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A Review on Anosmia.

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ABSTRACT

Quality of life for patients with anosmia is very low. They have problems in finding appropriate foods for eating and cannot even use perfumes due to overuse issues. According to reports of a summit of the Neurological and Communicative Disorders and Stroke National Council, it is estimated that about 3 million American adults suffer from disorders of taste and smell. This study reviews some etiologies of anosmia and quotes some studies that have investigated this disorder. Here are some reasons for anosmia reviewed in this study: trauma to the nasal cavity, Occlusive diseases of the nose and sinus; Nasal obstruction as a result of nasal polyps, severe colitis, (When the obstruction is removed, sense of smell will recover. However, the smallest degree of obstruction removal in which smell is recovered is not yet known. It is assumed that the place of this reopening or the area where the air flows through to reach the olfactory cleft is right medial and anterior to the lower part of the middle turbinate.), upper respiratory infection; In general, this loss of smell is associated with nasal airway obstruction and whenever it is reopened, these problems will be resolved in 1-3 days, Head Trauma; the rate of loss of smell is 5-10% among them. The rate of loss of smell to some extent depends on the site of trauma in the skull. Blows to the frontal area often lead to loss of smell. Senescence; Although older people may be afflicted with loss of smell due to any of the reasons discussed here, they may simply lose their sense of smell because of illnesses associated with dementia or the process of senescence. Congenital: History of individuals with congenital loss of smell shows that they are healthy from other aspects and at the age of about 8 they have gradually realized that their friends, parents, sisters, and brothers can perceive things that they are not capable of perceiving them, Exposure to toxic substances, Neoplasms; Intracranial and intranasal tumors can affect the sense of smell. The most common intranasal tumors include inverted papilloma, adenomas, squamous cell carcinoma (SCC), and esthesioneuroblastomas. Patients infected with human immunodeficiency virus, Epilepsy, Psychological disorders, Medications, Surgery, Idiopathic.

Keywords: anosmia, etiology, review article

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INTRODUCTION

Quality of life for patients with anosmia is very smooth and without soul. Such individuals mention that they select foods based on their ingredients and color and also nutritional habits. For instance, they should recognize sour milk from the masses that can be seen in its surface. Other patients do not use perfumes because of fear of overuse. Many patients express concerns about fire and toxic or dangerous gases and most of anosmic patients have faced at least one of such accidents. Smoke-sensitive alarms are really necessary for these individuals [1].

In addition to this absence of sensory input, there are people who have a fixed sense of smell (usually perceive a bad smell). These patients usually spend much time and money to solve this problem, although a successful result is not often achieved. As expected, some of the patients afflicted with olfactory dysfunction would face nutritional problems such as malnutrition, obesity, and anorexia, as foods smell bad to them [2].

Olfactory dysfunction in humans

According to reports of a summit of the Neurological and Communicative Disorders and Stroke National Council, it is estimated that about 3 million American adults suffer from disorders of taste and smell. Based on previous articles, more than 200 illnesses have been considered to be associated with changes in chemosensory power. Taking advantage of detailed history, physical examinations, chemosensory test, and imaging reviews, several research centers for chemosensory have managed to classify most of the patients with the impairment of smell into etiological categories. A rare group of patients that only have distortions in the sense of smell with no change in intensity (parosmia or phantosmia), are not included in this classification. Here is a detailed description of these etiological categories [3, 4].

Occlusive diseases of the nose and sinus

Nasal obstruction as a result of nasal polyps, severe colitis or even the simple closure of the nostrils with fingers will cause anosmia. When the obstruction is removed, sense of smell will recover. However, the smallest degree of obstruction removal in which smell is recovered is not yet known. It is assumed that the place of this reopening or the area where the air flows through to reach the olfactory cleft is right medial and anterior to the lower part of the middle turbinate [5]. This area may act as the regulator of airflow towards the olfactory cleft and any change in its anatomy clearly and directly affects the olfactory power. As a result, obstructions in this area or above it, caused by colitis, polyps, tumors, or deformities of the nasal bone, can reduce or eliminate sense of smell. This sometimes may happen in the case that the inferior nasal cavity seems to be normal. It has been observed that systemic treatment or steroids will improve anosmia in most patients with secondary nasal obstruction such as nasal polyps and chronic rhinitis. Although long-term treatment with systemic steroids has many side effects, a treatment period of one to two weeks may act as a diagnostic test for nasal diseases. What that is unclear so far is the etiology of anosmia in a few patients with open nasal tract that can be treated with long-term intake of systemic steroids [6, 7].

Although several authors have suggested that the deformity caused by trauma to the nasal cavity can cause loss of smell, none of these reports has used repeated olfactory tests and no significant change has been observed in the olfactory power following surgeries on the anatomy of the nose. Therefore, the reported olfactory defects may be the due to neurological damages. However, the scar resulting from previous surgery between middle turbinate and the nasal septum can be effective in the obstruction of airflow in the olfactory cleft [8].

Loss of smell because due to upper respiratory infection

Many people mention that they have completely lost their sense of smell once or more during an upper respiratory infection (URI). In general, this loss of smell is associated with nasal airway obstruction and whenever it is reopened, these problems will be resolved in 1-3 days [9]. There are concerns in some patients that their sense of smell would not recover after disappearance of other symptoms of URI. On the other hand, these individuals are mostly middle-aged and elderly and female with a significant difference (70-80%). The reason for this increase in women is unknown, but it can be attributed to the fact that women are more susceptible to URI [10].

Biopsies of the olfactory cleft in these individuals show reduced number of olfactory receptors or their full loss. The prognosis for recovery of this type of loss of smell is generally weak [11].

Head Trauma

A review of several comprehensive studies on adult patients with head trauma (including both major and minor trauma) reveals that the rate of loss of smell is 5-10% among them. The rate of loss of smell to some extent depends on the site of trauma in the skull. Blows to the frontal area often lead to loss of smell, but complete anosmia is 5 times more prevalent in the trauma to the occipital area [12]. Traumatic loss of smell usually emerges immediately, although, in some cases, olfactory impairment is either unimportant to the patient or intangible until months after the accident. According to most of major studies, possibility of the recovery of sense of smell is less than 10%. However, Duncan showed a slight or complete recovery in the discriminative power of smell after trauma in one-third of patients in a group of 20. Quality of the recovered sense of smell is usually poor [13].

The exact nature of the harm to the olfactory system as a result of trauma is unknown. However, the cutoff of olfactory nerves in the place where the upper part leaves the screening plate is an accepted theory [4].

Biopsies of the olfactory epithelium of patients with loss of smell caused by trauma have recently provided new information. After trauma, the olfactory cells generally deform, axons and axonal coils propagate in the lamina propria, and only a very small number of olfactory nodes and cilia remain. These findings suggest the following points [3-6]:

- Olfactory nerves are probably damaged in the screening plate at the time of trauma.
- The natural response of the olfactory nerves is recovery, but axons (for unknown reasons) cannot reach the olfactory bulb.
- Without this connection with the bulb, cells are not able to create olfactory nodes and cilia.

Therefore, the key point in helping these patients is the re-establishment of connection between olfactory axons and olfactory bulb. However, there is no known technique for doing so [14].

After trauma, another probable area for damage to the olfactory system is the frontal cortex. In a study on 40 patients with complete traumatic anosmia, all of them were facing with difficulties in their job performance. Most of these patients showed psychosocial problems along with damage to the frontal cortex. Similarly, Levin observed impairment in the olfactory function in patients with hematoma (contusion) caused by trauma to the frontotemporal area [15].

Senescence

Although older people may be afflicted with loss of smell due to any of the reasons discussed here, they may simply lose their sense of smell because of illnesses associated with dementia or the process of senescence. In fact, among the people who are healthy from other aspects, establishment of balance between odor perception and following by eyes clearly differs among persons whose age is above 85 and those below 74. It has been shown that olfactory detection power rapidly drops in the sixth and seventh decades of life. That's why most of individuals aged 65-80 show a reduction in the sense of smell [16]. This change of pattern, which is associated with age, is similar to something that is discussed about visual acuity and speech intelligibility. It has been observed that olfactory thresholds decline with age, which is less obvious in women than men [17].

Alzheimer and Parkinson are two known diseases related to dementia which are often followed by olfactory dysfunction. In patients with these diseases, there are probably damages to the central olfactory cortex and olfactory bulb, which can somewhat justifies the loss of olfactory perception [18].

Congenital

History of individuals with congenital loss of smell shows that they are healthy from other aspects and at the age of about 8 they have gradually realized that their friends, parents, sisters, and brothers can perceive things that they are not capable of perceiving them. Other chemosensory functions remain intact in most cases, so they can naturally feel the stimulating and sharp smells and flavors [19].

Loss of smell is seen in the greater number of people exclusively to a specific chemical substance or a particular group of chemicals, which is called specific anosmia. For example, musk, trimethylamine (with a fishy-like smell), hydrogen cyanide (like almond smell), butyl mercaptan (a gas additive), and isovaleric acid (a smell like cloakroom clothing) are some of the substances and chemicals that may cause specific anosmia. Jafek *et al.* have shown that congenital loss of smell is pathophysiologically associated with the degeneration or atrophy of olfactory epithelium or olfactory bulb in the final stages of evolution [5, 9]. This theory is based on the fact that in the biopsies of the olfactory cleft in individuals whose description suggests a congenital loss of smell, general lack of peripheral receptors or supporting cells can be observed and, instead, the normal respiratory epithelium is seen. In addition, individuals with congenital loss obtain a score on olfactory tests equal to or just slightly better than random test mode. Since in patients in other etiological categories (including head trauma and upper respiratory infection) at least a minimum of olfactory epithelium is retained (although with abnormal shapes), it would not be surprising that congenital patients obtain the lowest scores on the smell tests among the members of all etiological categories [12].

Family anosmia associated with early baldness and vascular headaches was firstly reported by Singh *et al.* and its autosomal dominant inheritance was described by Lygonis. However, the lack of complete permanent transfer of anosmia between families again suggests the varying influence of this disease. Kallmann syndrome is probably the most well-known type of congenital anosmia which is associated with hypogonadotropic hypogonadism. The gene responsible for this syndrome is located on the X chromosome. Men afflicted with this syndrome are diagnosed when they cannot complete the course of maturation. Such individuals exhibit a reduced, weakened or no olfactory power on olfactory tests. This dichotomy indicates the existence of various kinds of this disease, although their causes are still unknown [13].

Exposure to toxic substances

Reviewing the history of loss of smell associated with exposure to a particular chemical substance is the clinical method currently used for diagnosis. Loss of smell may occur within a few days or it may emerge many years later (as what occurs in the case of formalin). Even some common substances such as cigarette smoke can cause loss of smell. There are numerous reports on the loss of smell following the exposure to toxins that some of these losses are reversible and some others are irreversible. These factors are mainly gases or aerosols which enter into the nose through air inhalation. Concentration and duration of exposure to these toxic agents causing impairment of smell should be seriously taken into account by employers [14].

Neoplasms

Intracranial and intranasal tumors can affect the sense of smell. The most common intranasal tumors include inverted papilloma, adenomas, squamous cell carcinoma (SCC), and esthesioneuroblastomas. These tumors reduce the sense of smell by obstructing the airflow path to the olfactory cleft. Intracranial meningiomas, pituitary tumors, and gliomas can cause localized damages to the olfactory system. It is estimated that about 25% of tumors in the temporal lobe underlie olfactory disorders. Symptoms such as nasal obstruction, epistaxis, anosmia, hypoxemia, nasal lesions or other signs of central nervous system are warnings for the existence of these tumors. Olfactory test for each nostril separately is an appropriate way for diagnosis of these tumors [12, 20].

Patients infected with human immunodeficiency virus

It has been observed that HIV-infected patients show a reduced olfactory power on tests. The extent of these impairments is varying and depends on health parameters such as the number of T-helper cells (CD4), body weight, body composition, and diet [17].

Epilepsy

Olfactory auras are also observed in patients with epilepsy. Prevalence of olfactory auras is estimated to vary from less than 1% to more than 30%. The emergence of these auras, that are usually unpleasant, lasts a few minutes or less [18, 20].

Psychological disorders

Patients with depression, schizophrenia, and hallucinations may complain about loss of smell as part of their mental disorders. However, impairment in the olfactory system is only observed in patients with schizophrenia. Although the altered sense of taste has been observed in depressed patients, their sense of smell is usually normal. Thus, complaints of these patients about olfactory disorders are probably rooted in the central nervous system and the chemicals that are assumed to create symptoms of depression by affecting the nervous connections between the limbic system and hypothalamus [16, 21].

Medications

Although it seems that drugs can affect the taste system more than the olfactory system, there are many drugs that can cause impairment of olfactory function. After stopping the use of such drugs, the olfactory power usually recovers, although the changes are sometimes permanent [18].

Surgery

After making changes in the pathway of respiratory airflow or in the area surrounding the olfactory nerves, changes in olfactory power can be expected. Although the septal deformity that could affect the sense of smell have been reported and septum surgery has improved olfactory power in these cases, deformities that can be severe enough to block a nasal passage are extremely rare. Loss of smell has also been reported after Rhinoplasty [22]. These impairments can be due to nerve damage during surgery or narrowing of the secondary nasal airways in response to anatomic changes or scar tissue. Fortunately, advances in endoscopic sinus surgeries have brought the possibility of a more precise surgery and thus less damages to the olfactory system. Many surgeries on the skull and its base in the area of olfactory bulb have been followed by complete and permanent loss of smell. However, modern methods have been developed to protect the olfactory area during such surgeries [23].

Idiopathic

In some patients, even after a very quick review including many trials, no clear and concrete reason can be obtained for justifying the olfactory dysfunction. This group of patients usually includes young or middle-aged adults who appear to be healthy from other aspects. Some biopsies taken from these patients show the existence of olfactory epithelium. However, the observed changes were not specific enough to make for a certain diagnosis [21, 22].

Diagnostic surveys

The most important measure that a physician can do for a patient with olfactory dysfunction is to reach a correct diagnosis and be committed to the patient's condition. The fact that how severe patients estimate their olfactory impairment and how long it has lasted to emerge is an important point that should be considered when recording the history of patients. In addition, other events such as trauma or URI that have occurred around the beginning of the impairment should be determined [23].

A general checkup of all systems and organs and also the patient's general medical health status can be helpful in leaving aside the adverse side effects of drugs or the problems that may pose following some diseases such as hypothyroidism. With an accurate assessment of a patient who has been so far assumed to be afflicted with olfactory impairment caused by psychological problems, sometimes some pieces of evidence can be found for example from a metabolic disease that is seemingly irrelevant to the patient's problem. In

physical examinations, condition of nose, mouth, and the nervous system should be specially taken into account [24]. Nasal endoscopy is very useful especially in the examination of the nasal passages that are located right in the area under the olfactory cleft. Tests for the evaluation of patients with chemosensory complaints include measuring the taste and smell power. In clinics, tests for olfactory perception have been usually more useful than threshold ones [25].

Smell test from one nostril or both of them have shown to be useful in revealing the nose and skull tumors and also neurological impairments that were not already suspected. If the patient's medical condition requires a blood test (for example, level of thyroid), it should be done [26]. However, routine tests have not been useful. Rhinomanometry can be useful in assessing the overall state of the nose. If the upper nasal passages are open, any partial airflow in the nose may provide the sense of smell [24].

If an obstruction, an anatomic deformity or any history of nasal or sinus disease is suspected or if the diagnosis is not quite clear, a coronal CT (computerized tomography) scan should be prepared from the nose and sinus cavities. MRI (Magnetic resonance imaging) is not successful in depicting the delicate bony details of upper nasal cleft but it can be helpful in displaying soft tissues which sometimes include the olfactory groove. Simple radiographies of this area are too obscure to be useful in studies and examinations. Another advantage of the coronal CT scan is that it can be used in leaving aside the tumors or deformities of the skull [27].

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