Evaluation of the olfactory bulb volume and olfactory threshold in patients with nasal polyps and impact of functional endoscopic sinus surgery: a longitudinal study

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Background: **Debate still persists on the relation between olfactory bulb volume (OBV) and olfactory function. Many studies suggest that olfactory deprivation decreases the OBV. The aim of this study was to compare the olfactory threshold and OBV of patients with nasal polyps to healthy individuals and to evaluate the impact of functional endoscopic sinus surgery (FESS) on OBV and olfactory threshold.**

Methods: **A longitudinal study was carried out in Tehran between 2011 and 2012. Twenty-two patients with nasal polyps were compared with 37 healthy individuals. Olfactory threshold test and magnetic resonance imaging (MRI) were performed on all participants. Twenty-two patients in case group were followed for 6 months after FESS. OBV and olfactory threshold were measured after 6 months.**

Results: **There was no significant difference between the age, gender, and OBV of the 2 groups. However, the difference between olfactory threshold was significant ($p = 0.005$). The olfactory threshold showed no significant relation with OBV ($p > 0.05$). The correlation between Lund-Mackay score and the mean total OBV and left OBV was significant ($r = -0.15$, $p = 0.045$; $r = -0.22$, $p = 0.047$; respectively). The decrease in olfactory threshold measured after FESS was statistically significant. Right, left, and total OBV significantly increased after FESS.**

Conclusion: **The results of our study show that FESS has a significant impact on OBV increment and olfactory threshold decrement. The olfactory bulb is a plastic structure and improvement in peripheral olfactory function results in increase in OBV. However, further studies are mandated, in order to establish this result.** © 2015 ARS-AAOA, LLC.

Key Words:
olfactory bulb; olfactory threshold; FESS; nasal polyposis

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Nasal polyposis (NP) is a common benign medical problem affecting up to 4% of the population; the pathogenesis of nasal polyps is not completely understood, but it seems that chronic inflammation of mucosal membranes, allergy, and genetic predisposition are important factors in development of nasal polyps.[1]

Medical treatment is the initial management in NP. The surgical methods are reserved for patients with refractory disease. Nowadays, functional endoscopic sinus surgery (FESS) as a minimally invasive technique is considered the preferred surgical method for persistent nasal polyps.[2]

Nasal polyps are soft and lack sensation so small polyps may not result in symptoms. Multiple growths or a large polyp may block nasal passages and sinuses. Symptoms include nasal obstruction, loss of smell, loss of taste, headache, snoring, post nasal drainage, and sneezing. Although NP does not increase the mortality rate, it has a negative impact on patients' quality of life.[3] Several studies have shown that quality of life decreases with olfactory

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dysfunction. Moreover, olfactory dysfunction correlates with loss of appetite and depression.[4–7]

The olfactory bulb is the first place in the olfactory pathway and plays the main role in olfactory processing. It links the peripheral olfactory system to the central nervous system.[8]

Animal studies have shown that olfactory withdrawal reduces olfactory bulb volume (OBV).[9,10] There is some evidence that olfactory deprivation decreases olfactory bulb size and patients with anosmia or hyposmia have smaller olfactory bulbs; this is probably due to the decreased stimulation of olfactory bulb neurons.[11,12]

Most of the studies that have evaluated the olfactory system were based on subjective tests.[13–15] Magnetic resonance imaging (MRI) provides an accurate method for estimating OBV and an objective method for assessing olfactory function. MRI has previously been used to study the olfactory bulb in other causes of olfactory dysfunction, such as patients with congenital anosmia, posttraumatic patients, and postinfectious patients.[16,17] There is a shortage of studies evaluating OBV in patients with nasal polyps. In addition, to the best of our knowledge, no previous study has evaluated this relation in Iran; therefore, the present study was conducted to assess the olfactory threshold and OBV of patients with nasal polyps, to compare these values with those of healthy individuals, and to investigate the impact of FESS on olfactory function and OBV in patients with nasal polyps.

Patients and methods

This was a longitudinal study conducted in Imam Khomeini and Amir Alam Hospital of Tehran between 2011 and 2012. Our case group included 22 patients who presented with nasal polyps; controls consisted of 37 healthy individuals matched by the frequency-matching method for age and sex. The case group was followed for 6 months after FESS.

Patients with nasal polyps (according to diagnostic endoscopy and paranasal sinus computed tomography [CT] scan) who did not respond to standard treatment regimes including nasal corticosteroid and were candidates for FESS were eligible for the case group. Patients with a history of head trauma, nose or sinus tumors, diabetes mellitus, intracranial tumors, or any metal implants or pacemakers not compatible with MRI were excluded from the study.

Controls were randomly selected from participants of one of the Iranian institute of radiology projects conducted in Tehran. People with history of head trauma, polyps, olfactory dysfunction, severe cardiac disease, a pacemaker or other metal implants not compatible with MRI, and patients with severe claustrophobia were excluded from the control group.

The study was approved by the ethics committee of Tehran University of Medical Sciences and all participants formally consented to participate in all stages of the study.

FIGURE 1. Coronal T2-weighted magnetic resonance image of the olfactory bulbs.

All patients presented to the olfactory consultation service of Amir Alam hospital. Olfactory testing and MRI were performed after a comprehensive history taking and an ear, nose, and throat (ENT) physical examination to determine OBV and olfactory threshold. For each participant, age, sex, left OBV, right OBV, total OBV, and olfactory threshold were recorded. The Lund-Mackay score (degree of nasal polyps with the help of CT scan) and the degree of polyps (according to endoscopy) were documented for the patient group.

To estimate the olfactory threshold, the orthonasal test was performed with paper strips. A series of 8 solutions containing logarithmic dilutions of phenyl butyl alcohol in an odorless solvent (propylene glycol) beginning with concentration of 63% were used. The lowest concentration that the patient was unable to distinguish it from pure propylene glycol was considered as the olfactory threshold.

To assess the OBV all patients had brain MRI using a 1.5-T MR scanner in accordance to the standardized protocol for olfactory bulb analysis. Figure 1 shows a coronal T2-weighted MRI image of the olfactory bulbs.

The protocol comprised: (1) standard T2-weighted fast spin-echo images (5-mm-thick) covering the whole brain without interslice gap to exclude any parenchymal disorder; and (2) T2-weighted fast spin-echo images (2-mm-thick) without interslice gap in the coronal plane covering the skull base and olfactory track.

In order to calculate the OBV in cubic millimeters (mm^3), areas for all slices—determined by planimetric manual outlining–were added and multiplied by 2 considering the 2-mm slice thickness. The OBV was determined by a radiologist blinded to the study. Twenty-two patients in the

TABLE 1. Baseline characteristics of the study subjects factor case group*

Factor	Case group (n = 22)	Control group (n = 37)	*p*
Age, years	42.45 ± 11.29	40.29 ± 14.13	0.545
Male gender, n (%)	13 (59.1)	20 (54)	0.790
Right OBV, mm^3	66.59 ± 6.85	74.45 ± 13.26	0.052
Left OBV, mm^3	68.18 ± 16.94	75.67 ± 13.07	0.062
Total OBV, mm^3	134.77 ± 33.18	144.86 ± 29.21	0.228
Olfactory threshold (SD)	5.59 ± 1.76	1.67 ± 1.29	<0.001
Anosmic, n (%)	4 (18)	0 (0)	
Hyposmic, n (%)	16 (72)	4 (11)	
Normosmic, n (%)	2 (10)	33 (89)	
Lund-Mackay score	22.27 ± 1.93		
Stammberger's classification score	2.36 ± 0.78		

*Values are mean ± SD unless otherwise indicated.
OBV = olfactory bulb volume; SD = standard deviation.

case group were followed after FESS. After 6 months, OBV and olfactory threshold were measured once again. All images are saved at the otorhinolaryngology research center of Tehran University of Medical Sciences.

All statistical analyses were performed with the use of computer software (SPSS version 15; SPSS Institute, Chicago, IL). Baseline variables were compared between two groups using the independent Student *t* test. Distributions of continuous variables were analyzed using the 1-sample Kolmogorov-Smirnov test for normality. Correlations were analyzed using Pearson's correlation coefficient. Paired *t* test was used to compare the olfactory threshold and OBVs before and after the FESS. A *p* value less than 0.05 was considered statistically significant.

Results

A total of 22 patients with nasal polyps as well as 37 healthy individuals (control group) were recruited for the study. There were 33 male and 26 female participants within the age range of 19 to 71 years (mean ± standard deviation [SD], 41.10 ± 13.08).

Clinical characteristics of the study groups are given in Table 1. There were no statistically significant differences regarding age, sex, right OBV, left OBV and total OBV between the study and control groups. However, olfactory threshold was higher in the case group ($p = 0.005$). Anosmia was addressed to participants who failed to recognize any concentration.[18] The average olfactory threshold (mean ± SD = 1.87 ± 0.83) obtained from previous pilot study conducted by the first author (M.S.) in 100 healthy individuals. Patients with an olfactory threshold above normal (mean + 2SD) were considered as hyposmic.

No significant correlation was found between olfactory threshold and left OBV, right OBV, or total OBV in the study participants. The mean Lund-Mackay score of the patients was 22.27 ± 1.93.The correlation between this score and the mean total OBV and left OBV was significant ($r = -0.15$, $p = 0.045$; $r = -0.22$, $p = 0.047$; respectively). However, there were no significant relations between Lund-Mackay score and right OBV or olfactory threshold ($p > 0.05$ for both relations). Also, the average Stammberger's classification score was 2.36 ± 0.78. No significant correlation was found between this score with the average right, left, or total OBV and the olfactory threshold ($p > 0.05$).

TABLE 2. OBV before and after FESS*

	Volume before FESS	Volume after FESS	*p*
Right OBV, mm^3	66.59 ± 16.85	69.09 ± 16.78	<0.001
Left OBV, mm^3	68.18 ± 16.94	69.72 ± 17.60	0.001
Total OBV, mm^3	134.77 ± 233.18	138.81 ± 33.87	<0.001
Olfactory threshold (SD)	5.59 ± 1.76	3.5 ± 1.68	<0.001

*Values are mean ± SD unless otherwise indicated.
FESS = functional endoscopic surgery; OBV = olfactory bulb volume; SD = standard deviation.

OBV and olfactory threshold were measured again in the case group 6 months after FESS. The decrease in olfactory threshold measured after FESS was statistically significant.

As summarized in Table 2 right, left, and total OBV significantly increased after FESS. Figure 2 shows right and left OBV before and after FESS.

Discussion

The first part of the study evaluated the olfactory threshold and OBV in patients with nasal polyps and compared the results with healthy controls.

In this study, the olfactory threshold of patients with nasal polyps was significantly higher than those of the

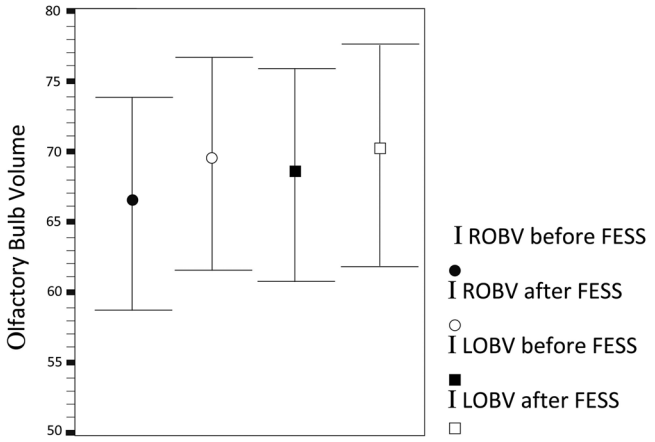

FIGURE 2. Right and left OBV before and after FESS. FESS = functional endoscopic sinus surgery; OBV = olfactory bulb volume.

control group. Other studies also showed that polyps decrease the olfactory function and threshold. According to the findings of our study, the difference of the total, right, and left OBV between the case and control groups was not significant. Total OBV and left OBV had a negative significant correlation with Lund-Mackay score. There was no significant correlation between Lund-Mackay score and right OBV or olfactory function.

The second part of the study investigated olfactory threshold and OBV changes in patients with NP after FESS. Our study demonstrated that patients had a significant decrease in olfactory threshold after surgery. There was also a significant increase in OBVs after FESS.

Goektas et al.[19] evaluated the relation between olfactory dysfunction, caused by different factors, and OBV; they found no significant relation between subjective olfactory tests (threshold, discrimination, identification score) and OBV. However, a significant correlation between objective tests (chemosensory evoked potentials) and OBV was present in their study ($p < 0.0001$).[19] In the study conducted by Buschhüter et al.,[20] left-sided OBV had a significant correlation with olfactory thresholds ($p < 0.05$), whereas right-sided OBV had no correlation with subjective olfactory tests ($p > 0.05$).

Rombaux et al.[21] compared the OBV of patients with postinfectious olfactory loss with a control group, and revealed that the OBV decreases with olfactory loss duration. Nonetheless, no significant relation between OBV and olfactory function was found.

Mueller et al.[22] evaluated the association between OBV and olfactory deprivation in posttraumatic and postinfectious patients, and showed a significant correlation between them.

In a study performed by Danielides et al.,[23] 116 patients with NP who underwent ESS were studied. Olfactory testing was performed using the Sniffin' Sticks test, preoperatively and postoperatively, and patients demonstrated a significant improvement of olfactory threshold after FESS.

Additionally, in a study performed by Gudziol et al.,[24] 37 individuals were evaluated (18 with rhinosinusitis and 19 healthy individuals) before and after FESS. A significant improvement was observed in both OBV and olfactory function of patients and the increase in OBV correlated significantly with an increase in odor thresholds.[24]

Many other studies have evaluated olfactory function and OBV. Remarkably, studies assessing disorders and injuries that directly affect OBV (such as head trauma) have demonstrated a significant correlation between olfactory function and OBV.[25,26]

On the other hand, studies in which olfactory dysfunction due to peripheral diseases such as nasal polyps (this study) and postinfectious olfactory loss is evaluated, show no significant association between olfactory function and OBV.

Conclusion

The results of our study show that FESS has a significant impact on OBV increment and olfactory threshold decrement. The olfactory bulb is a plastic structure and improvement in peripheral olfactory function results in enlargement of OBV. The limitations of this study bear mention; the duration of olfactory dysfunction was not assessed. In addition, the diagnosis of olfactory dysfunction was based on subjective tests and could have varied according to the state of patients at the time of evaluation, resulting in a possible bias.

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