

Hypertension in headache patients? A clinical study

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Objectives – The aim of the present study was to assess the prevalence of hypertension in patients with headache, coming to the observation of an Headache Center. **Materials and methods** – A total of 1486 consecutive outpatients were examined, and blood pressure was determined in all patients. **Results** – Migraine without aura (MO) was the most common diagnosis, followed by migraine associated with tension-type headache, migraine with aura (MA), episodic tension-type headache (ETTH), chronic tension-type headache (CTTH), cluster headache (CH), and medication-overuse headache (MOH). Hypertension was present in 28% of the patients, and it was particularly common in MOH (60.6%), CTTH (55.3%), CH (35%), ETTH (31.4%), less common in MO (23%) and MA (16.9%). In all headache groups, the prevalence of hypertension was higher than in the general population, within all age groups. After adjustment for age and gender, hypertension was found to be more common in tension-type, and especially in CTTH, than in migraine. These findings could be affected by ‘Berkson’s bias’: and should not be extrapolated to the general population, but apply only to the subpopulation of patients who come to the observation of an Headache Center, and who may have more disabling symptoms. **Conclusion** – Hypertension could be one of the factors leading to exacerbation of the frequency and severity of attacks, both in migraine and tension-type headache. Hypertension has important therapeutic implications and should be actively sought in headache patients, and more thoroughly investigated, with *ad-hoc* surveys in the general population.

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Considerable controversy surrounds the association of headache with hypertension, as some studies suggest a link with migraine and tension-type headache (1–3), possibly limited to high diastolic blood pressure and migraine in women (4), while other studies deny such an association (5–7) or, on the contrary, suggest a link between headache and lower values of blood pressure (8). In a large series of patients, however, headache was found to be very common in hypertensive patients, and to ameliorate after antihypertensive treatment (9). This finding has been confirmed in more recent

studies (10, 11). Moreover, a number of studies have shown an association between chronic daily headache and hypertension (12–16). The aim of the present study was to assess the prevalence of hypertension in outpatients with migraine, tension-type headache, and other forms of primary headaches, or medication-overuse headache (MOH), coming to the observation of an Headache Center.

Materials and methods

Consecutive outpatients coming for their first visit to the ambulatory of the Headache Center, Department of Internal Medicine, University of Florence, from January 2000 to December 2001 were considered for this study. At their initial visit all patients underwent a thorough medical visit

Abbreviations: CH, cluster headache; CTTH, chronic tension-type headache; ETTH, episodic tension-type headache; MA, migraine with aura; MO, migraine without aura; MOH, medication-overuse headache.

including their medical and headache history, general and neurological examination, and determination of blood pressure. In patients showing a systolic arterial blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg two other blood pressure determinations in a month were taken for diagnosis, according to the methods exposed in the 'Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure' (17), and the average of the three determinations was used for statistical analysis.

Patients were seated in a chair with their backs supported and their arms bared and supported at heart level. Measurements were taken after 5 min of rest with a mercury sphygmomanometer, and two readings separated by 2 min were averaged. The diagnosis of headache was made according to the IHS 1988 criteria (18), through a questionnaire followed by a structured interview. Eight subgroups were used for the analysis: migraine with aura (MA), migraine without aura (MO), episodic tension-type headache (ETTH), chronic tension-type headache (CTTH), 'mixed headache', i.e. association of migraine with tension-type headache (mixed), cluster headache (CH), other forms of primary headaches, including all other forms (other), and medication-overuse headache (MOH). The two diagnostic classes of the 1988 IHS classification 'ergotamine-induced headache' and 'headache induced by abuse of analgesics' were merged together, and subsequently reclassified as MOH, according to the latest IHS classification (19). When more than one symptomatic drug was overused, the patient was classified according to the most frequently used drug in the last 3 months, based on self-reporting by patients.

Patients with secondary headaches other than due to substance abuse were excluded from the study. Hypertension was defined as systolic blood pressure of 140 mmHg or higher, or diastolic blood pressure of 90 mmHg or higher, or current treatment with antihypertensive drugs. In order to test for the excessive prevalence of hypertension in (some of) the eight subgroups, we compared the actual to the theoretical frequencies of hypertensive patients in each of them. Theoretical frequencies were obtained with an indirect standardization, so as to keep into account the peculiar age and gender composition of each subgroup, and under the so-called 'null' hypothesis, i.e. assuming absence of influence of each diagnosis on the chances of being hypertensive (see the Appendix for the details). The significance of the differences (actual vs theoretical) was determined using a chi-square test. As this proved significant (see below) for the eight-column

table, we further investigated specifically whether the association with hypertension differed between migraine (MA + MO) and tension-type headache (ETTH + CTTH), and as the answer was positive, we also compared MA to MO, and, separately, ETTH to CTTH, in all cases standardizing by age and gender, in order to obtain unbiased theoretical frequencies. The other headache subgroups were not considered in this restricted analysis, as in the mixed headache group migraine and tension-type headache coexisted, while the other groups included too few patients.

Results

During the study period, 1486 patients (1008 females and 478 males) were diagnosed with primary headaches or MOH: MO was by far the most common diagnosis (718 patients), followed by 'mixed headache' (342 patients), MA (124 patients), ETTH (105 patients), CTTH (94 patients), CH (60 patients), and MOH (33 patients), while 10 patients presented rare forms of primary headaches. In all headache subgroups, women were more represented than men, with the exception of CH (m/f ratio = 3.62) and ETTH (m/f ratio = 1.1). In the MOH group, 28 of 33 patients overused non-steroidal anti-inflammatory agents (NSAIDs), three patients paracetamol, and two patients ergotamine (data not shown). Table 1 shows the frequency of the different headache subtypes in men and women. Hypertension was a common finding, as it was present in 28% of the patients, and it was particularly common in MOH (60.6%), in CTTH (55.3%), CH (35%) and ETTH (31.4%), and less common in MO (22.9%) and in MA (16.9%). As could be expected, patients with 'mixed headache' showed a frequency of hypertension intermediate between tension-type headache patients and migraine patients (Table 2).

After adjustment for gender and age, the difference in the prevalence of hypertension between the eight subgroups was less striking (Table 2, theoretical prevalence), mainly because patients in the MOH and CTTH were older, and the prevalence of hypertension is known to increase with age. In the statistical analysis however the difference in the prevalence of hypertension proved highly significant, both considering all the eight subgroups ($P < 0.001$) or only the four main subgroups (MA, MO, ETTH and CTTH) ($P < 0.001$). Merging MA with MO and ETTH with CTTH, to obtain a 'migraine group' and a 'tension-type headache group', the difference in the prevalence of hypertension was again significant ($P < 0.001$) with hypertension being more frequent in tension-

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Table 1 Demographic characteristics of the different headache subtypes in the patient sample

	MOH (<i>n</i> = 33)	CH (<i>n</i> = 60)	CTTH (<i>n</i> = 94)	ETTH (<i>n</i> = 105)	MA (<i>n</i> = 124)	MO (<i>n</i> = 718)	Mixed (<i>n</i> = 342)	Other (<i>n</i> = 10)	Total (<i>n</i> = 1486)
Females	30	13	64	50	90	493	263	5	1008
Males	3	47	30	55	34	225	79	5	478
Mean age (SD)	47.9 (14.5)	40.1 (11.8)	40.8 (18.1)	36.2 (18.7)	32.5 (14.2)	35.1 (14.1)	36 (14.4)	43.6 (15.7)	36.1 (14.9)

MOH, medication-overuse headache; CH, cluster headache; CTTH, chronic tension-type headache; ETTH, episodic tension-type headache; MA, migraine with aura; MO, migraine without aura; Mixed, mixed headache (see text); Other, all other forms.

Table 2 Actual and theoretical* prevalence of hypertension in patients with different headache subtypes

	MOH (<i>n</i> = 33)	CH (<i>n</i> = 60)	CTTH (<i>n</i> = 94)	ETTH (<i>n</i> = 105)	MA (<i>n</i> = 124)	MO (<i>n</i> = 718)	Mixed (<i>n</i> = 342)	Other (<i>n</i> = 10)	Total (<i>n</i> = 1486)
Actual	20 (60.6)	21 (35)	52 (55.3)	33 (31.4)	21 (16.9)	165 (23)	97 (28.4)	7 (70.0)	416 (28)
Theoretical*	14 (42.4)	23 (38.3)	33 (35.1)	33 (31.4)	29 (23.4)	190 (26.5)	90 (26.3)	4 (40.0)	416 (28)

Values in parentheses are in percentage. MOH, medication-overuse headache; CH, cluster headache; CTTH, chronic tension-type headache; ETTH, episodic tension-type headache; MA, migraine with aura; MO, migraine without aura; Mixed, mixed headache (see text); Other, all other forms.

*Assuming absence of influence of headache subtype on hypertension, and after adjustment for age and gender.

type headache than in migraine. Conversely, the differences within subtypes, i.e. between MA and MO on the one hand, and between ETTH and CTTH on the other, did not pass the significant test, although in the latter case the difference was greater.

Discussion

Although tension-type headache is more prevalent than migraine in the general population (20), MO was the more common diagnosis in our patients, in line with a similar study conducted in an other Headache Center (2). This may be due to the fact that only patients suffering from severe tension-type headache seek medical advice in specialized clinics. The number of patients with MOH (33 of 1486 patients) was very low, compared to what is reported in the literature (20, 21), as many patients with MOH were hospitalized at our clinic, and their clinical recordings were not included in this study, that was conducted in an outpatient setting. The link between headache and hypertension has been addressed in relatively few studies, and is a highly controversial subject. Both conditions are extremely common in the general population, and their coexistence in an individual patient could therefore be merely coincidental.

Comorbidity, e.g. between hypertension and migraine, or hypertension and tension-type headache, could be postulated only if the association between hypertension and some form of primary headache was observed systematically in the general population. Comorbidity, if present, could be due to different factors, e.g. a common physiopathology, or the association with a particular genotype, although a preliminary study on genotyping for the

complement C3F has apparently ruled out an association between migraine and hypertension (22). To further confound matters, 'headache' could simply be a generic symptom of hypertension (and therefore a secondary headache), and in fact as early as in 1913 headache was indicated as the most common complaint in hypertensive patients (23), and recently an association between hypertension and morning headaches was evidenced (24), but in neither of these two studies it was possible to distinguish true migraine, or true tension-type headache, or a secondary headache due to hypertension, from a generic complaint of 'headache'.

Other studies did not show a positive association between headache and hypertension (25, 26) or suggested that headache could be a side effect of antihypertensive treatment (27–29). Probably reflecting uncertainty about this matter, in the latest classification of headache disorders (19), under the heading 'secondary headaches', it is stated that 'mild or moderate hypertension does not appear to cause headache, and whether moderate hypertension predisposes to headache remains controversial'. We found a high prevalence of hypertension in patients with primary headaches, particularly in CTTH, CH and ETTH, and even higher in patients with MOH. The prevalence of hypertension in our study, for all headache and age subgroups (data not shown), was higher than that observed in the general population (30). After age- and gender-adjustment, hypertension was found to be more common in tension-type headache than in migraine, suggesting a possible comorbidity between tension-type headache and hypertension.

To our knowledge, this is the first report of such a finding. In another study on a sample of patients

observed at an Headache Center, Cirillo et al. (2) found a prevalence of hypertension comparable to our results for MO and MA, but not for tension-type headache, where a lower prevalence of hypertension was found. Another study still, once again at an Headache Center but on a small sample of patients, gave results in line with our findings for the prevalence of hypertension both in migraine and tension-type headache (3).

Other studies have questioned the association between headache and hypertension (5–7), or have shown a higher prevalence of headache in subjects with lower blood pressure values (8). Interestingly, however, in one of these negative studies (8), a link between high diastolic blood pressure values and headache in men and migraine in women was found in one of the analyses, rendering the results of the study less clear-cut. Moreover, one study giving negative results (5) was based on the behaviour of ambulatory blood pressure determinations surrounding episodes of headache in hypertensive patients, and addressed therefore a somehow different problem. We suspect that the discrepancies in the results of these studies could be due to the substantial difference in the observed populations: two of the remaining three studies showing negative results were conducted in the general population (6, 8), and headache characteristics is subjects sampled from the general population could be different from those of patients coming to the observation of Headache Centers, who normally have more disabling symptoms. In short, the results of our study could be limited to patients with more severe forms of headache, in whom hypertension could cause a higher frequency and a greater severity of attacks. The association between chronic daily headache and hypertension has already been reported (12–16). Only large and accurately planned studies conducted in the general population could help to assess the possible existence of comorbidity between hypertension and some forms of primary headache, and the prevalence of secondary headache, due to hypertension.

Patients enrolled in clinic-based study form a sample subject to the so-called Berkson's bias (31), as patients with *both* hypertension and headache are more likely to come to the observation of Headache Centers (or other hospital-based clinics) than patients with headache only, or hypertension only, giving rise to a spurious association. Indeed, we tend to think that this is in fact the point, and that hypertension causes an exacerbation in the frequency and severity of attacks, probably in tension-type headache more than in migraine, urging patients to seek medical help in Headache Centers. Interestingly we found a very high

prevalence of hypertension in patients with abuse of analgesics, and this seems to be only partially due to the demographic characteristics of this subgroup (Tables 1 and 2) so that the pharmacological effects of NSAIDs could be involved for patients taking these drugs, as the administration of some NSAIDs has been associated with an increase in blood pressure values (32, 33). An alternative explanation could again invoke hypertension causing an increase in the frequency and intensity of attacks, leading to overuse of analgesics.

In conclusion, we found a high prevalence of hypertension in MOH and in different forms of primary headaches, and in patients with tension-type headache more than in patients with migraine, although these findings could be limited to patients coming to the observation of Headache Centers. This is not without therapeutic implications: in our experience, a good control of hypertension (and particularly of diastolic blood pressure values) is essential in order to alleviate or resolve headache symptoms both in migraine and tension-type headache. Well designed population-based studies would be needed to estimate the true prevalence of hypertension in primary headaches such as migraine, tension-type headache and CH, and also the prevalence of secondary headache, due to hypertension.

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Appendix

The indirect standardization procedure with which we determined the theoretical number of hypertensive patients by headache subtype is as follows. Table A1 gives the distribution by sex and age class of our patients in general and of those with hypertension. We can therefore calculate the proportions with hypertension in each cell.

We now observe the sex and age distribution of patients with the various headache subtypes, and apply the proportions with hypertension obtained (column c in Table A1) to estimate the theoretical frequencies, i.e. the number of hypertensive patients we should expect in each case if age and sex had an

Table A1 Demographic characteristics of the different headache subtypes in the patient sample

Age class	(a) All patients			(b) Hypertensive patients			(c) % with hypertension		
	Females	Males	All	Females	Males	All	Females	Males	All
0–17	95	80	175	0	0	0	0.0	0.0	0.0
18–29	256	104	360	27	24	51	10.5	23.1	14.2
30–39	256	133	389	52	49	101	20.3	36.8	26.0
40–49	187	92	279	53	37	90	28.3	40.2	32.3
50–59	133	38	171	69	25	94	51.9	65.8	55.0
60–69	63	20	83	45	10	55	71.4	50.0	66.3
70+	18	11	29	15	10	25	83.3	90.9	86.2
All	1008	478	1486	261	155	416	25.9	32.4	28.0

Table A2 Demographic characteristics of the different headache subtypes in the patient sample

Age class	(a) Headache subtype: CTTH			(b) Theoretical hypertensive		
	Females	Males	All	Females	Males	All
0–17	5	4	9	0	0	0
18–29	17	7	24	1.8	1.6	3.4
30–39	9	6	15	1.8	2.2	4.0
40–49	8	7	15	2.3	2.8	5.1
50–59	10	2	12	5.2	1.3	6.5
60–69	12	1	13	8.6	0.5	9.1
70+	3	3	6	2.5	2.7	5.2
All	64	30	94	22.1	11.2	33.3

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