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Empty nose syndrome

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Abstract

Empty nose syndrome (ENS) is an iatrogenic condition that results from traumatic injury, often overresection, of the turbinates during sinonasal surgery. The underlying etiology is not entirely understood but is thought to have multifactorial contributions including alterations in the native nasal airway anatomy, abnormal mucosal and neural healing, and decreased trigeminal sensitivity, among other possibilities and contributors. Patients typically present with an intense fixation on their sensations of nasal obstruction and congestion despite an anatomically patent airway on examination. Because many patients with ENS have been shown to have significant psychiatric comorbidities, multidisciplinary specialist care including psychiatry and pain services is essential. Diagnosis is often difficult due to the variability of presentation and severity of symptoms, but standard assessments exist including the empty nose syndrome 6-item questionnaire (ENS6Q) and cotton test. Patients can be initially managed with conservative measures through humidification, moisturization, and psychiatric testing/referral. Procedural approaches to improve the nasal airway include submucosal implantation of temporary, semi-permanent, and permanent materials. A realistic and empathetic approach to patient communication is necessary in order to help manage patients with ENS, and all plastic surgeons performing septorhinoplasty should be aware of the risk and treatment options of the disease.

Keywords: Empty nose syndrome, rhinoplasty, inferior turbinate, nasal obstruction

INTRODUCTION

Empty nose syndrome (ENS) is an iatrogenic condition associated with decreased quality of life with significant physical, psychosocial, and emotional burdens. Thought to be a result of excessive turbinate reduction or resection during nasal or sinus surgery, ENS is a clinical entity with a spectrum of symptoms including nasal obstruction, dryness, burning, and feelings of suffocation. The exact incidence in turbinate reduction patients is currently unknown as there is a lack of primary literature reporting such data. Persistent empty nose syndrome symptoms can be distressing, requiring a nuanced and empathetic approach to diagnosis and management. There are a variety of different treatment options including both non-surgical and surgical methods involving reconstruction of the resected turbinate. A comprehensive review of ENS and suggested approach to management in post-rhinoplasty patients are discussed below.

PATHOPHYSIOLOGY

Located along the lateral walls of the nasal cavity are three pairs of turbinates which are the workhorse of nasal function, playing a key role in warming, humidifying, and filtering breathed air. As the most anterior turbinate pair, the inferior turbinates help regulate airflow through swelling and contracting in order to allow for proper flow rate and moisture levels within the nasal cavity. Pseudostratified ciliated columnar epithelium with goblet cells lines the sinonasal cavity and allows for rapid expansion and contracture through autonomic stimulation[1]. During the nasal cycle, which can last anywhere from thirty minutes to six hours, these structures alternate with each other so that only one turbinate is enlarged at a time[2].

Nasal microbiota plays a complex and essential role in regulating the mucosal immune system, which can play an important role in the histological expression in empty nose syndrome. Nasal dysfunction and reactive nasal inflammation may trigger a complex cascade of dysregulatory events, such as in diseases like chronic rhinosinusitis. Classically, disruption of the epithelial boundary allows for mucosal permeability and bacterial penetrance, promoting Th-2 inflammation and the release of inflammatory cytokines[3]. As a result of disruption to the mucosal barrier after turbinate surgery, patients may experience dysregulation of the mucosal immunity that can influence the overall histologic picture. One histopathology study found increased squamous metaplasia, submucosal fibrosis, and lower submucosal glands compared to controls[4]. The interactions of the nasal microenvironment in empty nose syndrome remain multifold and play an important role in the pathogenesis of this complex disease.

Alteration in the nasal physiological pathway can cause inhaled air to flow directly through the nasal cavity to the nasopharynx, losing the turbulent airflow that humans usually perceive with their nasal breathing. The most common reason for turbinate impairment is iatrogenic injury. Surgical resection of the inferior turbinates during sinonasal procedures can lead to excessive tissue reduction in the nasal cavity, thus impeding the natural physiologic processes of moisturization and humidification. Additionally, impairment of mucosal function secondary to surgical and non-surgical insult may occur. Abnormal neural healing after surgery can result in improper sensory connections, thus leading to increased nasal sensitivity and pain[5]. Several studies[6,7] have demonstrated impaired menthol lateralization detection thresholds in patients with ENS compared to healthy controls - menthol, a trigeminal agonist, is presented in serially diluted amounts to patients, who must identify which bottle contains the reagent. Patients with ENS had lower thresholds, suggesting decreased trigeminal sensitivity to volatile compounds, which may contribute to a lack of perception of airflow with inhalation. A recent meta-analysis by Kanjanawasee *et al*. corroborated these results, finding that menthol detection test was statistically impaired in ENS[8].

A combination of these physiological changes can cause patients to experience the significant discomfort that is characteristic of ENS. It has been thought that ENS symptoms were more common in more arid regions of the world due to lack of environmental humidity, but it has more recently been believed that symptom severity was not inherently related to climate or geographic factors[9]. Exacerbation of symptoms may, at times, be related to dry air, air conditioning, changes to weather, and transitioning between indoors and outdoors[9].

Aerodynamic studies have helped characterize nasal airflow patterns to better understand the profound implications of turbinate loss. In sinonasal models with bilateral radical inferior and middle turbinectomies, parameters including velocity, pressure, streamlines, air flux, and wall shear stress were measured during a laminar flow study[10]. Around the inferior turbinates, streamlines were less organized with decreased airflow rates near the inferior meatus, which may clinically correlate with the increased feelings of crusting and dryness that patients feel. Around the middle turbinates, velocities were increased around the sphenopalatine ganglion during inspiration and expiration, which is speculated to cause the headaches associated with respiration due to increased nerve stimulation. Computational fluid dynamics studies also demonstrated lower nasal resistance with lower air-mucosal stimulations, which were associated with worse symptoms[6,7]. While additional aerodynamic studies including an increased number of models are required for further investigation, these changes to airflow and turbulence can help explain the pathophysiology of the underlying disease.

SYMPTOMS

There are four different subtypes of ENS depending on the turbinate missing: inferior turbinate (ENS-IT), middle turbinate (ENS-MT), both inferior and middle turbinate (ENS-both), and after turbinate “sparing” procedure (ENS-type)[11]. ENS-IT is the most common subtype; patients typically present with complaints of paradoxical nasal obstruction despite no anatomical hindrances to airflow on examination and endoscopy. Other frequently reported symptoms include nasal congestion, nasal/pharyngeal dryness, crusting, headaches, and feelings of suffocation. Dyspnea, hypersensitivity to cold air, difficulty falling asleep, and general fatigue may also occur[12]. As nasal breathing is most physiologically preferred over mouth breathing, a drastic change in breathing pattern can cause significant distress[13].

Affected patients can also report a profound impact on quality of life and exacerbation of underlying mental health conditions. Psychological symptoms including anxiety, depression, fatigue, or lack of productivity are commonly associated with ENS. One systematic review with six studies found that anxiety and depression were elevated in ENS patients (65%-73% and 51%-71%, respectively)[8]. One cross-sectional study found a high prevalence of anxiety and depression warranting treatment, with decreased productivity at work and other activities[14]. Symptom severity correlated with depression and anxiety severity, overall pain/discomfort, and impairment in activities of daily living. In another study, suicidal ideation was identified in 23 of 62 (37%) ENS patients prior to nasal reconstruction surgery and in 4 patients after surgery[15]. While many patients with ENS can experience significant psychological distress, most studies to date have not analyzed preoperative psychological metrics[8]. It is also important to consider early psychiatric referral if concerned for an underlying psychiatric condition, as demonstrated in a case report of a patient ultimately diagnosed with somatic symptom disorder after having undergone numerous unsuccessful surgeries for ENS[16]. Close monitoring of the psychological burden of ENS is critical to ensure that patients receive multidisciplinary, specialist attention for comprehensive care.

ROLE OF TURBINATE SURGERY IN RHINOPLASTY

The aim of septorhinoplasty is to alter nasal anatomy for cosmesis and to relieve nasal obstruction for functional improvement. As inferior turbinate hypertrophy can be a frequent source of obstruction, many plastic surgeons concurrently address the turbinates in the operating room[17]. Hypertrophy is a heterogeneous disease process, with a multitude of surgical approaches to reduce tissue bulk[18]. Different types of turbinate reduction techniques include both mucosal and submucosal resection involving the use of radiofrequency, laser, turbinate shaver, and microdebrider. One systematic review assessing fifty-eight articles reporting surgical treatments and outcomes of inferior turbinate hypertrophy demonstrated that procedures such as partial and total turbinectomy and submucosal resection were associated with higher rates of crusting and epistaxis[19]. However, gentler techniques like cryotherapy and submucous diathermy failed to definitively address the underlying hypertrophy. Instead, submucosal resection and radiofrequency ablation were recommended as modalities that could provide lasting results while preserving turbinate function. Resection of the turbinate bone without destruction of the submucosa or mucosa has also been reported to have excellent postoperative functional results with improvement in nasal obstruction[20].

Though inferior turbinate resection is frequently performed as an adjunct to septorhinoplasty, there are mixed reports of the procedure’s long-term efficacy and quality-of-life benefits. A randomized controlled trial by Lavinsky-Wolff *et al.*[21] compared fifty patients undergoing septorhinoplasty with and without inferior turbinate reduction through submucosal diathermy. Looking at septorhinoplasty outcomes assessments, there was no significant difference between groups in Nasal Obstruction Symptom Evaluation (NOSE) scores, quality of life metrics, or acoustic rhinometry recordings, although patients with treatment used less topical corticosteroids. Similar findings were reported in a study of fifty patients undergoing septorhinoplasty with or without partial inferior turbinectomy (defined as the excision of one-third of inferior turbinates)[22]. There were no differences in complication rates between the two groups, but surgical time was considerably higher in the patients undergoing adjunct surgery (212 min *vs.* 159 min). One of the largest studies, including a total of 567 patients (391 undergoing septorhinoplasty alone, 176 with septorhinoplasty and turbinate resection), again corroborated an improvement of septorhinoplasty on disease-specific and general health quality of life outcomes[23]. Techniques included medial flap inferior turbinoplasty, microdebrider, electrocautery, or coblation submucosal resection. When controlling for patient characteristics and sinonasal comorbidities, patients with the combined procedure demonstrated a significant 6-point improvement in NOSE score compared to the septorhinoplasty group, though this was not clinically significant as the minimum clinically important difference for the NOSE score is 30 points. There is mixed evidence regarding the most efficacious approach of inferior turbinate reduction. One randomized double-blinded study found that patients undergoing medial flap turbinoplasty had less decongestant use and required less revision surgery compared to the electrocautery and submucosal approaches[24].

As some literature has reported a significant improvement in disease-specific outcomes irrespective of inferior turbinate reduction, it is important to evaluate the necessity of the procedure which can be associated with increased overhead operating costs, lengthened anesthesia time, and potential complications. Most importantly for this publication, turbinectomy may also contribute to ENS, which may not develop for years after the initial surgical insult. To date, there are currently no studies with long-term follow-up to determine the exact incidence of ENS after any nasal surgery.

DIAGNOSIS

Diagnosis of ENS is challenging due to the lack of objective data; clinicians must typically rely on patient-reported symptoms, which are highly variable in severity and presentation. The sino-nasal outcome test (SNOT-22) was initially created as a validated, self-administered questionnaire to assess chronic rhinosinusitis patients[25]. The SNOT-25 is an updated version that includes three additional questions assessing the impact of symptoms on job and household tasks[26]. The empty nose syndrome 6-item questionnaire (ENS6Q) was developed as an adjunct to SNOT-22 for patients with suspected ENS, including six disease-specific quality of life metrics assessing degree of "dryness", "lack of air sensation going through your nasal cavities", "suffocation", "nose feels too open", "nasal crusting", and "nasal burning”

[Table 1]. The questionnaire is then scored from 0 (no issues) to 30 (extremely severe). ENS6Q was found to reliably discriminate between ENS vs. control patients and ENS *vs.* chronic rhinosinusitis without polyposis patients[27]. The questionnaire can also distinguish ENS from patients with primary nasal obstruction (i.e., septal deviation, inferior turbinate hypertrophy)[28].

A thorough history and physical examination is necessary when evaluating patients with suspicion of ENS including comprehensive ear, nose, and throat examination with nasal endoscopy. Another physical exam maneuver that is commonly used to assess patients is the cotton test, which involves the placement of dry cottonoids along the area of missing inferior turbinate in the non-anesthetized nose. The test is positive if the patient reports an improvement in symptoms with cotton in place. In a case-control study comparing 15 patients with ENS and 18 controls, nearly all baseline differences in ENS6Q scores equalized after the cottonoids were placed in the ENS patients, demonstrating that cotton testing is a validated office test[29,30]. The minimal clinically important difference for ENS6Q was found to be 7, suggesting that the ENS6Q score needs to change by at least 7 to represent a clinically meaningful change experienced by the patient. The monofilament test is another assessment that utilizes monofilaments of variable diameters applied to the patient turbinate; the sensitivity threshold is recorded as the minimum monofilament size that patients can detect sensation[31].

The use of computed tomography (CT) in ENS patients has not been well studied in the literature. One study comparing patients with ENS with patients who had undergone inferior turbinate resection but without ENS found that ENS patients had increased central (> 2.64 mm) and posterior (> 1.32 mm) septal mucosal thickness compared to the septum in inferior turbinate reduction patients without ENS[32]. As these patients often undergo CT sinus imaging as part of their workup, measuring mucosal thickening may serve as an adjunct to the other diagnostic modalities discussed above in the appropriate patient.

There are a variety of patient-reported outcome measures and testing available to help diagnose patients with suspected ENS. The ENS6Q and cotton test are now the standardized first-line modalities, with CT sinus, computational fluid dynamics, and intranasal trigeminal nerve testing as useful but lacking sufficient evidence for routine use[30]. Due to high psychiatric comorbidity, patients with elevated suspicion of ENS should also undergo anxiety and depression screening.

MANAGEMENT

Non-surgical approaches

Conservative management is based on symptomatic relief by optimizing topical moisturization and treating any other comorbid psychiatric illnesses by obtaining a behavioral assessment. Strategies such as saline sprays, topical emollients, nasal lavage, and lubricant drops can be utilized to increase local humidification of the nasal cavity[33]. Regular use of a humidifier in the environment may also help alleviate symptoms[12]. While there are no original research studies assessing the efficacy of these conservative measures, they are low-risk and should be aimed at alleviating specific patient symptoms. As psychiatric comorbidities are common among patients with ENS, mental health specialists can be valuable to help diagnose and treat any underlying conditions. As a provider, an empathetic and honest discussion on the underlying cause and possible treatment options for ENS is crucial.

Surgical techniques

Should patients fail conservative treatments, a plethora of surgical approaches have been reported in the literature. In one systematic review, the most common technique involved a transnasal approach with submucosal implants in multiple strategic areas to ultimately narrow the nasal valve region or reconstruct

Table 1. Empty nose syndrome 6-item questionnaire (ENS6Q)

Symptom	No problem /NA	Very mild	Mild	Moderate	Severe	Extremely severe
Dryness	0	1	2	3	4	5
Sense of diminished nasal airflow	0	1	2	3	4	5
Suffocation	0	1	2	3	4	5
Nose feels too open	0	1	2	3	4	5
Nasal crusting	0	1	2	3	4	5
Nasal burning	0	1	2	3	4	5

NA: not applicable; This table is cited with permission from Velasquez *et al*.[27] published in *Int Forum Allergy Rhinol*.

the missing turbinate. Overall, among the 128 patients included, there was a mean improvement in SNOT-20 and SNOT-25 scores at the three-month postoperative time points, although not all patients derived benefit[34]. Among patients who felt that the intervention was beneficial, the biggest improvement was in the SNOT subdomains of ENS symptoms and psychological issues. No material was favored to have superior results compared to others, and implants included temporary fillers to semi-permanent and permanent options.

There are several case studies detailing numerous temporary filler options for submucosal injections including the use of carboxymethylcellulose/glycerin gel (Prolaryn, Merz Therapeutics)[35], hyaluronic acid[36], and calcium hydroxyapatite[37]. One case series assessing fourteen patients who underwent Prolaryn injection to the inferior meatus found a significant decrease in ENS6Q, SNOT-22, general anxiety disorder 7 (GAD-7) and patient health questionnaire-9 (PHQ-9) scores at 1 month[35]. Benefits of using fillers include the transient, resorbable nature of the material, safety/efficacy, ability to perform in the office, no operative room overhead costs, decreased healing times, and the ability for reversal in the case of hyaluronic acid. Submucosal fillers are also an appealing option for patients who do not wish to undergo a permanent surgical procedure or for those who may want to reduce symptoms until surgery can be scheduled in the future. Demonstration of improvement with fillers can furthermore confirm the utility of surgical augmentation. Downsides of fillers include resorption requiring revision procedures, limitation of adding bulk compared to surgical implants, and spillage from thick injections.

Semi-permanent or permanent implants can be used based on patient and provider preference. One of the earliest techniques utilized was acellular dermis, a material that is incorporated into the patient's tissue 3-6 months post-implantation[38]. Over time, the risk of infection from foreign body decreases as the dermis becomes infiltrated with blood vessels and collagen. Porous polyethylene implant (Medpor, Porex Surgical Inc.) is a biocompatible implant frequently used in aesthetic, reconstructive, and augmentation surgeries. Implantation of Medpor to reconstruct the inferior turbinate was found to improve SNOT-25 scores at the 3-, 6-, and 12-month time points[39]. A similar study found significant improvements in acoustic rhinometry assessments, including nasal resistance, nasal volume, and minimum cross-sectional area[40]. β-tricalcium phosphate, a synthetic bone graft substitute that is replaced by vital bone in 6 to 12 months, has also shown improvement in quality-of-life outcomes[41]. Benefits of using a semi-permanent or permanent implant include long-term and lasting benefits and increased tissue bulk compared to fillers.

With the many different implants described in literature, there is no clear consensus on the best material/strategic approach for implantation. One meta-analysis including 6 studies found that autografts/allografts were more effective than foreign body grafts when comparing preoperative and postoperative SNOT scores. This study, however, only included one randomized controlled trial directly comparing autografts/allografts (AlloDerm Regenerative Tissue Matrix, LifeCell Corporation, AbbVie) with foreign body grafts (silastic implant), which found no difference in SNOT-25 scores, rates of injection, rejection, or allergic reaction between both groups[42]. Heterogeneity of outcomes may even exist within distinct material types, such as cartilage. Among patients undergoing autologous cartilage implant, costal cartilage was superior to conchal cartilage in terms of SNOT-25 scores and depression-related symptom outcomes[43]. Another case series using cadaveric rib cartilage for inferior meatus augmentation showed disease-specific improvement via ENS6Q and SNOT-22 scores[44]. When assessing techniques, though most reports in literature utilize a submucosal implant, lateral nasal wall implantation may be superior to inferior nasal wall implantation[45].

Addressing psychiatric comorbidities

No matter which material and technique is selected for surgical augmentation, it is important to emphasize a holistic and comprehensive approach to management. Psychiatry or psychology consult in patients with comorbid psychological conditions is warranted. Patients with persistent pain issues should see a pain specialist for personalized treatment options. In one case-control series, patients with ENS after submucosal Medpor implantation experienced improvements in SNOT-25, ENS6Q, Beck Depression Inventory-II (BDI-II), and Beck Anxiety Inventory (BAI) postoperatively at 1 year, but all parameters were still significantly higher than those in the control group[46]. Repeat testing with anxiety and depression questionnaires can be helpful in evaluating the psychological burden of the disease and should be undertaken at regular postoperative intervals.

APPROACH TO THE POST-RHINOPLASTY ENS PATIENT

The expression "an ounce of prevention is worth a pound of cure" is certainly applicable to mitigating the risk of developing ENS after septorhinoplasty. Though commonly performed, turbinate reduction should be limited unless truly required. While there is mixed evidence regarding the most efficacious approach of inferior turbinate reduction, it is suggested that undergoing medial flap turbinoplasty may be superior to electrocautery and submucosal approaches[24]. In order to avoid unnecessary inferior turbinate surgery, additional studies predicting which patients would best benefit from the intervention are important. A thorough history and physical, as well as the use of validated objective outcome metrics including ENS6Q and the cotton test, is necessary if highly suspicious of ENS. A realistic but empathetic discussion with patients regarding pathophysiology, symptomology, and prognosis is warranted; refer to psychiatry or pain specialists when appropriate. Higher quality studies researching preoperative psychological features are necessary to predict which patients may be most at risk for developing ENS. Though there are a variety of surgical approaches, depending on patient and physician preference, a submucosal autograft/allograft with lateral nasal wall implantation appears to have the best evidence.

CONCLUSION

ENS is an iatrogenic condition after turbinate reduction that confers a significant physical and psychological burden on the patient. Plastic surgeons performing septorhinoplasty should be aware of the risk of this postoperative complication and be equipped with a variety of management strategies to best care for patients. While initial studies in CT imaging and computational fluid dynamics are promising, future studies involving more precise methods to accurately diagnose patients are warranted.

DECLARATIONS

Authors' contributions

Performed acquisition, analysis, and interpretation for the work, drafted the work, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Go BC

Substantially contributed to the conception and design of the work, reviewed it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Deane EC, Friedman O

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