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BLOOD PRESSURE PROFILE IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS

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ABSTRACT

Background: Cardiovascular mortality is the leading cause of death in end stage renal disease. Despite being on continuous ambulatory peritoneal dialysis (CAPD), blood pressure (BP) remains poorly controlled. A higher pulse pressure and non dipping are associated with increased cardiovascular mortality. We studied BP control and the prevalence of non dipping in CAPD patients.
Methods: All patients undergoing CAPD at our institution who met the inclusion criteria were recruited. We compared BP control and dipping status in diabetic and non diabetic patients on CAPD. We also determined whether BP and peritoneal membrane permeability were associated.
Results: Forty six patients with a mean age 45 ± 13 years were enrolled. Diabetic patients were older (mean age 54 ± 13 vs. 40 ± 11 yrs, p <0.001), had a lower mean diastolic BP (80 ± 14 vs. 90 ± 14 mmHg, p = 0.025) and a higher mean pulse pressure (59 ± 17 vs. 49 ± 14 mmHg, p = 0.035). They were also non dippers (n = 15 vs. n = 1, p = 0.007). The low and low average transporters tended to have a higher systolic BP (p = 0.054) and a higher pulse pressure (p = 0.058). On multivariate analysis, age was the main predictor of pulse pressure.
Conclusion: Despite being on chronic maintenance PD, BP was not well controlled. Diabetic patients had a higher pulse pressure and were non dippers thereby increasing their cardiovascular risk. We should therefore optimize BP control and aim to restore the nocturnal dip in these patients.

Keywords: ambulatory blood pressure monitoring, continuous ambulatory peritoneal dialysis, cardiovascular mortality, diabetes mellitus, dipping, diurnal variation, pulse pressure

INTRODUCTION

The incidence and prevalence of end stage renal disease (ESRD) is increasing worldwide. Diabetes and hypertension are the leading causes of ESRD in Malaysia. Once ESRD is reached, the options are hemodialysis (HD), peritoneal dialysis (PD) or renal transplantation. A small number of patients choose not to be dialysed and opt for conservative treatment.

Hypertension is very common in patients with ESRD either as a primary cause or secondary due the retention of salt and water. Only 26.7 % of PD patients achieved the target blood pressure of <130/80 mm Hg (Webb et al., 2009). There are studies showing that blood pressure control is better on HD than PD (Velasquez et al., 1997). Cardiovascular complications are the major cause of morbidity and mortality in these patients and account for 29 % of

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deaths in ESRD patients (Castledine et al., 2009).

The introduction of 24 hour ambulatory blood pressure monitoring (ABPM) has enabled a more comprehensive estimate of a patient's true blood pressure. It is well recognized that blood pressure (BP) varies during the course of the day and is characterized by a marked decrease in systolic and diastolic BP nocturnally (dipping). Loss of the normal nocturnal decline in BP is common in hypertensive and diabetic patients and is associated with target organ damage, a higher incidence of cardiovascular disease and poor long-term survival (Sturrock et al., 2000; Verdeecchia et al., 1994; White, 1999). Loss of the nocturnal dip in BP can only be determined by ABPM (Thompson and Pickering, 2006). Night time systolic BP from ABPM is more predictive than clinic BP readings for cardiovascular disease, stroke and death (Tonbul et al., 2002).

Diabetes per se is a major risk factor for cardiovascular disease. Studies have shown that non dipping is highly prevalent in diabetic patients and is associated with poor cardiovascular outcomes (Nakano et al.1998; Bouhanick et al., 2008).

Pulse pressure is an independent risk factor for mortality (Sesso et al., 2000; Benetos et al., 1997; Palmieri et al., 2006). The Hoorn study showed that the high pulse pressure in diabetics is associated with a worse cardiovascular mortality compared to non diabetic patients (Schram et al., 2002). The Strong Heart study demonstrated that a higher pulse pressure was associated with a higher cardiovascular mortality independent of traditional cardiovascular risk factors, left ventricular hypertrophy or reduced ejection fraction in adults without overt coronary heart disease (Palmieri et al., 2006).

Some studies have shown non-invasively determined central aortic systolic BP is more valuable than other blood pressure variables in the prediction of cardiovascular mortality (Wang et al., 2009).

The main aim of this study was to accurately measure the mean BP of patients on continuous ambulatory peritoneal dialysis (CAPD) using 24 hour ABPM and to compare the BP control, nocturnal dipping status, dialysis adequacy and peritoneal membrane permeability between diabetic and non diabetic patients.

METHODS

This study was a cross sectional observational study over a 3 month period. Patients on the CAPD programme at our centre who met the inclusion criteria were recruited and informed consent was obtained. Our inclusion criteria included patients on CAPD for a minimum of 5 months with a stable dialysis prescription. Patients under 18 years of age were excluded. Patients with severe fluid overload due to non compliance or membrane failure were excluded. Patients were recruited when they came to their clinic visit and their dry weight and fluid status was assessed during this visit.

Demographics including age, gender, race, body weight and height, body mass index, co morbidities like diabetes, hypertension, duration of peritoneal dialysis, number of antihypertensive agents used, use of angiotensin converting enzyme/angiotensin II receptor blockers, serum blood urea, creatinine and albumin were recorded. All patients had peritoneal membrane permeability function and dialysis adequacy tests performed during the study period. Results of peritoneal dialysis adequacy (weekly Kt/V), peritoneal membrane permeability, residual renal function and mean ultrafiltration volume were recorded. Peritoneal membrane permeability was divided into low and high transporters.

Twenty four hour ABPM was recorded using the BPRO machine (model T6400, Health stats). Patients were advised to carry out their normal activities as usual. BP readings were taken at 15 minute intervals throughout the 24 hour period. More than 80 % technically satisfactory readings were accepted to be a successful recording. Mean 24 hour daytime, night time systolic and diastolic BP, mean arterial BP was de-

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rived from 24 hour ABPM. Carotid artery systolic pressure (CASP) was also obtained using the same device.

Normal dippers were defined as patients who showed a fall in systolic or diastolic BP > 10 % during the night i.e. 10–20 %. Excessive dippers had > 20 % fall in night time BP; non dippers < 10 % fall in night time BP and reverse dippers as those who had no drop in night time BP but a paradoxical rise in BP. For analysis purposes, normal dippers and excessive dippers were considered as 'dippers' and non dippers and reverse dippers were grouped together as 'non dippers'.

Statistical analysis was done using SPSS (IBM, Chicago, IL) v. 18. Continuous variable data are presented as mean ± SD unless otherwise stated. We used students' independent and paired t test for most of the data analysis. We used Pearson correlation and linear and logistic regression analysis for univariate and multivariate analysis, respectively. A p value < 0.05 was considered statistically significant.

RESULTS

Forty six patients were enrolled and their demographics are shown on Table 1.

The results of BP profile between diabetic and non diabetic patients are tabulated on Table 2.

Table 1: Demographics of CAPD patients

	Mean	Std Deviation
Gender Male (n)	23 (50 %)	
Race		
Malay (n)	32 (69.6 %)	
Chinese (n)	14 (30.4 %)	
Hypertension (n)	43 (93.5 %)	
Diabetes (n)	16 (34.8 %)	
Age (years)	44.63	13.24
Dialysis vintage (months)	31.62	25.64
24hr Blood Pressure (mm Hg)		
Systolic	139.2	21.3
Diastolic	86.6	14.8
Mean arterial pressure (MAP)	104.2	15.5
Carotid arterial systolic pressure	130.8	21.7
Serum urea (mmol/L)	15.7	5.5
Serum creatinine (umol/L)	872.2	362.4
Serum albumin (g/L)	37.7	4.1
Mean ultrafiltration volume(mls)	1386	474
Residual renal function (mls)	301	341
Kt/V (dialysis adequacy)	2.18	0.64
Transporter (n)		
Low	34 (73.9 %)	
High	12 (26.1 %)	
Mean antihypertensive agents (n)	2.39	1.22
ACE inhibitors (n)	22 (47.8 %)	
ARB (n)	15 (32.6 %)	

ACE – Angiotensin Converting Enzyme ARB – Angiotensin II Receptor Blockers

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Table 2: BP profile in diabetic and non diabetic patients

	Diabetic (n = 16)	Non diabetic (n = 30)	P value
Number of patients	16	30	
Age (years)	53.5 ± 13.5	39.9 ± 10.5	**p < 0.001**
Dialysis vintage (months)	25.4 ± 25.7	34.9 ± 25.4	p = 0.23
Mean 24 hr SBP (mmHg)	139 ± 18	139 ± 23	p = 0.975
Mean 24 hr DBP (mmHg)	80 ± 14	90 ± 14	**p = 0.025**
Mean 24 hr MAP (mmHg)	100 ± 13	107 ± 16	p = 0.171
Mean 24 hr PP (mmHg)	59 ± 17	49 ± 14	**p = 0.035**
CASP (mmHg)	131 ± 20	131 ± 23	p = 0.96
Non dippers (%)	15 (93.7)	16 (53.3)	**p = 0.007**
Serum albumin (g/L)	36.2 ± 3.2	38.5 ± 4.3	p = 0.068
Ultrafiltration (mls)	1459 ± 555	1347 ± 430	p = 0.451
Residual renal volume (mls)	298 ± 407	303 ± 309	p = 0.964
Kt/V (dialysis adequacy)	2.18 ± 0.80	2.17 ± 0.55	p = 0.952
Mean anti-hypertensive agent (n)	2.56 ± 0.89	2.30 ± 1.37	p = 0.49
Transporters (n) High	2	10	
Low	14	20	

SBP – Systolic BP DBP – Diastolic BP MAP – Mean Arterial Pressure

Diabetic patients when compared to the non diabetics were older, had a lower mean diastolic BP and a higher mean pulse pressure. Thirty four out of 46 patients were low or low average (LA) transporters. There was no correlation between diabetes and the peritoneal membrane transporter status.

There was no relationship between peritoneal membrane transporter status and dipping status. However, there was an association between transporter status and BP although it did not reach statistical significance. The low and low average transporters tended to have a higher systolic BP (p = 0.054) and a higher pulse pressure (p = 0.058).

Thirty four out of 46 patients were low or low average (LA) transporters. Majority of the diabetic patients were low or low average transporters (14/16 = 87.5 %) whereas in the non diabetic group 20/30 (66.7 %) were low or low average transporters.

There was an inverse correlation with diastolic BP and age (R = -0.336, p = 0.002) and a higher pulse pressure correlated with increasing age (R = 0.443, p = 0.002,). Diabetes correlated with a lower diastolic BP (R = 0.330, p = 0.025) and a higher pulse pressure (R = -0.312, p = 0.035). There was an inverse correlation between age and diabetes (R = -0.498, p = <0.001).

On multivariate analysis age (p = 0.019) is the main determinant of pulse pressure compared to diabetic status (p = 0.445). Systolic BP is affected more by transporter status (p = 0.051) than diabetic status (p = 0.675).

DISCUSSION

Hypertension is common in renal disease. A majority of dialysis patients exhibit an elevated BP due to volume overload which is associated with increased cardiovascular mortality (Amar et al., 2000). Despite being on dialysis, BP is generally poorly controlled in ESRD (Harper et al., 2009). In our study cohort, ABPM showed that the mean BP was elevated despite being on PD. Increased dietary sodium, overestimation of patient's dry weight and inadequate ultrafiltration by the peritoneum

contribute to volume overload in these patients.

Pulse pressure is an indicator of vascular stiffness (Jensky et al., 2010). Pulse pressure was significantly higher in our diabetic population who were significantly older than the non diabetics but had been on dialysis for a shorter duration. Studies have shown that with increasing age, there is increased arterial calcification thereby leading to arterial stiffness (Eddington et al., 2009). This could explain why diabetics had a higher pulse pressure than the non diabetics despite the shorter duration of dialysis in our study.

ESRD is associated with increased arterial stiffness due to multiple factors including vascular calcification which starts as early as chronic kidney disease stage 4 (Eddington et al., 2009). Diabetic patients tend to have more vasculopathy than non diabetics and this may also explain the higher pulse pressure in the diabetic cohort. The combination of diabetes and high pulse pressure greatly increases their cardiovascular morbidity and mortality (Nilsson et al., 2009; Vaz-de-Melo et al., 2010). Studies have reported pulse pressure as an independent predictor for all cause mortality in PD patients (Liu et al., 2003). Pulse pressure is a potent indicator of mortality both in haemodialysis and PD patients (Fang et al., 2009; Liu et al., 2008). Even in non ESRD patients, pulse pressure is associated with increased cardiovascular mortality (Thomas et al., 2008).

On univariate analysis diabetes correlates inversely with age. We have shown on multivariate analysis age to be the main predictor of pulse pressure. There was a direct correlation with increasing age and increasing pulse pressure, hence the notion of age related vascular stiffness leading to higher pulse pressure.

The overall mean age of our patients is less than that reported by others. This is because choice of modality of renal replacement therapy is usually patients' choice. A lot of young working people chose PD compared to HD as they can still manage to do their PD whilst at work.

Although our patients were not overtly overloaded at the time of the ABPM study, we know that patients can have a few litres of fluid retention before oedema develops. There are also studies showing that diabetic patients tend to be more fluid overloaded than their non diabetic counterparts (Davenport and Willicombe, 2010). This could also partly explain the reason for the higher systolic blood pressure in our patients.

None of our patients in this study were on icodextrin (mainly due to the high cost involved). There is evidence that the use of icodextrin can improve blood pressure by improving the ultrafiltration (Boudville et al., 2007). None of our patients had membrane failure and the mean ultrafiltration in this group is commendable. The main reason for the suboptimal BP control is mostly likely due to non compliance with salt and fluid restriction.

Almost all these diabetic patients (93.7 %) were non dippers and therefore at higher risk for poor long-term outcomes. Studies have reported a higher incidence of cardiovascular events among reverse dippers and non dippers (Bouhanick et al., 2008). Some studies have reported a high incidence of non dippers in both CAPD and automated peritoneal dialysis (Jang et al., 2011). Others have shown analysis of 24 hour ABPM revealed BP reduction predominantly in the daytime and less in the night time after the introduction of CAPD (Shoda et al., 2000).

These results indicate that introduction of PD cannot reduce cardiovascular events because the nocturnal elevation of BP remains unchanged. The loss of nocturnal dip has been attributed to poorer sleep quality, autonomic dysfunction and volume overload. We need to bear in mind that even after introduction of PD, casual daytime BP readings may underestimate cardiovascular risk. It is well recognized that cardiovascular events tend to occur early in the morning. Just as blood pressure can be lowered in patients with chronic kidney disease, there is evidence that the dipping status can be restored (Portaluppi et al., 1995). Changing the timing of antihyper-

tensive agents from morning to night can improve dipping (Portaluppi et al., 1995).

There was no correlation between diabetes and transporter status in our study. However, others have reported diabetics to be high transporters but majority of the patients in their study were high transporters (Dwarakanathan et al., 2003). On the other hand, some have shown no difference in peritoneal membrane transport between diabetic and non diabetic patients (Chou et al., 2006). This is in keeping with our findings.

One study reported that high transporter status was directly associated with higher blood pressure (Tonbul et al., 2003). Our study showed the reverse, in that there was a trend towards the low and low average transporters having a higher systolic BP and pulse pressure. In general, most of our patients were low or low average peritoneal membrane transporters. Even when adjusted for diabetes, we still found this trend to persist. Larger studies recruiting a higher number of CAPD patients are indicated.

There was no relationship between transporter status and dipping status. We also found no significant difference in the dialysis adequacy between the diabetic and non diabetic patients. To the best of our knowledge there is no evidence at present to demonstrate any relationship between dialysis adequacy and diabetic status.

The management of BP includes achieving an accurate dry (target) weight, dietary sodium restriction, using anti hypertensive agents and changing the timing of anti hypertensive agents to achieve that nocturnal decline in BP. There is evidence that home BP monitoring is reflective of true blood pressure (Agarwal, 2010). This is advocated on all our patients on peritoneal dialysis but we have found at least 15 % of our patients do not regularly monitor their BP. This holds particularly true for our younger patients. Konings et al. (2002) have shown that both systolic and diastolic ambulatory blood pressure strongly correlate to left ventricular hypertrophy when compared to office BP readings. Despite home BP monitoring, we still feel that the nocturnal dip will not be picked up without ABPM.

Our study has few limitations in that it was a small study and therefore in some of our analysis we did not achieve statistical significance. In contrast to other studies, our study showed a trend towards a higher systolic BP and pulse pressure in low and low average transporters. Most of our diabetic patients were low or low average transporters and they were older. These two factors alone could explain the high pulse pressure and be confounding this trend. We need larger studies to look into this before any definitive conclusions can be made.

CONCLUSION

We need to bear in mind that even after introduction of PD, casual daytime BP readings may underestimate cardiovascular risk. The management of BP includes achieving an accurate dry (target) weight, dietary sodium restriction and using anti hypertensive agents.

ABPM needs to be used more frequently, especially on those patients who do not regularly monitor their BP at home and have an elevated clinic BP reading. Despite being on chronic maintenance PD, BP was not well controlled in our study cohort. Diabetic patients had a higher pulse pressure and were non dippers thereby increasing their cardiovascular risk. We should therefore aim to optimize BP control and to restore the nocturnal BP dip in these patients by adjusting the timing of their antihypertensive medications.

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