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Pulse Pressure and the Management of the Hypertensive Patients of Black Race

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Abstract: Present study was carried out to analyze the impact of pulse pressure in the occurrence of cardiovascular events in black hypertensive patients. It is a prospective study including old as well as new hypertensive patients followed up during 6 months with clinical assessments at 1, 3 and 6 months; cardiovascular complications were assessed according to the pulse pressure. At 6 months, 37% of patients had normal blood pressure against 5.2% at the inclusion. The percentage of patients having a $PP \geq 7999.2$ Pa (60 mmHg) regressed from 70.7 to 30.2% at 6 months. Under combination antihypertensive drugs, the percentage of patients having a $PP \leq 7999.2$ Pa (60 mmHg) increased from 20.8 (at Mo) to 71.7% (at M6). Cardiovascular complications were found in 21.2% of hypertensive patients. Twenty percent of patients having a $PP \geq 7999.2$ Pa (60 mmHg) during the three follow up visits had cardiovascular complications at 6 months against 80% in $PP \leq 7999.2$ Pa (60 mmHg) group at the three follow up visits. The PP is a factor to be taken more and more into account in the management of hypertension. In fact, the better the PP is mastered the less cardiovascular complications are noticed.

Key words: Pulse pressure, cardiovascular complications, black race

INTRODUCTION

At the beginning of seventies, the Harrison's Principles of Internal Medicine still affirmed that systolic hypertension involved a normal or low diastolic blood pressure is seldom regarded as responsible of a body attack. Indeed, with age increase, one witnesses a progressive increase of the Systolic Blood Pressure (SBP) and the Pulse Pressure (PP), ascribable mainly to a rise of arterial rigidity (Lakatta and Levy, 2003; Franklin *et al.*, 1997). It is now clearly established that the SBP and the PP themselves are very important cardiovascular risk factors. Recent studies showed that a rise of the SBP and the PP in the elderly is a major factor of reduction of life expectancy (Benetos *et al.*, 2005; Franco *et al.*, 2005). During the nineties, several studies showed a major benefit of the treatment of High Blood Pressure (HBP) pure systolic or systolic and diastolic in the elderly on the risks of cerebral stroke, myocardial infarction and cardiac failure (Staessen *et al.*, 1997; SHEP Cooperative Research Group, 1991). For several decades, the severity of High Blood Pressure (HBP) is assessed by considering, before all, the level of Diastolic Blood Pressure (DBP), although one knows that the SBP is a good factor to predict cardiovascular risk (Anonymous, 1999). These last years, therapeutic results obtained in the treatment of isolated systolic high blood pressure of elderly patients (Collins *et al.*, 1990) brought the specialists to consider both SBP and DBP as independent assessments of the level of severity of high blood pressure (Black and Yi, 1996). However, moderns' comparisons of the analysis of Arterial Pressure's (AP) curve associate two essential components

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(Safar and London, 1994). The Mean Arterial Pressure (MAP) and the pulse arterial pressure. The role of the pulse pressure in the cardiovascular mortality and morbidity namely coronary was clearly demonstrated not only in patients with coronary complications (Fang *et al.*, 1995; Darné *et al.*, 1989) but also in normotensive subjects (Blacher *et al.*, 2000). Most of those studies had been carried in western countries.

In sub-Saharan Africa, studies carried-out this direction are rare. The present study was carried out to analyze the impact of the pulse pressure in the occurrence of Cardiovascular (CV) events in the black race hypertensive patients.

MATERIALS AND METHODS

Bè hospital is the referral centre of N° III sub-division in the region of Lomé council. It has 14 services among which is found the department of internal medicine that has a unit cardiology where our study was carried-out.

It is a prospective study carried-out from January 1st, 2006 to February 28th, 2007. It concerned old (known hypertensives) as well as new hypertensive patients seen on out -patient basis and followed up during 6 months. One hundred and sixteen blacks patients aged from 18 years or above having been present to appointments given were included in the study. Hypertensives were subjects with SBP 18664.8 Pa (140 mm Hg) or DBP 11998.8 Pa (90 mmHg).

Hypertensive were assessed at inclusion (M0), at one (M1), at there (M3) and at 6 months (M6). A nurse measured supine blood pressure in the two arms using a manual sphygmomanometer (Mancia *et al.*, 2007). After a 10 min rest period, blood pressure was measured 3 times and the mean of the last 2 measurements was calculated. The first and fifth Korotkoff phases were used to define SBP and DBP. Plasma cholesterol was measured with a Technicon SMA-12 (Benetos *et al.*, 1998).

Patients were split into three categories according to the antihypertensive drugs received:

- Monotherapy: Treatment by a single antihypertensive drug
- Bitherapy: Treatment by an association of two antihypertensive drug
- Pluritherapy: Treatment associating more than two anti-hypertensive drugs

Hypolipodemic drugs, antidiabetics, antiplatelet drugs, nitreous derivatives and anti arrhythmic drugs were added to the treatments of our patients pending on their clinical state.

However, any other anti hypertensive could be added in every category to reduce the pulse pressure under 7999.2 Pa (60 mmHg), the value from which its increase is in relation with new cardiovascular events.

Treatment of patients was conducted by a cardiologist physician. His main objective was to control the arterial pressure and specifically the Pulse Pressure (PP). Cardiovascular events were defined using the following criterias of the definition of the complications of high blood pressure:

- The ischemic heart disease was defined by the presence of one of the following events: angina pectoris (chest pain started by exercise and improved by rest or trinitrin and electrocardiographic signs), Myocardial Infarction (MI), typical signs at Electrocardiogram (ECG)
- Cerebrovascular stroke was defined by transitory ischemic attack or thrombotic stroke or hemorrhagic stroke confirmed by CT-scan
- Cardiac failure was defined by clinical signs and at cardiac echodoppler

We have determined the PP of hypertensive patients at inclusion, at one, three and 6 months (M0, M1, M3 and M6) and analyzed the impact of this PP on new cardiovascular events. This

because epidemiological studies have shown that a $PP \geq 7999.2$ Pa (60 mmHg) is associated with a significant cardiovascular risk (Safar *et al.*, 2004).

Patients on admission, patients with congenital cardiopathy, patients that did not respond to appointments and patients from other races were excluded from this study.

Data Analysis

The quantitative parameters are presented as average $\pm$ Mean deviation and the qualitative parameters by the number and the corresponding percentage.

HBP was classified according to the Joint National Committee 7 (Chobanian *et al.*, 2003). We study the role of PP by dividing patients into PP classes: $PP1 \leq 50$, $50 \leq PP2 \leq 60$, $60 \leq PP3 \leq 70$, $70 \leq PP4 \leq 80$, $PP5 \leq 80$ mmHg. And cardiovascular events were evaluated according to the classes of PP and according to therapeutic groups.

The data were computerized and processed by a statistical word processor (statistical package for social sciences) using an univariate analysis.

RESULTS

Age and Sex

The 116 patients were made up of 27(23.3%) men and 89 (76.7%) women. The sex-ratio (men/women) was 0.3. The average age of the patients was 55.77 ± 2.55 years with extremes of 26 and 86 years. The age bracket from 39 to 59 years was the most representative, with 56 (48.3%) patients, followed by 60-80 years with 44 (37.9%) patients, then the 18 - 38 years with 15 (12.9%) patients and finally those above 80 years with one patient (0.9%).

At inclusion (M0), the average Body Mass Index (BMI) was 29.65 ± 1.22 kg m⁻² (extremes: 17.57 and 53.12 kg m⁻²). Thirty nine (33.6%) patients were over-weight, 42 (36.2%) were obese, eight (6.9%) had morbid obesity and 27(23.3%) had normal weight.

Six (5.2%) patients were diabetics, ten (8.2%) had high blood cholesterol. The average blood cholesterol was 2.12 ± 0.51 Kg m⁻³ (2.12 ± 0.51 g L⁻¹) with extremes of 0.74 and 3.75 kg m⁻³ (0.74 and 3.75 g L⁻¹).

Variation of Arterial Pressure (AP)

Table 1 presents the distribution of patients according to the classes of AP during follow up.

Variation of the PP

Table 2 presents the proportion of patients according to the classes of PP in the course of follow up.

At the end of 6 months of management, the medium BMI of patients was 28.52 ± 2.11 kg m⁻².

Treatment

The progression of patients' therapeutic profiles is summarized in Table 3.

Table 1: Progression of AP

Class of AP	At inclusion	M1	M3	M6
	n (%)			
Normal BP	3 (2.6)	6 (5.2)	7 (6.0)	10 (8.6)
Pre-HBP	3 (2.6)	15 (12.9)	22 (19.0)	33 (28.5)
HBP stage 1	29 (19.0)	50 (43.1)	62 (53.4)	60 (51.7)
HBP stage 2	69 (65.5)	41 (35.4)	24 (20.7)	8 (6.9)
Isolated systolic HBP	12 (10.3)	4 (3.4)	1 (0.9)	5 (4.3)

n = 116

Table 2: Modification of the PP in the course of follow up

Classes of PP (mmHg)	At inclusion	M0-M1	M1-M3	M3-M6
<50	12 (10.3)	27 (23.3)	37 (31.9)	24 (20.7)
[50 – 60]	22 (19.0)	39 (33.6)	37 (31.9)	57 (49.1)
[60 – 70]	30 (25.9)	24 (20.7)	28 (24.1)	26 (22.4)
[70 – 80]	21 (18.1)	13 (11.2)	11 (9.5)	5 (4.3)
≥80	31 (26.7)	13 (11.2)	3 (2.6)	4 (3.5)

n = 116

Table 3: Therapeutic profile during the follow up

Therapies	Admission	M1	M3	M6
Monotherapy	7 (6.0)	5 (4.3)	3 (2.6)	1 (0.9)
Bitotherapy	61 (52.6)	63 (54.3)	64 (55.2)	62 (53.4)
Pluritherapy	48 (41.4)	48 (41.4)	49 (42.2)	53 (45.7)

n = 116

Table 4: Complications found at 6 months

Complications	n (%)
Coronaropathies	11 (9.5)
Cardiac failure	2 (1.7)
Left Ventricular hypertrophy	16 (13.8)
Renal failure	1 (0.9)
CVS (A)	5 (4.3)
Total	35 (21.2)

A: Cerebrovascular stroke, n = 116

Table 5: Distribution of cardiovascular complications according to PP

Class of PP (mmHg)	Total No.	Cardiovascular complications n (%)
<60 at 3 visits	35	7 (20.0)
≥60 at 1 visit	45	7 (17.1)
≥60 at two visits	26	12 (46.2)
≥60 at 3 visits	10	8 (80.0)

n = 116

Complications

After 6 months of treatment, complications found in patients are contained in Table 4. The distribution of cardiovascular complications according to the PP is presented in Table 5.

DISCUSSION

In a population of black hypertensive patients initially managed on out-patients basis, we have assessed the modifications of antihypertensive treatment taking in to account the variations of the PP and have noted CV complications registered after 6 months of follow up. In the course of this study, limited financial means led to the reduction of the number of patients considered at inclusion.

At the end of the 6 months of treatment, the number of patients having a SAP < 18664.8 Pa (140 mmHg) and a DAP < 11998.8 Pa (90 mmHg) went from 5.2 to 37%. The number of hypertensives at stage 2 clearly regressed to the benefit of HBP stage 1.

As antihypertensive treatment was going on, blood pressure was becoming normal. The number of patients belonging to the class of PP < 7999.2 Pa (60 mmHg) had increased tremendously between inclusion and M6 going from 29.3 to 69.8%. The percentage of patients with PP ≥ 7999.2 Pa (60 mmHg) regressed over the 6 months: from 70.7% at first consultation, it went to 43.1% after a month, to 36.2% at 3 months to reach 30.2% at 6 months.

It appears from our results at 6 months that there is a connection between the regression of CV events and the decrease of the PP. The linear regression by stages (Safar *et al.*, 2004) has shown that

certain factors influenced the percentage of the variation of PP. the initial value of the PP and the treatment. Safar *et al.* (2004) also pointed out others factors such as the sex and the age.

We have noticed that a progressive increase of the number of patients under bitherapy or combination therapy with $PP < 7999.2 \text{ Pa}$ (60 mmHg) and same time an important decrease of the number of patients with $PP \geq 7999.2 \text{ Pa}$ (60 mmHg) that were under bitherapy or combination therapy.

In the study PHASTE 2000 (Safar *et al.*, 2004), the proportion of patients treated by combination therapy (angiotensin-converting-enzyme inhibitor + diuretic) went from 10% to more than 90%, while, this increase was only 5% in present study probably because the pluritherapy was administered at once in an important proportion of patients. This can be explained by the severity of the HBP of the subject of black race and by the therapeutic strategy we generally used in the treatment of the HBP which is low dose combination therapy. In this same PHASTE 2000 study (Safar *et al.*, 2004), the percentage of patients whom the PP was $\geq 7999.2 \text{ Pa}$ (60 mmHg), has definitely increased up to about 50%, whereas that of patients whom the PP was $\leq 10665.6 \text{ Pa}$ (80 mmHg) has decreased seriously to less than 5%, while we notice an increase of 40% having a $PP < 7999.2 \text{ Pa}$ (60 mmHg) and only a decrease of 23% of patients whom the PP was $\geq 10665.6 \text{ Pa}$ (80 mmHg). In spite of the important reduction of the number of patients with a $PP \geq 7999.2 \text{ Pa}$ (60 mmHg) and the increase of patients whom the PP was $\geq 10665.6 \text{ Pa}$ (80 mmHg), the differences observed can be explained by the absence of systematic use of combination therapy angiotensin-converting-enzyme inhibitor + diuretic in this study.

In the same perspective, the STRATHE study (Waeber, 2005) comparative of the effectiveness and the tolerance of the three categories of antihypertensives (Low dose combination therapy, sequential mono therapy and strategy <<step by step>>) in the treatment of non complicated hypertension has shown a significant increase of the percentage of patients having a normal arterial pressure in the combination therapy group compared to sequential monotherapy and <<step by step >> groups.

From all what has been said, it is clear that in hypertensives patients under antihypertensive treatment, the combination therapy is effective in bringing down the PP and limits the risk of occurrence of cardiovascular events.

During this study we have noticed a progressive return to normal of PP and AP in the patients.

Recommendations on management of high blood pressure are based most often on the measures of systolic and diastolic blood pressure.

The regression of cardiovascular complications was in connection with the mastery of PP in the group of patients having a $PP \geq 7999.2 \text{ Pa}$ (60 mmHg). Then, a meta-analysis (Blacher *et al.*, 2000) gathering and comparing the results of the three therapeutic trials has pointed out the fact that it was the PP and not the mean pressure which determined the cardiovascular risk in elderly hypertensives patients.

All the results agree the fact that the occurrence of cardiovascular complications is significantly more important for elevated pulse pressure.

Similarly, over these last years, studies from many countries have shown that the PP is a CV risk factor regardless of the systolic pressure, the diastolic pressure and the mean pressure (Madhavan *et al.*, 1994; Mitchell *et al.*, 1997). A $PP > 8665.8 \text{ Pa}$ (65 mmHg) may be associated with a straight elevation of cardiovascular risk, namely coronary, even though the absolute values of SAP and DAP did not exceed the upper limits of the normal (Benetos *et al.*, 1998). New studies have highlighted the role of this PP in association with other cardiovascular risk factors (Laugesen *et al.*, 2009). Although most studies were conducted at the old subject, it appears today that PP is a risk factor even among the young subjects by means of a left ventricular hypertrophy (Toprak *et al.*, 2009).

CONCLUSION

The pulse pressure is a factor to be taken more and more into account in the management of high blood pressure. The more the PP was mastered, the less cardiovascular complications were noticed. It is a reliable parameter to predict the occurrence of new cardiovascular events in hypertensive patients.

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