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Headache: Prevalence and relationship with office or ambulatory blood pressure in a general population sample (the Vobarno Study)

MARIA LORENZA MUIESAN[1], ALESSANDRO PADOVANI[2], MASSIMO SALVETTI[1], CRISTINA MONTEDURO[1], PAOLO POISA[1], BIANCA BONZI[1], ANNA PAINI[1], ELISABETTA COTTINI[2], CHIARA AGOSTI[2], MAURIZIO CASTELLANO[1], DAMIANO RIZZONI[1], AMEDEO VIGNOLO[2] & ENRICO AGABITI-ROSEI[1]

[1]*Internal Medicine and* [2]*Neurology, Department of Medical and Surgical Sciences, University of Brescia, 25100 Brescia, Italy*

Abstract
The association of headache and arterial hypertension is still controversial, although headache is usually considered a symptom of hypertension. The aim of this study is to evaluate the prevalence of headache in a general population sample and the relationship with arterial hypertension, as diagnosed by office measurements and ambulatory monitoring of blood pressure (BP). *Patients and methods.* In the randomized sample of the Vobarno population, 301 subjects (126 males, 175 females, age range 35–50 years) underwent a structured standardized headache questionnaire, office and 24-h ambulatory BP monitoring. *Results.* Prevalence of lifetime headache and of migraine was greater in females than in males. Office and 24-h BP values did not differ between subjects without headache and subjects with headache. No differences in headache prevalence (58% vs 55%), migraine prevalence (32% vs 28%) and use of analgesic drugs in the presence of headache (82% vs 78%) were observed between hypertensive patients (93.5% newly diagnosed, 6.5% treated) and normotensive subjects. *Conclusions.* In a general population sample, hypertension (diagnosed by office and/or 24-h BP) is not associated with headache.

Key Words: *Headache, ambulatory BP, blood pressure, migraine, masked hypertension, isolated office, hypertension*

Introduction

Headache is a common symptom and it has been reported to be the most frequently mentioned complaint that accompanies hypertension (1–8). In untreated hypertensive patients (diastolic blood pressure between 95 and 125 mmHg) the incidence of headache ranged from 15% to 20% (6). Despite the early recognition of an association, the link between headache and hypertension has been often attributed to anxiety or anger (9,10), which may trigger benign headache, or to the adverse effects of antihypertensive drugs (11–17).

Ambulatory BP monitoring (ABPM) provides an opportunity to analyse the relationship between the increase in blood pressure (BP) and headache, because it can more precisely identify truly normotensive and hypertensive patients (18). Some recent prospective studies have given conflicting results related to the association between BP values (measured both in the clinic and by ambulatory monitoring) and headache in hypertensive patients (19,20); in these studies, ABPM was used to evaluate the behaviour of BP during headache episodes, rather then to confirm the diagnosis of hypertension, or identify the presence of isolated office or isolated ambulatory hypertension (19,20).

Several main characteristics of headache have been rarely described in selected hypertensive patients groups, and only attempts of classification of various types of headache have been proposed (21,22). In a general population setting, migraine

Correspondence: Maria Lorenza Muiesan, Department of Medical and Surgical Sciences, University of Brescia, 25100 Brescia, Italy. Tel: +39-0303995829. Fax: +39-0303388147. E-mail: muiesan@med.unibs.it

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was found more frequently in subjects with optimal to normal BP (22), although elevated BP, stroke, epilepsy and psychiatric disorders have been associated with migraine (21).

The aim of this study is to evaluate the prevalence and the characteristics of headache in a young sample of a general population, living in a small town in Northern Italy, according to the diagnosis of hypertension, made by measurement of both office and ambulatory BP values.

Subjects and methods

Study population

We examined a sample of subjects 35–50 years of age selected from the general population of Vobarno, a small town in northern Italy. The participants in this ongoing epidemiological study were randomly extracted from the electoral rolls (23); almost 80% of the invited people agreed to participate in the study project and gave their informed consent. The study protocol was approved by the institution committee on human research.

After overnight fasting, each subject was admitted in the morning (08.00–09.00 h) to the outpatient clinic. Blood was drawn on the same day as the 24-h BP monitoring after fasting and abstinence from smoking for 12 h. Total serum cholesterol, triglycerides, glucose, uric acid and creatinine were determined.

A careful medical history was collected by a physician, with special attention to family and personal history of hypertension, ischaemic heart disease, stroke, diabetes mellitus and dyslipidaemia.

Information related to educational and occupational working activity was collected.

BP measurements

BP was measured three times by the same physician in all subjects, using a mercury sphygmomanometer and taking the disappearance of phase V Korotkoff sounds as diastolic pressure, with the subject in a sitting position after 10 min at rest. Hypertension was defined as a sustained increase in BP (systolic BP$\geqslant$140 mmHg and/or diastolic BP$\geqslant$90 mmHg) according to the World Health Organization/ International Society of Hypertension guidelines (24), and subjects with laboratory and/or clinical findings suggesting secondary forms of hypertension were excluded from analysis.

Twenty-four-hour BP and heart rate were evaluated by non-invasive automatic monitoring (model 90207; SpaceLabs, Redmond, WA, USA; 25). Readings were taken every 20 min during the daytime, defined as 07.00 to 22.59 h and at least every 30 min at night, defined as 23.00 to 06.59 h, with a total number of about 64 measurements per day. The subjects were fitted with the recorder at 09.00 h and it was removed at 10.00 h on the following day (25 h of monitoring). The subjects were allowed to follow their daily normal routines after they left the laboratory, and were requested to refrain from heavy physical exercise and to keep a diary indicating location and activities of the day. No recordings were made at weekends or during holidays, and shift workers did not undergo ambulatory recording while working at night. The 24-h BP profiles were used to calculate mean 24-h systolic and diastolic values, mean daytime systolic and diastolic values, mean night-time systolic and diastolic values. For more details, see reference 23.

Headache evaluation

Any information about frequency and clinical characteristics of headache was obtained from a self-administered, structured, standardized questionnaire, checked by an interviewer. Headache was diagnosed in the presence of any episode during lifetime, regardless of the presence of other symptoms. The diagnosis of different kinds of headache was formulated according to the International Headache Society criteria (26). Migraine was diagnosed in the presence of two among the following symptoms: unilateral location, pulsating quality, mild or moderate intensity, bilateral location, no aggravation by walking stairs or physical photophobia, phonophobia, lasting from 30 min to 7 days, occurring in less than 180 days per year. The occurrence of these episodes in more than 180 days per year characterized the diagnosis of chronic tension-type headache. Temporary disability caused by headache was evaluated with frequency and pain intensity scale (Migraine Disability Assessment Score, MIDAS; 27). According to the obtained score, headache was classified into four grades: grade I (mild, 0–5 points), grade II (moderate, 6–10 points), grade III (severe 11–20 points), grade IV (very severe, 21 points or more). In addition, level of anxiety was evaluated by two different anxiety scale tests (27–29).

Statistical analysis

Analyses were carried out with the SPSS 11.0 statistical package. All data are expressed as mean $\pm$ SD. Unpaired *t*-test or one-way analysis of variance (ANOVA), with Scheffe' correction for multiple comparisons, was used to evaluate

differences between and within groups. Frequency distributions were analysed by the χ^2 test. A p-value <0.05 was considered of statistical significance. The calculation of sample size power, based on the 24-h ambulatory BP values, indicated a statistical power of 70%, and confirmed that the number of subjects was adequate for evaluating differences between subjects with and without headache.

Results

All subjects were included in the analysis. Demographic characteristics of subjects are given in Table I. We identified 122 hypertensive patients, of whom 22 (eight males and 14 females) were receiving antihypertensive therapy (beta-blockers in five patients, calcium-antagonists in three, angiotensin-converting enzyme inhibitors in six and combination treatment in eight). All untreated hypertensive patients were not aware of their BP and newly diagnosed. Twenty-eight women were in treatment with contraceptive pill or hormonal replacement therapy, and other 14 subjects were treated with drugs that do not interfere with BP.

Headache prevalence and characteristics

Prevalence of lifetime headache was 57% and was greater in females in respect to males (67% vs 31%, χ^2, $p=0.001$); in the group of patients with headache, the frequency of headache episodes was more than twice/month in 20% of subjects. No significant differences were observed between subjects with and without headache as related to demographic characteristics and biochemical parameters, except for gender (Table II); prevalence of migraine was 30% (39% vs 18%, χ^2, $p=0.01$ in females and males respectively).

Clinical and mean 24-h, daytime and night-time arterial pressure values were similar in subjects with high and low frequency of headache (Table II). None of the subjects suffered headache throughout the 24-h non-invasive recording of the arterial pressure.

No correlation was observed between the MIDAS scale score and the arterial clinic or monitored BP values.

No differences were noticed in the anxiety scales, evaluated according to two different scores, among the three groups of patients without headache or with increasing frequency of headache.

BP and headache

No differences were observed in the prevalence and frequency of any lifetime headache type, and of migraine between normotensives and hypertensives (both untreated and regularly taking antihypertensive therapy; Table III). Prevalence of headache did not differ significantly when all subjects were divided according to ESH/ESC classification of BP values, and no differences in headache prevalence and episodes frequency, or in migraine prevalence were observed, considering subjects with optimal, normal or high-normal BP values (Table III).

In addition, in order more precisely to define the increase in BP values in the clinic and during 24 h, subjects were divided according to BP values measured in the clinic and during 24-h BP monitoring into four groups: normotensives (subjects with clinic office BP $<140/90$ and 24-h BP $<125/80$ mmHg), isolated clinic hypertension(subjects with clinic BP $\geqslant 140/90$ and 24-h BP $<125/80$ mmHg), hypertensives (subjects with clinic BP $\geqslant 140/90$ and 24-h BP $\geqslant 125/80$ mmHg) and isolated ambulatory hypertension (subjects with clinic BP $<140/90$ and 24-h BP $\geqslant 125/80$ mmHg). Prevalence of headache and migraine were not statistically significant among the four groups of subjects (Table IV).

No significant differences were observed for family history of headache, frequency and intensity (MIDAS scale score), and anxiety scale among the three groups of normotensives, untreated and treated hypertensives (Table V).

Table I. Demographic and clinical characteristics of the whole population.

	Range	Mean ± SD
Age, years	36–50	43.16 ± 3.70
BMI, kg/m^2	17.7–42.7	25.27 ± 4.19
Glucose, mg/dl	72–243	94.38 ± 14.57
S Creatinine, mg/dl	0.5–1.4	0.87 ± 0.16
Uric acid, mg/dl	1.2–9.1	4.37 ± 1.41
Total cholesterol, mg/dl	27–367	217.58 ± 38.67
HDL-cholesterol, mg/dl	27–126	59.12 ± 16.75
Tryglicerides, mg/dl	32–681	131.58 ± 93.49
Systolic BP, mmHg	90–176	128.62 ± 14.15
Diastolic BP, mmHg	58–134	84.62 ± 10.43
Mean BP, mmHg	70–148	99.28 ± 10.94
Heart rate, beats/min	58–110	78.50 ± 7.94
Systolic BP 24-h, mmHg	97–166	120.80 ± 10.70
Diastolic BP 24-h, mmHg	61–116	78.04 ± 7.83
Mean BP 24-h, mmHg	72–133	91.83 ± 8.65
Heart rate 24-h, beats/min	55–97	75.90 ± 7.82

SD, standard deviation; BMI, body mass index; HDL, high-density lipoprotein; BP, blood pressure.

Discussion

Our study has estimated the prevalence of headache and hypertension in a young sample of general

Table II. Demographic data, laboratory parameters and blood pressure (BP) values in the clinic and during 24-h ambulatory monitoring in subjects with and without headache.

	No headache	Headache	*p*
Age, years	42.5±4	43.6±4	NS
Male, %	56	31	0.001
BMI, kg/m^2	26±4	25±4	NS
Serum glucose, mg/dl	96±20	93±10	NS
Cholesterol T/HDL, mg/dl	220±35/57±16	219±39/60±17	NS
Creatinine, mg/dl	0.88±0.15	0.87±0.16	NS
Uric acid, mg/dl	4.59±1.38	4.24±1.46	NS
Heart rate, beats/min	78±10	77±18	NS
Clinic systolic BP, mmHg	128.23±14.33	128.94±14.43	NS
Clinic diastolic BP, mmHg	84.38±9.91	84.59±11.13	NS
Clinic mean BP, mmHg	99.01±10.67	99.35±11.53	NS
24-h heart rate, beats/min	76±7.8	76±7.5	NS
24-h systolic BP, mmHg	121.18±10.35	120.77±11.12	NS
24-h diastolic BP, mmHg	77.96±7.21	78.01±8.11	NS
24-h mean BP, mmHg	92.11±8.05	91.89±9.13	NS
Daytime heart rate, beats/min	78±7.8	79±7.5	NS
Daytime systolic BP, mmHg	125.3±11	125±11	NS
Daytime diastolic BP, mmHg	81.3±7.8	81.4±8.7	NS
Daytime mean BP, mmHg	96±8.4	96±9.5	NS
Night-time heart rate, beats/min	64±7	63.5±6	NS
Night-time systolic BP, mmHg	110.2±10.3	110±12	NS
Night-time diastolic BP, mmHg	68.6±7.4	68.2±8.4	NS
Night-time mean BP, mmHg	82±8.7	81±9.6	NS

BMI, body mass index; HDL, high-density lipoprotein; BP, blood pressure.

population sample in a small town in Northern Italy. The overall prevalence of lifetime episodes of headache was quite high and in agreement with previous reports (31–34). Women complained more frequently than men of headache, and in particular of migraine, while age, educational and occupational job were not related to the occurrence or increased frequency of headache (22,32). Our study confirmed previous findings (22), showing that migraine-like episodes of headache were slightly more frequent in normotensive subjects, as diagnosed by clinic and 24-h monitored BP values (32).

The lack of an association between headache and hypertension confirms previous results from cross-sectional studies (21,33,34). In a very recent meta-analysis of randomized, placebo-controlled trials with antihypertensive drugs, including 24,000 patients, the cross-sectional analysis across the placebo groups could not demonstrate any significant association between headache and diastolic or systolic BP (35).

In our study, BP values were measured in the clinic on two different occasions and confirmed by 24-h BP recordings, and therefore the diagnosis of hypertension was particularly accurate; as meticulous was the diagnosis of headache and its subtypes.

ABPM has been performed in two studies (19,20) in order to assess a possible relationship between the occurrence of headache and the simultaneous increase in BP; in both studies, examining mild to

Table III. Prevalence of headache and of high-frequency headache according to the degree of blood pressure (BP) increase.

	Headache prevalence (%)	Prevalence of frequent headache episodes (> 2/month) (%)	Migraine prevalence (%)
Optimal BP	17	14	18.5
Normal BP	25	23	26
High-normal BP	18	19	18
Grade 1	23	26	22.5
Grade 2	7	8	7.4
Grade 3	1	1	0
Antihypertensive treatment	8	9	7.4

Table IV. Prevalence of headache and migraine according to the presence of hypertension at clinical and/or 24-h blood pressure monitoring.

	Headache prevalence (%)	Migraine prevalence (%)
Normotension	53	58
Isolated office hypertension	11.8	7.4
Isolated ambulatory (masked) hypertension	6.5	2.5
Hypertension	27.5	30

Table V. Headache characteristics among the three groups of normotensives (NT) subjects, never treated hypertensive (HT) patients and HT patients receiving treatment.

	NT	Untreated HT	Treated HT	*p*
Family history of headache (%)	60	54	71	ns
Age of headache onset				ns
<20 years	29	19	14	
20–40 years	51	56	72	
>40 years	19	24	14	
Headache episodes frequency (>2/month)	27	25	18	ns
MIDAS score				ns
Grade I	6.5	4.2	17	
Grade II	44	46	33	
Grade III	43	43	33	
Grade IV	6.5	17	17	
Anxiety scale AST IX1	38±8	38±9	42±8	ns
Anxiety scale AST X2	37±7	37±9	38±7	ns

moderate hypertensive patients, BP levels in patients experiencing headache during the monitoring did not differ from those of patients without any symptom. The possibility that in subjects with headache, monitored BP values were not elevated because the subjects restricted their daily activities can be excluded by our study, since none of the subjects suffered of headache during the 24-h BP recording.

Anxiety may induce hyperventilation and an alert reaction, and has been invoked as a common mechanism to explain the occurrence of headache and increased BP (9,10). Anxiety may also be responsible for the greater incidence of headache reported in subjects, once they became aware of hypertension (1,36). In our study, we have taken into account this possible explanation, but could not demonstrate any difference in the anxiety profile, using two different scales, between patients with and without lifetime headache.

The results of our study can confirm that headache may be attributed to hypertension only in more severe conditions, such as pheochromocytoma or hypertensive encephalopathy (37,38). In our study in the group of patients with mild to moderate hypertension, none suffered high-frequency headache, while only one patient out of five patients classified as having severe hypertension (grade 3) reported suffering from high-frequency headache.

Several studies have attributed the development of headache in hypertension to the adverse effect of antihypertensive treatment, including diuretics, calcium antagonists and angiotensin-converting enzyme inhibitors (11,14,15). On the other hand, antihypertensive treatment with a calcium antagonist-based regimen (13) or with an Angiotensin II antagonist (16) could reduce headache episodes in hypertensive patients. Very recently, Law et al. have performed a meta-analysis of 94 randomized, placebo-controlled trials with four different classes of antihypertensive drugs, showing that BP-lowering drugs may prevent 30% of headache (35). We were not able to observe any relationship between the presence of headache and the class of antihypertensive drugs used, although the number of treated patients was very small. We have examined mainly newly diagnosed never-treated subjects, in the age range 35–50 years, 50% females, and therefore our observations cannot be extended to all hypertensive patients.

Conclusions

In conclusion, our study demonstrates that in patients with an accurate diagnosis of hypertension from a general population sample, the elevation in office and/or 24-h BP is not associated with increasing prevalence, frequency or severity of headache.

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