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RESEARCH PAPER

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Postoperative mometasone irrigations improve quality of life in skull base tumor patients

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Abstract

Objectives: The use of topical corticosteroids to manage postoperative sinonasal symptoms after endoscopic skull base surgery (ESBS) has not been well studied. We quantified long-term impact of postoperative steroid irrigations (SIs) on quality of life of patients after ESBS.

Methods: Retrospective review of patients at the University of Pennsylvania undergoing ESBS from 2010 to 2019. Data on patient demographics and postoperative treatment with nasal saline irrigation twice daily with and without dissolved steroids (mometasone or budesonide) was collected. Preoperative, and 1-, 3-, 6-, 12-, 18-, and 24-month postoperative Sino-Nasal Outcome Test (SNOT-22) scores were assessed.

Results: A total of 727 patients were assessed (53.4% males), with 479 patients in the no SI group and 248 patients in the SI group. Preoperative SNOT-22 scores did not differ significantly ($P = 0.19$). 1-, 3-, 6-, 12-, 18-, and 24-month post-op SNOT-22 scores did not significantly differ between groups. However, mometasone irrigations resulted in significantly lower postoperative 2-year SNOT-22 scores compared to budesonide ($P < 0.01$) and saline ($P = 0.03$).

Conclusions: Though corticosteroid irrigations are routine in managing inflammatory sinus disease, their role in postoperative management after ESBS for tumors is unclear. Our findings suggest that mometasone irrigation may be effective at improving postoperative quality of life in patients after ESBS.

KEYWORDS

postoperative steroid irrigations, skull base tumors

INTRODUCTION

In chronic inflammatory sinonasal disease, the addition of steroids to nasal saline irrigation improves patient symptoms, radiologic findings, and endoscopic appearance.[1,2] The addition of steroids to nasal irrigation postoperatively in patients who undergo endoscopic skull base surgery (ESBS) for resection of a skull base tumor has only been minimally investigated.[3] Existing literature suggests similar outcomes in quality of life (QoL) between patients treated postoperatively with steroids and with saline, however, the largest existing study was limited to a cohort of 59 patients followed for a short time of 3 months.[3] It is well documented in the literature that, following ESBS, patients experience transient nasal crusting (98%), nasal discharge (46%), hyposmia or anosmia (10%), and diminished nasal airflow (5%).[4] Within a year's time, a majority of patients report notable improvement in the aforementioned symptoms.[5] However, some patients continue with sinonasal symptoms and a reduced QoL despite these reported statistics.[5] For this subset of patients, optimal management of persistent symptoms is unclear.[6] This study sought to quantify the long-term impact of postoperative saline plus steroid nasal irrigations in patients undergoing ESBS, focusing primarily on the QoL and any associated radiographic changes.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board at the University of Pennsylvania. A retrospective review was performed of all patients who underwent ESBS at the University of Pennsylvania within the Division of Rhinology and Skull Base Surgery from 2010 to 2019. Patients were followed for up to 24 months postoperatively with the Sinonasal Outcome Test (SNOT-22) and Lund MacKay Score (LMS). Inclusion criteria for the study consisted of (1) diagnosis of benign or malignant skull base neoplasm; (2) completely endoscopic endonasal resection of skull base neoplasm; and (3) postoperative use of 240 mL nasal saline irrigations without dissolved steroids (saline only with no steroid irrigations [NSIs]) twice daily or use of 240 mL nasal saline irrigations with dissolved steroids (saline with steroid irrigations [SIs]), either 0.6 mg budesonide or 1–2 mg mometasone, twice daily. Patients under 18 years of age were excluded from the analysis.

Regardless of the extent of surgery, all patients were started on NSI or SI twice daily at 4 weeks postsurgery. Use of saline versus SIs was based on surgeon preference, with a gradual shift in more recent years to using steroid rinses based on presumed benefits. The decision to start patients on saline versus SI was not associated with specific patient factors or exam findings but instead represented a shift in practice from using saline irrigation earlier in time to using SI more recently due to presumed benefits. Use of steroid versus saline was determined based on the therapy initiated at the 1-month postoperative period. Patient symptoms were assessed using SNOT-22 preoperatively, 1-month postoperatively/preirrigation, and post-operatively/postirrigation at 3, 6, 12, 18, and 24 months. LMS were assessed preoperatively and at least 1 month postoperatively after using nasal irrigation either with or without dissolved steroids.

We performed subgroup analyses to determine if SI versus NSI results differed when stratified by tumor location (intracranial vs. intranasal only), by treatment with radiation therapy, or by malignancy status. Additionally, results of SNOT-22 score based on steroid treatment with budesonide versus mometasone was analyzed.

All statistical analyses were performed using SPSS (Version 26; IBM Corp.). Parametric data were expressed as a mean. Comparisons were made using Student's *t*-test with $P < 0.05$ determined to be statistically significant.

RESULTS

A total of 727 patients met inclusion criteria. Demographic information for the cohort is shown in Table 1. The mean age was 55.8 ± 19.8 years old. A total of 65.8% ($n = 429$) belonged to the SI group and 34.1% ($n = 248$) belonged to the NSI group. 40.9% of the SI group and 39.7% of the NSI group were current or former smokers ($P = 0.75$) as shown in Table 1. Baseline demographic data including age, gender, and smoking status, were similar between those in the saline group and those in the steroid group, including budesonide and mometasone subgroups. Basic data regarding tumor type and surgical approach are shown in Table 2. 19.1% ($n = 139$) were malignant skull base tumors and 80.8% ($n = 588$) were benign skull base tumors.

There was no significant difference in the SNOT-22 scores between the SI and the NSI groups at all time points measured:

TABLE 1 Baseline patient characteristics.

	SI group		
	Budesonide	Mometasone	NSI group
Total number	220	28	479
Mean age (years)	54.6	54.8	54.2
Gender	95 Female (43.2%)	13 Female (48.1%)	230 Female (47.9%)
	125 Male (56.8%)	14 Male (51.9%)	249 Male (52.1%)
Tobacco use	91 (41.4%)	11 (39.3%)	190 (39.6%)

Abbreviations: NSI, no steroid irrigation; SI, steroid irrigation.

TABLE 2 Tumor and operative characteristics.

	SI group	NSI group
Tumor type	*203 Benign (81.9%)*	*385 Benign (80.4%)*
	98 Inverted papilloma	40 Inverted papilloma
	28 Pituitary adenoma	260 Pituitary adenoma
	15 Meningioma	9 Craniopharyngioma
	2 Craniopharyngioma	19 Meningioma
	2 Rathke cleft cyst	1 SCC
	1 SCC	13 Rathke cleft cyst
	22 Fibro-osseous lesion/ osteoma	1 Chordoma
	6 JNA	6 Fibro-osseous lesion/ osteoma
	29 Other	5 JNA
		32 Other
	45 Malignant (18.1%)	*94 Malignant (19.6%)*
	1 Meningioma	1 Inverted papilloma
	12 SCC	1 Pituitary adenoma
	8 Esthesioneuroblastoma	17 SCC
	4 Chordoma	8 Esthesioneuroblastoma
	3 Adenocarcinoma	7 Chordoma
	3 SNUC	9 Adenocarcinoma
	14 Other	5 SNUC
		46 Other
Surgical approach	180 Intranasal only	127 Intranasal only
	5 Transplanum	11 Transplanum
	7 Transclival	12 Transclival
	5 Transtuberculum	16 Transtuberculum
	4 Transpterygoid	2 Transpterygoid
	7 Transcribiform	7 Transcribiform
	18 Transsellar	184 Transsellar
	9 Transsphenoidal	53 Transsphenoidal
	1 Transplanum, transcribriform, transsphenoidal	27 Transsellar, transsphenoidal
	1 Transfrontal	2 Transtuberculum, transsellar, transsphenoidal
	3 Transsellar, transsphenoidal	7 Transplanum, transsphenoidal
	1 Transtuberculum, transsellar, transsphenoidal	3 Transclival, transsphenoidal, Transsellar, transplanum
	1 Transtuberculum, transsellar	2 Transclival, transsphenoidal
	1 Transplanum, transsphenoidal	3 Transclival, transsphenoidal, transsellar
	5 Unspecified	1 Transplanum, transcribriform
		1 Transpetrosal
		18 Unspecified

Abbreviations: JNA, juvenile nasopharyngeal angiofibroma; NSI, no steroid irrigation; SI, steroid irrigation; SNUC, sinonasal undifferentiated carcinoma.

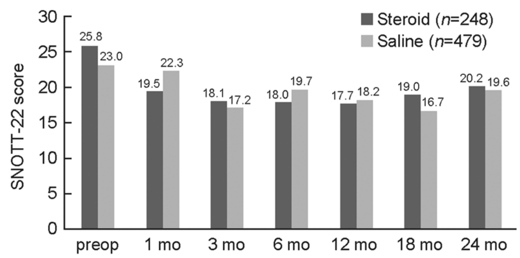

FIGURE 1 Comparison of SNOT-22 between steroid and saline groups ($P < 0.05$). SNOT-22, Sinonasal Outcome Test.

preoperative ($P = 0.19$), 1-month postoperative/preirrigation ($P = 0.15$), and postoperative/postirrigation at 3 months ($P = 0.67$), 6 months ($P = 0.49$), 12 months ($P = 0.85$), 18 months ($P = 0.51$), and 24 months ($P = 0.88$) (Figure 1). This trend was upheld in the subgroup analyses regardless of tumor location, treatment with radiation therapy, and malignancy status. The subgroup analysis of tumor location (intracranial vs. intranasal tumors) yielded statistically similar outcomes for SNOT-22 scores at 12 months between the SI and NSI groups ($P = 0.12$ for intracranial tumors vs. $P = 0.40$ for sinonasal tumors). Similarly, the analysis of SNOT-22 scores in the saline versus steroid groups at 12 months for tumors treated with adjunct radiation ($P = 0.92$) or without adjunct radiation ($P = 0.23$) were statistically similar. Finally, SNOT-22 scores at 12 months for malignant tumors ($P = 0.83$) versus benign tumors ($P = 0.43$) in the SI and NSI groups were also statistically similar.

For the subgroup analysis within the SI group, stratified by steroid type, the mometasone group achieved significantly lower SNOT-22 scores than the budesonide group at every time point after 6 months postoperatively ($P < 0.01$ at 6 months, $P = 0.02$ at 12 months, $P = 0.04$ at 18 months, and $P < 0.01$ at 24 months) (Figure 2A). The mometasone group also had significantly lower SNOT-22 scores compared to saline at every time point after 6 months, ($P < 0.01$ at 6 months, $P = 0.02$ at 12 months, $P = 0.32$ at 18 months, and $P = 0.03$ at 24 months), whereas the budesonide group showed no significant difference compared to saline at any time point (Figure 2B,C).

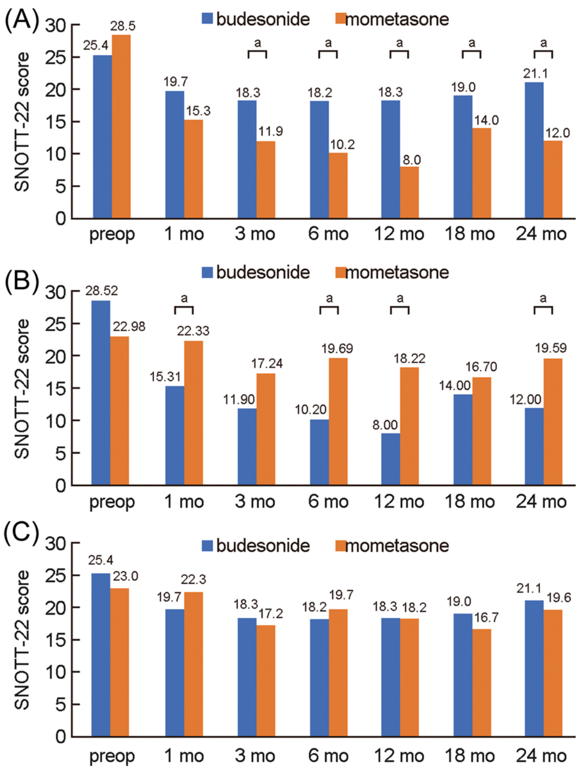

FIGURE 2 Comparison of SNOT-22 between groups (A) mometasone versus budesonide groups; (B) mometasone versus saline groups; (C) budesonide versus saline groups ($P < 0.05$). SNOT-22, Sinonasal Outcome Test.

Finally, although LMS differed significantly between the NSI group and the SI group preoperatively ($P < 0.001$), scores were similar to a statistically significant degree at 1 month postoperatively ($P = 0.104$) between the two groups.

DISCUSSION

The appeal of endoscopic surgery for skull base tumors stems from associated lower morbidity and faster recovery when compared to open approaches.[7–9] It has been reported that a patient's QoL at the very least transiently suffers following ESBS.[5] Routine postoperative care for these patients attempts to ensure an effective recovery and an overall improved QoL. Postoperative in-office debridement coupled with appropriate medical management allows help in improving QoL in these patients.[6] In chronic inflammatory diseases, adjunctive postoperative medical management includes nasal saline sprays and/or nasal saline irrigation. In the last decade, nasal saline irrigations with dissolved topical steroids have been integrated into the postoperative care of patients with chronic inflammatory disease who have undergone ESS. Compared to nasal saline irrigations without dissolved steroids, nasal saline irrigations with dissolved steroids have been demonstrated to improve long-term QoL outcomes in chronic inflammatory disease.[1,2,6]

An understudied area is the role of nasal saline irrigation with dissolved steroids for patients with skull base tumors undergoing ESBS. Despite the paucity of studies, nasal saline irrigation with dissolved steroids is occasionally empirically integrated into the postoperative management of skull base tumor patients. A retrospective study by Jo et al.[3] showed no efficacy associated with dissolved topical steroids in nasal saline irrigations after endoscopic resection of sinonasal neoplasms. Limitations to the study by Jo et al.[3] included a small sample size ($n = 59$), just once daily postoperative irrigation regimen, assessment of a single steroid agent (betamethasone), and short follow-up duration of 3 months postoperatively. To date, no other studies exist on the efficacy of nasal saline irrigations with dissolved steroids in patients undergoing ESBS.

This study assessed long-term QoL in patients who received nasal saline irrigations with or without dissolved steroids after undergoing endoscopic endonasal resection of skull base tumors. All patients were started on a standardized protocol of twice-daily nasal saline irrigations either independently or with dissolved steroids (mometasone or budesonide). Our practice has gradually shifted to placing more patients on SI due to improved postoperative healing and reduced sinonasal inflammation that was observed in our patients. There is also an apparent lack of evident side effects, as well as the appearance of improved healing, and anecdotally less CRS postoperatively.

Some studies suggest that patients experience only transient nasal symptoms postoperatively and return to baseline within 6–12 months of surgery.[10] Other studies demonstrate that a subset of patients develop ongoing chronic rhinosinusitis following ESBS for skull base tumors.[11] The differences in these conclusions lie mainly in the limitations of each study. Weaknesses of previous studies include omission of operative procedure details, inclusion of only a single surgeon's experience, enrollment of a limited number of patients, insufficient data on individual patient adherence to prescribed therapy, or a minimalist explanation of the techniques used, that is the uninostril approach.[3,5,10,11] Our current study included a variety of skull base tumors resected using a wide array of approaches and conducted by several different surgeons at a single institution to increase the external validity of our assessment.

With a more extensive cohort in this study, we discovered no difference in outcomes between NSI and SI groups overall and in subgroup analyses stratified by tumor location, adjuvant radiation, or malignancy status. Furthermore, we did not use cortisol testing in patients prescribed SIs, due to evidence from prior studies that showed no statistically significant changes to the hypothalamic–adrenal axis with use of steroid rinses.[12] However, we did find that nasal irrigations with dissolved mometasone twice daily offered significant improvement in long-term SNOT-22 outcomes compared to the group of patients who performed nasal saline irrigations without dissolved steroids or with saline irrigations combined with dissolved budesonide. This effect may be secondary to mometasone's increased first-pass metabolism compared to budesonide and the subsequent ability to increase the dosage without substantially increasing risk of side effects.[13] The cohort of patients receiving mometasone in this study therefore received higher intranasal steroid dosing of 1–2 mg versus the 0.6 mg of steroids used in the budesonide group. In this study, preoperative LMS in patients performing nasal saline irrigations with dissolved steroids was significantly higher than LMS in patients performing nasal saline irrigations without dissolved steroids, but these differences are no longer statistically significant at 1 month postoperatively.

Limitations of our study include the retrospective nature of the review and the lack of published literature on the most effective length of treatment with postoperative steroids. Additionally, patients received saline or steroids according to clinical practice, which evolved over the course of the study to favor steroid use based on lack of significant side effects, observational improvements in healing, and observation of lower rates of chronic rhinosinusitis at our center. Another limitation of this study is the small proportion of patients on mometasone; only 13% of the steroid group consisted of patients on mometasone due to initial issues with insurance coverage for this agent. Future work should be done to affirm these trends in a larger population of patients specifically treated with mometasone. Due to our intent to analyze, patients had varying lengths of follow-up that resulted in an overall smaller number of subjects for this study. SNOT-22 was used uniformly to assess symptom burden in all patients and we did not use alternate QoL surveys, such as the Skull Base Inventory, to assess patients. Future work should analyze results using other surveys specific to skull base tumor resection QoL. Because a standardized endoscopic grading scale is not routinely performed on all postoperative visits, we were unable to include this clinical information in our assessment. Future studies should include objective measures such as endoscopic and CT evaluations of disease burden before and after initiating irrigation therapy.

Further studies with randomized control trials are needed to adequately determine the optimal time to continue postoperative treatment with steroid rinses.

CONCLUSIONS

Patients with skull base neoplasms who undergo endoscopic surgical resection may benefit from nasal saline irrigation with dissolved steroids. Our current study demonstrates a significant improvement with mometasone at long-term follow-up after 6 months. Nevertheless, a randomized, double-blinded, controlled study is necessary to determine if there is clinical benefit from postoperative nasal saline irrigations with dissolved steroids in this patient population.

AUTHOR CONTRIBUTIONS

Mandy K. Salmon: Formal analysis; data curation; writing—review and editing. **Rijul S. Kshirsagar**: Writing—review and editing. **Jacob G. Eide**: Writing—review and editing. **Auddie M. Sweis**: Conceptualization; writing—original draft; data curation; writing—review and editing. **Kathleen Davin**: Data curation. **Aman Prasad**: Data curation. **Heather Ungerer**: Data curation. **Elizabeth Stevens**: Data curation. **Kevin Ig-Izevbekhai**: Data curation. **Siddhant Tripathi**: Statistical analysis. **Tran B. Locke**: Writing—review and editing. **Theodore Lin**: Conceptualization. **Brian M. Sweis**: Conceptualization. **Michael A. Kohanski**: Supervision; project administration. **Nithin D. Adappa**: Supervision; project administration. **James N. Palmer**: Supervision; project administration.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was approved by the Institutional Review Board of the University of Pennsylvania.

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