Nasal Nitric Oxide in Unilateral Sinus Disease

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Abstract

**Background:** Unilateral sinus disease (USD) can sometimes be difficult to accurately diagnose before surgery. The application of nasal nitric oxide (nNO) for USD diagnosis and its surgical outcome in USD has not been reported.

**Methods:** We prospectively enrolled sixty-six USD patients who underwent endoscopic sinus surgery for fungal rhinosinusitis (19), chronic rhinosinusitis (CRS) without nasal polyps (13), CRS with nasal polyps (12) and sinonasal mass lesions (22). nNO levels were measured preoperatively and at three and six months postoperatively. Correlations between nNO levels and potential parameters, type of disease, disease severity, and disease-related quality of life were assessed.

**Results:** Unlike bilateral CRS, in USD, nNO levels did not correlate with disease severity or postoperative QOL improvements. There were no differences in nNO levels between lesion and non-lesion sides in all groups, and nNO levels on both sides were significantly elevated six months postoperatively. Fungal rhinosinusitis patients had the lowest preoperative nNO levels; a cutoff of 228 ppb had the best sensitivity (83.3%) and specificity (83.0%) for preoperative diagnosis.

**Conclusion:** While preoperative nNO levels cannot serve as an alternative marker for disease severity of USD, they were lower in fungal rhinosinusitis than in other USD and may be useful for more accurate diagnosis prior to surgery.

Introduction

Unilateral sinus disease (USD) is not a rare condition among paranasal sinus diseases encountered in daily practice. Common presentations include unilateral nasal obstruction, purulent nasal discharge, nasal bleeding and facial symptomatology. Specific diagnosis among the different pathologies of USD made solely by endoscopy or computed tomography (CT) scan can be very difficult, and neoplasms should be considered even if CT scans show no bony destruction.1

Nasal nitric oxide (nNO), is mainly produced in the upper airway, particularly in the paranasal sinus mucosa. nNO levels are thought to be affected by rhinosinusitis status and may be implicated in the modulation of cilia beating.2,3 Thus, nNO has been used to screen for primary ciliary dyskinesia and as a potential postoperative biomarker after sinus surgery for chronic rhinosinusitis (CRS) because nNO levels are well correlated with radiographic staging and symptom severity.4 In our previous investigation of bilateral CRS with and without polyps, nNO levels were significantly inversely correlated with endoscopy scores and CT scores, elevated significantly after surgery and related to postoperative quality of life (QOL) improvements.5

nNO levels can be measured quickly, easily, and non-invasively, and measurements are feasible for following treatment outcomes of bilateral CRS. However, to our knowledge, nNO levels in USD have never been reported. Thus, the study aimed to assess the merits of nNO for an accurate preoperative diagnosis of USD in patients without bony destruction on CT scans and to determine correlations between nNO levels, surgical outcomes and QOL changes.

Methods and Materials

We prospectively recruited patients who underwent unilateral endoscopic sinus surgery (ESS) for USD and were refractory to medication therapy. We defined the operation side as the lesion side and the contralateral side as the non-lesion side. Patients with the following conditions were excluded: < 18 years of age, prominent contralateral sinus diseases (CT score > 1), obvious bony destruction on CT, previous sinonasal traumas/surgeries and currently pregnant. Potential clinical parameters, endoscopy scores, CT scores and SNOT-22 scores were also recorded. Measurements were made using an electrochemical analyzer (NIOX MINO®; Phadia AB/Aerocrine AB, Sweden) following American Thoracic Society/European Respiratory Society recommendations.6 Postoperative nNO levels were followed at three and six months postoperatively.

Results

Sixty-six consecutive USD patients receiving unilateral ESS for 19 fungal rhinosinusitis (mycetoma), 13 chronic rhinosinusitis without nasal polyps (CRSwNP), 12 chronic rhinosinusitis with nasal polyps (CRSsNP), and 22 sinonasal mass lesions, were enrolled. We excluded all sinonasal malignancies because adjuvant therapy may have interfered with nNO levels. Potentially related medical variables were analyzed, and only endoscopy scores (P = 0.047) and CT scores (P < 0.001) were higher on the lesion side in the CRSwNP group than in the other groups.

In this USD cohort, nNO level did not correlate with disease severity (endoscopy score and CT score, P = 0.969 and 0.891, respectively) or SNOT-22 scores (P = 0.533). The preoperative nNO level was significantly lower on the lesion side (Fig. 1A) and non-lesion side in the fungus group (Fig. 1B) than in the other groups. The other three groups had similar and higher preoperative nNO levels than those of the fungus group, but the latter did not present a more advanced CT score, which indicates that the nNO level in USD could not reflect the status of sinusitis.

Since in this study fungal rhinosinusitis (mycetoma) had a significantly lower nNO level than those of the other USD groups, we tried to determine a cutoff value by receiver operating characteristic (ROC) curve analysis. The sensitivity and specificity were 83.3% and 83.0%, respectively, for a cutoff value of 228 ppb nNO (area under the ROC curve = 0.903) (Fig. 2). The sensitivity was much higher than that for intranasal calcification on CT which was detected in 11 (57.9%) of the 19 fungus group patients. For the lesion side, nNO levels showed a continuously rising trend but only reached significant difference six months postoperatively (P = 0.002) (Fig. 3A). While nNO level on the non-lesion side showed a similar trend by six months postoperatively (P = 0.018), endoscopy scores improved gradually from three months after surgery and continued to improve until six months (both P < 0.001). Improvements in endoscopy scores were inversely correlated (r = −0.145) with elevation in mean nNO levels postoperatively (not significant, P = 0.162) (Fig. 3B).

Discussion & Conclusions

In our previous series of bilateral CRS, similar to the results of other studies, nNO levels were inversely correlated with endoscopy scores and CT scores in the CRSsNP and CRSwNP groups.7 In this study, however, nNO level did not correlate with the endoscopy/CT score in any group of USD patients. nNO level on the lesion side was similar to that on the non-lesion side in every group. In addition, unlike the results of the bilateral CRS study, preoperative nNO level was not correlated with postoperative improvements in endoscopy/SNOT-22 scores. Consequently, nNO level is not useful for assessing preoperative disease severity, or for predicting surgical outcomes, in USD. While preoperative nNO levels were not useful for assessing USD severity and prognosis, they were lower in fungal rhinosinusitis patients than in other USD patients and thus may be useful for the diagnosis of these patients.

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