Evaluation of Depression and Anxiety in Empty Nose Syndrome After Surgical Treatment

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Objectives/Hypothesis: Empty nose syndrome (ENS) is often associated with psychological symptoms. With the absence of psychiatric instruments utilized in the current literature, the assessment of psychological disorder is limited, and the effectiveness of surgical intervention in improving such disorders in ENS are not well understood. The aim of this study was to evaluate the change in depression and anxiety before and after surgical treatment for ENS.

Methods: ENS patients indicated for surgical treatment were enrolled. The Beck Depression Inventory II (BDI-II) and Beck Anxiety Inventory (BAI) questionnaires were completed by these patients before and after surgery to assess the level of depression and anxiety.

Results: A total of 20 patients completed the BDI-II and BAI before and after surgical treatment. A majority of patients developed depression and anxiety prior to surgical treatment. The severity of depression and anxiety were significantly decreased following the surgery; the mean scores of both the BDI-II and BAI improved from moderate severity to normal (both \( P < .001 \)). The preoperative total score was found to be a powerful predictor for the postoperative improvement in both BDI-II and BAI (\( P < .001 \)). Female patients had significantly worse preoperative scores (\( P = .005 \)) and greater postoperative improvement (\( P = .012 \)) in the BDI-II.

Conclusions: Depression and anxiety are psychological disorders prevalent among ENS patients. Surgical treatment for ENS is effective in improving depression and anxiety. Patients with worse preoperative BDI-II and BAI scores as well as female patients may be better candidates for surgical intervention.

Key Words: Empty nose syndrome, mental condition, psychological status, submucosal implantation, Beck Depression Inventory II, Beck Anxiety Inventory.

Level of Evidence: 4

INTRODUCTION

Empty nose syndrome (ENS) is currently recognized as an iatrogenic rhinitis, characterized by paradoxical nasal obstruction and history of turbinate or sinus surgery.\(^1\) This term was first introduced in 1994, describing the patent space of the nasal cavity on coronal view of computed tomography in these patients.\(^2\) Diagnosis of ENS is difficult due to the lack of reliable and objective measurements. Subjective symptomatology is the key-stone in the diagnosis and management of ENS. The diagnosis is basically founded on the combination of past operative history, reported symptoms, physical examination, and computed tomography. A cotton test is useful for diagnosis and surgical planning.\(^2\) The most common surgical intervention involves an implant, either a biosynthetic or autologous graft, secured within a submucosal pocket, which appears to result in clinical improvement.\(^3,4\)

The so-called “paradoxical nasal obstruction” is the main symptom of ENS, meaning the patient’s sensation of nasal stuffiness despite large air space in the nasal cavity. Other common presentations of ENS include dyspnea, nasal and pharyngeal dryness, hyposmia, rhinorrhea or postnasal drip, nasal crusting, inability to concentrate (aprosxia nasalis), chronic fatigue, frustration, irritability, anger, anxiety, or depression.\(^1,2\) The pathophysiology of ENS cannot be fully explained solely by anatomical change. Sozansky and Houser concluded that ENS remained a poorly understood disorder, and aberrations in the neurosensory system caused by surgical insult, improper healing, and alterations of airflow pattern may play the major role in the abnormal nasal sensations of ENS patients.\(^5\)

In our previous retrospective study, the 22-item Sino-Nasal Outcome Test was applied in patients with...
ENS, and it was found that submucosal implantation of Medpor over the septum or nasal wall is a feasible surgical treatment for long-term symptom relief.\cite{1,2,3,4} Houser and various other authors also showed clinical improvement after surgical intervention for ENS.\cite{1,2,3,4} The key outcome measurement used in our previous study and the studies mentioned above was the Sino-Nasal Outcome Test (SNOT). Although SNOT consisted of several symptoms in the psychological domain, it is not able to identify clinically meaningful psychological disorders and delineate nonclinical subjects.\cite{5} To date, there is an absence of studies that utilize psychiatric instruments measuring improvements of psychological disorders in ENS patients. The aim of this study was to evaluate the improvement in clinical psychological disorders, namely depression and anxiety, through surgical treatment in patients with ENS. This is the first prospective study conducted to evaluate psychological disorders in ENS patients.

**MATERIALS AND METHODS**

**Study Subjects**

This study was approved by the institutional review board of Chang Gung Memorial Hospital, Taoyuan, Taiwan (CGMH). Between 2012 and 2014, consecutive patients who visited the outpatient CGMH ear, nose, and throat clinic were assessed for eligibility. Patients were eligible for enrollment if they 1) had been diagnosed with ENS and 2) passed the cotton test. Patients were excluded if they had been diagnosed with 1) any psychiatric disorders or have received antipsychotics prior to the study; 2) congenital craniofacial anomaly, nasal valve collapse during inspiration, or nasal figure deformity due to trauma or augmentation surgery; and 3) ostiomeatal complex disease, sinusitis, nasal polyps, or other gross mass lesions. Subsequently, the eligible patients were enrolled into this study and underwent submucosal implantation of Medpor (Porex Surgical, Inc., Newman, GA) or autologous bone grafts performed by the same physician (T.-J.L.). Written informed consent was obtained from all patients prior to enrollment. Patients completed a baseline survey on the day prior to surgical implantation. This survey assessed general demographic factors such as age, gender, marital status, education level, and smoking status, followed by the assessment of psychological measures with the Beck Depression Inventory II (BDI-II) and Beck Anxiety Inventory (BAI). Patients also completed the BDI-II and BAI at 12 months following surgery.

**Diagnosis of ENS and the Cotton Test**

The diagnosis for ENS was based on the operative history of middle or inferior turbinectomies resulting in paradoxical nasal obstruction, breathing discomfort, pharyngeal dryness, and other related discomforts. Endoscopy was performed in all patients to examine the nasal cavity and mucosa before surgery. Patients with ENS showed an excessively wide nasal cavity and a broad view of the nasopharynx (Fig. 1A). Rhinomanometry and acoustic rhinometry were not compulsorily performed because they are beyond the coverage of our national insurance system. Once the diagnosis of ENS was established, the candidates for surgical intervention received a cotton test without local anesthesia or decongestant.\cite{6} A cotton ball moistened with isotonic sodium chloride was placed into the widest area of common nasal cavity where previous endonasal surgery or procedures were performed. The patient was asked to breathe through his or her nose to observe on any changes in symptoms for 30 minutes. If there was any improvement in symptoms, the patient passed the cotton test and was considered as a candidate for surgery.

**Surgical Intervention**

An endonasal submucosal implantation with porous high-density polyethylene (Medpor) or autologous bone grafts over the nasal wall was performed. Under local anesthesia, an incision was made on the nasal floor over the pyriform aperture to create a submucosal pocket. The emphasis of the surgery was to maintain the integrity of the mucosal flap and prevent the protrusion of the implant. If the patient has a sizeable and deviated septal bone, autologous bone graft was harvested for implantation. Otherwise, the patient was implanted with Medpor, a nonreactive material that allows tissue and vascular ingrowth. It is a surgical implant and has been used for over 20 years as a suitable framework biomaterial. We used the Medpor Ultra Thin Sheet, which is made in sizes of $38 \times 50 \times 0.85$ mm and cut it into $8 \times 25$ mm to $8 \times 40$ mm pieces. Multiple pieces of these grafts were used to form an ideal contour of submucosal implantation.

**Psychological Measurements**

The BDI-II and the BAI were applied in this study. BDI-II is a widely used self-administered instrument to detect symptoms of depression and to screen subjects with possible clinical

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Fig. 1. (A) The endoscopic finding of a right-sided nasal cavity with excessive volume before surgery. (B) The endoscopic finding of a right-sided nasal cavity with reduced volume after submucosal implantation on the lateral nasal wall.
depression. BDI was developed by Beck et al. in 1961 and was revised in 1996 as the BDI-II. Compared to its predecessor, the BDI-II showed improved clinical sensitivity and reliability.\textsuperscript{10} The BDI-II included 21 items, each of which is rated between 0 and 3. Depression is rated by the total score, where the score of 0 to 13 indicates normal, 14 to 19 indicates mild depression, 20 to 28 indicates moderate depression, and 29 to 63 severe depression. Similarly, the BAI was also developed by Beck et al. and is widely utilized to assess anxiety and delineate patients from nonclinical samples.\textsuperscript{11} It is a 21-item self-administered questionnaire, where each item is answered on a scale from 0 to 3. A final BAI score of 0 to 7 indicates normal, 8 to 15 indicates mild anxiety, 16 to 25 indicates moderate anxiety, and 26 to 63 indicates severe anxiety.\textsuperscript{12} The translated versions of the BDI-II and BAI in Chinese were used in this study. They were purchased from the Chinese Behavioral Science Corporation in Taiwan.\textsuperscript{12}

**Statistical Analysis**

The Wilcoxon signed rank test was used to compare the pre- and postoperative scores of each item and the total scores of the two questionnaires. Spearman correlation and Mann-Whitney U tests were applied to clarify the changes and links between BDI-II, BAI scores, and the potential factors. Multivariate linear regression was used to adjust potential confounding factors. Univariate linear regression was further conducted to investigate the prognostic significance of all variables in predicting ENS patients who may have the most significant postoperative improvement in BDI-II and BAI score. A stepwise linear regression model was fitted using a forward selection procedure in which the significance level of entry of a given variable in the model was 0.05, and the significance level of removal of a given variable in the model was 0.10 for the multivariate analysis including all the variables. A two-tailed \( P \) value of <.05 was considered to be statistically significant. Statistical analyses were performed using SPSS 16.0 statistical package for Windows (SPSS Inc., Chicago, IL).

**RESULTS**

**Study Subjects**

A cohort of 20 patients (12 men and eight women) was enrolled, with a mean age of 51.6 years (34–72 years). Sixteen of them were married. The educational level of five patients was higher education or above (e.g., university), and the others were secondary education or below (e.g., senior high school). None of them were smokers. One patient was excluded due to a psychiatric disorder diagnosed before prior nasal surgery. All patients had histories of turbinectomies, received submucosal implantation of Medpor or septal bone grafts over nasal wall, and completed BDI-II and BAI evaluations prior to surgery and at 12th months after surgery. Endoscopy was performed in all patients to examine the nasal cavity and mucosa after surgery. Figure 1B shows that the mucosa covering the graft was smooth and intact on the lateral nasal wall, reducing the width of the nasal cavity. The patients’ demographic data and total scores of both questionnaires are summarized in Table I.

**BDI-II**

Before surgical intervention, there were nine patients (45%) reported with severe depression, two (10%) reported with moderate depression, four (20%) reported with mild depression, and six (30%) reported as normal. The severity of depression improved after surgery in all patients with depression. In the normal group, four patients also had improvements in scores postoperatively. The mean BDI-II score improved significantly from 24.4 (moderate depression) to 6.3 (normal), with a \( P \) value of <.001 (Fig. 2A). Furthermore, all items in this questionnaire improved significantly after surgical treatment (Table II).

**BAI**

The results of the BAI scores are listed in Table III. Similarly, there were eight (40%) patients reported with severe anxiety, three (15%) reported with moderate anxiety, three (15%) reported with mild anxiety, and seven (35%) reported as normal before surgical intervention. The severity of anxiety improved after surgery in all patients with anxiety. In the normal group, four patients also had improvements in scores postoperatively. The mean BAI score improved significantly from 19.0 (moderate anxiety) to 6.8 (normal), with a \( P \) value of <.001 (Fig. 2B). All items except “wobbliness in legs” and “hot/cold sweats” improved significantly after operation (Table III).

**Correlation Analysis**

Regarding the Spearman correlation, the preoperative score was found to be related to BDI-II score improvements after surgical treatment (\( P < .001 \)). Female patients tended to have worse preoperative total scores and greater postoperative improvements in BDI-II scores (\( P = .005 \) and .012, respectively). In addition, multivariate linear regression analysis was conducted to adjust the potential confounding factors, where preoperative BDI-II score and gender were found to be powerful predictors for postoperative improvement (\( P < .001 \) and \( P = .006 \), respectively). For BAI, the preoperative score was the only significant predictor for postoperative improvement after multivariate regression analysis (\( P < .001 \)).

**DISCUSSION**

In this study, it was found that a majority of ENS patients developed depression and anxiety before surgical intervention. The pathophysiology on the changes in the mental status of ENS patients is not well understood, but the development of psychological symptoms in ENS patients has been confirmed.\textsuperscript{1,2} Although anatomical change caused by ENS may not be fully accountable for emotional impacts, there are some reports describing the relation between ENS and mental status.\textsuperscript{3,13,14} Freund et al. studied the activation of limbic system, which is normally involved in processing emotions, using functional magnetic resonance imaging in ENS patients at a resting condition. Limbic activation may result in...
an unstable mental condition for ENS patients.\textsuperscript{13} Lemogne et al. reported that a patient developed anxiety and depression due to ENS and was treated with cognitive behavior therapy and a serotonin reuptake inhibitor. The patient's anxiety and depression subsided after medical treatment; however, the patient's nasal symptoms, including dryness and dyspnea, remained unimproved.\textsuperscript{14} In our previous study, it was confirmed that surgical treatment could significantly improve nasal symptoms in ENS patients.\textsuperscript{3} To date, our study is the first to prove that psychological symptoms related to ENS could be improved solely via surgical treatment without cognitive behavior therapy or antipsychotic medication. This may suggests that ENS is composed of rhinological and psychological factors.

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BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory II; F = female; M = male; Post-op = postoperative; Pre-op = preoperative.
psychological symptoms, and surgical treatment alone could significantly improve both aspects without medical treatment.

Naftali et al. have demonstrated that inspired air directed into a wide passageway resulted in ineffective air conditioning due to the lack of inferior turbinates and turbulence. The surgical treatment for ENS rebuilt more appropriate nasal anatomic structure and airflow patterns that could significantly relieve related nasal symptoms. The present study showed that both depression and anxiety status also significantly improved after surgery. The reason for the significant improvement in psychological symptoms may be due to the improvement in “dyspnea sensation” after surgery. In ENS patients, thermoreceptors fail to be stimulated by airflow due to poor nasal air conditioning, resulting in the sensation of nasal congestion and shortness of breath. ENS patients at rest had been presented with temporal and cerebellar activation similar to experiments involving respiratory distress and air hunger during CO₂ inhalation, respectively. This abnormal signaling to the brain may produce the constant feeling of respiratory distress in ENS patients, leading to functional impairment such as distraction, chronic fatigue, frustration, irritability, depression, and anxiety. Thus, it is reasonable that improvement in “dyspnea sensation” after surgical intervention would change not only anatomical figures but the abnormal brain signals, resulting in improvement in mental status. To our knowledge, the present study provided direct evidence regarding the psychological changes after surgical treatment for patients with ENS.

In the present investigation, preoperative total score was found to be significantly related to postoperative improvement for both BDI-II and BAI. In addition, female patients had significantly worse preoperative scores and greater postoperative change in BDI-II scores. For BAI, there is a trend that females had a worse preoperative level and better postoperative improvement but without statistical significance. This may be due to a relatively small sample size. No other medical parameters, including age, education, marriage, type of implant, allergy tests, and blood tests, were found to be markedly correlated with postoperative improvement for either questionnaire. These results implicated that ENS patients with a worse preoperative score and of the female gender would be expected to have more improvement in mental status after surgical treatment. In a literature review, Leong performed a systematic review of ENS studies published to date, in which all seven studies included for analysis were case series. The sample size of these studies ranged between three and 31 patients, with a follow-up period from 6 to 48 months. In this study, a larger sample size and a longer follow-up period may be required for a more definitive conclusion regarding the long-term improvement of...
ENS patients’ psychological disorders. According to previous studies and our experience, implantation is the main technique utilized in the treatment of ENS. The key difference is the type of implant materials used, and the most appropriate implant material has to be compared in future studies. There is currently also a lack of guidelines on the amount and size of implants, which may result in inconsistent surgical results. It would be ideal if the placebo effect could be taken into account by having a control group, although sham surgery would not be considered ethical. Hence, to our knowledge, there have not been any controls in existing studies.

CONCLUSION
This study found that a majority of ENS patients developed depression and anxiety. Surgical treatment is effective in improving both depression and anxiety in patients with ENS. ENS patients with worse preoperative BDI-II and BAI scores and females may have better outcomes after surgical treatment.

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BIBLIOGRAPHY