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Relation between Pulse Pressure, Hypertensive Retinopathy, and Other Cardiovascular Risk Factors among Hypertensive Patients in Cameroon

Relation entre la pression pulsée et la rétinopathie hypertensive et d'autres facteurs de risque cardiovasculaire chez des patients hypertendus au Cameroun

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ABSTRACT

Introduction. There are few studies on the prevalence of hypertensive retinopathy and the specific role of pulse pressure in the occurrence of cardiovascular complications in general and hypertensive retinopathy in particular in Cameroon. The aim of this study was to investigate the relationship between pulse pressure, hypertensive retinopathy and cardiovascular risk in a group of hypertensive patients in Cameroon. **Methods.** We carried out an analytic cross-sectional study from October 2016 to May 2017 in three hospitals in Garoua (Cameroon). We included all known hypertensive patients aged over 18 years consulting in selected hospitals, who provided their written inform consent. Patients with concomitant diabetes or presenting a contraindication to eye dilation were excluded. Each patient underwent an interview using a standard questionnaire, physical examination with including measurement of blood pressure and anthropometric parameters. A complete eye examination was carried out in search of hypertensive retinopathy. **Results.** We included 130 participants (65.4% females) with a mean age of 53.18 ± 10.7 years, and a mean duration of hypertension of 5.9 years. 79.2% of participants were on pharmacological treatment – mainly calcium inhibitors (50.3%) and thiazides diuretics (17.2%). 23.9% already presented with target organ lesions. Hypertensive retinopathy was seen in 16% of patients, and was associated with male sex, target organ damage, and age ≥65 years. Pulse pressure correlated with age, mean arterial blood pressure and systolic blood pressure. However, we found no association between pulse pressure and hypertensive retinopathy. **Conclusion:** Hypertensive retinopathy is frequent in Cameroonian hypertensive patients, and is associated with other target organ lesions but not with pulse pressure.

RÉSUMÉ

Introduction. Au Cameroun, il existe peu de données sur la prévalence de la rétinopathie hypertensive et le rôle du niveau de pression pulsée dans la survenue des complications cardio-vasculaire. L'objectif de notre travail était d'étudier la relation entre une élévation de la pression pulsée et la rétinopathie hypertensive chez un groupe de patients hypertendus au Cameroun. **Méthodes.** Il s'agissait d'une étude transversale à visée descriptive et analytique, qui s'est déroulée sur une durée de 08 mois allant d'octobre 2016 à Juin 2017 dans trois hôpitaux de la ville de Garoua. Nous avons recruté les patients hypertendus âgés de 18 ans révolus consentants, venus consulter dans ces formations hospitalières. Les patients diabétiques ou avec une contre-indication à la réalisation d'un fond d'œil ont été exclus. Les données socio-démographiques, les antécédents personnels et familiaux du malade ont été collectés. Un examen physique complet avec une prise des paramètres anthropométriques a été réalisé au premier contact. Par la suite un fond d'œil a été réalisé à la recherche de rétinopathie hypertensive. **Résultats.** Nous avons recruté 130 patients (65,4% des femmes), âgés de 53 ± 10,7 ans, avec une durée moyenne de l'hypertension de 5,9 ans. 79,2% des patients étaient sous traitement antihypertenseur dont 50,29% sous inhibiteurs calciques et 17,2% sous diurétiques thiazidiques. 23,9% des patients sous traitement antihypertenseur ont présenté une atteinte d'organe cible de l'HTA. La prévalence de la rétinopathie hypertensive dans la population des hypertendus était de 16% et était associée à l'âge avancé (>65 ans), au sexe masculin et à l'existence d'une lésion d'organe cible. La pression pulsée était statistiquement corrélée à l'âge, à la pression artérielle moyenne et à la pression artérielle systolique. Il n'y avait pas d'association entre la pression pulsée et la rétinopathie hypertensive. **Conclusion.** La rétinopathie hypertensive est fréquente dans notre contexte bien qu'elle ne soit pas associée à la pression pulsée. Les facteurs associés à sa survenue sont l'âge avancé (> 65 ans), le sexe masculin et l'existence d'autres lésions d'organes cibles de l'hypertension.

INTRODUCTION

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure [1]. Hypertension was diagnosed in about 40% of adults over 25 years in 2008 and was responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke [2]. It is the most important preventable contributors to the global burden of disease and death and remains a major risk factor for cardiovascular and renal morbidity and mortality [3]. In Cameroon, this condition affects one in three adults [4]. Hypertension can lead to various complications affecting large vessels such as stroke, myocardial infarction as well as complications due to lesions of small vessels of the kidneys, nerves and eyes. Ocular manifestations of high blood pressure are common and result in vascular compromise at the level of the retina, the choroid, or the optic nerve. It is estimated that 10.7% of hypertensive patients over the age of 40 have hypertensive retinopathy and over a 5-year follow-up period [5]. Hypertensive retinopathy is the most common ocular sign of hypertension and is a result of the breakdown of the inner blood-retinal barrier [6]. Given that, current guidelines recommend routine ophthalmoscopy examination to detect signs of retinopathy in people with hypertension [7,8]. Hypertensive retinopathy is independently associated with long-term cardiovascular mortality [9]. Prevalence of retinal lesions due to arterial hypertension in Cameroonian milieu is estimated at 30.5%. In addition to systolic (SBP), diastolic (DBP) and/or mean arterial blood pressure (MAP), pulse pressure (PP) has recently emerged as an independent cardiovascular risk factor, associated with hypertensive and cardiovascular complications [10,11]. For instance, in a population-based study of Tehranian adults, SBP and PP had similar discrimination and fitness characteristic for prediction of CVD events and total mortality among both younger and older adults, which were stronger than MAP and DBP [12].

Whether pulse pressure is associated with retinal complications of high blood pressure is unknown, and study on the topic are scarce. Therefore, we aimed to investigate the relationship between pulse pressure and hypertensive retinopathy in Cameroon.

MATERIALS AND METHODS

Study design and setting

We carried out an analytical cross-sectional study from October 2016 to May 2017 in three hospitals in Garoua (Cameroon) namely the Regional Hospital, the Medico-Social Center of the National Social Welfare Fund, and the Notre Dame Hospital of the Apostles of Garoua.

Participants

We included every known hypertensive patient aged over 18 years with or without treatment consulting in the selected hospitals, and who provided a written inform consent. Patients with concomitant diabetes or presenting a contraindication to eye dilation were excluded.

Procedure

Recruitment was carried out in the emergency departments, outpatient clinics, internal medicine and medical resuscitation units. Eligibility criteria were checked and eligible patients were invited to participate in the study. During the first visit, patients were interviewed using a standard questionnaire. This served to collect socio-demographic data, other cardiovascular risk factors, past medical history: duration of hypertension, lifestyle, treatment adherence, pharmacological treatment, compliance, and complications. This was followed by a detailed physical examination for blood pressure and anthropometric parameters. This was an office blood pressure measured in mmHg using an automated electronic device (OMRON® M2 INTELLISENSE). The measurement was done on a patient at rest since at least 5 minutes, with an adapted cuff on both arms, and repeated on the arm with highest values. Then, the average of these two measures was considered. The height was measured in cm on a patient standing, while the weight was measured in light clothes to the nearest 0.5 Kg. Body mass index (BMI) was calculated using the formula Weight/(height)^2. Pulse pressure was calculated by the equation systolic blood pressure – diastolic blood pressure. Retinal perfusion was estimated by the following relation: Retinal perfusion pressure = 0.666 Mean arterial blood pressure – Intraocular pressure. Mean arteria blood pressure was defined as diastolic blood pressure + 1/3 pulse pressure. Following this first visit, the patient was invited to a second visit at the ophthalmic department of the Garoua Regional Hospital. During this visit, a complete eye examination was done with intraocular pressure measurement, visual acuity, and eye dilation for retinal examination. The third visit served for the measurement of biological parameters such as fasting glucose, dipstick in search of proteinuria.

Sample size

The sample size was calculated using the Cochrane formula $N = Z^2 \times p\,(1-p)/d^2$. Based on previous findings in our population study, that estimated the prevalence of high blood pressure to about 29.7% and that of hypertensive retinopathy at 30.47% among hypertensive patients. The calculated minimum sample size for the study was estimated to of 123 patients.

Statistical analysis

The data were entered into the CDC Epi-info ™ software version 7.2, then exported to the IBM SPSS Statistics ™ software version 20 for analysis. Qualitative data are expressed as count and percentages, and quantitative variables are expressed as mean ± standard deviation. The normality of the variables was checked using the Shapiro-Wilk test. Association between qualitative data was done using Chi-square test while correlation served to evaluate relation between quantitative variables. The level of significance was set at 0.05.

Ethical consideration

Ethical clearance was obtained from the Ethics Committee of the Faculty of Medicine and Biomedical

Sciences of the University of Yaounde I. Administrative authorizations were obtained locally from the study sites. Our study was conducted according to the principles of the Helsinki Declaration. All participants provided written informed consent.

RESULTS

General characteristics of the study population

Overall, we included 130 participants (65.4% females) with mean age of 53.2 ± 10.7 years, and a mean duration of hypertension of de 5.9 years. 89.23% of patients lived in urban settings. More than 2/3 (109/130) of participants were taking pharmacological treatment for high blood pressure. The average duration of hypertension in treated patients was 6.4 years versus 3.3 years in untreated patients. Other cardiovascular risk factors (obesity, smoking, sedentarily) were more frequent among already treated individuals. Calcium channel blockers (50.3%) and thiazide diuretics (17.2%) were the most prescribed molecules. 23.9% of treated patients presented with target organ damage. This was 19% among hypertensive individuals without pharmacological treatment. Only 2 (1.5%) of our patients were smokers, 12 (9.2%) consumed alcohol, and 19 (11.5%) practiced regular physical activity. The average body mass index was 28 ± 6 kg / m².

Blood pressure levels of our study population

The study population was then divided in two groups, treated and untreated patients, and subsequent analysis were done accordingly. Blood pressure levels of untreated patents were higher than those of treated individuals (SBP: 166 ± 25mm Hg vs 147 ± 23mm Hg; DBP: 99 ± 13mm Hg vs 92 ± 17mm Hg, MAP: 122 ± 15mm Hg vs 108 ± 21mm Hg; p<0.001). Similarly, retinal perfusion pressure and pulse pressure were much higher in untreated individuals and reached critical threshold set at 65mmHg (PP: 66 ± 21mmHg vs 55 ± 15mmHg; RPP: 67 ±10mmHg vs 58 ± 14mm Hg; p<0.001).

Prevalence and classification of hypertensive retinopathy

Overall, hypertensive retinopathy was found in 16.1% of patients. The frequency of hypertensive retinopathy in treated individuals was 17.4% versus 9.5% among untreated patients. Using Keith and Wagner classification stage 1 (31.57% vs 50%) and 2 (47.36% vs 50%) were the most found in treated and untreated patients respectively. Stage 3 was reported only in patients already receiving treatment (21.05).

Correlation between pulse pressure and cardiovascular risk factors

There was a correlation between pulse pressure and age in treated patients as well as untreated patients, systolic blood pressure, mean arterial pressure, and retinal perfusion pressure in both groups (Table 1). However, we found no statistically significant association between pulse pressure and duration of hypertension/follow-up.

Table 1: Factors correlated to pulse pressure

	Treated patients		Untreated patients	
	r (Pearson)	*p* value	r (Pearson)	*p* value
Age	**0.16**	**0.04**	**0.46**	**0.03**
BMI	-0.009	0.30	-0.06	0.78
Waist to Hip ratio	0.03	0.70	-0.18	0.42
SBP	**0.62**	**<0.001**	0.86	**<0.001**
DBP	0.10	0.28	0.03	0.87
MAP	**0.29**	**0.002**	**0.51**	**0.01**
RPP	**0.26**	**0.005**	**0.50**	**0.01**

Relation between hypertensive retinopathy and cardiovascular risk factors

Hypertensive retinopathy was associated to male sex [OR: 2.89; 95% CI 1.05 - 7.96; p = 0.03], age ≥65 years and existence of any target organ damage [OR: 3.86; 95% CI: 1.3 - 10.97; p = 0.008]. Table 2 summarizes the different factors associated to hypertensive retinopathy

Table 2: Factors associated with hypertensive retinopathy

	Treated patients			Untreated patients		
	Chi²	P	OR [95%CI]	Chi²	P	OR [95%CI]
Sex (male)	4.45	**0.03**	2.89 [1.05– 7.96]	0.83	0.36	3.7 [0.19 – 74.06]
Age ≥65 years	1.47	**0.02**	2.14 [0.33 – 3.88]	0.52	0.47	0.88 [0.74 – 1.05]
Smoking	1.50	0.22	4.9 [0.29 – 82.76]	/	/	/
Other target organ damage	7.00	**0.008**	3.86 [1.3 – 10.97]	0.52	0.47	0.88 [0.74 – 1.05]
Sedentarity	1.03	0.31	1.91 [0.53 – 6.82]	/	/	/
Waist to Hip ratio	2.51	0.11	2.22 [0.81 – 6.05]	0.36	0.54	0.88 [0.74 – 1.04]
SBP≥140 mm Hg	0.35	0.55	0.74 [0.27 – 2,00]	0,36	0,54	1,12 [0,95 – 1,32]
DBP≥90 mm Hg	0.46	0.49	0.70 [0.26 – 1,91]	0,69	0,40	1,14 [0,95 – 1,37]

Hypertensive retinopathy and pulse pressure

There was no association between elevation of pulsed pressure (≥65 mmHg) and the presence of hypertensive retinopathy in hypertensive patients.

Table 3: Association between pulse pressure and hypertensive retinopathy

	Treated		Untreated	
	Chi²	*p*	Chi²	*p*
Hypertensive retinopathy	0.00	0.99	0.005	0.95
Stages of hypertensive retinopathy				
Stage 1	0.57	0.45	0.95	0.32
Stage 2	0.007	0.93	1.15	0.28
Stage 3	1.11	0.29	/	/

DISCUSSION

Our study aimed to investigate the relation between hypertensive retinopathy, pulse pressure and cardiovascular risk factors in a group of treated and untreated hypertensive patients in Cameroon. We found that 20% of hypertensive patients were untreated and among treated individuals, the most prescribed pharmacological molecules were calcium channel blockers and thiazide diuretics according to international recommendations. Despite this treatment, blood pressure remained above the targets. About one quarter already had target organ damage. Hypertensive retinopathy was seen in 16% of patients, mainly stages 1 and 2. This was more frequent in already treated patients with long duration of hypertension. Pulse pressure correlated with age, mean arterial blood pressure, systolic blood pressure, and retinal perfusion pressure. Hypertensive retinopathy was associated with sex (male) and age ≥65 ans. However, we found no association between pulse pressure and hypertensive retinopathy.

The treatment rate of hypertension in our study is more than two third, which is much higher than previous findings in similar settings [13-15]. This suggests an increase in awareness for this condition in our context.

Moreover, the commonly prescribed pharmacological molecules largely agreed with the current recommendations, which proposed as first-line monotherapy with calcium channel blockers and / or thiazide diuretics [16]. However, the improved management illustrated by a high proportion of subjects undergoing pharmacological treatment and the adequacy of prescriptions with international recommendations is not accompanied by a better control of blood pressure figures, which remained above targets as previously described by in the same context one year ago [17]. This again shows, if need be, the difficulties associated with blood pressure control in the sub-Saharan African subject. This revives the debate on the previously described limitations of monotherapy for blood pressure control in sub-Saharan African subjects, and the need for more aggressive treatment from diagnosis, to ensure optimal control of blood pressure figures in these patients [18]. Target organ damage was also frequent in our population certainly due to sub optimal control of blood pressure figures affecting at least one quarter of our patients. Among complications of high blood pressure, retinopathy was mostly found in patients with long duration of hypertension despite pharmacological treatment. This could be attributed to an association between duration of hypertension and retinopathy. However, further analysis did not find this association, suggesting that important prevalence of retinopathy in this population is most related to uncontrolled blood pressure figures as described elsewhere [19]. Pulse pressure was correlated to other blood pressure components except diastolic blood pressure. Moreover, there was a positive correlation between pulse pressure and retinal perfusion pressure suggesting that an increase in pulse pressure is associated with an increase in retinal pressure which is considered as a contributor to hypertensive retinopathy [20]. Hypertensive retinopathy was associated with older age. Therefore, age could represent a cofactor in the effect of high blood pressure of the eye.

This could be that arterial hypertension is accompanied by an increase in retinal perfusion pressure which normally causes a reflex reaction of vasoconstriction of retinal arterioles to protect the retina from the detrimental effects of too high perfusion pressure. This reflex vasoconstriction may deteriorate with age, especially in the elderly, and lead to greater fragility of the retinal capillaries at changes in central and peripheral blood pressure. Finally, we found no association between elevated pulse pressure and the presence of hypertensive retinopathy in our study population, suggesting that elevated pulse pressure is neither a predictor nor a modulator of hypertensive retinopathy.

Limitations

Our study was a Hospital based study. As a result, it has a selection bias, in particular for the study of parameters such as the treatment rate and prevalence of hypertensive retinopathy. Patients regularly followed up in Hospitals are less prone to complications than those who are not regularly followed up. Consecutive sampling used increased this selection bias.

DISCLOSURE

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Author's contributions: Study conception and design: HB, HS and SK. Data collection: HB, HS, and SK . Statistical analysis and interpretation: HB, CNN, HS, and SK. Drafting: HB, CNN and SK. Critical discussion and manuscript revision: All authors.

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