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Response of Treatment in Patients with Primary Headaches and Hypertension: A Prospective Observational Pilot Study

Kan Basıncı Yüksekliğinin Eşlik Ettiği Primer Baş Ağrılı Hastalarda Tedaviye Yanıt: Prospektif Gözlemsel Pilot Bir Çalışma

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Abstract

Objective: To determine the priority in the treatment of patients with primary headaches accompanied by high blood pressure. In our study, we investigated whether there was a relationship between the decline in headache after treatment and the change in the average arterial pressure.

Materials and Methods: This prospective observational study was performed with 101 patients who were admitted to the hospital emergency department with primary headache accompanied by high blood pressure. After treatment, the decrease in the severity of headaches, mean arterial pressure, and percentage value for the drop of mean arterial pressure were calculated for all patients.

Results: In the study, 25 (24.8%) patients' headache decreased 3 levels, 43 (42.6%) patients' headache decreased 2 levels, and 23 (22.8%) patients' headache decreased one level. The mean arterial pressure value at admission was 118.58±12.65 mmHg, and after treatment at the 30th minute decreased to 98.41±13.43 mmHg. Although there was a statistically significant ($p<0.001$) decrease in the mean arterial pressure value of patients with 2-3 level decrease in the headache severity, there was no statistically significant ($p>0.05$) drop in the mean arterial pressure value of the patients with one level decrease in headache severity after treatment.

Conclusion: This study showed that when a primary headache, which is often associated with high blood pressure, was treated instead of treating high blood pressure as a secondary cause of headache, blood pressure decreased spontaneously.

Keywords: Emergency department, hypertension, primary headaches

Öz

Amaç: Bu çalışmanın amacı, kan basıncı yüksekliğinin eşlik ettiği primer baş ağrılı hastalarda tedavi önceliğinin belirlenmesine katkıda bulunmaktır. Çalışmamızda baş ağrısına yönelik uygulanan tedavi sonrası baş ağrısındaki gerileme ile ortalama arteriyel basınçtaki değişim arasında ilişki olup olmadığını karşılaştırdık.

Gereç ve Yöntem: Bu prospektif gözlemsel çalışma hipertansiyonun eşlik ettiği primer tip baş ağrısı şikayeti ile acil servise başvuran 101 hasta ile yapıldı. Tüm hastaların tedavi sonrası baş ağrılarındaki düşme düzeyleri, ortalama arteriyel basınç ve ortalama arteriyel basınçtaki düşme yüzdeleri hesaplandı.

Bulgular: Tedavi sonrası 25 (%24,8) hastanın ağrısı 3 alt düzeye, 43 (%42,6) hastanın ağrısı 2 alt düzeye, 23 (%22,8) hastanın ağrısı 1 alt düzeye düşmüştü. Başvuru anında hastaların ortalama arteriyel basınç değerlerinin ortalaması 118,58±12,65 iken baş ağrısına yönelik tedavi sonrası 30. dakikada hastaların ortalama arteriyel basınç değerlerinin ortalaması 98,41±13,43'e gerilemişti. Baş ağrısına yönelik verilen tedavi sonrasında baş ağrısında değişme olmayan ve bir alt düzeye gerileyen hastaların ortalama arteriyel basınç oranında anlamlı düşme olmazken ($p>0,05$), baş ağrısı iki ve üç alt düzeye gerileyen hastalarda ortalama arteriyel basınç oranlarında anlamlı düşme oldu ($p<0,001$).

Sonuç: Bu çalışma göstermiştir ki hipertansiyonla birlikteliği sık olan primer tip baş ağrılarında sekonder nedenler göz önünde bulundurularak yüksek kan basıncını kontrol etmeye yönelik tedaviler yerine baş ağrısı tedavi edilmelidir.

Anahtar Kelimeler: Acil bölümü, hipertansiyon, primer baş ağrısı

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Introduction

There is no consensus on the management of patients with high blood pressure (BP) and with no symptoms of acute target organ damage (TOD) (1). How to manage the patients admitted to the emergency deparment with headache and accompanying high BP is not exactly clarified (2). According to our clinical observations in cases where headache accompanied by high BP, it could be very difficult for physicians to understand what they are dealing with. It is not always possible to differentiate whether it is a headache because of high BP or it is high BP because of headache. Therefore, physicians may have doubts about which they should primarily treat. Headaches constitute an important portion of admissions to the emergency department and neurology clinics (3,4). In the United States (US), approximately 3 million people (2-3% of all emergency department presentations) are admitted to the emergency department due to headache every year (5). Headache, in which the clinical findings vary from 'very serious' to 'mild discomfort,' could be primary headache or a symptom caused by acute or chronic diseases (6). The majority of headaches encountered in emergency departments are primary headaches, which are classified as migraine, cluster-type, and tension-type. The severity of headaches in these patients generally decreases with symptomatic treatment (7). However, the pre- and post-treatment approach to headache requires a multifaceted perspective. Emergency department doctors should make the differential diagnosis between secondary headaches caused by structural and metabolic causes and primary headaches in which no cause and etiology is detected. This becomes more important, especially in the case of headaches accompanied by co-morbidities or a coincidental diseases (8). Hypertension (HT), as it is seen in one-third of the population of the US and one billion of the world population, is an important co-morbid condition that may accompany migraine (9). There are difficulties in the management of patients with HT who account for up to 45% of emergency department presentations. In the emergency department, a sufficient consensus has not been provided for the management of patients with moderate HT [systolic blood pressure (SBP) <180 mmHg, diastolic blood pressure (DBP) 90-120 mmHg] or with serious HT (SBP >180 mmHg, DBP >120 mmHg) without end organ damage (10,11). For patients admitted to the emergency department with high BP, there is insufficient evidence regarding the benefit or harm of reduction of high BP not accompanied with acute organ damage (1). However, it is known that ongoing HT changes the auto-regulation of cerebral perfusion. The reduction of BP more than 20-25% causes a disturbance in the auto-regulation and this in turn leads to a treatment-related decrease in cerebral perfusion and the development of various complications (7).

The purpose of this study was to contribute to the determination of the priority in the treatment of the patients with primary headaches accompanied by high BP. In our study, we investigated whether there was a relationship between a decline in headache after treatment and the change in the mean arterial pressure (MAP).

Materials and Methods

Study Design and Subjects

This prospective observational study was performed with 101 patients with primary headache accompanied by HT admitted to a second step city hospital emergency department, between May 5th, and July 31st, 2013 (Figure 1). The study was approved by the Dr. Lutfi Kirdar Kartal Training and Research Hospital of Local Ethics Committee (approval number: 8951337/1009/120).

Study Criteria

Inclusion criteria: Male and female patients aged over 18 years, who agreed to participate in the study, and who presented to the emergency department with symptoms of headache that were considered as primary-type headache accompanied with HT were included in our study. Consent forms were filled by all participants.

Exclusion criteria: Patients with evidence or suspicion of secondary headache conditions (trauma history, neurologic deficits, suspected intracranial infection, neck stiffness, suspected intracranial aneurysm, bleeding, surgical and tumor history, toxic exposures), patients with HT-associated TOD clinical and electrocardiologic findings (patients with clinical and electrocardiologic findings of HT-associated TOD), pregnancy or suspected pregnancy, patients with mental retardation or cognition

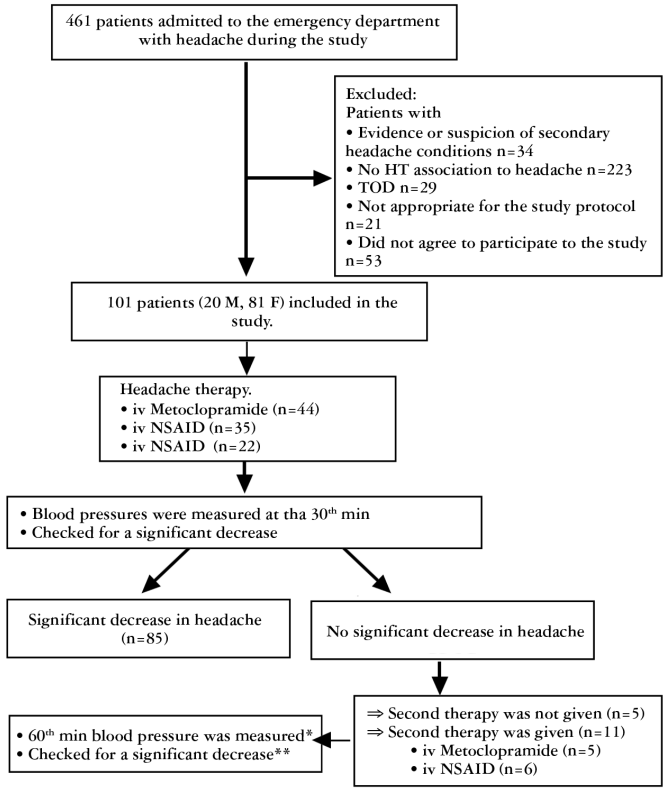

Figure 1. Study design and patient flow chart

*Intravenous vasodilator was given to one patient who had no decrease in blood pressure.

**No significant decrease was observed for one patient's headache.

M: Male, F: Female, HT: Hypertension, TOD: Target organ damage, IV: Intravenous, IM: Intramuscular, NSAID: Non-steroidal anti-inflammatory drug

impairment, allergies or adverse effect history for non-steroidal anti-inflammatory drug (NSAID) and metoclopramide, patients aged under 18 years, and those who did not agree to participate in the study were excluded from the study.

Study Protocol

Patients who presented to the emergency department with symptoms of headache and met the criteria for inclusion in the study were questioned for age, sex, and comorbid diseases (e.g., cerebrovascular disease, cardiovascular disease, HT, primary-type headache). Their headaches were evaluated in terms of duration, character, distribution, severity and associated symptoms, and data were recorded. The patients were questioned as to whether they had experienced a similar headache and if so what was their frequency. The severity of headache was classified into five categories based on a visual analog scale (VAS) (Figure 2). After resting for five minutes, all patients' right arm BPs were measured in the sitting position using a 13 x 47-cm cuff size manual BP measurement device (Erka, Perfect Aneroid Adult Sphygmomanometer, Germany). SBP ≥140 mmHg or DBP ≥90 mmHg values were considered as HT. The patients with HT were further investigated to identify TOD by evaluating clinical findings, imaging, and laboratory values; if TOD was identified, patients were excluded from the study. Intravenous (IV) metoclopramide, NSAID (tenoxicam) and intramuscular (IM) diclofenac were administrated to the patients for the treatment of headache. IV treatments in 100 cc saline solution were administrated over 15 minutes. Metoclopramide was preferred in patients with accompanying nausea. The administration type (IV or IM) of NSAID drug was left to the discretion of the patient. After the first treatment, the severity of headache as determined using the VAS scale and measured BP values were recorded at the 30th min. After treatment, the decrease in the severity of headache, MAP, and the percentage value for the drop of MAP were calculated for all patients. After the first treatment, the second treatment (metoclopramide instead of NSAID, NSAID instead of metoclopramide) was administrated to 11 out of 16 patients whose headache did not adequately decline, the other 5 patients did not agree to the second treatment. The severity of headache and BP values of these 16 patients were again recorded in the 60th minute.

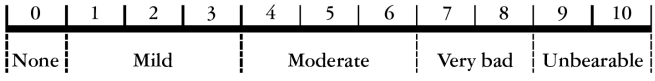

Figure 2. The headaches of the patients in the study group were classified into five groups according to a visual analog scale

Statistical Analysis

All data was recorded on the SPSS 19.0 software (SPSS Inc., Chicago, IL, USA) and frequencies and descriptive statistics were calculated. The Wilcoxon signed-rank test was used to calculate the relationship between decline in the severity of headache and drop of MAP.

Results

A total 101 patients, 20 (19.8%) males and 81 (80.2%) females, were included in the study. The mean age of the patients was 55.55±12.94 years (min: 22 max: 93 years). Of the patients, 6 (5.9%) had cerebrovascular disease, 10 (9.9%) had cardiovascular disease, 17 (16.8%) had primary headache syndrome, 55 (54.5%) had a history of HT. Thirty-nine (38.6%) of the patients were admitted to the emergency department with headache lasting more than 12 hours, 19 (18.8%) patients for 6-12 hours, 32 (31.7%) for 2-6 hours, and 11 (10.9%) patients were admitted in the first 2 hours. During the patients' admission to the emergency department, the severity levels of headaches were classified as excruciating for 40 (39.6%) patients, very bad for 42 (41.6%) patients, and moderate for 19 (18.8%) patients (Table 1). Thirty-eight (37.6%) patients described their headache as throbbing (pulsating), 26 (25.7%) patients as pressing/tightening, and 23 (22.8%) patients as a heaviness sensation in the head; the remainder described their headache in various ways. The pain localization for 35 (34.7%) patients was defined as the neck, 21 (20.8%) patients defined it as in both sides of the head, 11 (10.9%) patients defined it as one side of the head, and 6 (5.9%) patients defined it as both sides of the head and in the neck. The other 28 patients defined their pain locations as the forehead, localized in the retro-orbital area, orbital, periorbital and temporal areas, the top of the head or different combinations thereof. Although headaches were not accompanied by any symptoms in 22 patients (21.8%), 22 (21.8%) patients had nausea, 16 (15.8%) patients had nausea, photophobia and phonophobia, and 10 (9.9%) patients had symptoms such as restlessness and agitation accompanied by headache. The other 31 (30.7%) patients had these symptoms separately or in different combinations.

IV metoclopramide treatment was given to 44 (43.6%) patients, IV NSAID to 35 (34.7%) patients, and IM NSAID to 22 (21.8%) patients (Table 1). Only one treatment was performed

Table 1. The severity of headaches at admission and the treatment used

	The first therapy			
	IV Metoclopramide	IV NSAID	IM NSAID	
The severity of headache at admission	n (%)	n (%)	n (%)	Total (%)
Moderate	8 (42.1)	2 (10.5)	9 (47.4)	19 (100.0)
Very bad	16 (38.1)	15 (35.7)	11 (26.2)	42 (100.0)
Unbearable	20 (50.0)	18 (45.0)	2 (5.0)	40 (100.0)
Total	44 (43.6)	35 (34.7)	22 (21.8)	101 (100.0)

NSAID: Non-steroidal anti-inflammatory drug, IV: Intravenous, IM: Intramuscular

to 90 (89.1%) patients and the other 11 (10.6%) patients received the second drug therapy. An antihypertensive drug was given as a second therapy in one of these patients because they had an increase in MAP. When the severity of headaches was checked at the 30th minute, 5 (5.0%) patients had no headache, 69 (68.3%) patients had mild headache, 14 (13.9%) patients had moderate level, 8 (7.9) patients had a very bad headache, and 5 (5.0%) patients had excruciating headaches (Table 2). The decreases in the headache severity were divided into five levels as follows: 25 (24.8%) patients' headache decreased 3 levels, 43 (42.6%) patients' headache decreased 2 levels, and 23 (22.8%) patients' headache decreased one level. Ten patients had no change in the severity of their headache (Table 3). When the MAP value of the patients at admission was 118.58±12.65 mmHg, after treatment the patients' MAP value at the 30th minute was decreased to 98.41±13.43 mmHg. The rates of the decline in MAP values were found as >30% for 13 (12.9%) patients, 20.1-30% for 38 (37.6%) patients, 10-20% for 30 (29.7%) patients, <10% for 16 (14.9%) patients. Although MAP values of four patients were found to be increased, one remained the same (Table 4).

The decline in levels of headaches and MAP values of each decline level before and after treatment were calculated for patients with decline in headache after treatment. Whether there was a decline in MAP values after treatment was tested using these calculated values with the Wilcoxon signed-rank test. Although there was a statistically significant ($p<0.001$) decrease in the MAP rates of patients with a 2-3 level decrease in headache severity, there was no statistically significant ($p>0.05$) drop in the MAP rates of patients with a one level decrease in headache severity after treatment (Table 5). The comparison of decrease level in headache severity and MAP decline percentage after treatment is shown in Table 6.

Eleven patients who received the second therapy and 5 patients who did not agree to the second therapy were examined after 60 minutes and the decreases in headache and BP values were recorded. The severity of headache remained the same in one (6.2%) patient, decreased one level in 1 (6.2%), two levels in 9 (56.2%), 3 levels in 4 (25.0%), and 4 levels in 1 (6.2%) patient. For the same group of patients, the MAP value decreased from 107.29±17.25 to 100.42±16.32 mmHg. The decline rates in

Table 2. The severity of headache at admission vs. the 30th min after analgesia

	The severity of headache 30th min after analgesia					
	Absent	Weak	Moderate	Very bad	Unbearable	
The severity of headache at admission	n (%)	n (%)	n (%)	n (%)	n (%)	Total (%)
Moderate	4 (21.1)	14 (73.7)	1 (5.3)	-	-	19 (100.0)
Very bad	1 (2.4)	33 (78.6)	4 (9.5)	4 (9.5)	-	42 (100.0)
Unbearable	-	22 (55.0)	9 (22.5)	4 (10.0)	5 (12.5)	40 (100.0)
Total	5 (5.0)	69 (68.3)	14 (13.9)	8 (7.9)	5 (4.8)	101 (100.0)

Table 3. The severity of headache at the admission vs. decrease rates of headaches at the 30th min after analgesia

	The rate of decrease in the headache 30th min after analgesia				
	Same	1 level	2 levels	3 levels	
The severity of headache at admission	n (%)	n (%)	n (%)	n (%)	Total
Moderate	1 (5.3)	15 (78.9)	3 (15.8)	-	19 (100.0)
Very bad	4 (9.5)	4 (9.5)	31 (73.8)	3 (7.1)	42 (100.0)
Unbearable	5 (12.5)	4 (10.0)	9 (22.5)	22 (55.0)	40 (100.0)
Total	10 (9.9)	23 (22.8)	43 (42.6)	25 (24.8)	101 (100.0)

Table 4. The severity of headache at the admission vs. decrease rates of mean arterial pressure values at the 30th min after analgesia

	The rate of decrease in the MAP values at the 30th min after analgesia						
	<10%	10-20%	20.1-30%	>30%	Increased	Same	
The severity of headache at admission	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Total
Moderate	2 (10.5)	8 (42.1)	6 (31.6)	2 (10.5)	-	1 (5.3)	19 (100.0)
Very bad	5 (11.9)	11 (26.2)	18 (42.9)	6 (14.3)	2 (4.8)	-	42 (100.0)
Unbearable	8 (20.0)	11 (27.5)	14 (35.0)	5 (12.5)	2 (5.0)	-	40 (100.0)
Total	15 (14.9)	30 (29.7)	38 (37.6)	13 (12.9)	4 (4.0)	1 (1.0)	101 (100.0)

MAP: Mean arterial pressure

Table 5. The mean arterial pressure decrease levels before (0 min) and after (30th min) analgesia			
Decrease level for headache	MAP at 0 min Median (min-max)	MAP at 30th min Median (min-max)	p*
Same	112.0 (100.7-123.0)	106.7 (83.3-115.3)	0.384
One level	115.3 (92.7-143.3)	96.7 (80.0-146-7)	0.059
Two levels	116.3 (104.7-160.0)	96.7 (73.3-123.6)	<0.001
Three levels	120.0 (103.3-163.3)	96.7 (73.3-130.0)	<0.001

*p values were generated by using Wilcoxin signed-rank test. MAP: Mean arterial pressure, min: Minimum, max: Maximum

Table 6. The comparison of the decrease levels in the headache and decrease rates of mean arterial pressure at the 30th min							
	The rate of decrease in the MAP values 30th min after analgesia						Total
	<10%	10-20%	20.1-30%	>30%	Increase	Same	
Decrease level for headache	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Same	4 (40.0)	-	3 (30.0)	-	3 (30.0)	-	10 (100.0)
One level	5 (21.7)	8 (34.8)	6 (26.1)	2 (8.7)	1 (4.3)	1 (4.3)	23 (100.0)
Two levels	5 (11.6)	13 (30.2)	17 (39.5)	8 (18.6)	-	-	43 (100.0)
Three levels	1 (4.0)	9 (36.0)	12 (48.0)	3 (12.0)	-	-	25 (100.0)
Total	15 (14.9)	30 (29.7)	38 (37.6)	13 (12.9)	4 (4.0)	1 (1.0)	101 (100.0)

MAP: Mean arterial pressure

MAP values were <10% for 2 (12.5%) patients, <10-20% for 3 (18.8%) patients, <20.1-30% for 8 (50.0%) patients, and >30% for 1 (6.2%) patient. MAP values were increased in 2 (12.5%) patients.

Discussion

To the best of our knowledge, this is the first study to examine BP response for the headache therapy for the patients with primary headache accompanying HT in the emergency department. In this study, we identified that when the headache was treated, the accompanying HT was significantly decreased.

Headache and HT are two common causes of admission to the emergency department. However, these findings may be seen together. This combination occurs because HT is a frequent comorbid condition and acute headache leads to vascular sympathetic stimulation, which causes an increase in heart rate and BP (12). In the pathogenesis of vascular headache, in the earlier stage, there is a cerebral vasoconstriction that can reduce cerebral blood flow by 25% (13). Treating patients with HT who also have headache with antihypertensive drugs may cause cerebral perfusion that is already impaired to worsen, and this leads to a risk of ischemic stroke and cerebral cell loss (14,15).

The disease groups with high prevalence accompanying migraine are angina, acute myocardial infarction, affective disorders (depression, mania, anxiety and panic disorder), and stroke (16). In a migraine attack accompanied by stroke, BP increases to maintain cerebral perfusion in the border line ischemic area. In these conditions, which may be considered as a headache caused by HT, if antihypertensive agents are used the infarct area may grow larger. In the same way, diuretics, which aim at reducing HT, may cause an increase in blood viscosity and hematocrit, which in turn cause a reduction in blood fluidity and an increase in the infarct area (17). In order to provide the correct treatment, hypertensive emergencies should be accurately diagnosed, and in order to avoid possible complications, physicians should be familiar with the pharmacologic and clinical effects of drugs used (18).

Ferreira et al. (19) conducted a survey with physicians regarding hypertensive emergencies. In this study, the response by 95.2% of 250 physicians was that headaches were the second alarm finding of hypertensive emergencies. However, mild (140-159/90 mmHg to 99 mmHg) or moderate (160-179/100 mmHg to 109 mmHg) chronic arterial HT does not cause headaches, but headache can be observed as a result of severe and sudden fluctuations in BP (20). Headaches caused by HT are not an indicator of an end-organ damage, so immediate treatment for BP is not needed (21).

When clinical signs of acute organ damage findings, which are suggestive of hypertensive emergency are not apparent, and evaluation and follow-up of patients in the emergency department are not clear, these can mislead physicians in decisions (22). They may connect the headache to HT and treatments to reduce BP can be given to patients.

Study Limitations

Pain treatments were given because the patients were admitted for headaches and because they had the expectation for quick medication. The limitation of our study is that we had to give medication to these patients without being able to differentiate patients whose high BP would fall spontaneously without medication (e.g., caused by anxiety, HT related with the white coat effect).

Conclusion

This study showed that in the primary headaches, which are often associated with HT, instead of treating high BP by considering secondary causes, when headache was treated, BP spontaneously decreased. We believe that detailed, multi-centered studies are need regarding patients with headaches accompanied by symptoms of high BP or admission because of high BP accompanied by headache

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Ethics

Ethics Committee Approval: The study was approved by the Dr. Lutfi Kırdar Kartal Training and Research Hospital of Local Ethics Committee (approval number: 8951337/1009/120).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.C.H., H.H., Concept: A.C.H., H.H., Design: A.C.H., Data Collection or Processing: A.C.H., H.H., Analysis or Interpretation: H.H., V.Ü., Literature Search: A.C.H., H.H., V.Ü., Writing: A.C.H., H.H.

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