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RHINOLOGY

Osmophobia and olfactory functions in patients with migraine

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Abstract Olfactory dysfunction and migraine has been associated for a long time. In this study, we planned to compare olfactory functions in patients with migraine and osmophobia with patients having migraine but no osmophobia, in addition with a normal control group using "Sniffin' Sticks" test. The main distinction of this study is that all qualitative and quantitative properties of olfactory functions; threshold, discrimination and identification, are evaluated separately and jointly. Thirty healthy person aged between 16 and 56 (18 women, 12 men) and 60 migraine patients aged between 15 and 54 (39 women, 21 man) were included in the study. All patients have been inquired about osmophobia and have been assessed with Hedonic tone assessment. Osmophobia has been tested for perfume, cigarette smoke, leather, stale food, soy sauce, fish, spices and coffee smells. Olfactory functions has been assessed with "Sniffin' Sticks" smell test. Thresholds, discrimination and identification have been determined for each patient. In migraine patients with osmophobia, threshold was 7.75 ± 2.3, in migraine patients without osmophobia threshold was 8.25 ± 1.5 and threshold was 10.75 ± 1.3 for the control group. Discrimination score was 6 ± 1.2 in migraine patients with osmophobia, 9 ± 0.8 in patients without osmophobia and was 12 ± 1.4 in the control group. In migraine patient with or without osmophobia Threshold/Discrimination/Identification (TDI) scores were lower than the control group. The most important parameter in our study is that discrimination scores were especially lower in patients with osmophobia. We believe that this decrease in discrimination in migraine patients with osmophobia; who claim that they smell everything and they are sensitive to all smells, is significant. Further studies about smell discrimination will help better understand some conditions; especially anosmia and hyposmia after upper respiratory tract infections and parosmia.

Keywords Migraine · Osmophobia · Smell tests · Sniffin' Sticks · Hyposmia

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Introduction

Migraine is a syndrome which can be triggered by intrinsic or extrinsic factors, affecting quality of life. As a cause for primary head-ache, it is encountered frequently by neurologists and ent specialists. The incidence of migraine is 10.5–16.5 % in Europe and USA, 2–3 % in Arabic Peninsula and Africa. In two studies conducted in Turkey, the incidence was found 16.4 %. Migraine is seen two times more frequently in females. The peak age of migraine is 20–40 [1]. One of the most significant properties of migraine is the reccurence. According to International Headache Society-IHS-2004 classification

migraine can be classified as; with aura, without aura, childhood syndromes, retinal migraine, complications of migraine and probable migraine. Practically 90 % of migraine cases are in first two groups [2].

The relationship between olfactory disfunction and migraine is known for a long time and there are various studies. In addition to the quantitative changes in other neurological diseases, the olfactory dysfunction in migraine has a qualitative change also [3–10]. In some cases it is reported that olfactory hallucinations are part of aural symptoms or some smells can trigger migraine. Stages of migraine are prodromal stage, aura, head-ache and postdromal periods. Especially in prodromal and aural periods; patients report an increase in smell discomfort. Prodromal olfactory hypersensitivity can be explained with the relation of prodromal symptoms with frontal lobes, hypothalamus, cerebral hemispheres and central noradrenergic systems [11]. Migraine and olfactory functions are studied with subjective psychophysical olfactory function tests and objective electrophysiological tests.

Olfactory dysfunction is diagnosed in up to 15 % in various populations [12–16]. In Turkish population in a study using questionnaires incidence was 6.7 % [17]. The most frequent causes of olfactory dysfunction are upper respiratory system infections, head trauma and various sinonasal diseases [18]. Other reasons for olfactory dysfunction are age, toxic materials, congenital anomalies, neurological diseases such as multiple sclerosis, Parkinson and Alzheimer's disease [19–23].

Conscious olfaction is the result of interaction of stimulants with orbitofrontal cortex and neocortical areas with the intermediary of thalamus. Learning and remembrance of a smell stimulant happens in a waste neuronal network. Olfactory meningioma and temporal epilepsy are diseases characterised with a decrease in smell discrimination [24].

Psychophysical smell tests, electrophysiological smell test, psychophysiological smell tests and structural imaging techniques are used to assess olfactory functions. Most frequently used tests are psychophysical tests. In those test; identification, discrimination and thresholds are evaluated. University of Pennsylvania Smell Identification Test (UPSIT), Sniffin' Sticks, Connecticut Chemosensory Clinical Research Center Test (CCCRCT), Barcelona smell test 24, Smell Discettes Test are some of the most used smell tests. In psychophysiological test cardiovascular and respiration changes are evaluated. In electrophysiological test an electro-olfactogram is used. Cranial magnetic resonance to measure olfactory bulbus, positron emission tomography, SPECT, are some of the imaging techniques [29–31].

Because of every cultures different smell sensibilities, test in accordance to that culture must be used. For Turkish population Sniffin' Sticks test is appropriate [25].

The purpose of this study is to compare patients with migraine with and without osmophobia and control group using Sniffin' Sticks. The main distinction of this study is that all qualitative and quantitative properties of olfactory functions; threshold, discrimination and identification, are evaluated separately and jointly.

Materials and methods

After having approval from the ethical committee of our university, 30 healthy (18 female, 12 male) aged between 20 and 56 and 60 migraine patients (39 female, 21 male) aged 20–54 are included in the study, after having informed consent. This study is designed as randomised prospective blind study, and is conducted with collaboration of University of Sakarya ENT and Neurology Clinics. Patients in the migraine group were randomly selected from patients referring to the Head-Ache policlinic run by neurology deparment. İnclusion criterias were; being between 20 and 60 ages, being diagnosed as migraine with/without aura according to HIS-2004 criterias, at least 2 years of migraine history, more than 6 attacks a month, visual pain scale score greater than 3. Patients with history of drug abuse, brain diseases, sinonasal diseases, neıropsychiatric diseases, or upper respiratory tract infections in last 3 weeks were excluded. Sixty migraine patients according to theses criterias, 30 with, 30 without aura were included. When forming groups, having no statistical difference between genders and age was ensured. Neurological, ENT and physical examination were done on all patients. All participants were questioned for osmophobia and Hedonic Tone Assessment was applied. Osmophobia has been tested for perfume, cigarette smoke, leather, stale food, soy sauce, fish, spices and coffee smells. Olfactory functions have been assessed with "Sniffin' Sticks" smell test. The test was conducted (with both nostrils together) to achieve the threshold, discrimination, and identification (TDI) ranking (the sum of the TDI scores) for each subject. Odorants were made available in commercial felt-tip pens (Sniffin Sticks, Burghart Medical Technology, Wedel, Germany). For the purpose of smell display, the pen cap was removed by the same experimenter for just a few seconds, and the tip of the pen was positioned about 1–2 cm from the nose. With regard to odor thresholds, three pens were provided in a randomized order: one made with phenyl ethyl alcohol in various dilutions (with an enhancing dilution fraction of 1:2), and two that contained the solvent. *N*-Butanol was not used to avoid osmophobia in migraine patients. Once a person recognized the pen with the odorant twice, reduced content levels were introduced until the person could not detect the pen with the odorant (a spectrum of 1–16). When this level

Table 1 Olfactory scores

	Migraine patients with osmophobia ($n = 30$)	Migraine patients without osmophobia ($n = 30$)	Control group ($n = 30$)	p value
Threshold scores	7.75 ± 2.3	8.25 ± 1.5	10.75 ± 1.3	<0.001
Discrimination scores	6 ± 1.2	9 ± 0.8	12 ± 1.4	<0.001
Identification scores	13 ± 0.9	12 ± 2.4	14 ± 1.3	0.6
TDI score	25 ± 1.7	30 ± 1.6	35 ± 1.3	<0.001

was reached, the pen with a one step greater level was used until the pen with the odorant was accurately recognized. The test was completed when seven reversals had been determined. For identification, 16 widespread odorants were used. To avoid olfactory desensitization, a minimum 30 s break was used between exposures. Subjects were asked to identify each scent on an odorant form by means of deciding four odorants. Smell discrimination was determined with 16 triplets of odorant pens in which the odor in 1 pen was different from the other 2. Final results of the TDI tests were considered one-by-one and summed for a complete TDI score.

Statistical analysis

All data was prossesses with SPSS 21.0 (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL). Statistical difference between groups was assessed with ANOVA (including post hoc Tukey test) and Chi square tests. $P < 0.05$ was deemed statistically significant.

Results

All participants were grouped as migraine with osmophobia, without osmophobia and control gorup. Every group was compared in the group and between groups.

Identification score was 13 ± 0.9 in migraine with osmophobia, 12 ± 2.4 in migraine without osmophobia and 14 ± 1.3 in the control group. There was no statistically significant difference between smell identification scores.

In migraine patients with osmophobia, threshold was 7.75 ± 2.3, in migraine patients without osmophobia threshold was 8.25 ± 1.5 and threshold was 10.75 ± 1.3 for the control group. Discrimination score was 6 ± 1.2 in migraine patients with osmophobia, 9 ± 0.8 in patients without osmophobia and was 12 ± 1.4 in the control group. In migraine patient with or without osmophobia Threshold/Discrimination/Identification (TDI) scores were lower than the control group. The decrease in these scores was significantly higher in migraine with osmophobia group (Table 1). In osmophobia group, 80 % parfum, 70 % cigarette smoke, 63.3 % stale food, 46.6 % fish, 40 % coffee, 40 % leather, 6.6 % soy sauce was expressed as annoying smells (Table 2).

Discussion

There are several psychophysical measurement methods to assess olfactory function. One of the most important factors to success in these tests is the cultural accordance. Tests such as UPSIT, CCCRCT, Sniffin' Sticks, Smell diskettes are used to in many studies. The reason for us to use Sniffin' Sticks test in this study is that this is the most detailed and validated test for Turkish population [25]. UPSIT tests validation for Turkish population was a version of "short identification test". Sniffin' Sticks is much more detailed to measure threshold values. Threshold measurement which consists of 16 stages in Sniffin' Sticks, is seven stages in CCCRCT. This difference is important when measuring minimal differences. Smell diskettes can only be used as a screening test.

In our study, migraine patients with and without osmophobia had lower TDI scores than control group. This result is in concordant with the knowledge that stress and emotional factors can affect olfactory functions. Croy et al. also have studies that support our findings [26].

The peculiarity of our study is that discrimination scores were lower especially in patients with osmophobia. We believe that this decrease in discrimination in migraine patients with osmophobia; who claim that their olfaction is increased and that they are sensitive to all smells, is

Table 2 Osmophobia rates for specific smells, of migraine patients with osmophobia

Disturbing smell	%
Perfume	80
Smoke	70
Stale food	63.3
Fish	46.6
Coffee or spices	40
Leather	40
Soy sauce	6.6

significant. This particular point is similar to olfactory changes is pregnancy. Several studies indicated that two-thirds of pregnant women rate their sense of smell as higher than normal [27] or as abnormally sensitive [28, 29]. Cameron et al. [27] found that 85 % of pregnant women ($n = 60$) identified at least one odor to which they were more sensitive. Nordin et al. [28] reported that, relative to non-pregnant women ($n = 76$), more of the pregnant women ($n = 144$) reported "stronger-than-normal smell sensation" of particular odors, including spices, coffee, cooking odors, cigarette smoke, spoiled food, perfumes. This was particularly evident early in pregnancy.

Pregnant women tend to be more sensitive to smells they don't like. A similar mechanism can be the cause of the osmophobia in migraine patients.

Further studies about smell discrimination will help better understand some conditions; especially anosmia and hyposmia after upper respiratory tract infections and parosmia.

Studies about smell and migraine are focused on osmophobia. Saisu et al. have reported that smell identification scores were lower in migraine patients with and without aura [8]. Nowadays it has become more important to asses the quality and quantity of smell functions in neurological diseases. Studies were conducted mostly on neurodegenerative diseases. In diseases like Alzheimer's; decrease in olfactory functions can be an early sign. There are several studies linking migraine and qualitative olfactory disfunction [30, 31]. In addition to these studies we aimed to evalute changes in discrimination and threshold scores.

These changes are more manifest in patients with osmophobia, which is an important finding of this study. Osmophobia scores were higher for perfume and fish smells, which is in accordance with other studies.

Because of challenges of measuring olfactory functions during an episode, there are fewer studies in literature [31]. In addition studies comparing quantitative olfactory functions with control groups and the presence of aura are needed. UPSIT-T which is validated for Turkish population must be used in studies to come [32].

Compliance with ethical standards

Conflict of interest All authors declare that there is no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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