Journal of Human Hypertension (2003) 17, 787–790

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ORIGINAL ARTICLE

Headache is not more frequent among patients with moderate to severe hypertension

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The association between hypertension and headache has been a contentious issue. Most studies have showed that mild hypertension and headache are not associated, but this may not be the case in patients with hypertension classified at more severe stages. We investigated the association between hypertension classified at moderate to severe stages and headache in a cross-sectional study conducted in the hypertension clinic of a tertiary care University hospital. In total, 1763 referred patients with a medical diagnosis of hypertension in most cases (95.7%) were evaluated by an extensive protocol questionnaire, detailed physical examination, laboratory examination, and had their blood pressure classified according to the VI Joint National Committee (JNC-VI) recommendation. Logistic regression models were used to explore the association between severity of hypertension and pulse pressure with the presence of headache, controlling for several potential confounders. The complaint of headache was referred by 903 (51.3% of whole sample), and a total of 378 patients (21.4%) were classified at the moderate to severe stage (stage III of the JNC-VI report). The diagnosis of moderate to severe hypertension was not associated with the complaint of headache (OR 1.02, 95% CI from 0.79 to 1.30). Pulse pressure and headache were inversely associated (OR 0.91, 95% CI from 0.86 to 0.97, for 10 mmHg). We concluded that headache and hypertension classified at moderate to severe stages were not associated in patients attending to a hypertension clinic. The novel finding of an inverse association between pulse pressure and headache should be addressed in further investigations.
Journal of Human Hypertension (2003) **17,** 787–790. doi:10.1038/sj.jhh.1001621

Keywords: blood pressure; pulse pressure; headache

Introduction

The absence of association between headache and hypertension has been consistently demonstrated.[1–9] More recent studies, with ambulatory blood pressure monitoring,[10,11] have showed that blood pressure did not vary around episodes of headache in patients already suffering from hypertension. In a population-based study, we demonstrated that not only blood pressure was unrelated to the complaint of headache, but that individuals with migraine tended to have lower blood pressure than individuals without migraine.[12]

Despite this large volume of evidence, reviewers and authors of book chapters are still asserting that hypertension causes headache, at least in certain conditions, such as severe and secondary hypertension.[13,14] Studies on the relationship between the hypertension classified at moderate to severe levels and headache, particularly in patients attending to outpatient clinics, are still lacking. In this report, we demonstrate that patients classified at the moderate to severe stages of hypertension did not complain of headache more frequently than patients classified at lower stages of hypertension, and that pulse pressure was inversely associated with headache in these patients.

Methods

Our data come from a prospectively planned cohort study of patients with hypertension in the hypertension clinic of the Divisions of Cardiology and Clinical Pharmacology of the Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil. Details of its design, data collection, and some results have been reported.[15–18] During baseline evaluation, patients answer to an extensive questionnaire and undergo a

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Received 3 June 2003; revised 3 July 2003; accepted 4 July 2003

detailed physical examination. The classification of blood pressure, according to the VI Joint National Committee (JNC-VI) recommendations,[19] is based on the average of six blood pressure measurements taken in three visits separated by intervals of 1–2 weeks. The diagnosis of hypertension and its classification are established during the first visit when blood pressure is within normal levels, in patients with severe hypertension and in patients with clinical consequences of high blood pressure. Secondary hypertension is sought in patients with any finding of suspicion on the basis of international recommendations.

Sitting blood pressure is determined twice with 2-min interval, after 5 min of rest, through indirect auscultatory method, using mercury or aneroid sphygmomanometers with standard cuff ($12 \times 23\,cm^2$), keeping the arm at the fourth intercostal level. In patients with arm circumference greater then 33 cm, a large cuff ($15 \times 33\,cm^2$) is used. The first phase of Korotkoff sounds is considered as systolic and the fifth phase as diastolic blood pressure.

The presence of 21 symptoms associated with cardiovascular diseases or other diseases is systematically questioned, such as chest pain, dyspnea, headache, insomnia, and anxiety. In the case of headache, the patient answers to the question 'do you use to have headache?' without any additional characterization.

Blood pressure and other continuous variables in patients with and without headache were compared using Student's *t*-test for independent samples. Categorical variables were compared using χ^2 test. The proportion of patients classified at the several stages of hypertension was compared between individuals who complained and who did not complain of headache. A logistic regression model was used to explore the association between gender, age, severity of blood pressure, use of blood pressure lowering medications, and other symptoms, with the presence of headache. An α level of 0.05 was regarded as significant and 95% confidence intervals (CIs) were calculated when appropriate.

Results

The study population consisted of 1869 patients. After the exclusion of 106 cases with missing data, 1763 patients (94.3% of the whole cohort) constituted the final sample. Most patients (95.7%) had a previous diagnosis of hypertension. The complaint of headache was referred by 903 patients (51.3% of whole sample).

The characteristics of patients with and without headache are presented in Table 1. Individuals with headache were younger, were more frequently women, and complained of anxiety and insomnia more frequently than individuals without headache. A total of 378 patients (21.4%) were classified as moderate to severe hypertensives (stage III of the JNC-VI report). More patients without headache tended to be classified at this stage than patients with headache. Body mass index and the proportion of current smokers, non-white individuals and patients using blood pressure-lowering drugs were similar in both groups. Patients with headache had systolic blood pressure (SBP) significantly lower than individuals without headache, and diastolic blood pressure (DBP) had a tendency to be higher in headache sufferers.

In logistic regression models, we explored the association between hypertension classified at the JNC-VI stage III and pulse pressure with the presence of headache, controlling for confounding variables. As can be seen in Table 2, the diagnosis of moderate to severe hypertension was not associated with the complaint of headache. When blood pressure was included in the model as a continuous variable, there was an inverse association between SBP and headache (OR = 0.98; 95% CI of 0.98–0.99) and a direct association between DBP and the symptom (OR = 1.02; 95% confidence interval of

Table 1 Characteristics of patients with and without headache (*N* and % or mean ± s.d.)

	Headache		
Characteristics	*Yes (N=903)*	*No (N=860)*	P
Females	678 (75.2)	533 (62.1)	<0.001
White	698 (79.8)	664 (80.4)	0.83
Current smoker	179 (20.1)	173 (20.3)	0.91
Using antihypertensive treatment	593 (65.3)	593 (69.0)	0.106
Anxiety	279 (30.1)	174 (21.1)	<0.01
Insomnia	266 (29.8)	158 (19.2)	<0.001
Hypertension stage III	179 (19.8)	199 (23.1)	0.09
Age (years)	48.2 ± 12.6	54.4 ± 12.9	<0.001
SBP (mmHg)	152.6 ± 25.0	157 ± 27.6	<0.001
DBP (mmHg)	94.1 ± 15.1	92.9 ± 15.0	0.106
BMI (kg/m^2)[a]	29.1 ± 5.5	29.1 ± 5.5	0.78

[a]Body mass index.

Table 2 The association between headache, moderate to severe hypertension, and other potential confounders, results of the logistic regression model

Variable	*Beta*	*OR*	*95% CI*	P
Age (years)	−0.03	0.96	0.95–0.96	<0.001
Anxiety (yes)	0.16	1.18	0.92–1.50	0.17
Hypertension stage III[a]	0.01	1.02	0.79–1.30	0.87
Sex (male)	−0.58	0.55	0.44–0.69	<0.001
Use of antihypertensive drugs	−0.12	0.88	0.71–1.09	0.26
Insomnia (yes)	0.55	1.73	1.35–2.22	<0.001

OR: odds ratio.
[a]The control group consist of patients classified at lower stages of hypertension or normal blood pressure.

Table 3 Association between headache, pulse pressure, and other potential confounders, results of the logistic regression model

Variable	*Beta*	*OR*	*95% CI*	P
Age (years)	−0.03	0.96	0.95–0.97	<0.001
Sex (male)	−0.62	0.53	0.42–0.67	<0.001
Use of antihypertensive drugs	−0.10	0.90	0.72–1.11	0.34
Pulse pressure (10 mmHg)	−0.009	0.91	0.86–0.97	0.023
Anxiety (yes)	0.16	1.17	0.92–1.49	0.17
Insomnia (yes)	0.54	1.72	1.34–2.20	<0.001

OR: odds ratio.

1.01–1.03). As a result of these opposite trends, pulse pressure was inverse and independently associated with headache (Table 3).

Discussion

We demonstrated, in a large sample of patients with hypertension attending to an outpatient clinic, and controlling for several potential confounders, that there is no association between the diagnosis of hypertension at moderate to severe stages and headache. These findings are in agreement with the results of most epidemiological,[3–5] clinical,[6–9] and studies with ABP monitoring,[10,11] which have not shown any consistent association between blood pressure and the diagnosis of hypertension with headache. Our findings extended these observations to patients classified at more severe stages of hypertension,[19] and suggest that finding of high blood pressure in patients with headache may be secondary to a reverse causality. The inverse association with pulse pressure was unforeseen, but showed to be independent of several confounders. There is no apparent explanation for this finding, which may be related to the opposite association with SBP and DBP, and the mechanisms of headache production.[20,21] The association with age would be a potential confounder, but it was controlled in the multivariate analysis. The play of chance cannot be ruled out.

Despite of being usually accepted as a potential cause of headache,[13] the association between severe hypertension and headache was predominantly described in previous studies, not controlling for confounding and for the awareness of hypertension.[22–25] It has been suggested that the awareness of the diagnosis may be a reason for the higher frequency of headache among patients with hypertension.[7,8] Since almost all participants of our study knew that they had hypertension, this potential bias on the association between the diagnosis of hypertension and the complaint of headache was naturally controlled.

A few more recent studies have suggested the existence of an association between headache and hypertension. Cooper *et al*[26] described a close relationship between SBP and DBP with headache, but they did not control for gender, age, and the awareness of the diagnosis. Hansson *et al*,[27] using pooled data from seven randomized double-blind, placebo-controlled trials with ibesartan, demonstrated that fewer patients with DBP between 90 and 99 mmHg complained of headache than patients with DBP higher than 100 mmHg. Moreover, individuals treated with the drug had also lower frequency of headache than patients receiving placebo. This study did not include, however, moderate to severe hypertensive patients. The small differences between the groups may be a result of a type I error or may be secondary to an effect of ibesartan unrelated to its blood pressure-lowering properties. The lower frequency among patients treated actively may be attributed to the general improvement in quality of life in patients treated with antihypertensive drugs.[28]

The possibility that there is a real association between hypertension classified at moderate to severe stage and headache cannot be completely discarded by our study, since the diagnosis of headache was not made at the same time of the classification of blood pressure. Since the complaint of headache was a highly prevalent condition, however, it is unlikely that any association could have been masked. The absence of any variation of blood pressure around episodes of headache strengthens the interpretation that there is no such association.[10,11] We cannot discard, also, a potential association between headache and blood pressure in patients with secondary hypertension. This possibility is also unlikely, since patients with such condition were just a small proportion of the whole sample. Moreover, if the prevalence of headache is different among patients with secondary hypertension, this could be secondary to the underlying cause of hypertension in these patients, and not to blood pressure itself.

The almost homogeneous demonstration of the absence of any consistent association between blood pressure, hypertension, and headache needs to be incorporated into clinical practice. Patients and physicians still believe on such association, despite the demonstration that the majority of patients could not identify if their blood pressure was high or low based on the presence of headache.[29] The suggestion that this belief should not be discouraged, in order to use the complaint of headache as a herald of uncontrolled blood pressure, is unjustifiable, since the contrary may also be happening.

In conclusion, we did not find a relationship between the complaint of headache and hypertension classified at moderate to severe stages in patients attending to a clinic for patients with hypertension. The finding of an inverse association between pulse pressure and headache should be evaluated in further investigations.

Acknowledgements

This is study was partially funded by CNPq and FAPERGS, Brazil.

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