Prevalence of hypertension in patients on peritoneal dialysis: results of an Italian multicentre study

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Abstract

Background. The tenet that peritoneal dialysis is capable of either normalizing or improving blood pressure control in uraemic patients is based on outdated or monocentric experiences. Therefore, we assessed the prevalence of hypertension and the efficacy of antihypertensive therapy in a large, multicentric cohort of patients on peritoneal dialysis.

Methods. Twenty seven out of the 50 centres belonging to the Italian Co-operative Peritoneal Dialysis Study Group took part in the study. The main patient selection criteria were: peritoneal dialysis therapy for at least 3 months and no peritonitis or changes in dialysis technique for at least 1 month. Clinical blood pressure was measured according to WHO/ISH guidelines. Ambulatory blood pressure monitoring was carried out using a SpaceLabs 90207 recorder. Hypertension was defined according to WHO/ISH criteria and staged according to the criteria of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC), 5th Report. Ambulatory blood pressure monitoring recordings were used to evaluate white-coat hypertension, blood pressure load and the dipping phenomenon.

Results. Five hundred and four subjects were evaluated. Hypertension was prevalent in 88.1% of the population, and 362 out of 444 hypertensive patients were on antihypertensive therapy. JNC staging revealed that 188 patients had moderate to severe hypertension. Blood pressure load was pathological in 77.3% of the patients receiving antihypertensive therapy. JNC staging revealed that 188 patients had moderate to severe hypertension. Blood pressure load was pathological in 77.3% of the patients receiving antihypertensive therapy. White-coat hypertension was identified in 9.1% of the hypertensive patients not on antihypertensive therapy, and 53.1% of the patients were non-dippers.

Conclusions. The study demonstrates that hypertension is a dramatic, unsolved problem in uraemic patients treated with peritoneal dialysis, and casts doubts on the effectiveness of our current peritoneal dialysis strategies and pharmacological management of hypertension.

Key words: ambulatory blood pressure monitoring; antihypertensive therapy; prevalence of hypertension; peritoneal dialysis; white-coat hypertension

Introduction

Cardio- and cerebrovascular events are the main causes of morbidity and mortality of patients on peritoneal dialysis [1]. Although high blood pressure (BP) is the leading factor causing cardiovascular mortality in the general population, scant attention is paid to arterial hypertension in recent peritoneal dialysis studies. This might be due to the general belief that end-stage renal disease (ESRD)-related hypertension is easily controlled by peritoneal dialysis. Unfortunately, this assertion is at least in part based on outdated reports [2]. In recent years, ambulatory blood pressure monitoring has been applied in peritoneal dialysis patients. This evaluation technique offers some advantages over traditional office measurements as it avoids ‘observer bias’, ‘digit preference’ of the operator and the stress reaction of the patient, and provides mean BP levels representing the average of >90 measurements per day. Nonetheless, only a few small studies have been carried out using ambulatory blood pressure monitoring in peritoneal dialysis patients [3].

We were thus prompted to conduct a large multicentre study to evaluate the prevalence of hypertension and the efficacy of antihypertensive therapy in peritoneal dialysis patients using traditional clinical sphygmonanometric measurements and 24 h ambulatory blood pressure monitoring recordings.

Subjects and methods

All 50 centres in the Italian Co-operative Peritoneal Dialysis Study Group (ICPDSG) were invited to take part in this study.
transversal, observational, multicentre study. All patients on peritoneal dialysis for at least 3 months and without peritonitis episodes or changes in dialysis technique for at least 1 month were considered eligible. Exceptions included cases in which an adequate ambulatory blood pressure monitoring recording was not possible due to arrhythmia (frequent extrasystoles, chronic atrial fibrillation), those with a differential BP < 20 mmHg or > 90 mmHg, or patients engaged in heavy physical work. Patient consent was required. The first 30 consecutive and consenting subjects in each centre were enrolled in the study. A monitor of the study confirmed that the appointment schedule of the patients was not altered before recruitment began. The patients selected for the study were asked to visit the out-patient clinic of their peritoneal dialysis centres on pre-determined days between 8 and 10 a.m. for BP measurement and ambulatory blood pressure monitoring evaluation.

Information regarding age, weight, height, kidney disease, blood haemoglobin, peritoneal dialysis schedule and pharmacological therapy at the time of office BP measurement was reported on a patient card completed by the local nephrologists.

BP was measured by a local nephrologist with a mercury sphygmomanometer using Korotkoff phase I and V to identify systolic and diastolic BP values (SBP and DBP), respectively. Three subsequent readings were taken after a 10 min rest in the sitting position, and their averages were used for statistical analysis. Hypertension was defined according to WHO/ISH criteria (presence of one of the following criteria: SBP > 140 mmHg, DBP > 90 mmHg, current antihypertensive therapy), and staged according to the criteria of the Joint National Committee (JNC) on Detection, Evaluation and Treatment of High Blood Pressure, 5th Report [4].

Ambulatory blood pressure monitoring was carried out shortly after clinical BP measurement, using a SpaceLabs 90207 recorder with a DIU90219 interface (SpaceLabs Inc, Redmond, Washington, USA). BP was measured at pre-set 15 min intervals from 6 a.m. to 12 p.m. (day time) and at 20 min intervals from 12 p.m. to 6 a.m. (night time). The patients were requested to maintain their usual physical activities and peritoneal dialysis schedule during the monitoring, to adhere to their regular sleeping hours, to fill in a patient diary of their therapy, daily activities and quality of night rest, and to return to the hospital 24 h later. Editing of the raw data was performed according to the standard criteria encoded in the monitoring software. Twenty four hour BP recordings were not considered suitable for analysis if they lasted < 24 h, if < 75% of the expected number of readings were available after the removal of artefacts (by automatic editing of the SpaceLabs software) or if BP readings were missing during 1 h or more. Ambulatory blood pressure monitoring records were used to evaluate BP load as a percentage of SBP and DBP values up to the cut-off (140 and 90 mmHg daily, 120 and 80 mmHg nightly); a BP load > 30% was considered abnormal [5]. White-coat hypertension was diagnosed when no antihypertensive therapy was given, office BP were values ≥ 140/90 mmHg and daytime BP episodes were < 130/85 mmHg [6]. According to O’Brien’s recommendations, a patient was considered a dumper if day–night SBP/DBP variation was > 10/5 mmHg [7].

Statistics

Patient cards, patient diaries and ambulatory blood pressure monitoring records were collected by the co-ordinating centre and loaded into a general file, and the statistical processing was performed using the SPSS statistical package (SPSS Inc., Chicago, USA). A multivariate analysis was performed by using MANOVA (dependent variables: SBP and DBP values; independent variables: gender, peritoneal dialysis technique and recombinant human erythropoietin therapy (rHuEpo); covariates, age and peritoneal dialysis duration) and logistic regression (dependent variable: hypertension according to WHO criteria; qualitative and quantitative independent variables as in MANOVA). The linear regression analysis was used to evaluate the relationships between age and DBP levels (the only significant correlation found with the multivariate analysis) and between haemoglobin and BP levels. The χ² contingency tables were used to evaluate the possibility of a predominant gender in the whole population and the difference in the use of antihypertensive multitherapy between rHuEpo-treated and untreated patients. The disagreement between JNC staging and BP load evaluation was tested by means of McNemar’s test. Data are reported as mean ± SD. The null hypothesis was refused for two-tailed P-values < 0.05.

Results

Characteristics of the study population

Twenty seven out of the 50 ICPDSG centres, with an overall peritoneal dialysis population of 829 patients, participated in the study. A total of 181 patients were not eligible for the following reasons: 35 for a peritoneal dialysis duration < 3 months, 93 for peritonitis, 21 for arrhythmia, 10 for differential BP < 20 mmHg or > 90 mmHg, and 22 for heavy physical work. Of the 648 eligible patients, 144 did not participate in the study due to their refusal (43 patients) and randomized discarding (101 patients). Table 1 summarizes the main characteristics of the 504 patients submitted to the study. All patients were Caucasians. There was a significantly higher prevalence of males than females (59.3% vs 40.7% respectively, χ² = 8.5, P < 0.005). Forty five per cent of the patients were over 64 years of age, 5.4% were under 40 years, and middle-aged patients accounted for the remaining 49.6% of the population. Of the patients in the study, 70.2% had been on rHuEpo therapy at the time of office BP measurement and loaded into a general file, and the statistical processing was performed using the SPSS statistical package (SPSS Inc., Chicago, USA). A multivariate analysis was performed by using MANOVA (dependent variables: SBP and DBP values; independent variables: gender, peritoneal dialysis technique and recombinant human erythropoietin therapy (rHuEpo); covariates, age and peritoneal dialysis duration) and logistic regression (dependent variable: hypertension according to WHO criteria; qualitative and quantitative independent variables as in MANOVA). The linear regression analysis was used to evaluate the relationships between age and DBP levels (the only significant correlation found with the multivariate analysis) and between haemoglobin and DBP levels. The χ² contingency tables were used to evaluate the possibility of a predominant gender in the whole population and the difference in the use of antihypertensive multitherapy between rHuEpo-treated and untreated patients. The disagreement between JNC staging and BP load evaluation was tested by means of McNemar’s test. Data are reported as mean ± SD. The null hypothesis was refused for two-tailed P-values < 0.05.

Table 1. Characteristics of the study population

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of patients</th>
<th>Males/females</th>
<th>Age (years)</th>
<th>Time on dialysis (months)</th>
<th>Renal diseases</th>
<th>Glomerulonephritis</th>
<th>Vascular nephropathy</th>
<th>Not determined</th>
<th>Interstitial nephropathy</th>
<th>PKD</th>
<th>Diabetic nephropathy</th>
<th>Other</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>504</td>
<td>299/205</td>
<td>61.4 ± 12.3</td>
<td>32.0 ± 28.5</td>
<td>143 (28.4%)</td>
<td>113 (22.4%)</td>
<td>85 (16.9%)</td>
<td>80 (15.9%)</td>
<td>40 (7.9%)</td>
<td>39 (7.7%)</td>
<td>4 (0.8%)</td>
<td></td>
</tr>
</tbody>
</table>
nocturnal peritoneal dialysis. The distribution of the various peritoneal dialysis techniques was similar between genders. One hundred and ninety patients were treated with rHuEpo at the mean dose of 4539 ± 2907 UI/week.

**Antihypertensive therapy**

Three hundred and sixty two patients (71.8% of the study population, 81.5% of the hypertensive patients) were on antihypertensive therapy; 181 patients were treated with one drug, 128 patients with two drugs, and 53 patients were taking three or more drugs. Calcium antagonists were the most widely used drugs (65.7%), followed by angiotensin-converting enzyme inhibitors (32.6%), clonidine (30.1%), beta-blockers (22.6%), vasodilators (13.0%), angiotensin II receptor antagonists (1.9%) and α-methyldopa (1.1%). The comparison of the patient cards with the patient diaries revealed that 4.7% of the patients did not adhere completely to the therapeutic prescription of the physicians.

**BP levels and prevalence of hypertension**

Average office SBP and DBP values of the whole study population were 147.8 ± 24.3 and 85.0 ± 12.2 mmHg, respectively. Four hundred and forty four patients (69.3% of the population with a valid ambulatory blood pressure monitoring recording) had a pathological BP load. Among the patients on antihypertensive therapy, 82 hypertensive patients were off antihypertensive therapy.

Multiple regression analysis showed that the only statistically significant relationship among the variables studied was between age and DBP levels (F = 39.6, P < 0.001). The linear regression analysis showed a negative correlation between these two parameters: r = −0.27, P < 0.001.

Figure 1 shows the average SBP and DBP values for successive decades of life. With advancing age, SBP levels remained substantially stable and DBP levels tended to diminish progressively.

No differences in the use of antihypertensive drugs were found with respect to gender, age, peritoneal dialysis technique and peritoneal dialysis duration.

| Table 2. BP stages according to the JNC classification |

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension</td>
<td>78</td>
</tr>
<tr>
<td>High normal</td>
<td>58</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>stage 1</td>
<td>180</td>
</tr>
<tr>
<td>stage 2</td>
<td>123</td>
</tr>
<tr>
<td>stage 3</td>
<td>54</td>
</tr>
<tr>
<td>stage 4</td>
<td>11</td>
</tr>
</tbody>
</table>

Discussion

A greater number of patients on rHuEpo therapy were treated with two or more antihypertensive drugs (84 out of 190 vs 97 out of 314; χ² = 8.5, P < 0.005). No relationship was found between haemoglobin and BP levels in either the whole population or in the two groups of patients with and without rHuEpo therapy.

**Ambulatory blood pressure monitoring evaluation**

Four hundred and fourteen out of the 504 ambulatory blood pressure monitoring recordings were valid and suitable for analysis. The causes of failure in the other 90 cases were: one or more hours without BP readings in 90 cases, ambulatory blood pressure monitoring duration < 24 h in 27 cases and < 75% of the expected number of readings in 22 cases. The 24 h mean values of SBP and DBP were 139.0 ± 19.4 and 80.6 ± 10.8 mmHg; the mean values were 140.7 ± 19.6 and 82.1 ± 11.0 mmHg during the daytime, and 132.0 ± 21.3 and 74.4 ± 11.4 mmHg at night time, respectively.

Two hundred and eighty two out of 414 patients (69.3% of the population with a valid ambulatory blood pressure monitoring recording) had a pathological BP load. Among the patients on antihypertensive therapy, BP load evaluation revealed residual hypertension in 235 out of 304 patients and it agreed with the office BP evaluation in 243 patients (37 with BP control, 206 with poor BP control) and disagreed in the other 61 patients (32 with hypertension according to office BP evaluation and normal BP load, 29 with normotension according to office BP evaluation and pathological BP load). The McNemar’s test showed that the disagreement between JNC staging and BPL evaluation was not significant.

Among the hypertensive patients off drugs, white-coat hypertension was identified in six out of 66 cases. Two hundred and twenty patients (53.1% of the whole population with valid ambulatory blood pressure monitoring) were non-dipper cases, 39 of whom had a reversed circadian rhythm.

Our study, involving 30% of the peritoneal dialysis population of the ICPDSG centres, i.e. ~15% of the
Italian peritoneal dialysis population, represents one of the largest and most recent epidemiological investigations on hypertension in ESRD patients treated with peritoneal dialysis. The number of centres involved (~25% of the main Italian centres) and the large sample sizes of the study provide a fairly realistic picture of the prevalence of hypertension in patients in Italy.

A large percentage (88.1%) of peritoneal dialysis patients were hypertensive according to WHO/ISH criteria, and JNC staging documented poor BP control in 73% of the study population, with moderate to severe hypertension in half of the hypertensive patients.

The prevalence of hypertension was much higher than in the healthy population [8]. This difference may be partially accounted for by the advanced age of our population (almost half of the patients were elderly). It is interesting to note, however, that the younger subjects seemed to behave like the older patients with respect to BP levels and hypertension, with an interference of gender and age substantially different from that of the healthy population. Ageing was associated with decreasing DBP levels beginning in the first decades of life, whereas in the healthy population, this phenomenon is not observed until the seventh decade of life. Moreover, SBP levels were high and stable for all the decades of life, differing from the healthy population, in which SBP increases progressively throughout life. The absence of a ‘gender effect’ on BP levels and on the prevalence of hypertension is another sign supporting the hypothesis of a premature ageing of uraemic patients on peritoneal dialysis treatment.

Although a comparison with the PD-CIS report [9] is limited by differences in age, nationality and race distribution, our findings are similar to, or even more disheartening than, those contained in the report. By adopting the same limits of normotension as the PD-CIS study (SBP ≤150 mmHg and DBP ≤90 mmHg), 45% of our population is hypertensive vs. a prevalence of 35% in the PD-CIS study. Moreover, our results are similar to those recently found by Salem in a large haemodialysis population [10] suggesting that peritoneal dialysis does not offer any advantage over haemodialysis with respect to BP control.

In contrast to a previous report [11], we did not observe any improvement in BP control after the first months of peritoneal dialysis treatment. Moreover, our data did not confirm Diaz-Buxo’s results [12] regarding a positive effect of continuous cyclic peritoneal dialysis on pharmacological BP control; in fact, BP levels and the prevalence of hypertension were similar in all the peritoneal dialysis modalities.

Our data also showed a negative impact of rHuEpo on BP regulation, since the patients on rHuEpo therapy needed more antihypertensive drugs to maintain their BP levels at levels similar to those not receiving rHuEpo. This effect did not appear to be mediated by the level of haemoglobin, and could be explained by the well-documented vasoconstrictor activity of rHuEpo [13].

Despite the wide use of effective antihypertensive drugs, the majority of patients (79%) had residual hypertension. On the other hand, the lack of treatment of one out of five hypertensive patients does not seem to be justified, as white-coat hypertension was a rare event in our population.

Based on BP load calculations using the two BP measurement techniques, ambulatory blood pressure monitoring does not seem to provide any real advantage over sphygmomanometric measurement in evaluating who should be treated and when treatment should be changed. However, the high prevalence of non-dippers found in our peritoneal dialysis population is worthy of study and deserves a longitudinal evaluation, since several studies have already documented that cardiovascular complications due to hypertension are greater in non-dippers than in dippers [14].

In conclusion, the data of this epidemiological investigation document the fact that BP control in peritoneal dialysis patients, described in the past as satisfactory and easy to achieve, is today more a ‘myth’ than a ‘reality’. These figures cast doubts on the effectiveness of our current peritoneal dialysis strategies and pharmacological management of hypertension, and should stimulate further studies aimed at evaluating the clinical outcomes over a period of time.


References


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