Outcome Analysis of Endoscopic Sinus Surgery in Patients with Nasal Polyps and Asthma

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Objective: To investigate the efficacy of endoscopic sinus surgery (ESS) in the management of chronic sinusitis and asthma in patients with nasal polyps and steroid-dependent asthma. Study Design: Retrospective chart review. Methods: The study included 17 patients who underwent ESS with nasal polyps, steroid-dependent asthma and a minimum of 1 year postoperative follow-up. Nine patients were ASA sensitive, and eight patients were ASA tolerant. Chronic sinusitis and asthma were evaluated using subjective (patient complaints) and objective (computed tomography scans, pulmonary function tests, steroid doses) criteria. Preoperative data were compared with data obtained 12 to 18 months post-ESS. Tissue samples were graded for degree of inflammation and edema. Results: Thirteen of the 17 (76.5%) patients reported improved clinical symptoms post-ESS. The postoperative Lund-Mackay scores were statistically lower for the 17 patients (P < .0001). The group experienced improvement in postoperative forced expiratory volume at 1 second (FEV₁) (P < .014). Twelve of 17 (70.6%) experienced reduction in systemic steroid usage (P < .048). The ASA sensitive patients did not have a statistical improvement in postoperative FEV₁ (P > .08) and sinonasal symptoms (P > .16) compared with the ASA tolerant group. Polyp tissue from the ASA sensitive patients demonstrated more edema and more inflammation on average than ASA tolerant polyps, but the results were not statistically significant. Conclusion: ESS demonstrates a beneficial effect on the sinonasal and asthma symptomatology in patients with nasal polyps and asthma using objective measures. Subset of aspirin-tolerant patients have statistically better outcome for sinonasal symptoms and pulmonary function testing than aspirin-sensitive patients. Keywords: Nasal polyps, asthma, sinus surgery, Samter's triad.

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INTRODUCTION

The association between asthma and nasal polyposis has been established since the 19th century. The exact nature of this relationship is still not well understood. From an epidemiologic standpoint, the frequency of polyps ranges within 10% to 15% in asthmatic patients over 40 years of age. The frequency of polyps in aspirin-sensitive asthmatics ranges from 36% to 96%. The frequency of asthma in the setting of nasal polyposis lies within 30% to 70%.

The disease process in patients with nasal polyps and asthma tends to be more severe and refractory to conventional medical and surgical treatment strategies, especially in the subset of aspirin-sensitive asthmatics. Objective data assessing outcome in patients with nasal polyps and steroid-dependent asthma is sparse. This patient population will be the focus of the current study with analysis of sinonasal and asthma symptomatology after surgical intervention using objective measures. The subsets of aspirin-tolerant and aspirin-sensitive (i.e., Samter's triad) patients are subsequently compared.

MATERIALS AND METHODS

The study design was a retrospective data analysis performed at a tertiary-care referral center. The subject population was 17 patients undergoing surgical intervention by the two senior authors (R.C.K., D.B.C.) between the period of January 1995 and December 2000. The patients underwent nasal polypectomy and endoscopic sinus surgery (ESS) as described in the Messerklinger technique.

The inclusion criteria for the study were as follows: nasal polyps, steroid-dependent asthma, and presence or absence of aspirin sensitivity. All of the patients underwent maximal medical management of the sinonasal and asthma symptomatology by the Department of Otolaryngology and the Division of Allergy and Immunology, Northwestern University Medical School, before undergoing surgery. A minimum of 1-year postoperative follow-up was required before inclusion in the study. Patients

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with allergic fungal sinusitis, immunodeficiency disorders, and cystic fibrosis were excluded from evaluation.

Patient demographic data were obtained from chart review. The sinus symptoms were analyzed using objective and subjective measures. Objectively, the pre- and postoperative Lund-Mackay scores were determined by evaluating the sinus computed tomography scans. Postoperative scans were performed between 12 and 18 months after surgery in all cases and compared with preoperative scans. A score of 0 to 24 was calculated as described by Lund and Mackay. On the basis of the chart review, the patients overall sinonasal symptomatology was placed into one of five categories: cured, much improved, improved, unchanged, or worse.

The asthma symptoms were evaluated using two measures. First, pre- and postoperative pulmonary function testing was reviewed. Specifically, the predicted pre- and postoperative forced expiratory volume at 1 second (FEV₁) values were calculated. Second, pre- and postoperative systemic steroid usage was determined and placed in one of the following categories: none, occasional (2–3 bursts/week), intermittent (burst/1–2 month), and QOD (every other day). The above variables were then compared between the subsets of aspirin-tolerant and aspirin-sensitive patients.

Histologic analysis was performed on archival specimens of polyps on all 17 patients by a pathologist blinded to outcome. Tissue was graded as mild, moderate, or severe with regard to degree of edema and intensity of inflammation.

Statistical Analysis

Mean differences between pre- and postoperative scores were evaluated for statistical significance using within-subjects t-tests for Lund-Mackay scores and for pulmonary function testing scores (for the total sample, and separately by group). The number of patients showing better post-op steroid usage was compared statistically versus chance (defined as a 50% likelihood of post-op reduction in steroid usage) using the binomial formula, for the sample considered as a whole, and separately by group. Similarly, the number of patients reporting improved postoperative clinical symptoms was compared statistically versus chance (defined as a 50% likelihood of post-op improvement in clinical symptoms) using the binomial formula, for the sample considered as a whole, and separately by group. Finally, the association between dummy coded change in clinical symptoms and change in steroid use was assessed for the sample considered as a whole using chi-square analysis, and the association between dummy coded change in clinical symptoms (treated as the independent variable) and pre- and postoperative Lund-Mackay scores and pre- and postoperative pulmonary function testing scores. The level of significance for all tests was P < 0.05.

RESULTS

The study included 17 patients with an average age of 51 (range 31–80) years. There were 10 males and 7 females. Table I shows the demographic data for the subsets of aspirin-sensitive and aspirin-tolerant patients. The total number, age, and preoperative Lund-Mackay scores were not statistically different.

Table I. Demographic Data for Subsets of Aspirin-Sensitive and Aspirin-Tolerant Patients.

<table>
<thead>
<tr>
<th></th>
<th>Aspirin Sensitive</th>
<th>Aspirin Tolerant</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Age</td>
<td>53 years</td>
<td>49 years</td>
</tr>
<tr>
<td>Preoperative L-M</td>
<td>22 (1-14)</td>
<td>19 (1-5)</td>
</tr>
</tbody>
</table>

L-M = Lund-Mackay.

Figure 1 illustrates the pre- and postoperative Lund-Mackay scores. The patients as a whole improved from 21 to 12 (P < 0.0001). The aspirin-sensitive patients improved from 22 to 14 (P < 0.006). The aspirin-tolerant patients improved from 19 to 9 (P < 0.001).

Figure 2 illustrates the overall sinonasal symptomatology for the patient population. Thirteen of the 17 (76.5%) patients in the group reported reduced sinonasal symptoms (cured, much improved, or improved) postoperatively (P < 0.019). For aspirin-sensitive patients, six of nine (66.7%) patients reported reduced symptoms after surgery (P < 0.16). For aspirin-tolerant patients, seven of eight (82.5%) patients reported reduction of symptoms (P < 0.031). Four patients did not report change in symptoms after ESS. No patients reported worsening of symptoms postoperatively.

Figure 3 shows the pre- and postoperative pulmonary function testing data. For the group, the predicted FEV₁ value improved from 83% to 90% (P < 0.014). For the aspirin-sensitive patients, the FEV₁ improved from 85% to 92% (P > 0.08). For the aspirin-tolerant patients, the FEV₁ improved from 81% to 86% (P < 0.047).

The pre- and postoperative systemic steroid usage data are illustrated in Figure 4. Only one patient required occasional steroids preoperatively. Six patients required intermittent bursts on monthly or bimonthly basis, and 10 patients required steroids QOD. Postoperatively, nine patients were completely weaned from steroids. Three re-

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required steroids on occasional basis after the surgery. Another three required bursts, and two required QOD regimen. For the whole group, 12 of 17 (70.6%) patients had reduction in steroid usage ($P < 0.048$). For aspirin-sensitive patients, six of nine (66.7%) needed less steroids ($P > .16$). For aspirin-tolerant patients, six of eight (75%) used less steroids postoperatively ($P < 0.11$).

There was no statistical association between postoperative sinonasal improvement and the change in steroid usage ($P > 0.82$) or pulmonary function testing ($P > 0.14$).

Improved clinical symptomatology was significantly related to lower postoperative Lund-Mackay scores ($P < 0.003$).

Histologic analysis demonstrated greater edema and inflammation in the ASA sensitive patients when compared with the ASA tolerant patients, but the results were not significant. Specifically, the degree of tissue edema on average was 2.3 in the ASA sensitive patients versus 1.6 in the ASA tolerant patients. The intensity of inflammation was 2.7 on average for the ASA sensitive patients versus 2.1 for the ASA tolerant patients. These trends were not statistically significant.

**DISCUSSION**

A strong association between asthma and polyps exists from a clinical and epidemiologic standpoint in the literature. The precise mechanisms involved in the pathophysiology of these processes yet remain to be elucidated. Nevertheless, the beneficial effect of surgery on the outcome of upper and lower airway disease in this setting has been has been documented by several authors.

Nishioka et al. examined the effect of ESS in 20 patients with chronic sinusitis and asthma. A subjective questionnaire was administered to this patient population. Eighty-five percent reported that ESS resulted in improvement of the asthma. Seven (53.8%) patients required less inhalers and systemic asthma medications. Eighteen (90%) patients had emergency department or urgent physician visits within the year before ESS; all of these patients had a reduction in these visits. The authors concluded that because 43% of asthma costs result from hospitalizations and emergent or urgent care visits, "a significant impact on health care costs can be realized with functional ESS in this patient population."8

Dunlop et al. determined the efficacy of ESS on asthma in 50 adult patients with chronic rhinosinusitis or nasal polyps. Twenty patients reported improvement of asthma control postoperatively. Twenty percent required less steroid inhalers, whereas 28% needed less bronchodilators. A statistically significant reduction in oral steroid usage and hospitalization for asthma was also noted. In addition, there was an improvement in sinonasal symptoms using the mean visual analogue scores, especially for nasal obstruction and sense of smell. Importantly, no difference was noted for asthma and sinonasal outcomes between the chronic rhinosinusitis and nasal polyg groups.

Uri et al. evaluated 34 asthmatic patients with massive nasal polyps who underwent ESS. Follow-up endoscopy revealed satisfactory results in 30 (88%) patients. A positive correlation was noted with the patients' subjective assessment of their nasal status. A statistically significant decrease was documented for steroid and inhaler usage. In the subpopulation of 13 patients followed at the asthma clinic, no difference was noted between the pre- and postoperative asthma condition. Seven patients had minimal improvement, and six noted worsening of their asthma.

The patient population with massive nasal polyposis and steroid-dependent asthma was also the focus of this study. The goal was to determine the efficacy of ESS on the sinonasal and asthma symptomatology in this patient population. The bulk of the sinonasal disease was evaluated objectively by determining the pre- and postoperative Lund-Mackay scores. The Lund-Mackay score improved from 21 to 12 for the group as a whole. Subjectively, 13 of 17 (76.5%) patients reported reduced sinonasal symptoms postoperatively. Importantly, improved sinonasal symptoms positively correlated with lower postoperative Lund-Mackay scores. Thus, reduction of bulk of nasal polyposis actually translated to subjective improvement, although the postoperative Lund-Mackay score was on average 12 with 1 year of follow-up.

Asthma symptoms were assessed using objective measures, specifically pulmonary function testing and steroid usage data, from the patient records. Although other studies have also reported on oral steroid inhalers and bronchodilators, this data in the aforementioned studies has been subjectively assessed. Subjective questionnaires rely on patient recall and, thus, introduce a confounding variable in the data analysis. In addition, there is an inherent difficulty in assessing this variable objec-
tively because the patients may be taking several inhalers concomitantly. In this patient population, the variables of systemic steroid usage and pulmonary function testing were most amenable to objective evaluation.

The FEV$_1$ value improved from 83% to 90% in this group as a whole. This improvement was statistically significant. Note that from a clinical standpoint, it is difficult to ascertain how the change in the FEV$_1$ value affects the asthma in this patient population. However, this data must be assessed in light of the steroid usage data. Postoperatively, 12 of 17 (70.6%) patients required less steroids, with 9 patients being completely weaned from oral steroids. An additional three required steroids on an occasional basis. The patient population was able to maintain same or better FEV$_1$ values, with a statistically significant reduction in systemic steroid usage. For patients with nasal polyps and steroid-dependent asthma, the findings are significant. The long-term effects of chronic steroid usage, including osteoporosis, cataracts, hypertension, weight gain, and psychologic disturbances, are well established. Thus, it is imperative to reduce the steroid requirement in this patient population and avoid the adverse sequelae.

The effect of ESS in the subsets of aspirin-sensitive and aspirin-tolerant patients was also studied. The association of asthma, nasal polyps, and sensitivity to aspirin, known as Samter’s triad, is well recognized. The exact mechanisms remain to be elucidated but are likely caused by a defect in eicosanoid synthesis. Eicosanoids are by-products of arachidonic acid metabolism that are released mainly by two enzymes, cyclooxygenase and lipooxygenase. Aspirin and aspirin-like products inhibit the activity of cyclooxygenase and, thus, increase the activity of lipooxygenase and its products, leukotrienes. Leukotrienes result in increased vascular permeability, mucus secretion, and smooth muscle constriction in the upper and lower airways. The resultant airway edema and bronchoconstriction manifest as acute asthmatic attacks and nasal symptoms characteristic of these patients.

The objective and subjective data for the aspirin-sensitive and aspirin-tolerant patients was compared to attempt to assess the clinical implications of this putative leukotriene effect. The postoperative Lund-Mackay scores improved from 22 for the aspirin-sensitive and from 19 for the aspirin-tolerant patients to 14 and 9, respectively. The improvement was statistically significant for both of the groups. However, on average, the postoperative Lund-Mackay score was significantly higher for the aspirin-sensitive patients. Subjective improvement was noted in six of nine (66.7%) of aspirin-sensitive patients. In contrast, seven of eight (87.5%) patients in the aspirin-tolerant group noted improvement in the sinonasal symptoms. When the subsets were evaluated separately, the sinonasal symptom improvement was statistically significant for only the aspirin-tolerant group. Thus, in general, the sinonasal disease in the Samter’s patients tends to be more refractory to surgical interventions using both subjective and objective criteria.

Parallel results for the two groups were noted with regard to their postsurgical pulmonary status. The postoperative improvement in the predicted FEV$_1$ value was statistically significant only for the aspirin-tolerant patients. Improvement was noted in the ASA sensitive patients as well, but it was not statistically significant. In addition, six of nine (66.7%) aspirin-sensitive patients noted reduction in steroid usage, whereas six of eight (75%) aspirin-tolerant patients had reduction in steroid usage. When both of the groups were evaluated separately, neither group reached statistical significance. Thus, the postoperative benefit on asthma symptoms was evident in both groups, although it was less pronounced in the aspirin-sensitive group.

CONCLUSION

The data analysis in this review demonstrates that ESS after maximal medical management results in beneficial effect on the asthma and sinonasal symptomatology in this patient population utilizing objective measures. The postoperative Lund-Mackay scores were statistically lower and the sinonasal symptoms were also statistically better. The FEV$_1$ value improved and the requirement for systemic steroid usage decreased for the patients. When the data are compared between the aspirin-sensitive and aspirin-tolerant subsets, the positive effect in the aspirin-sensitive population was less pronounced. Nevertheless, the study illustrates that ESS is important for optimal management of this difficult subset of rhinologic patients.

BIBLIOGRAPHY

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