บทฟื้นฟูวิชาการ ■ Review Article

ผลของการสูงวัยต่อจมูกและโพรงอากาศข้างจมูก: สิ่งที่ทราบในปัจจุบันและการทบทวนวรรณกรรม

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The Effect of Aging on the Nose and Paranasal Sinuses: What We Now Know and a Review of the Literature

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ในช่วงทศวรรษที่ผ่านมา ปรากฏการณ์ของสังคมผู้สูงอายุได้กลายเป็นประเด็นหลักทั่วโลก รวมทั้งในประเทศไทย จุดประสงค์ของการทบทวนวรรณกรรมนี้เพื่อให้แพทย์ได้ทราบถึงความรู้ที่ทันสมัยในปัจจุบันเกี่ยวกับผลของการสูงวัยต่อจมูกและโพรงอากาศข้างจมูกในหลายๆ ด้าน ซึ่งการเปลี่ยนแปลงนี้สามารถพบได้ทั้งในผู้สูงอายุปกติและผู้สูงอายุที่เป็นโรคทางจมูก ความเสื่อมทางสรีรวิทยาของเยื่อบุจมูกในผู้สูงอายุก่อให้เกิดอาการคัดแน่นจมูก จมูกแห้ง มีสะเก็ดในจมูก น้ำมูกไหลลงคอ และกระแอมบ่อยๆ การเสื่อมถอยของระบบภูมิคุ้มกันทำให้ผู้สูงอายุมีแนวโน้มที่จะมีการติดเชื้อในจมูกได้ง่าย ซึ่งจะส่งเสริมทำให้มีการอักเสบในจมูกมากขึ้น นอกจากนี้ แพทย์ควรจะมีความตระหนักและระมัดระวังเกี่ยวกับการใช้ยาร่วมหลายขนาน (polypharmacy) ในผู้สูงอายุ เพื่อที่จะลดความเสี่ยงเกี่ยวกับอันตรกิริยาของยา (drug interaction) และผลข้างเคียง (side effect) ปัญหาการดมกลิ่นสามารถเกิดได้ทั้งในผู้สูงอายุปกติหรืออาจเป็นอาการนำของโรคทางระบบประสาทหลายโรค ความเข้าใจที่มากขึ้นเกี่ยวกับการเปลี่ยนแปลงของโพรงจมูกและไซนัสทั้งหมดนี้ จะนำไปสู่การวินิจฉัยและการดูแลรักษารวมถึงคุณภาพชีวิตของผู้ป่วยที่ดีขึ้น

คำสำคัญ: การสูงวัย; สูงอายุ; จมูก; การดมกลิ่น;จมูกผู้สูงวัย; จมูกอักเสบ; ไซนัสอักเสบ

Over the past decade, the phenomenon of the aging society has become a major topic around the world, and many countries (including Thailand) are now classified as aged societies. Accordingly, the aim of this review was to provide physicians with a multi-perspective update regarding what is now known about the effect of aging on the nose and paranasal sinuses. Multiple changes in the nose and paranasal system can be observed in older aged healthy populations and rhinologic patients. Physiologic deterioration of nasal mucosa that occurs when people get older contributes to nasal obstruction, dryness, crusting, postnasal drip, and frequent throat clearing. Age-related immunosenescence renders people more vulnerable to infection, which may intensify nasal inflammation. Moreover, polypharmacy among older people requires awareness and caution on the part of the physician to decrease the risk of drug interaction and side effect. Olfactory disturbance can occur as a result of physiologic change or premotor manifestation of neurodegenerative diseases. Enhanced understanding of sinonasal change in older adults will improve diagnosis, patient care, and quality of life.

Keywords: Aging; Elderly; Nose; Older; Olfaction; Presbynasalis; Rhinitis; Sinusitis

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Introduction

Over the past decade, the phenomenon of the aging society has become a major topic around the world. Many countries around the world (including Thailand) are now classified as aged societies. In 2016, the Foundation of Thai Gerontology Research and Development Institute (TGRI) reported that 3 member nations within the Association of South East Asia Nations (ASEAN) regional intergovernmental organization (Singapore, Vietnam, and Thailand) are already classified as aged societies. Of the approximately 65.9 million registered Thai citizens in 2016, eleven million (16.5%) were aged 60 years or older, and this trend shows no signs of leveling off or decreasing. Accordingly, it has been predicted that the proportion of people in Thailand aged 60 years or older will reach 20% (complete aged society) in 2021, and 30% (super aged society) in 2036.[1]

The nose and paranasal sinuses comprise one of the body's systems that change with age. However, these changes are often either overlooked or misunderstood by a majority of physicians, even otorhinolaryngologists. Although many published articles focus on defined singular aspects of this important system, such as olfaction, only a few articles undertake a comprehensive review of the nose and paranasal sinuses. Edelstein identified several age-related changes in the normal adult nose in 1996.[2] Since that time, a plethora of new knowledge has been discovered and reported. In 2016, DelGaudio and Panella established the term presbynasalis to describe multiple changes in the aging sinonasal tract.[3]

The aim of this review was to provide physicians with a multi-perspective update regarding what is now known about the effect of aging on the nose and paranasal sinuses. Some changes to the nose and paranasal sinuses are due to normal physiological changes, while others are caused by pathologic conditions. For an example of the latter, many age-related neurodegenerative diseases often adversely affect olfaction. The information provided herein will assist clinicians to differentiate, diagnose, and manage nose and sinus-related conditions in their geriatric patient population.

Nasal epithelium and histology

Several older studies using computerized microscopic photometric technique found no change in nasal ciliary beat frequency with advancing age, even in subjects older than 70 or 80 years.[2, 4, 5] In contrast, multiple more recent studies reported significantly decreased nasal ciliary beat frequency, and increased percentage of cilia ultrastructure defect with increasing age.[3, 6, 7] Furthermore, many studies found a decrease in nasal mucociliary transport in aging population; however, it remained unchanged in some studies.[6, 8-10] Inconsistent findings among studies may be explained by ciliary beat frequency that did not correlate with mucociliary clearance. Multiple potential factors influence mucociliary transport, including cililary ultrastructure, nasal airflow, temperature, toxin exposure, inflammatory mediators, and the amount, viscosity, and composition of mucous.

Sahin and Corey also found change in nasal mucosa, with a reduced number of goblet cells and elastic fibers.[11] Most older adults tend to have some degree of dehydration. Consequently, nasal secretions become sticky. Excessively thick mucous combined with decreased mucociliary clearance may contribute to common complaints among older adults that include postnasal drip and frequent throat clearing.

Riedler, et al. studied nasal septal cartilage from 33 fresh cadavers (age range: 55-93 years) and found that chondrocytes decrease in size and number with advancing age. Glycosaminoglycan within the cartilage matrix was found to decline 2.4% per year, which is in contrast to collagen content that remain unchanged.[12] These changes contribute to changes in the biomechanical properties of cartilage. Specifically, cartilage becomes weaker, it has less integrity, and it has less capacity to repair itself when intentionally (surgery) or unintentionally traumatized. Lee, et al.[13] harvested nasal septal cartilage from 50 patients undergoing rhinologic surgery and found the same results as Riedler, et al.[12]

Nasal airflow

Lindemann, et al. found a significantly decreased ability to control temperature and to humidify inhaled air among older adults compared to a younger study group.[14] Atrophy of nasal mucosa caused by epithelium/basement membrane thinning and reduction in submucosal blood supply may contribute to this functional change, and these factors may effectuate an increase in minimal cross-sectional area and nasal cavity volume.[14-17] Enlarged nasal cavity volume reduces contact time and contact surface between mucosa and the air stream. When combined,

these changes cause recurrent crusting, dryness, and feelings of irritation in the older adult nose. In addition, nasal mucosa in older population tends to respond decreasingly to trigeminal and chemosensory irritation.[18] This is another possible explanation why older people develop feelings of nasal obstruction.

Morphology

Tip ptosis, which is characterized by drooping of the nose due to loss of nasal tip support, can be caused by weakening of septal cartilage and tip muscle, separation of upper and lower lateral cartilages, and maxillary alveolar hypoplasia.[2, 13, 15] Columella retraction and nasal valve collapse are also seen, both of which exacerbate the sensation of nasal obstruction.

Immune system

Immunosenescence, which is defined as the decline in both innate and adaptive immune function in aging, comprises depletion and exhaustion of naive T cells, increased antigen-experienced cells (CD8+ suppressor/cytotoxic T cells), and decreased CD4+ T cells and CD19+ B cells.[7, 19] This combination of changes leads to a global reduction in immunological space due to the expansion of these memory cells. IgG isotype class switching also declines with age, and this results in a decrease in antigen-specific antibodies.[20] The neutrophils of older adults also have less phagocytic function, and they are more susceptible to apoptosis.[21] This aforementioned group of factors inclines older patients to increased vulnerability for infection, autoimmune disease, and malignancy.[22]

'Inflamm-aging', which is a term that was proposed by Franceschi, et al., is an aging-related change in innate immunity, and is thought to be one component of immunosenescence.[23] It is provoked by a continuous antigenic load (bacteria, virus, and/or parasite), physical (climate or radiation) stress, and/or chemical (free oxygen radicals) stress for an extended period of time. Chronic activation of macrophages with age or 'macroph-aging' results in a progressive increase in proinflammatory status over time.[23] Many studies found a direct relationship between age and inflammatory cytokines.[24-27] This subclinical low-grade chronic inflammatory process in aging can lead to inflammatory age-related diseases (atherosclerosis, neurodegenerative disease, osteoporosis, and arthritis) in individuals that have frail genetic components.[28, 29] However, impact on nasal inflammation remains inconclusive.

Rhinitis and chronic rhinosinusitis (CRS)

Rhinitis can be categorized as either allergic rhinitis or non-allergic rhinitis. The prevalence of allergic rhinitis in older adults, which is approximately 12%, decreases with advancing age due to a decline in allergic sensitization.[30, 31] As a result of immunosenescence, older adult patients tend to have less allergic symptoms, and decreased total/specific IgE and skin reactivity.[32-34] Blunting response of eosinophil degranulation to IL-5 stimulation is also found in older people.[19] The management of allergic rhinitis in older patients, (e.g., allergen avoidance, environmental change, and medical treatment) is similar to that of younger patients. Multiple comorbidities and polypharmacy are common among older adults, so medications should be carefully prescribed to avoid adverse effect on underlying disease, hepatic/renal impairment, and/or drug interaction. Intranasal corticosteroids are safe and effective for treating allergic rhinitis in older patients. There is no evidence that intranasal corticosteroid increases the risk of cataract.[35] However, concomitant steroid use via other routes in patients of any age, such as inhaled or ophthalmic steroid, may increase the risk of increased intraocular pressure, which can lead to glaucoma in some patients. Second-generation antihistamines can be safely used in older adult patients due to the low rate of blood-brain barrier crossing. The sedative and anticholinergic effects of first-generation antihistamines (e.g., constipation, urinary retention, dry mouth, visual disturbance, postural hypotension, and angle-closure glaucoma) limit their use in this advanced age group. Physicians should be cautious when prescribing oral decongestants for relief of nasal obstruction in older adults, as they may aggravate urinary retention, hypertension, glaucoma, and heart disease. Allergen-specific immunotherapy can be prescribed safely in older patients. However, increasing risk of severe systemic reaction was reported in patients taking angiotensin-converting enzyme inhibitors and/or beta-blockers. Hence, discontinuation of these medications is recommended before administration of immunotherapy.[36, 37]

In contrast to allergic rhinitis, non-allergic rhinitis tends to occur with increasing regularity in older

adults. Imbalance of the autonomic nervous system in the nasal cavity may play a role. Many aggravating stimulants, such as climate change, chemical/irritating agents, tobacco smoke, strong odors, and emotions, can trigger the onset of symptoms. Polypharmacy among older adults tends to increase the risk of drug-induced rhinitis. Many medications that are commonly used by older people were reported to cause non-allergic rhinitis (Box 1).[16] Rhinitis medicamentosa, which is caused by prolonged use of topical decongestants, is common in patients that self-treat themselves with over-the-counter medications. Treatment of non-allergic rhinitis is similar to that of its allergic counterpart; however, second-generation antihistamines have little to no benefit in non-allergic rhinitis, because there is no histamine release. Parasympathetic overactivity is thought to be one of the mechanisms of non-allergic rhinitis. Hence, first-generation antihistamines that have anticholinergic properties and topical anticholinergic drugs (e.g., intranasal ipratropium bromide) have all been proven efficacious for treating this disorder. Rhinitis medicamentosa can be treated by discontinuation of the topical decongestant.

Reh, et al. reported no difference in the presentation of CRS (allergy, polyp, asthma, and aspirin sensitivity) between older and younger patients.[38] In contrast, Cho, et al. found that older patients with CRS had a greater prevalence of nasal polyps than younger groups, and that age-related blunting of the IL-6-S100A8/9 signaling pathway that causes impaired epithelial barrier may have contributed to this finding.[39, 40] Change in microbiome was observed between healthy older and younger people, and imbalance in the sinonasal microbiome may contribute to the development and persistence of this disease.[41] There is currently no difference in the management guideline for CRS compared between younger and older patients. Medication is still the mainstay of treatment, and surgery is mandatory in selected cases where maximal medical treatment failed to maintain symptom control. Increasing age showed no impact on the outcome of endoscopic sinus surgery[38, 42, 43]; however, it may increase the risk of surgery-related complications, because older patients tend to have more previous surgical procedures.[43]

Olfaction

Many studies have confirmed that the sense of smell declines with age.[44-48] In United States population, half of people aged 65 to 80 years, and three-quarters of those aged 80 years or more have smell disturbance.[49] Multiple assessments, including psychophysical (threshold, identification, and discrimination), electrophysical, and phychophysiological testing, have confirmed age-related olfactory deficit.[50] One of the most important factors relating to smell deficit is that older individuals may not be able to detect leaking gas, fire, toxic substances, and spoiled food. Some previous studies reported association between olfactory impairment in older age and mortality.[51, 52] Change in external nose morphology, enlarged nasal volume resulting in decreased amount of airstream reaching the olfactory area, and decrease in both size and number of patent foramen in the cribiform plate were found in older adults.[53] The olfactory receptor cell axon can be severed, and can progress to degeneration of nerve fila to olfactory bulb. In contrast to knowledge about changes in non-olfactory elements, molecular and cellular mechanisms were largely unknown in the past. Researchers are now investigating and reporting the mechanisms that underlie olfaction in non-pathologic normal aging.[50, 54] Olfactory sensory neurons in the nasal lining were found to change with age. The observed decline in the number of these neurons results from impaired neurogenesis relative to the replacement of dead neurons. Reduction in defense metabolizing enzymes (e.g., heat-shock protein, glutathione, and cytochrome P-450) and prolonged exposure to toxic substances, air pollution, inflammation, and recurrent infection (viral or bacterial) may influence this change.[50] In addition, a decrease in the selectivity of and sensitivity to odors was found in aging olfactory receptor neurons.[54] There are also a combination of changes that occur in the olfactory bulb, in neurotransmitters, and in the olfactory processing system in the central brain that contribute to age-related olfactory perception. A collection of the causes of age-related olfactory change is given in Box 2. The reader is herewith referred elsewhere for a more detailed review.[50]

In addition to non-pathologic aging-related changes, olfactory disturbances can occur as part of some neurodegenerative diseases (e.g., Parkinson's disease, Alzheimer's disease, Huntington's disease,

and multiple sclerosis), and may present as early symptoms that precede motor manifestation by several years.[55-58] Unfortunately, smell-related problems that develop in older adults are often overlooked by medical providers, and many older people also underestimate or altogether fail to recognize their olfactory deficit. Enhanced awareness of this age-related medical phenomenon will help clinicians better recognize, counsel, and treat their older patients that develop this disorder.

Conclusion

The proportion of older adults is increasing in many countries around the world. Multiple changes in the nose and paranasal system can be observed in older aged healthy populations and rhinologic patients. Physiologic deterioration of nasal mucosa that occurs when people get older contributes to nasal obstruction, dryness, crusting, postnasal drip, and frequent throat clearing. Age-related immunosenescence renders people more vulnerable to infection, which may intensify nasal inflammation. Moreover, polypharmacy among older people requires awareness and caution on the part of the physician to decrease the risk of drug interaction and side effect. Olfactory disturbance can occur as a result of physiologic change or premotor manifestation of neurodegenerative diseases. Enhanced understanding of sinonasal change in older adults will improve diagnosis, patient care, and quality of life.

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Conflict of interest declaration

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Box 1. Medications that can cause rhinitis

- Acetylsalicylic acid/nonsteroidal anti-inflammatory drugs (ASA/NSAIDs)
- Alpha/beta-blockers
- Angiotensin-converting enzyme (ACE) inhibitors
- Calcium channel blockers
- Diuretics
- Oral contraceptives
- Phosphodiesterase 5 inhibitors
- Psychotropics

Box 2. Causes of olfactory dysfunction in aging

- Alteration of nasal airflow
- Decrease in size and number of cribriform foramina
- Impaired regeneration of olfactory sensory neurons
- Change in central brain processing

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