



## Accuracy of osmophobia in the differential diagnosis between migraine and tension-type headache



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### ABSTRACT

Our objective was to determine the accuracy parameters of osmophobia in the differential diagnosis between migraine and tension-type headache. Migraine or tension-type headache patients, diagnosed according to the criteria of the International Classification of Headache Disorders-II, were interviewed about osmophobia during the crisis and in the period between episodes. We studied 200 migraine patients and 200 tension-type headache patients. During the crisis, osmophobia occurred in 86.0% (172/200) of patients with migraine and 6.0% (12/200) of those with tension-type headache. In migraine, osmophobia was associated with photophobia and phonophobia (57/172, 33.1%) or with nausea, photophobia and phonophobia (92/172, 53.5%) and presented high sensitivity (86.0%, 95% CI 80.2–90.3) and specificity (94.0%, 95% CI 89.5–96.7), with low percentages of false positives (6.5%, 95% CI 3.6–11.4) and negatives (13.0%, 95% CI 8.9–18.4). In the period between attacks, osmophobia was restricted to migraine patients (48/200, 24.0%). The areas under ROC curves were:  $0.903 \pm 0.017$  to osmophobia during crisis;  $0.784 \pm 0.025$  between crises;  $0.807 \pm 0.023$  to photophobia/phonophobia, and  $0.885 \pm 0.017$  to pain developed by odors. Osmophobia may be a specific marker to differentiate migraine from tension-type headache, which suggests its inclusion within the criteria to diagnose migraine.

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### 1. Introduction

Osmophobia is defined as intolerance to odors and it is associated to primary headaches, particularly to migraine with or without aura [1–7], and it may be present in tension-type headache. The literature of its occurrence in secondary headaches is very scarce [8].

The prevalence of osmophobia during an attack in patients with migraine ranges from 20% to 81.7% [2,4–7,9–11]. However, osmophobia may be present in the absence of pain (period between attacks) [2,3,9,12–15].

Migraine is a chronic neurological disorder with a prevalence of 15.2% in Brazil [16]. It is defined as an abnormal neurovascular reaction that occurs in a genetically vulnerable organism. It externalizes itself clinically by recurrent attacks of headache and associated manifestations, depending on triggering factors [17].

These associated manifestations include nausea or vomiting, photophobia, phonophobia, dizziness and osmophobia [1,2,18,19]. However, only nausea and/or vomiting, photophobia and phonophobia are part

of the diagnostic criteria for migraine. The inclusion of osmophobia as an additional criterion in the appendix of the International Classification of Headache Disorders (ICHD)-2 is proposed [14,19].

In three comparative studies between migraine and tension-type headache conducted with children and adolescents (aged 4 to 18 years) with headache [5,10,12] and in another study with adults [20], osmophobia was more prevalent in migraine patients, in a demonstration that it is a symptom of low sensitivity and high specificity for the differential diagnosis between these two forms of headache. The presence of osmophobia in juvenile patients with tension-type headache has prognostic value, since this form of headache may change to migraine during development [21–23].

The aim of this study was to determine the parameters of accuracy of osmophobia in the differential diagnosis between migraine and tension-type headache.

### 2. Patients and methods

#### 2.1. Study design and patients

This was a prospective study with comparison of groups. The study population comprised a non-random and convenience sampling, consisting of the first 200 migraine patients and 200 tension-type headache patients (comparison group) treated at a headache clinic in the city

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of Teresina in northeastern Brazil. Data for this study were collected from August to December 2011.

## 2.2. Inclusion and exclusion criteria

Patients aged between 18 and 60 years, with migraine or tension-type headache, according to the diagnostic criteria of ICHD-II [19], and the presence of headache in the last six months at a frequency less than 15 days per month were included in the study.

In order to obtain consistent and valid data, the study excluded patients without a headache in the last six months, association between migraine and tension-type headache, concomitantly or at different times, the presence of other primary or secondary headaches, the presence of associated diseases or the use of medications that might impair olfaction, and pregnant women.

## 2.3. Data collection

The patients underwent a thorough standard medical history performed by a headache specialist to record the typical characteristics of their pain over the past six months. They were questioned about osmophobia, both during the headache attack and the period between attacks. Having met the criteria for inclusion and exclusion, patients were invited to participate in the study by signing the informed consent form. There was, then, a structured interview based on a questionnaire to investigate the research objectives. Excluded at this stage were uncooperative patients or those who answered the interview incompletely.

## 2.4. Statistical analysis

Once the information was organized in the database, the Statistical Package for Social Sciences (SPSS®) version 17.0 for statistical analysis was used. The chi-square test with Yates correction, Fisher's exact test and Mann-Whitney test for differences between averages of unpaired samples were used, assuming a significance level of 0.05. Sensitivity and specificity parameters and positive and negative predictive value were determined.

## 2.5. Ethical aspects

This study was approved by the Ethics in Research Involving Human Subjects Committee at the State University of Piauí, Brazil, protocol number 049/11 and the National Ethics in Research System, registry number 439715. All patients signed the informed consent form.

## 3. Results

There were 400 patients averaging  $38.6 \pm 9.9$  in age (95% CI 37.7–39.6) and ranging from 22 to 58 years old, 219 (54.7%) of whom were women, which corresponded to the sex ratio of 0.83:1 male/female.

Two hundred patients (50.0%) were diagnosed with tension-type headache and 200 (50.0%) with migraine, whose distribution differed according to sex and age, as observed in Table 1. Tension-type headache was predominant in men, with a 4.4:1.0 ratio male/female, whereas in migraine this ratio equaled 0.1:1; thus, predominantly female. These differences were significant. Regarding age, tension-type headache was present in patients aged  $40.0 \pm 10.4$  years old, while migraine was diagnosed in younger patients, aged  $37.3 \pm 9.0$  years old, and these differences were significant.

As for symptom differences between tension-type headache and migraine, it was found that, during an attack, migraine patients more often reported osmophobia (172/200, 86.0%), were female (164/172, 95.3%) and reported an association of osmophobia to photophobia and phonophobia (57/172, 33.1%) or to nausea, photophobia and phonophobia (92/172, 53.5%). Patients going through a tension-type headache attack more often did not report osmophobia (188/200,

**Table 1**

Distribution of sex and age according to diagnosis of 200 patients with migraine and 200 with tension-type headache.

Variables	Diagnostic		P value
	Migraine	TTH	
Sex			<0.001*
Female (n; %)	182 (83.1)	37 (16.9)	
Male (n; %)	18 (9.9)	163 (90.1)	
Age (years)			0.008†
Mean	37.3 (9.0)	40.0 (10.4)	
95% CI	36.0–38.6	38.5–41.4	

Legend: TTH – tension-type headache; CI – confidence interval.

\* P value based on the chi-square test.

† P value by the Mann-Whitney test for average difference test between averages of unpaired samples.

94.0%), were male (158/188, 84.0%) and had no other symptoms (164/200, 82.0%) (Table 2).

In the period between attacks, there was a predominance of absence of osmophobia for both migraine patients and patients with tension-type headache, regardless of sex. However, when present, it was restricted to migraine patients (48/200, 24.0%). Odors triggered headache in 140/200 (70.0%) of the migraine patients, including the 48 patients with osmophobia between attacks and 92 patients without it. Both differences reached statistical significance (Table 2).

Table 3 shows the results of sensitivity, specificity, and positive and negative predictive values, as well as false positive and negative values of associations, statistically significant, of osmophobia during attack and between attacks, photophobia/phonophobia, and the triggering of headache by odors with the diagnosis of migraine.

While osmophobia during the attacks and photophobia/phonophobia showed high indicative values of accuracy for diagnosis of migraine, with low percentages of false positives and negatives, osmophobia between episodes and the triggering of headache by odors had low sensitivity and high specificity, from those resulting in high positive predictive values.

In the presence of osmophobia during an attack, the probability of not being migraine was 6.5%, while the probability of being migraine in the absence of osmophobia during the attack was 13.0%. The same reasoning used in relation to osmophobia between attacks made it possible to state that, when present, the probability of not being migraine

**Table 2**

Distribution of symptoms as diagnosis in 200 patients with migraine and 200 with tension-type headache.

Symptoms	Diagnosis				P value
	Migraine		TTH		
	n	%	n	%	
Osmophobia during attack	<b>172</b>	<b>86.0</b>	<b>12</b>	<b>6.0</b>	<0.001*
Female	164	95.3	7	58.3	
Male	8	4.7	5	41.7	
Osmophobia between attacks	<b>48</b>	<b>24.0</b>	<b>0</b>	<b>0.0</b>	<0.001†
Female	36	75.0	0	0.0	
Male	12	25.0	0	0.0	
Osmophobia associated with other symptoms	<b>172</b>	<b>86.0</b>	<b>12</b>	<b>6.0</b>	<0.001*
Photophobia and phonophobia	57	33.1	0	0.0	
Photophobia or phonophobia	0	0.0	12	100.0	
Nausea, photophobia and phonophobia	92	53.5	0	0.0	
Nausea and/or vomiting	23	13.4	0	0.0	
Odor as a trigger to headaches	<b>140</b>	<b>70.0</b>	<b>0</b>	<b>0.0</b>	<0.001*
Female	134	95.7	0	0.0	
Male	6	4.3	0	0.0	

Legend: TTH – tension-type headache.

\* P value based on Fisher's exact test.

† P value by chi-square test.

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