PAPER

Blood pressure and risk of headache: a prospective study of 22 685 adults in Norway

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Objectives: Prevalence studies of the association between blood pressure and headache have shown conflicting results. The aim was to analyse the relation between blood pressure and risk of headache in a prospective study.

Methods: A total of 22 685 adults not likely to have headache, had their baseline blood pressure measured in 1984–6, and responded to a headache questionnaire at follow up 11 years later (1995–7). The relative risk of headache (migraine or non-migrainous headache) was estimated in relation to blood pressure at baseline.

Results: Those with a systolic blood pressure of 150 mm Hg or higher had 30% lower risk (risk ratio (RR)=0.7, 95% CI 0.6–0.8) of having non-migrainous headache at follow up compared with those with systolic pressure lower than 140 mm Hg. For diastolic blood pressure, the risk of non-migrainous headache decreased with increasing values, and these findings were similar for both sexes, and were not influenced by use of antihypertensive medication. For migraine, there was no clear association with blood pressure.

Conclusion: In the first prospective study of blood pressure and the risk of headache, high systolic and diastolic pressures were associated with reduced risk of non-migrainous headache. One possible explanation may be the phenomenon of hypertension associated hypalgesia, which probably involves the baroreflex system influencing nociception in the brain stem or spinal cord.

In 1913, Janeway noted that migraine was common in subjects with arterial hypertension,[1] and since then the relation between blood pressure and headache has been examined in many studies.[2–26] There is a consensus agreement within the International Headache Society that chronic arterial hypertension of mild to moderate degree does not cause headache.[27] Most cross sectional studies performed in unselected populations have shown no association (negative or positive) between blood pressure and the prevalence of headache.[2–14] In some studies, however, a higher prevalence of headache[15–18] and migraine[19 20] has been reported in hypertensive patients than among normotensive controls. Other studies have found a higher prevalence of hypertension among patients who have headaches[21–23] or migraine[24–26] than among headache free people.

In this prospective study of a large unselected population, we have examined the relation between blood pressure measured between 1984 and 1986, and the subsequent risk of developing non-migrainous or migrainous headache at follow up 11 years later (1995–7). We also assessed the cross sectional association between blood pressure and headache prevalence as estimated at follow up in 1995–7.

MATERIAL AND METHODS

In Nord-Trøndelag County in Norway, two population based epidemiological studies have been performed (The HUNT studies).[28 29] The first investigation (HUNT-1) took place between 1984 and 1986, and the main topics included blood pressure, diabetes mellitus, and health related quality of life. The second investigation (HUNT-2) was carried out between 1995 and 1997; it was more extensive than the first, and among several topics, HUNT-2 included 13 questions related to headache.[29]

In HUNT-1 (1984–6), all residents 20 years and older were invited to participate, and a detailed description of the study population has been given by Holmen *et al*.[28] Briefly, out of 85 100 eligible people, 77 310 (91%) answered the questionnaire that was sent with the invitation, and participated in a medical examination that included measurements of height, weight, blood pressure, pulse, and blood glucose. Blood pressure was measured according to a standardised method that has been described in detail elsewhere.[28] The participants were seated, and blood pressure was measured using a mercury sphygmomanometer after at least 4 minutes rest with the cuff placed on the right upper arm. The cuff was inflated twice with an interval of at least 1 minute. Systolic and diastolic pressures were registered to the nearest 2 mm Hg, and the second measured pressure was used in the analysis of this study.

The HUNT-1 questionnaire did not include headache items, but 59 471 persons responded to a question on use of analgesics ("How often have you taken pain relieving medication during the last month?"). A total of 41 581 responded that they "never" used analgesics. For the purpose of the present study, we have assumed that among those who had never used analgesics, the proportion of those with headaches would be negligible. Among the 41 581 subjects, 22 720 also attended HUNT-2 and responded to the headache questionnaire. Out of these, 22 685 people had their blood pressure measured in HUNT-1 (1984–1986), and were eligible for the prospective analysis. Among the 22 720 people assumed to be free of headache in HUNT-1, 6317 (28%) reported having headaches in HUNT-2 (migraine 7% and non-migrainous headache 21%).

In HUNT-2 (1995–7), all inhabitants 20 years of age and older were also invited to participate, and details of the study have been reported elsewhere.[29] Briefly, the participants answered two questionnaires. One (Q1) was included with the invitation, and the other (Q2) was handed out to those who attended the medical examination. Blood pressure was measured using an oscillometric method, and the cuff was inflated three times with 1 minute intervals. Analyses are based on the mean values of the second and third measurement. The Q2 included 13 questions on headache,[29]

designed to determine frequency of headache, and to diagnose migraine according to a modified version of the migraine criteria of the International Headache Society. Out of 92 566 invited subjects, 51 326 (56%) completed the headache questionnaire in Q2 and had their blood pressure measured.

By using the responses to the 13 headache questions in HUNT-2 we classified those who answered "yes" to the question "Have you suffered from headache during the last 12 months?" as "headache sufferers". Also, subjects who reported having migraine in the questionnaire were diagnosed as migraineurs. In addition, those who fulfilled the following criteria were diagnosed as having migraine:

- Headache attacks lasting from 4 to 72 hours (equal or less than 72 hours for those who reported frequent visual disturbances before the attacks).
- Headache had at least one of the following three characteristics: pulsating quality, unilateral location, or aggravation by physical activity.
- During headache, at least one of the following was present: nausea, photophobia, or phonophobia.

Our criteria for migraine were a modified version of the migraine criteria of the International Headache Society,[27] the most notable modification being that severity of pain was not included among the pain characteristics (item number 2**).** As a consequence, our migraine criteria were less rigorous regarding number of pain characteristics required for diagnosis. Also, our migraine criteria differed from the International Headache Society criteria —for examle, by not considering the number of previous attacks experienced over the lifetime. More details of the discrepancy between our migraine criteria and the International Headache Society criteria have been described previously.[29]

Headache that did not satisfy the criteria for migraine was classified as non-migrainous headache.

The questionnaire based headache diagnosis that we used has been validated by comparing it to diagnoses made in a clinical interview in a sample of participants.[29] For migraine, the positive predictive value of a questionnaire based diagnosis was 84%, and the chance corrected agreement (κ) was 0.59 (95% CI 0.47–0.71), which is considered moderate. For non-migrainous headache, and for the total group of "headache sufferers", κ values were 0.43 and 0.57, respectively, which indicate moderate agreement.[29]

Ethics

The study was approved by the regional committee for ethics in medical research, and by the Norwegian data inspectorate.

Statistical analysis

Differences between proportions were analysed by χ^2 test. p Values <0.05 were considered statistically significant. In multivariate analyses using multiple logistic regression, we used blood pressure values measured in HUNT-1 to estimate the relative risk of headache, as registered in HUNT-2. Risk was calculated for total headache ("all headache types"), and for the subtypes migraine and non-migrainous headache. Blood pressure was divided into three categories: <140 mm Hg, 140–149 mm Hg, and ⩾150 mm Hg for systolic, and <90 mm Hg, 90–99 mm Hg, and ⩾100 mm Hg for diastolic blood pressure. Initially, we also analysed headache risk by eight categories of blood pressure using increments of 10 mm Hg, but the results were not materially different from those presented in table 1. We evaluated potential confounding variables by adjusting for age (5 year categories), years of education (three categories: <10, 10 to 12 years, and >12), occupational status (four categories: employed, unemployed, retirement, and disability pension), use of antihypertensive medication (yes/no), current smoking (yes/no), alcohol consumption (three categories), and body mass index.

When appropriate,blood pressure was treated as a single ordinal variable (categories 1 to 3) and was incorporated in a two sided test for trend to evaluate the probability of a linear relation between blood pressure categories and headache risk ("dose-response relation"). The trend test was considered statistically significant at $p<0.05$.

To ensure that the use of antihypertensive medication did not influence the relation between blood pressure and risk of headache, we repeated the analyses after excluding the 3678 participants who used or had used antihypertensive medication, as assessed from information collected in HUNT-1 or HUNT-2. The precision of the relative risks was assessed with 95% confidence intervals (95% CIs). Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 8.0 (SPSS Inc, Chicago, USA).

RESULTS

High systolic blood pressure at baseline tended to be associated with low headache prevalence 11 years later in all

Table 1 Risk ratio (RR)* of headache related to blood pressure11 years earlier

		All headache types		Non-migrainous headache		Migraine	
Variable	Total number	n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)
Women:							
Systolic blood pressure (mm Hg)							
<140	7926	3091	1.0 (reference)	2168	1.0 (reference)	923	1.0 (reference)
140–49	1044	248	0.8 (0.7 to 0.9)	184	0.8 (0.7 to 1.0)	64	0.8 (0.6 to 1.1)
⩾150	1728	289	0.7 (0.6 to 0.8)	222	0.7 (0.6 to 0.8)	67	0.7 (0.5 to 1.0)
		p for trend <0.0001		p for trend <0.0001		p for trend <0.01	
Diastolic blood pressure (mm Hg)							
<90	8278	3033	1.0 (reference)	2137	1.0 (reference)	896	1.0 (reference)
90–99	1784	470	1.0 (0.9 to 1.1)	336	0.9 (0.8 to 1.1)	134	1.1 (0.9 to 1.4)
⩾100	636	125	0.8 (0.6 to 1.0)	101	0.8 (0.6 to 1.0)	24	0.7 (0.4 to 1.1)
		p for trend <0.05		p for trend <0.01		p for trend=0.44	
Men:							
Systolic blood pressure (mm Hg)							
<140	7879	1964	1.0 (reference)	1539	1.0 (reference)	425	1.0 (reference)
140–49	2022	420	0.9 (0.8 to 1.1)	321	0.9 (0.8 to 1.0)	99	1.1 (0.8 to 1.3)
⩾150	2086	295	0.8 (0.7 to 0.9)	225	0.7 (0.6 to 0.9)	70	0.9 (0.7 to 1.3)
		p for trend <0.0002		p for trend <0.0005		p for trend=0.25	
Diastolic blood pressure (mm Hg)							
<90	8191	1939	1.0 (reference)	1520	1.0 (reference)	419	1.0 (reference)
90–99	2804	593	1.1 (1.0 to 1.2)	450	1.0 (0.9 to 1.2)	143	1.2 (1.0 to 1.5)
⩾100	992	147	0.8 (0.6 to 1.0)	115	0.8 0.6 to 1.0)	32	0.8 (0.6 to 1.2)
		p for trend=0.10		p for trend <0.01		p for trend=0.17	

*Adjusted for age, occupational status, and use of antihypertensive drug therapy.

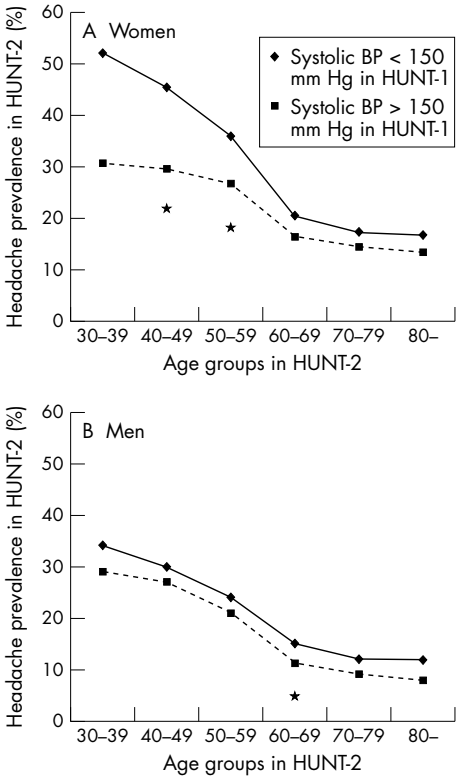

Figure 1 Headache prevalence (%) in HUNT-2 by age in those with systolic blood pressure ⩾150 mm Hg and <150 mm Hg in HUNT-1. *p<0.05.

age groups (fig 1). Among those with systolic blood pressure 150 mm Hg or higher, the relative risk of headache was 0.7 (95% CI 0.6–0.8) compared with those with systolic blood pressure below 140 mm Hg. For each sex, there was a strong linear trend (p<0.0002) of decreasing risk of headache with increasing systolic blood pressure (table 1). Excluding the 3678 people with a history of antihypertensive medication did not change the results (data not shown). We also analysed the data according to subtype of headache, and found that high systolic blood pressure was associated with reduced risk of non-migrainous headache for both sexes. For migraine, a similar relation was found only in women (table 1).

For diastolic blood pressure there was a trend of decreasing risk of non-migrainous headache with increasing pressure, evident for both sexes (p trend<0.01) (table 1). For migraine, however, there was no clear association with diastolic blood pressure.

In the cross sectional analysis (table 2), high systolic blood pressure was associated with slightly lower prevalence of headache, but this was statistically significant only for "all headache types" and for non-migrainous headache in women. Headache was slightly more prevalent in men with high diastolic blood pressure. Among women, there was an increasing prevalence of migraine with increasing diastolic blood pressure.

DISCUSSION

In this first prospective study to evaluate blood pressure as a risk factor for headache, the most striking finding was that high systolic and diastolic blood pressure at baseline was associated with a consistent reduction in risk of non-migrainous headache 11 years later. These findings were not influenced by the use of antihypertensive medication. In the cross sectional part of the study, we found an overall inverse relation between systolic blood pressure and headache among women but not among men.

The present results differ from those of cross sectional studies, which have either found no association[2–14] or a positive association between blood pressure and the prevalence of headache.[15–25] In cross sectional studies, however, the relation between cause and effect cannot be distinguished, as the blood pressure measurements are performed at the same time as the information on headache is obtained. Therefore, headache may influence the value of the measured blood pressure. Two major advantages of our study with regard to indicating an aetiological factor, is the prospective design, and that the blood pressure measurements were performed on a presumably headache free population.

It is a limitation of our study, however, that no headache questions were included in HUNT-1, and that headache status at baseline had to be determined indirectly by using information on the use of analgesics. Thus, we assumed that "never users" of pain relieving medication during the past month in HUNT-1 were unlikely to have had headache. It has, however, been reported that some patients with headache do not relieve their pain with medication.[30–34] If we included a substantial number of subjects at baseline who had headaches, this could have influenced our results, but it is difficult

Table 2 Cross sectional study (HUNT 2): Prevalence odds ratio (OR)* for headache in different blood pressure categories

		All headache types		Non-migrainous headache		Migraine	
Variable	Total number	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)
Women:							
Systolic blood pressure (mm Hg)							
<140	17960	9381	1.0 (reference)	6051	1.0 (reference)	3330	1.0 (reference)
140–59	5410	2236	1.0 (0.9 to 1.0)	1498	1.0 (0.9 to 1.0)	729	1.0 (0.9 to 1.1)
⩾160	4290	1324	0.8 (0.8 to 0.9)	927	0.8 (0.8 to 0.9)	397	0.9 (0.8 to 1.1)
Diastolic blood pressure (mm Hg)							
<90	22896	11041	1.0 (reference)	7229	1.0 (reference)	3812	1.0 (reference)
⩾90	4764	1900	1.0 (1.0 to 1.1)	1247	1.0 (0.9 to 1.0)	653	1.2 (1.0 to 1.3)
Men:							
Systolic blood pressure (mm Hg)							
<140	13003	4130	1.0 (reference)	3051	1.0 (reference)	1079	1.0 (reference)
140–59	7127	2015	1.0 (0.9 to 1.0)	1514	1.0 (0.9 to 1.1)	501	1.0 (0.9 to 1.1)
⩾160	3536	740	0.9 (0.8 to 1.0)	578	0.9 (0.9 to 1.1)	162	0.8 (0.7 to 1.0)
Diastolic blood pressure (mm Hg)							
<90	17822	5239	1.0 (reference)	3908	1.0 (reference)	1331	1.0 (reference)
⩾90	5844	1646	1.2 (1.1 to 1.2)	1235	1.1 (1.0 to 1.2)	411	1.1 (1.0 to 1.3)

*Adjusted for age, occupational status, and use of antihypertensive medication.

to ascertain in which direction. Identification of a completely headache free population is difficult, as most subjects will have had headaches during the past year.[35] It seems reasonable to assume that our "analgesic free" population had relatively minor headache problems compared with the general population.

It could be argued that non-migrainous headache was less frequent in subjects with high blood pressure because headache was better treated among those with a tendency to hypertension, as they probably visit doctors more often than normotensive people. However, this explanation seems unlikely, as our result was not influenced by use of antihypertensive medication.

A possible biological explanation for the inverse relation between systolic blood pressure and risk of headache may be the phenomenon called "hypertension associated hypalgesia".[36] The mechanisms are not clear, but data from humans and rats suggest that the baroreflex system may modulate nociception, probably involving both endorphinergic and noradrenergic neurons in the brain stem and spinal cord. Of particular relevance to the results of the present study is that an inverse relation between blood pressure levels and sensitivity to painful stimuli extends into the normotensive range.[36]

We found that high blood pressure was associated with reduced risk of non-migrainous headache. Among those with non-migrainous headache as many as 80% have tension-type headache according to our validation study.[29] If correct, we suggest that the phenomenon of "hypertension associated hypalgesia" has a protective effect against tension type headache. This was, however, not clearly demonstrated for migraine, because an inverse relation between blood pressure and risk of migraine did not reach statistical significance.

CONCLUSIONS

In this first prospective study of blood pressure and the risk of headache, we found that high systolic and diastolic blood pressure were associated with reduced risk of non-migrainous headache. A possible explanation for this surprising result may be hypertension associated hypalgesia, which may involve the baroreflex system influencing nociception in the brain stem or spinal cord.

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