Assessment of Olfaction Using the “I-Smell” Test in an Indian Population: A Pilot Study

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Abstract The objective of our study was to assess the olfactory function in patients having sinonasal disease and in normal healthy individuals and to establish a clinical test for olfaction in Indian population. Odor threshold and odor identification testing in patients of sinonasal disease and in subjects with no sinonasal disease was done in an academic tertiary medical center. Fifty patients with sinonasal disease (Group A) and 100 normal subjects with no complaints of olfactory dysfunction (Group B) were prospectively recruited. Group A was evaluated using visual analogue scales for subjective grading of olfactory function, nasal endoscopy and odor threshold and identification abilities. Group B was evaluated using nasal endoscopy and combined olfactory score. The combined olfactory score (COS) in group A ranged from 0 to 15 (mean 7.85, SD 2.26). The score in group B ranged from 7 to 19 (mean 14.57, SD 4.78). Statistically significant correlation was observed between VAS and COS ($r = 0.764, p < 0.001$) and nasal endoscopy score and COS ($r = 0.55, p < 0.001$) in group A. The “I-Smell” test could effectively discriminate between subjects with olfactory dysfunction and the normosmic subjects and is feasible to be used in Indian population.

Keywords Olfaction · Olfactory threshold test · Olfactory identification test

Introduction

A proper functioning sense of smell allows a person to discriminate between thousands of largely organic, low molecular mass, volatile compounds. When combined with gustatory and somatosensory stimuli, the sense of smell determines the flavors of foods and beverages, and aids the process of digestion by triggering normal gastrointestinal secretions. While some of these functions may be less vital to a person's well being and functionality than vision and hearing, their loss may still impact negatively the person's quality of life [1]. Routine clinical quantitative measurement of smell function can allow a physician to validate and characterize a patient's olfactory complaint and longitudinally follow the course of smell function after therapeutic intervention or during recovery from previous loss [2]. Smell function was largely left unassessed by physicians because it was found inconvenient and time consuming. Therefore, the clinical need for a brief, simple and reliable screening test was realized and has been studied in the past [3]. The objectives of our study were to assess the olfactory function in individuals having sinonasal disease and in normal healthy individuals and to compare the olfactory score in these two groups. We aimed to develop a test which will be portable, inexpensive to create and suitable for Indian population.

The most widely used tests for assessing the ability to smell are those of odor threshold detection and odor identification. The more successfully used tests include the University of Pennsylvania Smell Identification Test (UPSIT) [4], the “Sniffin’ Sticks” test [5, 6], the Connecticut Chemosensory Clinical Research Center (CCCRC) test [7] and the 12-odor Brief Smell Identification Test (B-SIT), also known as the Cross-Cultural Smell Identification TestTM [8]. A modification of the CCCRC test; the

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combined olfactory test (COT) for Chinese population has also been developed [9]. The use of these tests in Indian population is limited by factors such as cost, differences in familiarity with the odors and difficulty in procurement of these test kits. We therefore proposed to develop a test; the “I-Smell” test for evaluation of olfaction in the Indian population.

Materials and Methods

All test procedures were explained in full detail to the participants and a written informed consent was taken. The study was performed in accordance with the Declaration of Helsinki and was approved by the Institutional ethics committee.

The “I-Smell” test comprises of two components; threshold testing and odor identification.

The threshold test employs 1-butanol as the test odorant. 1-butanol is commonly used in odor experiments as it is low in toxicity, colorless, water-soluble, readily available in high purity and has a neutral odor quality [9]. It has attained wide acceptance as a reference odorant in various applied settings because of these same attributes [7]. The test kit contained nine glass bottles each containing ~20 ml of test solution which were labeled as, solutions one to nine and another identical glass bottle filled with ~20 ml of sterile water. The 1-butanol solution was diluted by successive factors of three; the highest concentration being 4 % (vapor phase of ~3,000 ppm), designated as solution one while lowest concentration being 0.00061 %, designated as solution nine. Participants received two bottles at a time, one with sterile water and one with odorant (solutions one to nine). The test began with the weakest solution in an ascending order of concentration to avoid desensitization. The *method of ascending limits* was used. The patient needed to identify the bottle containing the odorant on four successive occasions. The lowest concentration of odorant that the patient identified was defined as the threshold. Scores of one to nine were given depending on the lowest concentration of solution successfully identified. Zero was scored if solution one was not identified. After determination of the threshold in one nostril, testing was done for the other nostril in the similar manner. A standard technique was followed [9].

Odor Identification Testing

The odorants used in previous studies from various centers were modified for the study according to our local dietary and cultural habits. The odors were chosen based on their properties of pleasantness, familiarity and practicality. The substances were kept in opaque plastic bottles and the

patient's eyes were covered when the substances were presented to them to prevent any chance of visual identification. To perform the test, the cap was removed by the examiner for ~3 s, and the mouth of the bottle was placed ~2 cm in front of the nostril and patient was asked to sniff normally without any force. There was an interval of at least 30 s between successive presentations to prevent olfactory desensitization [6]. Patients were asked to choose from a list of four choices for each substance presented. Ten items were presented in random order for monorhinal smelling [7]. To restrict the stimulus to one nostril, the participant was asked to hold the irrelevant nostril closed. The total odor identification score was calculated by adding the number of substances correctly identified. The total score of the threshold test and the odor identification test was taken up as the combined olfactory score for the nostril being tested. Both the tests were done in a well-ventilated and quiet room. Substances used for odor identification were asafoetida (heeng), naphthalene balls (moth balls), garlic (lahsun), vicks vaporub[®], rose water, sandalwood oil, cardamom (elaichi), clove oil (laung), lemon and cumin seeds (jeera).

The study was conducted over a period of 8 months. Fifty patients having nasal complaints and sinonasal disease were taken as “cases” (group A). Additionally, one hundred normal healthy individuals were assessed and taken as “controls” for sense of olfaction using the same test method (group B). The age group was from 14 to 60 years for both the groups. People having history of smoking and patients with complete nasal obstruction (extensive polyposis) were excluded from group A. Individuals having history of smoking; past history of nasal surgery; any disease known to affect olfactory dysfunction and having history of any chronic drug intake, were excluded from group B. Assessment of olfactory dysfunction included detailed history and examination for potential causes of olfactory dysfunction. Visual analogue scale (VAS) was used for subjective grading of olfactory dysfunction, ‘zero’ score being worse and ‘five’ being normal. The olfaction test, routine ENT examination including anterior rhinoscopy and nasal endoscopy were done. Scoring for nasal endoscopy was done according to Lund and Kennedy scoring system. Each side was graded separately and scores from each side were taken as ‘right nostril’ and ‘left nostril’ individual scores.

All relevant data from case record forms and olfactory test scores was tabulated and systematically analyzed.

Statistical Analysis

The demographic data, clinical information, visual analogue score and the results of the olfactory test were

analyzed. The differences in olfactory score between the two groups (normal and subjects with olfactory dysfunction) were statistically analyzed using the one-way ANOVA followed by post hoc Tukey tests. For comparison of age between the two groups, we used Pearson correlation method and for sex comparison, unpaired student *t*-test. The diagnostic nasal endoscopy (DNE) scores and combined olfactory scores (COS) were correlated using the Pearson correlation. The VAS scores and the combined olfactory scores were correlated using the one-way ANOVA followed by post hoc Tukey test. A *p* value < 0.05 was taken as statistically significant.

Results

Group A consisted of 26 male (54 %) and 24 female (46 %) subjects, mean age being 30.8 years (SD 12.83 years) and male-to-female ratio being 1.08:1. Group B consisted of 58 male and 42 female subjects, mean age being 33.4 years (SD 11.04 years) and male-to-female ratio being 1.3:1. The likely causes of olfactory dysfunction in the fifty cases of rhinological disease are outlined in Table 1.

Olfaction was evaluated in all subjects using the “I-Smell” test. The mean time spent on threshold detection was 4.4 min and odor identification was 5.2 min and the whole test took a mean time of 9.4 min. The range of score in controls i.e., group B, was from 7 to 19 (mean score 14.57, SD 4.78); while in cases i.e., group A, was from 0 to 15 (mean score 7.85, SD 2.26).

The subjects in the group A were classified in four groups on the basis of VAS scores for the purpose of analysis and for the purpose of correlation between the subjective sense of olfaction and the result on objective testing of olfaction.

As depicted in Table 2, the mean olfactory scores of the right as well as left nasal cavities increased, as the VAS score increased from 0 to 5 in group A. Using one-way ANOVA test followed by post hoc test Tukey, it was seen that the lower VAS scores (0, 1, 2) were correlated with lower mean olfactory scores (1.33, 6.50) and patients having normal VAS scores (5) were having higher olfactory scores (12.22). Using this correlation, we were able to

Table 2 Correlation of VAS and COS

No. of patients (<i>n</i> = 50)	VAS score	Mean combined olfactory score	Grading of olfactory dysfunction
9	0	1.33	Anosmia
18	1–2	6.5	Moderate hyposmia
14	3–4	11.25	Mild hyposmia
9	5	12.22	Normal

classify the patients in four classes viz., anosmia, moderate hyposmia, mild hyposmia and normal. Significant correlation was found between the visual analogue score and the combined olfactory score (COS) [$r = 0.764$, $p = 0.000$ (<0.001)]. The mean COS in the four groups was as follows:—allergic rhinitis—6.61, chronic rhinosinusitis with or without polyps—9.44, deviated nasal septum—4.50 and miscellaneous (atrophic rhinitis, nasal mass)—1.8

The subjects in group A were also assessed using nasal endoscopy. The DNE score and COS were correlated using Pearson’s correlation and the correlation was found to be significant [$r = 0.55$, $p = 0.000$ (<0.001)]. On correlation of DNE score with the COS, in each of the four groups in group A, it was found that the correlation was significant in all the disease groups except in chronic rhinosinusitis perhaps due to inclusion of cases with and without nasal polyps. The correlation observed was; in allergic rhinitis [$p = 0.015$], $r = 0.796$], in chronic rhino sinusitis [$p = 0.405$], $r = 0.120$], in deviated nasal septum [$p = 0.021$], $r = 0.59$] and in miscellaneous [$p = 0.015$], $r = 0.945$]. However the correlation needs to be interpreted with caution, as, the number of subjects in each disease group was less.

We observed that in the normal healthy individuals, acuity of olfaction decreased as the age progressed as showed on correlation of age with the COS, using Pearson’s correlation [$r = -0.365$, $p < 0.001$]. On comparison of sex with the COS in subjects of group B, it was found to be non-significant ($p > 0.05$), using unpaired student *t*-test.

On comparison of combined olfactory scores in the two groups, it was found that the difference was statistically significant [$p = 0.000$ (<0.001)], using one-way ANOVA followed by post hoc test Tukey. The mean difference with 95% confidence interval was 6.725 (5.59–7.86). The difference is highlighted in a graph which has been plotted between the number of subjects and the total combined olfactory score of left and right nostrils, with series 1 being the group A and series 2 being the group B (Fig. 1). This implies that on the “I-Smell” test, the patients with sino-nasal disease performed poorly and our test could effectively discriminate between subjects with olfactory dysfunction and subjects with normal olfaction.

A receiver operating characteristic curve was drawn for butanol threshold test (BAT) and odor identification test

Table 1 Causes of olfactory dysfunction in group A

Aetiology	Frequency (<i>n</i> = 50)	Percentage (%)
Chronic rhinosinusitis	17	34
Deviated nasal Septum	15	30
Allergic rhinitis	13	26
Miscellaneous	5	10

Fig. 1 Graph between total olfactory score and number of subjects

and the area under the curve was determined. Higher value of area under the curve indicates better classifying test for cases and controls. Butanol threshold detection test had [area = 0.938 (0.899–0.977)] which was greater than odor identification test [area = 0.837 (0.823–0.932)] as shown in Fig. 2. The correlation between the threshold and identification tests equaled +0.83 which indicated that the score on butanol test predicted 70 % of the variance on the other. This implies that in our study, BAT was more appropriately classifying cases and controls.

Discussion

A successful test for olfaction should be able to establish the olfactory threshold and should have an odor identification component using common odors to have a practical relevance in a particular cultural setup. Various other authors have published reports of modifying the established tests, to suit the needs of their population [10–12]. As there

is no established test for the Indian population, leading to neglect of this important chemosensation, we carried out this study to develop a clinical test for olfaction for use in our population.

We used the standard methodology, as in olfactory threshold testing, the subject is asked to report which of two or more stimuli (i.e., an odorant and one or more blanks) smells rather than to simply report whether or not an odor is perceived. Such “forced-choice” procedures have been reported to be less susceptible to contamination by response biases than non-forced choice procedures. In addition, they are more reliable and produce lower threshold values [13].

To provide a brief overview of the available tests; among the various tests the UPSIT has been used most widely. This is a simple self-administered clinical test which utilizes “scratch and sniff” odorants for odor presentation. The UPSIT is highly reliable, with test–retest reliability coefficients exceeding $r = 0.90$ [4].

Sniffin Sticks is a test based on felt-tip pens devised by Kobal in Erlangen, Germany. It comprises tests for odor threshold, odor discrimination, and odor identification [5]. Further studies have been done to bring out modifications of this test, such as to create a screening test which would need less time for application [14], and to investigate a threshold like measure for olfactory sensitivity [15]. The Connecticut Chemosensory Clinical Research Center (CCCRC) test combines stability of outcome with sensitivity to variables known to affect olfaction such as age and sex [6].

Major nonclinical findings derived from modern sensory tests, primarily the UPSIT, are that—women are better able than men to identify odors, significant loss of olfactory function occurs after the age of 65 years, the decreased smell ability associated with smoking is present in prior cigarette smokers, and olfactory function is compromised in urban residents and in workers in some industries, including the paper and chemical manufacturing industries [16].

On analyzing the data obtained from our test, on correlation of age with the combined olfactory scores in the normal population, it was found that as the age progresses, the olfactory score declines [$r = -0.365$, $p < 0.001$]. This has also been shown in other studies [6, 7]. The possible explanations given for this decline are psychologic factors such as age-related deterioration in memory or attention and various morphologic alterations in the elderly nasal mucosa such as changes of epithelial blood flow, reduced metabolism or increased mucus viscosity [6].

Olfactory sensitivity was found to be higher for females than males in previous studies [6, 7]. The reason for this may be the positive influence of various hormonal factors, especially estrogens, on the female olfactory epithelium.

Fig. 2 Receiver operating characteristic curve

In our study, no statistically significant correlation of sex with olfactory score was established ($p > 0.05$), which may be due to a smaller sample size.

Previous studies have shown that the sense of olfaction is frequently affected in sinonasal disease [17, 18]. In our study the range of COS for the patients of sinonasal disease was 0–15 and the range of score for normal population was 7–19 [mean difference with 95% CI being 6.725 (5.59–7.860)]; thereby establishing that there was considerable difference in the olfactory scores between the two groups. This observation is concurrent with previous studies [3, 7, 9].

In the group consisting of patients of olfactory dysfunction with nasal complaints, we classified the patients into four sub-groups: chronic rhinosinusitis with or without polyps, allergic rhinitis, deviated nasal septum and miscellaneous group. In the combined olfactory test performed by Lam et al. [9], out of a total of 188 Hong Kong Chinese subjects, 55 had normal function while 133 subjects had either hyposmia ($n = 89$) or anosmia ($n = 44$). The potential causes of olfactory dysfunction were rhinitis, nasal polyposis, idiopathic, post-URI, rhinosinusitis, head injury, atrophic rhinitis and syphilis. In another study involving 278 patients; the major causes of olfactory loss were upper respiratory tract infection (36 %), sinonasal disease (21 %), trauma (17 %), congenital anosmia (3 %) and other causes (3 %). In 18 % patients, no definite cause could be identified [19]. Though we do not have a large number of subjects with an olfactory impairment, we do have a representative group of patients with sino-nasal disease.

A correlation between the subjective severity of olfactory dysfunction graded by the VAS and the combined olfactory score (COS) was demonstrated in our study ($r = 0.764$, $p < 0.001$), as shown previously by Lam et al. ($r = 0.56$, $p < 0.01$) [9] and Hashimoto et al. [20].

The “I-Smell” test, required an average of 9.4 min, while the mean time spent on each COT was 8.6 min [9].

On correlation of DNE score with the COS in each of the four groups of diseases in our study, significant correlation was found indicating to some extent that the test could predict correlation between olfactory dysfunction and severity of disease; the limitation being a small sample size.

In a study conducted by Cain et al. [7] the identification component consistently yielded a higher frequency of anosmic scores, leading them to conclude that odor identification may be having higher sensitivity than threshold component. On the grounds of ease of use, speed of administration, and resolution between patients and controls, the identification component might seem more desirable. However, in our study, by estimating area under the curve (receiver operating characteristic curve) we

found that the butanol threshold test is better in classifying the subjects as cases or controls, while other authors have found that tests of odor identification and detection are typically correlated with one another [13].

Our study compared the combined olfactory score with the visual analogue score for the subjective severity of olfactory dysfunction and we classified the patients into groups (normal, mild hyposmia, moderate hyposmia and anosmia). Even though, our test score correlated with the visual analogue score ($p < 0.05$) and was effective in discriminating between patients with olfactory impairment and subjects with normal sense of smell, suggesting that the test is a feasible method of olfactory assessment, we will validate it further in a larger number of subjects and do further testing for test–retest reliability. In routine otorhinolaryngological practice, the test could help both to establish the initial severity of olfactory disorders and to chart the course of changes after surgery, during or after medication. Such use would decrease sole reliance on the subjective impressions of the patient and could assist in appropriate and timely decision making. With the help of this study, we have tried to establish a simple, easy-to-use, portable, inexpensive and easily administrable test for olfaction. The test has also been suitably modified for Indian population.

Summary

- Though various tests for olfaction are in use in the western population, no standardized test is available for the Indian population with a large population suffering from olfactory impairment
- The developed test could effectively discriminate between olfactory function in patients and normal individuals
- The “I-Smell” test is a simple, easy-to-use, portable, cost effective test, suitably modified for the Indian population

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