

## Research Article

# Presence of Symptoms of Dysautonomia in Patients with Migraine with Aura and Migraine without Aura: A Retrospective Study

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### Abstract

**Objectives:** To investigate symptoms of autonomic dysfunction in patients with migraine with aura and without aura.

**Methods:** A retrospective chart review was conducted for 36 migraine patients who presented to our hospital and autonomic nervous system symptoms were assessed using the COMPASS-31 questionnaire in comparison to a control group of 18 subjects.

**Results:** A total of 54 patients, including 36 migraine patients and 18 control groups, were included in the study. Twenty-six of the migraine patients (72.2%) were female and others were male. The average age is 35.5 It was observed that autonomic nervous system symptoms were more frequently observed in patients with aura migraine.

**Conclusion:** We believe that it is important to recognize and watch out for symptoms of autonomic dysfunction particularly in patients with migraine with aura to develop specific treatment strategies and to reduce associated functional disability.

**Keywords:** Autonomic dysfunction, migraine with aura, migraine without aura

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The autonomic nervous system (ANS) consists of the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS) and its regulation involves numerous complex and integrated steps. Dysautonomia, also known as ANS dysfunction, refers to a multitude of clinical conditions that develop because of faulty regulation of these complex steps. It presents with multiple symptoms including constipation, insomnia, dizziness, blurred vision, cold and clammy palms and soles, abnormal blood pressure, headaches, lightheadedness with orthostatic intolerance and palpitations.

Autonomic dysfunction has also been associated with in-

creased pain sensitivity as in reflex sympathetic dystrophy with pain out of proportion to the cause.<sup>[1-3]</sup>

Migraine is an episodic syndrome consisting of a variety of clinical features that result from dysfunction of the sympathetic nervous system. During headache-free periods, migraineurs have a reduction in sympathetic function compared to non-migraineurs.

Migraine is most similar to pure autonomic failure in terms of reduced supine plasma norepinephrine levels, peripheral adrenergic receptor supersensitivity, and clinical symptomatology directly related to sympathetic nervous system dysfunction. The peripheral sympathetic nervous system

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dysfunction is much more severe in pure autonomic failure than in migraine. Migraine differs from both pure autonomic failure and multiple system atrophy in that migraineurs retain the ability, although suboptimal, to increase plasma nor-epinephrine levels following physiological stressors.

Autonomic dysfunction has been predominantly assessed and reported in adult migraine patients. Sympathetic hyperfunction and hypofunction<sup>[4]</sup> as well as parasympathetic hyperfunction and hypofunction<sup>[5]</sup> have been described in the literature.

The goal of this preliminary study was to investigate the frequency of symptoms suggestive of autonomic dysfunction specifically in patients diagnosed with migraine with aura and migraine without aura.

## Methods

The frequency of autonomic dysfunction was assessed retrospectively in patients with migraine. Patients with migraine were divided into two groups and a control group was also included in the study. The control group was selected from the healthy persons.

The study was conducted in Gaziantep Sanko University in 2017. The Second Edition of the International Classification of Headache Disorders (ICHD-2) was used for diagnosis of headache<sup>[6]</sup> and the frequency, severity, duration of pain, and demographic characteristics such as patient age and gender were reviewed in detail by a neurologist. Autonomic dysfunction was assessed using the COMPASS-31 (Composite Autonomic Symptom Scale) questionnaire.

The COMPASS-31<sup>[7]</sup> questionnaire, a validated and internally consistent measure of autonomic functioning across several domains, was adapted to create the "autonomic symptom checklist." The autonomic symptom checklist assessed the following six symptoms of autonomic dysfunction: "constipation," "insomnia," "dizziness," "blurred vision," "abnormal blood pressure," and "cold and clammy palms and soles" (Table 1 for the clinical operationalization of each symptom). The presence of these six symptoms was

investigated by reviewing the clinical notes of the neurologist from the initial evaluation for participants in either of the headache groups or for the control group.

## Statistical Analysis

Normality of numerical data was checked by Shapiro-Wilk test. Student's t test was used for normally distributed data and Mann-Whitney U test was used to compare differences between two independent groups when the distribution was not normal. Kruskal-Wallis test was used to compare non-normal numerical variables for more than two groups. Relationships between categorical variables were tested by Chi-square test. All analyses were performed using SPSS for Windows, version 24 and a p value less than 0.05 was considered statistically significant.

## Results

The study was conducted on a total of 54 patients including 36 patients with migraine and 18 control subjects. There was a predominance of female patients among the migraineurs (n=26, 72.2%) whose mean age was 35.5 years. Twenty-one patients (58.3%) had a diagnosis of migraine with aura and others had migraine without aura. The mean duration of pain was 17.5 hours for migraine patients with an average frequency of 5.5 migraine episodes per month. The mean age was 29.67 and 37 years in patients with migraine without aura and migraine with aura respectively, and 29.72 years in control subjects. There were 11 females (61.1%) among control subjects. No significant difference was observed with respect to age between the study groups (p=0.145).

## Comparison of Study Groups

### A. Patients with Migraine with Aura Versus Patients with Migraine Without Aura:

#### a. Demographic Findings

Pain associated with migraine headache was severe in 16 patients with migraine with aura and in 6 patients with migraine

**Table 1.** Description of autonomic symptoms assessed

Symptom description	
Constipation	No bowel movements for greater than 2 days; difficulty, straining or hard bowel movements
Insomnia	Greater than 1 h to fall asleep; frequent waking; unable to maintain sleep
Dizziness	Greater than 15 days of lightheaded/near-syncope; vertigo; unsteadiness
Blurry vision	Subtle pupillary asymmetry; visual cortex interpretation of sensory imbalance as visual blurriness
Abnormal blood pressure	Cold and clammy palms and soles sympathetic response in extremities: palmar and plantar sweating, color changes, and temperature changes associated with sudomotor and vasomotor change
	Blood pressure above or below the normal range for adolescents and children: systolic (110–131 mm Hg), diastolic (64–83 mm Hg)

The frequency of symptoms was assessed through a review of patient notes utilizing the above criteria.

without aura. A statistically significant difference was found between two groups of migraineurs with pain being more severe among patients with migraine with aura ( $p=0.036$ ).

#### aa. Comparison of Autonomic Functions:

Constipation was found in 14 patients with migraine with aura and 6 patients with migraine without aura. Insomnia was present in 16 patients with migraine with aura and 10 patients with migraine without aura. Dizziness was present in 19 patients with migraine with aura and 10 patients with migraine without aura. Migraineurs did not differ statistically significantly with respect to the occurrence of constipation, insomnia and dizziness (Table 2).

Blurred vision ( $p=0.004$ ), cold and clammy palms and soles ( $p=0.048$ ) and abnormal blood pressure ( $p=0.037$ ) were statistically significantly more common in patients with mi-

graine with aura.

Patients with migraine with aura showed statistically significantly greater duration and frequency of pain ( $p=0.007$ ,  $p=0.033$ , Table 3).

#### B. Comparison of migraineurs versus control group:

Patients with migraine with aura showed statistically significant differences for all six autonomic symptoms in comparison to control group: constipation ( $p=0.001$ ), insomnia ( $p=0.001$ ), dizziness ( $p=0.001$ ), blurred vision ( $p=0.002$ ), cold and clammy palms and soles ( $p=0.014$ ), abnormal blood pressure ( $p=0.011$ ) (Table 4).

For patients with migraine without aura, only symptoms of constipation ( $p=0.013$ ), insomnia ( $p=0.003$ ) and dizziness ( $p=0.025$ ) showed statistically significant differences compared to control group (Table 5).

## Discussion

Headaches, migraine and tension-type headaches in particular, were shown to result in functional disability by causing autonomic dysfunction symptoms in both adult and pediatric studies. Specifically, some characteristic symptoms of a migraine episode including nausea vomiting, watery eyes and eyelid drooping or change in skin color have been associated with impaired autonomic functioning. Many studies

**Table 2.** Comparison of autonomic dysfunction symptoms among migraine patients: Severity of pain, and frequencies of blurred vision, sweating and abnormal blood pressure were significantly greater in migraine with aura

Variables	Migraine with aura (n=21)	Migraine without aura (n=15)	P
Gender			
Female	17 (0.81)	9 (0.6)	0.168
Male	4 (0.19)	6 (0.4)	
Intensity of pain			
Mild	1 (0.05)	5 (0.33)	0.036*
Moderate	4 (0.19)	4 (0.27)	
Severe	16 (0.76)	6 (0.4)	
Constipation			
Yes	14 (0.67)	6 (0.4)	0.111
No	7 (0.33)	9 (0.6)	
Insomnia			
Yes	16 (0.76)	10 (0.67)	0.531
No	5 (0.24)	5 (0.33)	
Dizziness			
Yes	19 (0.91)	10 (0.67)	0.075
No	2 (0.1)	5 (0.33)	
Blurred vision			
Yes	18 (0.86)	6 (0.4)	0.004*
No	3 (0.14)	9 (0.6)	
Cold and clammy palms and soles			
Yes	14 (0.67)	5 (0.33)	0.048*
No	7 (0.33)	10 (0.67)	
Abnormal blood pressure			
Yes	13 (0.62)	4 (0.27)	0.037*
No	8 (0.38)	11 (0.73)	

\*Significant at 0.05 level; n (%). Chi-square test.

**Table 3.** Comparison of demographic findings between migraine patients: Duration of pain and frequency of pain were significantly greater in migraine with aura

Variables	Migraine with aura (n=21)	Migraine without aura (n=15)	p
Age (years)	37±11.65	29.67±12.99	0.085
Time of pain	24.52±11.93	13.87±9.52	0.007*
Frequency of pain	6 [5-8] <sup>†</sup>	3 [2-8] <sup>‡</sup>	0.033*
Duration of illness	6 [3-10] <sup>†</sup>	5 [1-6] <sup>‡</sup>	0.062

<sup>†</sup>Mean±std.deviation; Student's t test; <sup>‡</sup>Median [25%-75%]; Mann-Whitney U test.

**Table 4.** Comparison of patients with migraine with aura versus control group

	P
Gender	0.170
Constipation	0.001*
Insomnia	0.001*
Dizziness	0.001*
Blurred vision	0.002*
Cold and clammy palms and soles	0.014*
Abnormal blood pressure	0.011*

\*Significant at 0.05 level; n (%). Chi-square test

**Table 5.** Comparison of patients with migraine without aura versus control group

	P
Gender	
Female	0.948
Male	
Constipation	
Yes	0.013*
No	
Insomnia	
Yes	0.003*
No	
Dizziness	
Yes	0.025*
No	
Blurred vision	
Yes	0.948
No	
Cold and clammy palms and soles	
Yes	0.730
No	
Abnormal blood pressure	
Yes	0.767
No	

\*Significant at 0.05 level; n (%); Chi-square test.

have shown abnormalities in RR-variation test (a sensitive test for autonomic dysfunction) and diastolic blood pressure in migraine patients.<sup>[4, 8]</sup> In our study, symptoms such as blurred vision, cold and clammy palms and soles and abnormal blood pressure indicative of autonomic dysfunction were more common in patients with migraine with aura compared to patients with migraine without aura. When autonomic symptoms were compared between patients with migraine with aura and control group, all six relevant symptoms were found to significantly more common in patients with migraine with aura. Insomnia was common in both migraine with aura and migraine without aura.<sup>[9]</sup> In the present study, although insomnia was common in both groups of migraineurs, there was no statistically significant difference between the two groups. Dizziness and vertigo are common complaints and migraineurs and patients with frequent disabling headaches report these symptoms in conjunction with migraine headaches.<sup>[10]</sup> Dizziness symptom was significantly more frequent in both groups of migraine patients compared to control group. This finding suggests that vertiginous migraine should be questioned more carefully.<sup>[10]</sup> All of these results indicate that in addition to sympathetic hyperfunction and parasympathetic hypofunction, some small nerve fibers may be affected. Further studies may assist in

developing a standardized questionnaire to assess functioning of the autonomic nervous system for general use.

## Conclusion

Pain and disability experienced by migraine patients during a migraine episode may be associated with dysfunction of the autonomic nervous system. Our study findings suggest that autonomic dysfunction might either be a risk factor for migraine attacks or be a cause of disability particularly in patients with migraine with aura. More frequent autonomic symptoms observed in migraine with aura suggest that ANS dysfunction and migraine may share a common neural substrate in the neural pathways from the central to the peripheral nervous system. We believe that it is important to recognize and watch out for symptoms of autonomic dysfunction in migraine to develop specialized treatment strategies and to reduce associated functional disability.

## Disclosures

**Ethics Committee Approval:** The study was approved by the Local Ethics Committee.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

## References

- Butler IJ, Lankford JE, Hashmi SS, Numan MT. Biogenic amine metabolism in juvenile neurocardiogenic syncope with dysautonomia. *Ann Clin Transl Neurol* 2014;1:251–7. [\[CrossRef\]](#)
- Wadhwanian R, Butler I, Hashmi S, Numan M, Lankford J. Dysautonomia: Retrospective study of amino acids, cytokines and neurotransmitter metabolites. *Ann Neurol* 2016;80:S299.
- Gordon N. Reflex sympathetic dystrophy. *Brain Dev* 1996;18:257–62. [\[CrossRef\]](#)
- Shechter A, Stewart WF, Silberstein SD, Lipton RB. Migraine and autonomic nervous system function: a population-based, case-control study. *Neurology* 2002;58:422–7. [\[CrossRef\]](#)
- Yerdelen D, Acil T, Goksel B, Karatas M. Heart rate recovery in migraine and tension-type headache. *Headache* 2008;48:221–5.
- Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004;24 Suppl 1:9–160.
- Sletten DM, Suarez GA, Low PA, Mandrekar J, Singer W. COMPASS 31: a refined and abbreviated Composite Autonomic Symptom Score. *Mayo Clin Proc* 2012;87:1196–201.
- Gazerani P, Cairns BE. Dysautonomia in the pathogenesis of migraine. *Expert Rev Neurother* 2018;18:153–65. [\[CrossRef\]](#)
- Uhlig BL, Engstrøm M, Ødegård SS, Hagen KK, Sand T. Headache and insomnia in population-based epidemiological studies. *Cephalalgia* 2014;34:745–51. [\[CrossRef\]](#)
- Kirkim G, Mutlu B, Olgun Y, Tanriverdizade T, Keskinoglu P, Güneri EA, Akdal G. Comparison of Audiological Findings in Patients with Vestibular Migraine and Migraine. *Turk Arch Otorhinolaryngol* 2017;55:158–61. [\[CrossRef\]](#)