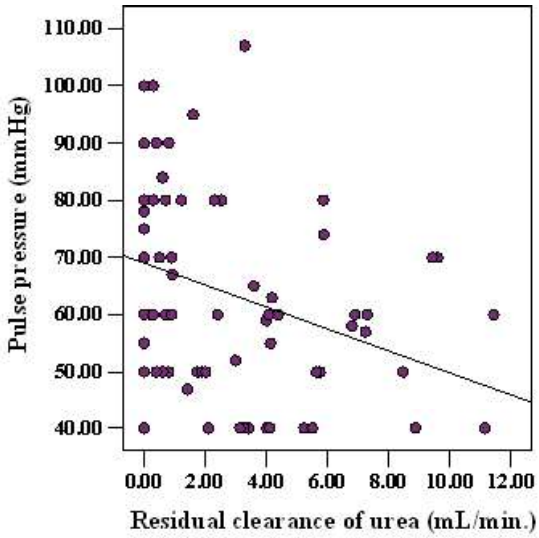

Fig. 2. Correlation between residual clearance of urea and pulse pressure rho= - 0.400, p<0.0005

Discussion

The role and importance of preserving residual diuresis or residual renal function (RRF) is recognized and clearly defined in patients treated by peritoneal dialysis, and residual diuresis is considered the "heart" of peritoneal dialysis. It has been shown that preserving RRF plays an important role in patients on hemodialysis in recent years [3,4,13]. Accurate measurement of RRF in patients with chronic renal failure remains a challenge. The most commonly recommended average value are the sum of creatinine clearance and the clearance of urea [4]. Values of residual urea clearance and diuresis have been used to estimate RRF. If the residual urea clearance was less than 1 ml/min and the daily urine output of less than 200 ml, then RRF was lost, which was supported by other researchers [4,8]. There are various factors that have an impact on the loss of RRF. It is believed that the length of hemodialysis treatment is one of the factors contributing to the loss of RRF [6]. In our study, patients without preserved RRF had significantly longer duration of hemodialysis compared to patients with preserved RRF (38.0 vs.16,0 months, p<0.0005).

One of the important factors in the development of heart disease and vascular disease in patients with CKD is anemia, which occurs in the early stages of CKD. Patients with preserved RRF have better control of anemia [8]. Our research has not found a significant difference regarding hemoglobin of patients with and without preserved RRF. Although the loss of RRF was linked with hypoalbuminemia in the studies of some authors, our study results did not find significant difference in albumin concentrations in the two groups. Hyperphosphatemia is common in dialysis patients. It is associated with the development of vascular calcification, and an increased risk of cardiovascular diseases [10,11]. RRF role in controlling the balance of phosphate is clearly proven in patients on PD and patients on hemodyalisis [9]. In our study there was a significant difference in the level of phosphorus in the observed groups. Patients with preserved RRF had lower values of serum phosphorus in comparison to patients without RRF (1.5 vs. 2.1, $p < 0.001$). In addition to phosphorus, an important factor associated with an increased risk of cardiovascular diseases is secondary hyperparathyroidism. In our study, we showed that patients with preserved RRF had significantly lower levels of parathyroid hormone compared to patients without preserved RRF (226.24 vs. 504.37, $p < 0.001$).

Hypertension is a common finding in patients treated with hemodialysis [11]. Although the causes of hypertension are multifactorial, the significance of the volume status impact in the control of blood pressure [15]. Patients with preserved RRF have better control of body water volume, hence it can be assumed that they will have better blood pressure control. Our research revealed a significant difference in interdialytic weight gain in the dialysis patients with and without preserved RRF (2.4 vs. 3.5, $p<0.05$), which clearly indicates that patients with preserved RRF have better body water volume control. Since hypertension in the majority of these patients depends on the volume status and considering that blood pressure is alternating between dialysis, there is no consensus of blood pressure (BP) values before and after hemodialysis needed in the diagnosis of hypertension. It is considered that predialysis values of BP exceeding 150/85 mmHg and postdialysis BP greater than 130/75 mmHg may be used as a threshold to define hypertension, with a sensitivity of at least 80% [15]. In our study, hypertension is defined as the value of BP greater than 140/90 mm Hg, measured as average value of blood predialysis pressures in ten consecutive hemodialysis treatments. Taking this into consideration, there is a statistically significant difference in the BP values in the two groups. Hypertension was more frequent in patients without preserved RRF (68.4 vs. 25.6%, $p<0.001$). Significantly higher values of systolic blood pressure (150 vs 130 mmHg, $p<0.001$), mean arterial (101.2 vs. 95.5, $p<0.05$) and pulse pressure (70.0 vs. 57.0, $p<0.001$) were found in patients without RRF, but not in the values of diastolic blood pressure. There was a positive linear correlation between the volume residual diuresis, residual urea clearance, systolic blood pressure (rho=-0.272, $p<0.005$; rho=-0.388, $p<0.0001$), mean arterial pressure (rho=-0.272, $p<0.05$; rho=-0.261, $p<0.005$) and pulse pressure (rho=-0.387, $p<0.005$; rho =-0.392, $p<0.005$). Pulse pressure per se is a better predictor of CV events and mortality in hemodialysis patients. Pulse pressure increase of 10 mmHg increases the risk of CV events by 22% [11,12].

The results of our study clearly show that patients with preserved RRF have a lower incidence of predialysis hypertension and significantly better control of blood pressure.

Conclusion

Residual renal function contributes significantly to the overall health and well-being of patients on hemodialysis. RRF has been implicated to be important in maintaining the fluid balance of patients on hemodialysis. Loss of RRF is associated with higher systolic blood pressure, higher mean arterial blood pressure and higher pulse pressure. RRF also plays an important role in phosphorus control, and removal of middle weight uremic toxins. Patients without RRF have more severe anemia, greater degree of inflammation and malnutrition. It is therefore crucial to develop effective therapeutic strategies that may preserve RRF in dialysis patients. Assessment of RRF is currently not part of routine hemodialysis care in our country. These results provide a strong rationale for routine monitoring of RRF in HD patients. Furthermore, development of methods to assess and preserve RRF is important and may improve dialysis care. Possible limitation of the study was the small study sample.

Conflict of interest statement. None declared.

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