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Arterial hypertension in migraine: Role of familial history and cardiovascular phenotype

Laura Babayan [a,b], Oleg V. Mamontov [a,b,c], Alexander V. Amelin [a,b], Mikhail Bogachev [d], Alexei A. Kamshilin [b,*]

[a] Pavlov First Saint Petersburg State Medical University, St. Petersburg, Russia
[b] ITMO University, St. Petersburg, Russia
[c] Federal Almazov North-West Medical Research Centre, St. Petersburg, Russia
[d] Saint-Petersburg Electrotechnical University, St. Petersburg, Russia

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ABSTRACT

Recent studies indicate that migraine is associated with increased risk of cardiovascular diseases. However, links between autonomic cardiovascular regulation, arterial hypertension (AH) and migraine are still little explored. In this study, we evaluated autonomic regulation in migraine patients with and without hypertension. We studied 104 patients with migraine, aged 34 ± 10 y, including 28 with and 76 without hypertension (M + AH and M − AH groups, respectively). The control group consisted of 88 healthy volunteers matched by age and sex. The autonomic regulation of circulation was examined with the tilt-table test, deep-breathing and Valsalva Maneuver, handgrip test, cold-stress induced vasoconstriction, arterial baroreflex, and blood pressure variability measurements. We found that migraine patients with concomitant hypertension demonstrated reduced arterial baroreflex, whereas other parameters of cardiac autonomic regulation were unchanged. In contrast, most indicators of vasomotor reactivity (blood pressure response to the hand-grip, Valsalva maneuver and cold vasoconstriction) were enhanced in migraine patients with no significant differences between migraine patients with and without hypertension. Patients from both M + AH and M − AH groups more commonly had a family history of cardiovascular disorders. Our data revealed increased vasomotor reactivity in migraine patients, with or without concomitant hypertension. This was associated with the family history of cardiovascular diseases.

1. Introduction

Migraine affects between 10 and 20% of the active adult population, with women being affected about three to four times more frequently than men (Lipton and Bigal, 2005). However, some particular pathophysiological mechanisms and comorbidities of migraine still have to be understood. In migraine patients pathological vascular reactivity has been reported (Mamontov et al., 2016), (Vanmolkot et al., 2007). Currently, the deficiency of autonomic cardiovascular regulation is considered as one of the possible mechanisms leading to the onset and persistence of headaches (Matei et al., 2015). Several large population trials have shown the relationship between the migraine and the ischaemic stroke (Etminan et al., 2005) additionally supported by the meta-analysis data (Schürks et al., 2009). While the reasons for increased stroke frequency in migraine patients are not yet fully understood, they are often associated with the higher risk of accompanying factors such as predisposition to cardiovascular disorders from family history as well as a wide range of concomitant diseases that may lead to cardiovascular complications (Sacco et al., 2012). In particular, 64% higher risk of arterial hypertension (AH) in migraine patients have been reported (Scher et al., 2005). Similar conclusions have been drawn in other studies (Schwaiger et al., 2005). Furthermore, several recent studies have associated migraine not only with hypertension, but also with ischemia (Kuo et al., 2013).

On the other hand, in several studies migraine has been associated with the family history of cardiovascular disorders. Early myocardial infarctions (before age 60) are more frequently reported in parents of migraine patients (Scher et al., 2005). This is also supported by the HUNT study that reported higher rates of myocardial infarction or stroke history in close relatives of migraine patients (Tronvik et al., 2011). It is well known that hypertension patients, like migraine patients, have abnormal autonomic regulation (Palatini and Julius, 2009), mainly in the vascular reactivity (Mamontov et al., 2016). However, the autonomic regulation in migraine patients with normal and increased arterial blood pressure was not systematically analyzed. Furthermore, the role of cardiovascular complications in the family history of migraine patients in their autonomic regulation status and arterial hypertension development is not fully understood.

In the current study, in order to explore the links between the autonomic cardiovascular regulation, hypertension, and migraine we analyzed the autonomic regulation status and family history of

* Corresponding author.
E-mail address: alexei.kamshilin@yandex.ru (A.A. Kamshilin).

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cardiovascular pathologies in migraine patients with and without concomitant arterial hypertension.

2. Materials and methods

The study involved 104 migraine patients aged 34.4 ± 10.0 years (Table 1). Most patients had episodic migraine, including 13 with rare episodes (<3 occurrences per month), 64 with frequent episodes (3–14 occurrences per month). Twenty-six patients suffered from chronic migraine (15 or more episodes per month). The majority of patients had migraine without aura ($n = 91$). Migraine with aura was observed in 12 patients. The diagnosis of migraine was made using the criteria of the International Classification of Headache Disorders, 3rd edition (Headache Classification Committee of the International Headache Society, 2013). The study included patients with normal blood pressure, as well as at early stages of the concomitant arterial hypertension determined following published recommendations (Mancia et al., 2014). Patients with long lasting arterial hypertension, essential organ damage and associated clinical complications were excluded from this study.

The control group included 88 healthy volunteers of comparable age 35.3 ± 12.1 y, sex (14 males and 74 females) and anthropometric characteristics (Body mass index of 22.1 ± 3.3) with the patients groups. There were no significant differences between groups in systolic blood pressure and heart rate, while migraine patient had higher diastolic blood pressure.

Family history of cardiovascular disorders and autonomic regulation status assessment was performed in all subjects.

2.1. Questionnaire

All subjects were questioned about known medical history of their close relatives including:

1. documented arterial hypertension development before 50 y in their first-degree relatives;
2. known ischemia-associated episodes (angina, myocardial infarctions) as well as cerebral circulation diseases in their first- and second-degree relatives before 55 y (male) and/or 65 y (female);
3. cases of sudden death, likely of cardiovascular origin, chronic cardiac failure in their first- and second-degree relatives before 55y (male) and/or 65y (female);
4. diabetes mellitus type II, ancestral dyslipidemia cases in their first- and second-degree relatives.

In those cases where the history could not be confirmed or could be ambiguously interpreted the data were not taken into account. Altogether 59 (57%) patients and 57 (65%) volunteers provided supported family history.

2.2. Autonomic cardiovascular regulation assessment

To address the autonomic regulation of circulation, we performed the following tests: the tilt-table test, deep breathing and Valsalva Maneuvers, handgrip test, cold-stress induced vasoconstriction, arterial baroreflex, and blood pressure variability. The non-invasive beat-to-beat blood pressure monitor Finometer-Pro (FMS, The Netherlands) was used along with the simultaneously recorded electrocardiogram (ECG). The forearm blood flow was measured by venous occlusion plethysmography using custom-made Dohn plethysmograph.

The following tests have been used in this study:

- The tilt-test allowed us to evaluate the role of the sympathetic nerves in hemodynamic control (Furlan et al., 1998), (Novak, 2011). This test was performed on a tilt-table, the hemodynamic parameters were assessed both in the supine and in the orthostatic positions.
- The application of the deep-breathing test allowed us to evaluate the parasympathetic cardiac control (Novak, 2011). Expiration/inspiration (E/I) coefficients essential for this test were estimated from the ratio of ECG intervals during six respiratory cycles.
- The Valsalva Maneuver was performed to address the autonomic regulation of the heart rate and vascular reactivity (Novak, 2011). To this end, the heart rate and blood pressure were recorded before, during, and 30 s after the expiration. Valsalva index was estimated from the ratio of the longest and shortest R-R intervals of the ECG. The sympathetic reactivity was obtained from the blood pressure elevation at the end of the second phase of Valsalva Maneuver (Lu et al., 2001), (Mamontov et al., 2016).
- During the handgrip test, one-third of the maximum force was applied for three minutes on the handle dynamometer to measure the diastolic blood pressure (Ewing et al., 1974).
- The sympathetic cardiovascular responses were evaluated by applying a cold ice pack to the chest area for two minutes (a cold-pressure test, as presented by Imaizumi et al. (Imaizumi et al., 1984).
- The spontaneous arterial baroreflex was measured by the cross-correlation method (Wehrwein and Joyner, 2013).
- The blood pressure variability related to the neurogenic control of the vascular tone was estimated at the rest and supine position as proposed by Parati et al. (Parati et al., 2013).

All the above listed tests were carried out during interictal period of migraine patients at least two days after the last migraine attack. Moreover, all participants were asked to refrain from taking medications during 48 h before the survey.

2.3. Ethics statement

This study was conducted in accordance with ethical standards presented in the 1964 Declaration of Helsinki. The Ethics Committee of the Pavlov First Saint-Petersburg State Medical University prior the research approved the protocol of this study. All subjects provided a written consent for the study.

2.4. Statistical analysis

Statistical analysis was performed using the software STATISTICA 10. The comparative analysis was carried out by using the non-parametric Mann-Whitney test for independent samples. Differences occurrence of family history were assessed using the chi-square test. All data are presented as the mean value ± standard deviation (SD). Significance was assumed when $p < 0.05$.

3. Results

3.1. Concomitant arterial hypertension

Concomitant arterial hypertension was observed in 28 migraine patients which were classified as belonging to the M + AH group. This group was next compared against the migraine group without hypertension (M − AH), comprising 76 patients. Patients in both groups

Table 1
Migraine patients and control group.

	Control group ($n = 88$)	Migraine group ($n = 104$)	p-Value
Age, y	35.3 ± 12.1	34.5 ± 10.0	>0.05
Body mass index, a.u.	22.1 ± 3.3	22.7 ± 4.1	>0.05
Systolic blood pressure, mmHg	120.7 ± 11.5	118.3 ± 11.2	<0.005
Diastolic blood pressure, mmHg	67.0 ± 9.7	69.6 ± 7.1	<0.05
Heart rate, beats/min	72.9 ± 12.1	75.5 ± 11.4	>0.05
Sex m/f	16/72 (81.8%)	17/86 (83.5%)	>0.05
Aura yes/no	No	12/92 (11.5%)	>0.05
Episodes rare/freq/chro	No	13/65/26	>0.05
Arterial hypertension yes/no (%)	No	28/76 (26.9%)	