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Clinical Diagnosis and Treatment of Olfactory Dysfunction

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Olfactory dysfunction is a relatively common disorder that is often under-recognized by both patients and clinicians. It occurs more frequently in older ages and men, and decreases patients' quality of life, as olfactory dysfunction may affect the emotion and memory functions. Three main causes of olfactory dysfunction are sinonasal diseases, upper respiratory viral infection, and head trauma. Olfactory dysfunction is classified quantitatively (hyposmia and anosmia) and qualitatively (parosmia and phantosmia). From a pathophysiological perspective, olfactory dysfunction is also classified by conductive or sensorineural types. All patients with olfactory dysfunction will need a complete history and physical examination to identify any possible or underlying causes and psychophysical olfactory tests are essential to estimate the residual olfactory function, which is the most important prognostic factor. CT or MRI may be adjunctively used in some indicated cases such as head trauma and neurodegenerative disorders. Functional MRI (fMRI) and psychophysiological tests (olfactory event-related potential, OERP) are also used in the research setting. Compared to rapid progress that has occurred in fields of basic science and diagnostic tools for the therapy of other diseases and disorders, treatments for olfactory loss are still in a state of unmet need. In most olfactory dysfunctions, there has been no well-designed randomized controlled study to justify or prove effective treatment modalities. Therefore, with more attention to the problem and further research we can expect breakthroughs in the treatment of smell loss in the near future.

Key Words: Smell; Olfaction; Olfaction Disorders ; Diagnosis; Therapeutics

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INTRODUCTION

Smell is one of several special sensations (visual, auditory, and olfactory) used to monitor the human environment. Also it provides a clue to escape or avoid from dangerous situations (spoiled foods, fire, and leaking natural gas). Smell is tightly associated with taste and flavor in eating and nutrition, and is essential for memory and emotion. Olfaction is a conserved biological function from ancient times but its relative functional volume in the brain has been decreased with the development of higher brain functions in evolution. Although olfaction is not rudimentary in human and still provides very important functions, its significance is easily ignored or neglected.

In 1837, there was the first scientific case report of traumatic anosmia. Recently, there have been big advancements in the olfactory science with the discovery of G-protein (1994) and G-protein coupled receptor (GPCR, 2004). In line with the development of olfactory tests (psychophysical and electrophysiological tests) and imaging studies such as computed tomography (CT), magnetic resonance image (MRI), and functional MRI (fMRI), there have been many investigations ongoing in clinical practice (otolaryngology, neurology, and neuropsychiatry). Here, we will discuss the clinical diagnosis and treatment of olfactory dysfunction focusing on hyposmia and anosmia.

TERMINOLOGY AND DEFINITIONS OF OLFACTORY DYSFUNCTION

1. Qualitative olfactory dysfunction

The qualitative olfactory dysfunctions are disorders of odor iden-

tification (dysosmia), which include parosmia (altered odor perception with odor present) and phantosmia (perception of smell without odor present). In special form of dysosmia, some patients interpret the smell of all odors as unpleasant (cacosmia).

Parosmia is less frequent than hyposmia/anosmia and is prevalent in the following conditions; head trauma (29-55%), post-URI (upper respiratory tract infection, 35-51%), sinonasal diseases (17-28%), and toxins/drugs (17-28%) [1]. Patients with parosmia showed smaller volume of olfactory bulb than patients without parosmia.

Information regarding the pathogenesis of parosmia has been lacking but some hypotheses have been suggested; 1) partial loss of olfactory receptor neurons, 2) dysfunction of olfactory bulb by interneuronal loss, 3) pathology of the interpretive central nervous system, 4) abnormalities in axonal targeting from regenerating fibers after injury, and 5) altered olfactory map after olfactory injury. Further studies will be warranted to uncover which of these hypotheses are causal to parosmia.

Both parosmia and phantosmia may lead to a significantly decrease in quality of life because of foul odor, altered taste, and weight loss. There are case reports of severe parosmia (lethal appetite and weight loss) and phantosmia (horrible odor perception, extensive hygiene, and social isolation) [2,3].

2. Quantitative olfactory dysfunction

The quantitative olfactory dysfunctions are categorized into hyposmia (decrease in smell) and anosmia (lack of smell) compared with normosmia (normal olfactory function). In most cases of chronic rhinosinusitis with nasal polyposis and head trauma, anosmia results while most patients with post-viral dysfunction exhibit hyposmia accompanied by dysosmia [4]. Often, qualitative and quantitative olfactory disorders occur simultaneously. Landis et al reported that anosmic and hyposmic participants had 6% of parosmia and 1.5% of phantosmia, respectively [5] and Bonfils et al analyzed a series of 56 patients with parosmia, in which 71.4% were associated with hyposmia and 28.6% reported anosmia [6].

PREVALENCE AND ETIOLOGY OF OLFACTORY DYSFUNCTION

Although there have been few population-based studies, most authors reported frequencies of 1-3% of olfactory disorders [7]. Self-report usually underestimates olfactory dysfunction compared to olfactory test and this discrepancy may be due to unawareness of gradual decline in olfactory function in elderly [8]. Recently, one population-based study reported that the prevalence of olfactory dysfunction was 19.1%, composed of 13.3% with hyposmia and 5.8% with anosmia [9]. Dysosmia appears to be less common than odor sensitivity loss and a recent population-based study reported a prevalence of 4.0% in adults [10]. Aging, male, and smoking are well known risk factors for olfactory dysfunction. Smoking affects olfactory function less than age or sex, and it seems to be dose- and duration-dependent. Smoking cessation may improve olfactory function over time. Common risk factors such as head trauma, stroke, epilepsy, diabetes mellitus, depression, neurodegenerative disorder (Parkinson's disease), toxin (gasoline), medications (adrenergic and cholinergic agents), nasal obstruction, and upper respiratory tract infection are associated with increased prevalence of olfactory impairment [11].

Olfactory dysfunction can be classified into conductive (physical blockage of airflow to olfactory mucosa) or sensory-neural types (disruption of the olfactory-neural signaling pathway). Conductive types include diseases of the nasal and paranasal sinuses (including nasal stenosis, allergic rhinitis, chronic rhinosinusitis with polyposis, and tumors), and show a relatively good prognosis after medical and/or surgical management. Sensory-neural types include URI, traumatic head injury, neurodegenerative disorders, congenital (Kallman's syndrome), and toxins. The prognosis of sensory-neural types remains poor and is sometimes irreversible. Although more than 200 causes of olfactory disorders exist, the vast majority of olfactory dysfunction occurs as a result of sinonasal diseases, post-URI, and head trauma (Table 1). Cases where the cause of olfactory dysfunction is idiopathic has been estimated to be about 20-30%.

1. Age

Olfactory function peaks around the third or fourth decade of life and then decreases with increasing age and is significantly reduced above the age of 55 years [12]. A decline in olfaction may be sharp in the sixth and seventh decade of life. In addition to age-related declines in memory and attention, surface area of the olfactory mucosa decreases as a result of a loss of primary olfactory receptor neurons with replacement by respiratory epithelium [13]. Other pathological processes involved in the loss of olfactory function in aging may include a reduced rate of basal cell proliferation, decreases in cilia and supporting cell microvilli, reduced metabolism, occlusion of the cribriform plate, changes of epithelial blood

Table 1. Causes and treatment of olfactory dysfunctions

Underlying causes of olfactory loss	Treatment of olfactory loss
Sinonasal diseases Allergic and non-allergic rhinitis Septal deviation Chronic rhinosinusitis with nasal polyposis	Topical steroids Oral steroids (in severe cases, short-term) Desensitization (immunotherapy) Surgery (endoscopic sinus surgery)
Post-viral	No effective therapy Expectation for spontaneous recovery Nasal or oral corticosteroid (no RCT, randomized controlled trial) Reassurance
Head trauma	No effective therapy Recovery is unlikely and requires longer time periods up to 18 months Counseling for danger risk and appropriate compensatory strategies
Toxins Smoking Work-related toxins	 Stop smoking Eliminate additional toxin exposures
Drugs Local anesthetics (cocaine) Anti-hypertensives (nifedipine) Antimicrobials (streptomycin, amphotericin B) Angiotensin (carbimazole, thiouracil) Anti-depressant (amitryptilline) Immune suppressant (methotrexate) Antiotensin-converting enzyme inhibitors	Removal of offending drugs Change dose of offending drugs Change to an alternative medication

flow, or increased mucus viscosity. In one animal study, increased pro-apoptotic gene expression was observed in the olfactory mucosa of older rats.

2. Post-viral

URI is the most frequent cause of olfactory dysfunction. Human rhinovirus, picornavirus, parainfluenza virus type 2, human coronavirus, and Epstein-Barr virus have all been demonstrated in post-viral olfactory dysfunction [14]. Olfactory dysfunction commonly occurs in women over 40 years of age after a severe or prolonged course of common cold. Virus can damage the olfactory epithelium resulting in abnormalities in the number and function of receptors with replacement by respiratory epithelium. Hyposmia is more frequent than anosmia in post-viral olfactory dysfunction. In addition, parosmia and phantosmia seems to be combined with post-viral olfactory disorder. In case of sensorineural type of loss, topical or oral steroid may not be effective. Post-viral olfactory dysfunction shows poor response to treatment and if recovered, the majority of patients show improvement within 6 months but has been reported up to 3 years post infection [15]. However, a 1-year follow up study reported that post-viral olfactory loss showed better incidence of improvement than that of post-traumatic loss (30% vs 10%, respectively).

3. Sinonasal diseases

Olfactory loss related to sinonasal diseases shows common characteristics of a gradual decrease over several years or a fluctuating course. Chronic rhinosinusitis with and without nasal polyposis (CRSwNP and CRSsNP) is the most common ENT diseases causing olfactory dysfunction. CRSwNP shows more frequent olfactory loss and more severe form (anosmia) than CRSsNP [16]. CRSwNP is not pure conductive olfactory loss but mixed with sensory-neural type due to inflammatory changes in the olfactory mucosa. Also, altered olfactory mucus (Bowman's gland) and olfactory receptor cells may explain olfactory loss associated with CRSwNP. Squamous metaplasia, increased apoptosis, and a significant change in the normal cell-cycle dynamics were found in the olfactory epithelium of CRSwNP [17]. In mixed type, the prognosis of olfactory recovery after medical (steroids) and surgical (endoscopic sinus surgery) therapies would be poor. The importance of olfactory cleft patency remains in controversy.

Many patients (21.4%) with allergic rhinitis report of olfactory dysfunction accompanied by nasal obstruction. Olfactory threshold in allergic rhinitis showed a correlation with blood eosinophilia, radiographic changes, and number of sensitized allergens [18]. However, nasal resistance measured by rhinomanometry was not related to olfactory threshold [19]. Therefore, inflammatory process not merely mechanical obstruction may play a role in allergy-

related olfactory dysfunction. Medical and surgical treatments could restore olfactory function in allergic rhinitis.

4. Head trauma

Anosmia occurs in 15% or less of patients after head trauma and 15-30% of anosmia is related to head trauma. Anosmia is more common than hyposmia after head trauma. Poor prognosis is expected in cases of severe trauma, loss of consciousness, post-traumatic amnesia, and radiological abnormalities. But anosmia can occur even after minor blows and occipital blows produce more severe loss than frontal blows (coup-contrecoup). Post-traumatic anosmia occurs secondary to olfactory mucosal damage, stretching or shearing of the olfactory nerves at the site of cribriform plate, and edema of the olfactory tract and bulb, and hemorrhage (or contusion) in the olfactory brain area. Hence, anosmia can occur without definite cribriform plate fracture. Most post-traumatic olfactory dysfunction are recognized soon after the injury but can be delayed due to late-onset of cell death in some cases. The connections between axons and the olfactory bulb are injured and decreased sensory input may also cause decreased volume of olfactory bulb [20]. Also, scar formation and fibrosis in the olfactory bulb have been found in post-traumatic smell loss [21]. Regeneration of the olfactory nerve is a possible mechanism of recovery but aberrant connections may lead to olfactory distortion (dysosmia). Complete history and physical examination including nasal endoscopy will be essential and tests for cranial nerve functions including olfaction and taste should be done. CT and MRI scans are useful adjuncts to diagnose the olfactory dysfunction. There are no specific treatments available for post-traumatic anosmia. Olfactory function returned in just 10-30% of cases while 20% of patients worsened [22]. Recovery is unlikely if improvement is not observed within 6 months to 1 year following head trauma. All patients should be informed regarding the risks of olfactory loss and appropriate compensatory strategies.

5. Neurodegenerative disorders

Olfactory dysfunction can be the earliest sign of Parkinson's disease, Alzheimer's disease, and multiple sclerosis. Devanand et al reported that an abnormal olfactory test was more sensitive to predict the development of Alzheimer's disease than a low score on the Mini-Mental State Examination [23]. Therefore, simple olfactory tests may prove to be useful as a screening test and to monitor patient response to treatment.

6. Psychiatric disorders

Schizophrenia and depression are associated with smell disorders. The amygdala and cortex are involved in these psychiatric diseases. However, self-reported depression did not relate to the severity of olfactory dysfunction [24].

7. Brain tumors

Frontal and temporal lobe tumors can lead to olfactory dysfunction. Anterior fossa tumor such as esthesioneuroblastoma and Foster-Kennedy syndrome shows progressive hyposmia leading to anosmia, and one quarter of temporal lobe tumors cause olfactory loss. Therefore, association between brain tumors and olfactory dysfunction will be site-specific.

8. Autoimmune and endocrine disease

Olfactory dysfunction can be caused by autoantibody (anti-ribosomal P) in patients with systemic lupus erythematosus (SLE). Labeling and mouse studies have demonstrated the association between SLE and olfactory dysfunction [25]. In addition, some endocrine diseases such as diabetes mellitus, hypothyroidism, and hypogonadism are associated with olfactory dysfunction.

9. Toxins and drugs

Local exposure of chemicals (formaldehyde, cadmium, benzene, cyanoacrylates, gasoline, ammonia, hairdressing chemicals, herbicides, pesticides, and zincs) can cause smell loss. Degrees of olfactory dysfunction are correlated with the concentration of the toxins and the length of exposure. Toxin-induced olfactory dysfunction is usually permanent.

Often, systemic drugs (chemotherapy, anticonvulsants, antidepressants, antirheumatics, immunosuppressants, antimicrobials, antithyroids, and antihypertensives) appear to cause taste and olfactory dysfunction [26]. However, the precise causal mechanisms for olfactory loss as a side effect of pharmacotherapy have not been well defined. In most cases, changing or removing the offending drugs will reverse the effects on the olfactory functions.

TRIGEMINAL AND OLFACTORY DYSFUNCTION

The nasal cavity is innervated by two cranial nerves: the trigeminal and olfactory systems. Most odors stimulate both nervous systems and interaction between the two systems has a powerful influence on odor and touch perception. Many studies have shown that

olfactory loss will lead to decreased responsiveness to trigeminal stimulation [27,28]. Atrophic rhinitis is a unique clinical setting which can result in loss of both olfactory and trigeminal functions [29].

EVALUATION OF OLFACTORY DYSFUNCTION

The clinical evaluation of patients with olfactory dysfunction should include a thorough history taking, physical examination, psychophysical olfactory tests, and/or imaging. The medical history should encompass the onset and degree of olfactory dysfunction and details regarding medical, occupational and family history. Possible risk factors such as smoking, viral infection, and head trauma should be evaluated. Olfactory testing should be performed to estimate the degree of olfactory loss. Unlike in the auditory system, no site-of-lesion study is available and histopathological studies are lacking. Imaging study will be helpful to diagnose the neurodegenerative disorders and head trauma associated with olfactory dysfunction.

1. History and physical examination

A detailed history should be taken to characterize the olfactory and/or taste function such as onset (sudden or gradual) and severity (complete or partial) of olfactory dysfunction. Some patients with olfactory dysfunction complain of decreased or altered food flavor. Self-reporting questionnaires may be helpful to estimate the severity of olfactory dysfunction. However, self-assessment may reflect nasal airway patency and may be limited by other factors such as underestimation of olfactory loss and the influence by patient's mood and motivation [30]. A well-designed questionnaire can be useful to get good informations from patients. Generally symptoms are reported as more severe with hyposmia than anosma, the younger than the eldery, and women than men. Family history should be determined to detect neurodegenerative and psychiatric disorders. Any preceding events such as cigarette smoking, occupational toxin exposure, URI, head trauma, and nasal surgery should be determined. In suspected case of dementia, a mini-mental status examination may be helpful. For parosmia, relation to the environment (specific odor), peripheral/central origin, and unilaterality should be sought.

A complete head and neck examinations should be performed to check the nasal cavity, oral cavity, cranial nerve functions (II-V, VII-IX, and XII) and any neurologic signs. Nasal endoscopy should be performed to identify possible causes of conductive olfactory loss (nasal polyps or tumors). In case of unilateral parosmia or phantosmia, local anesthesia can help to identify the indication for endoscopic removal of olfactory epithelium. Signs of Foster Kennedy syndrome in tumors of the olfactory groove and sphenoidal ridge include ipsilateral olfactory loss, optic nerve atrophy, and central papilledema. Quality of life is poor if the olfactory deficit has a sudden-onset or is accompanied by parosmia. The decrease in quality of life is related to the degree of impairment.

2. Psychophysical (olfactory) test

Psychophysical test is mandatory to detect the severity of olfactory dysfunction by a trained specialist, and it is helpful to follow up the progression or reversal of olfactory dysfunction. The University of Pennsylvania Smell Identification Test (UPSIT, 1984) is a quick and simple test and is a 40-items 'scratch-and-sniff' test (Fig. 1). The patient is forced to check each odor from four choices [31]. Malingering is suspected if a score less than 5 or 6. The Cross-Cultural Smell Identification Test (CC-SIT) is a variant of UPSIT and uses 12 items, which are commonly identified in different countries. The Connecticut Chemosensory Clinical Research Center Test (CCCRC, 1988) use 10 stimuli (7 olfactory stimuli and 3 trigeminal stimuli) in an opaque jar to each nostril. Patients have to choose 10 correct answers among a 20-items list.

Finally, Sniffin's stick test (SST, 1997) is an olfactory test based

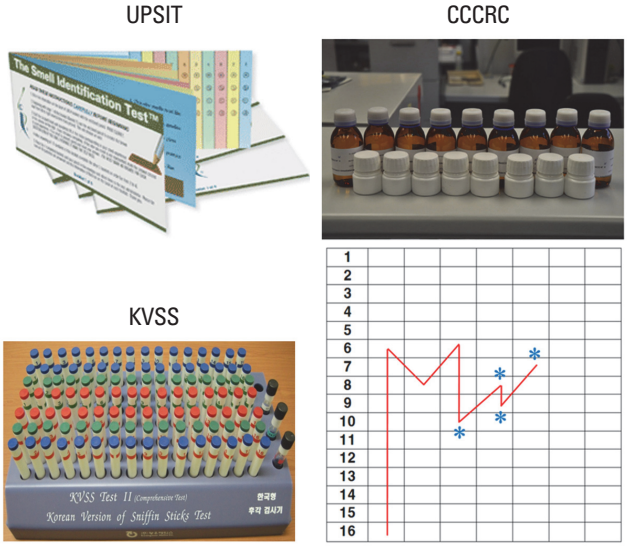

Fig. 1. Types of psychophysical olfactory tests of University of Pennsylvania Smell Identification Test (UPSIT, 40 items), Connecticut Chemosensory Clinical Research Center Test (CCCRC, 10 items) and Korean Version of Sniffin's stick test (KVSS, 16 items). A graph (right-inferior panel) shows an example of odor threshold test in KVSS.

on felt-tip pens and assesses odor threshold, discrimination, and identification. Currently, we use a Korean version of Sniffin's Stick Test (KVSS). *Odor thresholds* are assessed with n-butanol of 16 dilution by a single-staircase starting from the lowest dilution; it is a random triple-forced choice procedure in which the subjects have to identify the odor-containing pen in comparison with two pens containing the solvent only. Triplets are presented at intervals of 20 s. Reversal of the staircase is triggered when the odor is correctly identified in two successive trials. A single wrong identification triggers the reversal of the staircase to the next higher concentration. Threshold is defined as the mean of the last four out of seven staircase reversal points. The subjects' scores range between 0 and 16. In the *odor-discrimination* task, triplets of pens (red, green, and blue colored pens) are presented in a randomized order, with two containing the same odorant and the third a different odorant. Subjects have to determine a different and odor-containing pen after three trials of smelling. The presentation of triplets is separated by 20-30 s. The interval between the pens of a triplet was approximately 3 s. As a total of 16 triplets were tested the subjects' scores ranged from 0 to 16. *Odor identification* is assessed by means of 16 common odors. The subjects should choose the perceived odor from a list of four choices. The interval between odor presentations is 20-30 s. Again, the subjects' scores range from 0 to 16. Both the odor discrimination and identification test are the suprathreshold test. Results of the three subtests were presented as a composite "*TDI score,*" which was derived from the sum of the results obtained for threshold, discrimination and identification measures. An increased TDI score of more than 5.5 points should be demonstrated to determine if a patient has an improved sense of smell. Odor threshold seem to reflect mainly peripheral processes while odor discrimination and identification seem to be more related to higher order cognitive functions.

3. Electrophysiologic test

There have been three electrophysiologic tests such as electro-olfactogram (EOG), electroencephalogram (EEG), and olfactory event-related potential (OERP). EOG is an invasive procedure and has not been shown to be a reliable test, and EEG reflects just the indirect influence of olfactory stimuli. Therefore, these two tests are not commonly used in clinical practice and research setting. Like the auditory brainstem response (ABR), OERP can detect residual olfactory functions and be used to discriminate malingering. OERP could be recorded in some of hyposmia but in none of the anosmic patients [32]. Absence of OERP in hyposmia may reflect the prognosis but further studies will be necessary. At the current time, electrophysiologic test are used mostly in the research setting. There are some limitations in both psychophysiologic and electrophysiologic tests. They cannot discriminate reliably between central and peripheral loss, and moreover provide no information about the site-of-lesions.

4. Imaging study

Imaging study is not routinely indicated because in most cases it is negative and therefore should be used judiciously for the diagnosis of olfactory dysfunction. Even if detailed histories (risk factors and preceding events) and physical examinations (nasal endoscopy) are negative, imaging study such as CT and MRI could not add more information. Still, in selected cases of structural, inflammatory, traumatic, neurodegenerative, and tumorous conditions, imaging may be helpful. MRI can be used to confirm Kallmann syndrome (congenital agenesis of olfactory bulbs). Brain tumors are rarely associated with olfactory dysfunction and therefore image screening for brain tumor is not necessary. Recently, the fMRI has been used to evaluate activated areas in the brain by olfactory stimulation and will be helpful in the screening and early diagnosis of Alzheimer's disease, Parkinson's disease, multiple sclerosis, or other neurodegenerative diseases. However, it is now used primarily for research.

TREATMENT OF OLFACTORY DYSFUNCTION

Prognosis of olfactory dysfunction depends on the etiologies because conductive smell loss shows a good prognosis after intervention compared to sensory-neural type. Olfactory test could not discriminate between conductive and sensory-neural types. For this purpose, multidisciplinary approaches including history, physical examination and imaging will be warranted. Generally, presence of residual olfactory function is the most important factor for prognosis. Other secondary factors such as sex, age, smoking history, and parosmia may influence the prognosis. Unfortunately, evidence-based treatment protocol for olfactory loss is limited at the current time.

1. Treat the underlying causes

There are currently no pharmacologic methods to treat olfactory loss especially in sensory-neural types. Any underlying causes such as smoking, systemic and local diseases, and medications

should be ameliorated and treat first underlying diseases if present such as temporal lobe seizures, migraines, psychiatric disorders, and metabolic diseases. Evidence is limited but toxin-induced olfactory dysfunction may recover after the exposure terminates. In cases of hyposmia in the elderly, food flavoring and tastes can be amplified with the use of concentrated essences or extracts to stimulate a positive effect on intake and nutritional status.

2. Medical treatment

There have been a few case reports for a natural history of spontaneous recovery from anosmia after post-URI and head trauma, mostly within the first year [33]. Various medical treatments have been tried, including topical and systemic steroids, but well-controlled studies have been lacking. Systemic steroids may improve conductive, post-viral, and idiopathic olfactory loss. Topical steroids have been used as monotherapy or adjuvant therapy. In a placebo-controlled randomized double-blind study, it was reported that long-term topical steroids after initial therapy of combined topical and systemic steroids showed a lack of further improvement in patients with hyposmia and anosmia [34]. Systemic steroids can restore many patients (83%) who still complained smell loss after endoscopic sinus surgery but long-term prognosis is less promising [35]. Although olfactory improvement is often possible in CRSwNP, it is frequently transient and incomplete [36]. Steroid-dependent anosmia indicates the presence of a conductive mechanism for olfactory dysfunction.

Systemic steroids are more effective for olfactory dysfunction than topical steroids. The reasons for this difference have not been clearly demonstrated but several explanations for weak efficacy of topical steroids have been suggested. Only a small volume of topical steroids can reach the olfactory cleft. And the site of inflammation may not always be in the olfactory mucosa but may be in the cribriform plate or olfactory bulb. Standard recommendation for dosage and duration of steroids treatment has been missing. Moreover, the efficacy and regimen of topical steroids have not been clearly established. Long-term use of systemic steroids is usually unwarranted and results in side effects including gastric ulceration, osteoporosis, and diabetes but short course pulsed use of systemic steroids may be effective and may likely avoid undesirable side effects. Zinc deficiency has been suggested as a possible factor for hyposmia but a randomized, placebo-controlled trial of zinc sulfate reported no therapeutic effect [37]. Furthermore, Jafek reported a case that topical use of zinc resulted in permanent anosmia [38]. Other drugs such as Gingko biloba and vitamin B have not proven to be effective to treat olfactory dysfunction. Alpha-lipoic acid was reported to improve the post-viral olfactory loss but this study was not a placebo-controlled study.

Dysosmia tends to diminish over time and Reden et al reported that 29% of parosmia and 53% of phantosomia reported improvement within the first year [39]. Phantosmia sometimes responds to medical intervention by avoiding nasal airflow (blocking the nares) and application of topical anesthetics. Endoscopic removal of olfactory mucosa on the affected side may improve severe phantosmia.

3. Surgical treatment

The purpose of surgical treatment (septoplasty, turbinoplasty, and endoscopic sinus surgery) primarily aims at elimination of nasal obstruction and removal of inflamed mucosa or nasal polyps. Improved olfactory function after these surgeries may be a secondary benefit. Delank and Stoll showed that 25% of hyposmia and 5% of anosmia improved olfactory function after surgery [16]. And a longitudinal MRI study showed increased olfactory bulb volume after endoscopic sinus surgery in patients with CRSwNP [40]. While effective in most cases, nasal surgery may rarely cause olfactory loss by synechia, crusting, and damage to the olfactory epithelium.

In cases of severe, debilitating unilateral phantosmia, selective olfactory bulb removal [41] or endoscopic removal of olfactory mucosa may be performed on the affected side.

4. Olfactory training

Although it has not been extensively studied, olfactory training may be helpful to improve olfactory function. When olfactory receptor neurons regenerate after functional deficit, olfactory cues may modulate this regenerative process. Olfactory training consists of a 12 weeks program in which patients expose themselves twice daily to four intense odors (rose, eucalyptus, lemon, cloves) [42].

CONCLUSION

Olfaction is an important special sense and olfactory dysfunction leads to disturbance of quality of life, taste, and food intake. Smell loss is commonly underestimated by patients and there can be mismatch between self-rating of olfactory loss and psychophysical test especially in the elderly. Better insight into the mechanisms

of olfactory loss enables us to develop new strategies for therapeutic intervention. However, treatment of olfactory dysfunction remains an unmet need.

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