Clinical Trial/Experimental Study

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Effects of nasal irrigation after endoscopic transsphenoidal resection in patients with pituitary adenomas

A randomized controlled trial

Peng Xu, RN, MSc[a,*], Shuling Liu, RN, PhD[b,c], Yahong Dong, RN, BSc[d], Wei Liang, RN, BSc[e], Zijun Li, RN, BSc[a], Fang Liu, RN, BSc[a]

Abstract

Purpose: We aimed to explore the methods to reduce or prevent nasal complications after endoscopic transsphenoidal pituitary adenoma resection. We also examined the effects of nasal irrigation after this procedure was performed.

Methods: A randomized controlled trial was performed. Sixty patients of a tertiary hospital were enrolled in this study. The subjects were randomly divided into a control group and an intervention group. The subjects of the control group were given routine guidance, and 20 mL of normal saline was atomized through inhalation. The gauze was removed 7 days after surgery. The patients of the intervention group were given 50 mL of a 2% saline solution at 37°C to 38°C for bilateral nasal irrigation for 1 week. After that, patients were given 50 mL of a 0.9% normal saline solution at 37°C to 38°C for bilateral nasal irrigations. The complications of the two groups were collected at baseline, 1 week after intervention, 1 month, and 3 months after intervention. The data were analyzed using the chi-square test.

Results: A 1-month after intervention, there were significant differences in dysosmia, epistaxis, and nasal adhesion between the intervention and control groups. A 3-month after intervention, only olfactory disturbances were significantly different between the two groups.

Conclusions: Nasal irrigation helps reduce the incidence of complications such as epistaxis and nasal adhesions in the early postoperative period. It can also promote the elimination or reduction of olfactory disturbances.

Abbreviations: Bid = Bis in die, CT = computed tomography, D = odor discrimination, DSA = Digital Subtraction Angiography, I = odor identification, TDI T = odor threshold.

Keywords: endoscopic transsphenoidal resection, nasal complications, nasal irrigation, pituitary adenomas, randomized controlled trial

1. Introduction

Pituitary tumors are common benign neurosurgical tumors, accounting for 10% to 12% of all intracranial tumors, and the population incidence is about 1/100,000.[1] These tumors have been increasing in prevalence in recent years. Transsphenoidal resection of these tumors is currently considered an effective and safe treatment method. Common surgical methods include a microscopic and endoscopic transsphenoidal resection of pituitary tumors. The main complications include diabetes insipidus, cerebrospinal fluid rhinorrhea, hypopituitarism, intracranial

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[a] Department of Otolaryngology, Tianjin Huanhu Hospital, Tianjin, China, [b] Department of Neurology, Tianjin Huanhu Hospital, Tianjin, China, [c] Department of Nursing Management, Tianjin Huanhu Hospital, Tianjin, China, [d] Department of Neurosurgery, Tianjin Huanhu Hospital, Tianjin, China, [e] Department of Operating Room, Tianjin Huanhu Hospital, Tianjin, China.

[*] Correspondence: Peng Xu, Department of Otolaryngology, Tianjin Huanhu Hospital, No.6 Jizhao Road, Jinnan District, 300350, Tianjin, China (e-mail: xupeng73@yeah.net).

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infection, sphenoid sinusitis, nasal adhesions, perforation of the nasal septum, olfactory disorders, and dry nasal cavities. Some complications are the nasal symptoms caused by the varying degrees of nasal cavity structural damage associated with the surgical approach. However, neurosurgeons often pay more attention to diabetes insipidus, cerebrospinal fluid rhinorrhea, and hypopituitarism. Complications such as sphenoid sinusitis, nasal adhesions, and olfactory disorders are often ignored by healthcare professionals because these disorders do not pose a serious threat to patient lives. Therefore, these disorders have not garnered much attention in the medical literature. However, a few studies have shown that these nasal problems exist and have a significant impact on postoperative patient recovery.[1,2]

The present research on transsphenoidal pituitary tumor resection has primarily focused on surgical approaches, trans-sphenoidal resection techniques, patient positioning for the transsphenoidal techniques, and transnasal pituitary tumor surgeries. However, these approaches have been shown to be safe and effective for the prevention of nasal complications in previous studies. They are also easy to perform, and patient compliance is better than when other techniques have been used.

Patients undergoing pituitary tumor resections through a transnasal route have been shown to have fewer postoperative complications. In terms of post-surgical food and wound care management, the prevention and treatment of nasal-related complications are more about "cooperating with specialists." There are no standardized, specific, or feasible interventions regarding postoperative nasal irrigation methods in any relevant guideline.[1] However, post-surgical nasal cavity irrigation has also been shown to reduce nasal mucosal edema,[3] thereby ensuring normal ciliary movement, the first line of defense in the nasal mucosal layer. Ciliary movement changes can lead to nasal cavitary and sinus complications. Therefore, this study used experimental research methods to analyze and explore the effects of nasal irrigation on nasal complications in patients receiving the endoscopic transsphenoidal approach to pituitary tumor resections.

2. Objectives and methods

2.1. Research objective

From April 2019 to December 2019, 60 patients with pituitary tumors were convenient sampling collected as research subjects from a first-class tertiary hospital.

The inclusion criteria were that patients:

1. needed to be from 18 to 70 years of age;
2. needed to have confirmed pituitary adenomas; and
3. patients provided informed consent.

Exclusion criteria were patients with:

1. have received the endoscopic transsphenoidal approach to resect the pituitary adenomas previously;
2. had prior sphenoid sinusitis, nasal adhesions, nasal septum perforation, olfactory disorders, or nasal bleeding disorders;
3. had serious heart, lung, or kidney diseases;
4. postoperative or possible cerebrospinal fluid rhinorrhea;
5. recurrent pituitary tumors and sellar resections of septal defects;
6. aggressive pituitary tumors that extend outside of the cavernous sinus;
7. coagulation disorders and other blood system diseases;
8. consciousness impairments or uncooperative;
9. cognitive impairment; and
10. an inability to communicate through language.

2.2. Ethical considerations

This study involving human participants were reviewed and approved by ethical committee of Tianjin Huanhu Hospital. Written informed consent for study participation was obtained from each patient following a detailed explanation of the protocol and objectives.

2.3. Methods

All patients were given routine treatment and nursing care according to the nursing protocols at this first-class tertiary hospital.

The patients in the control group were given 20 mL of normal saline as an inhalation therapy twice daily (BID) after the surgical resections as directed by a neurologist. The gauze was removed 7 days after surgery, and the nasal cavity was cleaned. The nasal cavity crust was cleaned using nasal endoscopy until the nasal cavity wound was completely epithelialized. The intervention group was given the same nursing therapy as the control group. However, these patients received 50 mL of 2% saline at 37°C to 38°C through bilateral nasal irrigation the first week after the gauze removed. This was followed by a bilateral nasal flush BID for another 1 week consisting of 50 mL 0.9% normal saline at 37°C to 38°C. All the patients in both groups were followed after discharge (see Fig. 1).

2.4. Research tools

At the research institute, we used the PrevenCo Otology Cleaner (Ruifu Biological Medicine Science and Technology, Shanghai) after nasal passages were washed using type J bottles.

Nasal irrigation refers to a treatment method in which nasal secretions are washed out using water flow pressure. It is mainly used to treat atrophic rhinitis, caseous rhinitis, fungal infections of the nasal cavity. It is also used to clean nasal cavities after nasal and sinus surgery and radiotherapy to treat nasal and nasopharyngeal tumors. The specific method is as follows: The patient sits upright, with his/her head tilted slightly forward. The patient breathes open mouth, holding the nasal cavity flushing bottle in one hand and placing an olive into one nostril; the flushing bottle is switched on to gently spray the medicine into one nasal cavity. The medicine first flows into the nasopharynx and then flows out through the contralateral nasal cavity or through the mouth.

Flushing frequency: twice daily
Each rinse volume: 50 mL, rinse time is about 5 minutes

Since the patient needs to perform the nasal cavity irrigation treatment on their own, the otolaryngology nurse trains each patient in the intervention group before treatment and emphasizes any precautions and gives guidance during the first 3 days of the nasal cavity irrigation treatment. Any errors during training are corrected to avoid errors that could jeopardize therapeutic efficacy.[4]

According to the case information and discharge results, data were collected before the operations and then, after 1 week, 1 month, and 3 months of intervention. The data included the

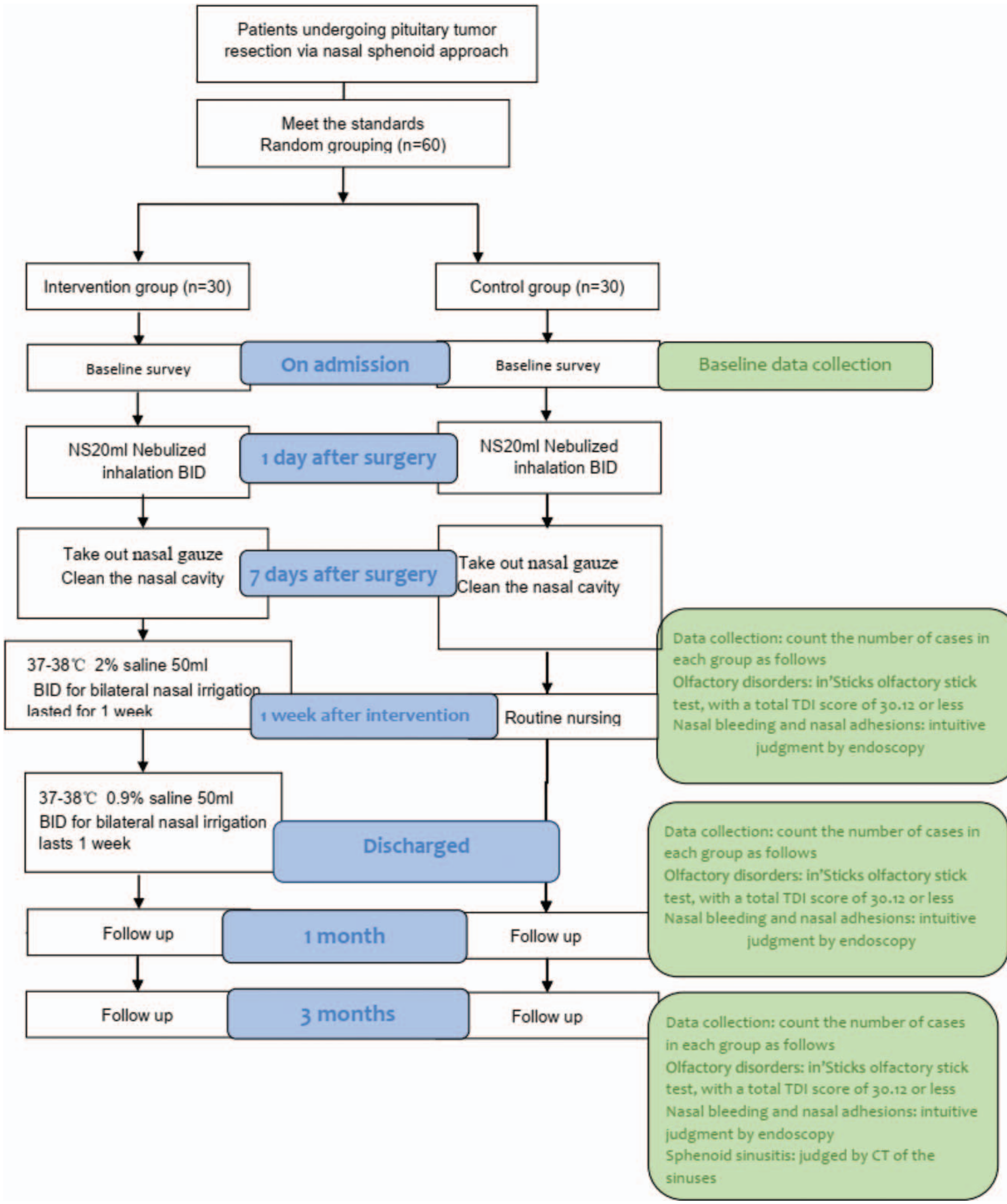

Figure 1. The flow chart of this study.

occurrence of olfactory disorders, epistaxis, and nasal adhesions. The starting point of the procedures in the control group was the first time the nasal cavity was cleaned after surgery.

The diagnosis of olfactory disorders and nasal adhesions in this study is based on the clinical judgment of the otolaryngologist, such as a patient's complaint and doctor's objective examination. Sniffin' Sticks olfactory stick test was used to assess olfactory function, TDI total score $\leq$ those with a score of 30.12 were assessed as olfactory disorders. (TDI refers to T=odor threshold, D=odor discrimination, I=odor identification.)[5] Nasal bleeding and nasal adhesions can be intuitively judged by nasal endoscopy.

By reviewing postoperative and follow-up records, we examined the occurrence of sphenoid sinusitis 3 months after intervention, which was determined with CT scans of the sinuses for the first 3 months after an intervention.

2.5. Statistical methods

Statistical analyses were performed using statistical package of SPSS (version 25.0, IBM). Measurement data were expressed as the means ± standard deviations (SDs). Comparisons between the two groups were analyzed using the *t* test. The count data were expressed by rates, and comparisons between groups were assessed using the chi-squared test. The rank-sum test analyzed the survey scores, and the repeated measurement data were analyzed using the generalized estimating equation (GEE). $P<.05$ was considered to represent a statistically significant difference.

3. Results

During the study period, 60 participants with pituitary tumors were admitted and gave wrote consent forms. Table 1 summarizes the participants' general characteristics and clinical symptoms. No statistically significant differences regarding general characteristics and clinical symptoms of patients were found between the intervention and control groups ($P>.05$). The two groups were found to be comparable (see Table 1).

Based on the data analyses obtained in this study, the occurrence of complications, such as olfactory disturbances, epistaxis, and nasal adhesions was statistically different between the intervention group at 1 week vs 1 month post-surgery. For the group analyses, only olfactory dysfunction was found to have a statistical difference between the two patient groups, 3 months post-resection. These results indicated that a reasonable nasal irrigation technique could significantly reduce nasal symptoms, effectively promote benign nasal mucosal lesion outcomes, and help improve postoperative olfactory function in patients after transsphenoidal resection of pituitary adenomas. However, the results also showed that the influence of this intervention method on the occurrence of postoperative sphenoid sinusitis was not statistically different from that of the control group (see Table 2).

Table 1

Characteristics of the control and intervention groups.

Variables	Control group (n=30)	Intervention group (n=30)	χ^2/t	P
Age (years)	53.97±13.09	55.2±13.52	0.359	.843
Operation time (min)	219±71	198±66	0.085	.771
Gender			0.069	.793
Male	13	12		
Female	17	18		
Marital status			0.351	.554
Married	29	28		
Single	1	2		
Education			2.47	.650
Elementary	2	2		
Junior school	2	3		
High school	4	8		
Junior college	11	10		
Bachelor degree and above	11	7		
Smoking			0.659	.417
Yes	12	9		
No	18	21		
Drinking			0.073	.787
Yes	10	11		
No	20	19		
Disease history			3.353	.340
Hypertension	3	1		
Diabetes	0	2		
Hyperlipidemia	1	2		
Heart disease	0	0		
Other	26	25		

The analytic results regarding the GEE for the occurrence of olfactory disorders (see Table 3) showed that the time after the intervention was negatively correlated with the probability of postoperative olfactory disorders with a coefficient of −0.594, which was statistically significant ($P=.001$). The probability of olfactory dysfunction after the operation was 0.552 times that of the before the operation, indicating that the probability of olfactory dysfunction in both the intervention and control groups decreased as the time after intervention increased. There was also

Table 2

Comparison of complications between the control and intervention groups in patients receiving transsphenoidal resections of pituitary adenomas.

Complications	Control group (n=30)		Intervention group (n=30)		χ^2	P
	Yes	No	Yes	No		
Intervention after 1 week						
Olfactory disturbance	10	20	3	27	3.277	.028*
Epistaxis	8	22	2	28	4.320	.038*
Nasal adhesions	10	20	3	28	3.277	.028*
Intervention after 1 month						
Olfactory disturbance	8	22	2	28	4.320	.038*
Epistaxis	7	23	1	29	3.126	.023*
Nasal adhesions	6	24	1	29	4.012	.044*
Intervention after 3 month						
Olfactory disturbance	3	27	1	29	5.963	.015*
Sphenoid sinusitis	4	26	2	28	0.741	.389
Epistaxis	1	29	0	30	1.017	.313
Nasal adhesions	1	29	0	30	1.017	.313

* $P<.05$.

Table 3

Analytic results of the generalized estimation equation for the occurrence of olfactory disorders.

Variable	Coefficient	Standard error	OR value (95%CI)	*P*
Grouping				
Control group	0.000	0.000	1	–
Intervention group	−1.514	0.7300	0.220 (0.053,0.920)	.038
Time	−0.594	0.1716	0.552 (0.394,0.773)	.001

CI=confidence interval, OR=odds ratio.

a statistically significant difference in postoperative olfactory disturbances between the intervention and control groups ($P=.038$); the regression coefficient was −1.514, indicating that the incidence of an olfactory disturbance in the intervention group was 0.220 times that of the control group. These results suggested that nasal irrigation interventions could reduce the postoperative probability of olfactory disorders.

The GEE for the occurrence of sphenoid sinusitis suggested (see Table 4) that there was no statistically significant difference in postoperative sphenoid sinusitis between the intervention and control groups ($P=.398$).

The GEE for the occurrence of epistaxis and nasal adhesions (see Tables 5 and 6) showed that post-intervention times were negatively correlated with the probability of postoperative epistaxis and nasal adhesions, showing that the probability of having epistaxis and nasal adhesions decreased by extending the time after resection in both the intervention and control groups. The differences in the occurrence of epistaxis and nasal adhesions between the intervention and control groups were statistically significant, suggesting that the nasal irrigation interventions might reduce the incidence of these complications after surgery.

4. Discussion

The pituitary gland is located in the center at the base of the skull. Since the most important and dense vascular nerves of the skull base are gathered in this location, the associated relationship with the pituitary gland is complicated. For example, pituitary tumors are usually removed with craniotomy. In this procedure, not only can the surgical trauma be substantial, but tumor exposure is often unsatisfactory. The sphenoid sinus is the only natural space that can expose the central area of the skull base. In recent years, neurosurgeons have performed transnasal pituitary tumor resections to change the surgical approaches and achieve the safety goals of being minimally invasive with satisfactory tumor exposure. This technique is now widely used.[6,7] However, due to the narrow space of the nasal cavity and paranasal sinuses,[8,9] the injuries that occur during the transsphenoidal approach with repeated instrument access into the nasal cavity and sinuses and the mucosal damage caused by the instrument crowding, postoperative complications are inevitable. In other words, there are hidden dangers related to the healing process.

Generally speaking, neurosurgeons are trained to treat complex and serious diseases, such as cerebrospinal fluid rhinorrhea,[10] diabetes insipidus,[11] hypopituitarism, intracranial infection, and serious complications after transsphenoidal pituitary tumor resections and have less training in treating simple nasal problems. Nasal complications often include sphenoid sinusitis, nasal bleeding, olfactory disturbances, and dry nasal cavities.[12] Therefore, this study adopted a nasal cavity irrigation technique used in the Department of Otolaryngology at the Tianjin Huanhu Hospital to reduce postoperative nasal complications in patients undergoing pituitary tumor resection using the transnasal approach.

The nasal cavity irrigation method used in this study promotes nasal mucosal ciliary movement, increasing the rates at which cilia can eliminate secretions and inflammatory factors and reducing nasal mucosal congestion and edema. This method, thereby, reduces nasal symptoms caused by internal complications.[13,14]

Since hypertonic saline (2% saline) can improve nasal mucosal edema, but hypertonic saline promote the release of histamine and substance P, it can also increase pain and other symptoms of discomfort.[15] To avoid the long-term use of hypertonic saline for flushing a patient's nasal cavity, we stopped using hypertonic saline 1 week after surgery, when nasal edema is usually significantly eliminated. After that, the patients continued to receive bilateral nasal irrigation with 50 mL of 0.9% normal saline at 37°C to 38°C to enhance local blood circulation and improve symptoms of nasal discomfort.

4.1. Olfactory disorders

Olfactory disorders are primarily caused by damage to the nasal mucosa during endoscopic transsphenoidal pituitary tumor resection. Damage to the turbinates and nasal septum mucosa that contain a distribution of olfactory nerve endings is more likely to cause olfactory disorders after surgery. In this study, the

Table 4

Analytic results of the generalized estimation equation for sphenoid sinusitis.

Variable	Coefficient	Standard error	OR value (95%CI)	*P*
Grouping				
Control group	0.000	0.000	1	–
Intervention group	−0.767	0.9078	0.464 (0.078, 2.751)	.398
Time	−2.8612E−17	0.0000	1.00	–

CI=confidence interval, OR=odds ratio.

Table 5

Analytic results of the generalized estimation equation for epistaxis.

Variable	Coefficient	Standard error	OR value (95%CI)	*P*
Grouping				
Control group	0.000	0.000	1	–
Intervention group	−1.734	0.8325	0.176 (0.035,0.902)	.037
Time	−0.845	0.1794	0.430 (0.302,0.611)	<.001

CI=confidence interval, OR=odds ratio.

Table 6

Analysis of results of generalized estimation equations for nasal adhesions.

Variable	Coefficient	Standard error	OR value (95%CI)	*P*
Grouping				
Control group	0.000	0.000	1	–
Intervention group	−1.629	0.7115	0.196 (0.049,0.791)	.022
Time	−1.059	0.2122	0.347 (0.229,0.526)	<.001

CI=confidence interval, OR=odds ratio.

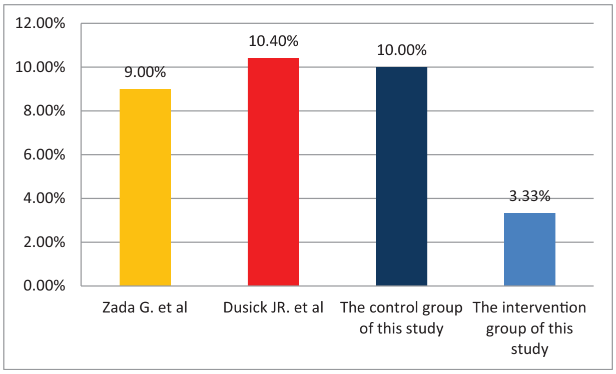

Figure 2. Comparison of the incidence of olfactory disorders of different groups and studies.

postoperative comparison of the two patient groups found that the occurrence of olfactory dysfunction decreased gradually over time, and the incidence of olfactory dysfunction was 10% in the control group 3 months after of intervention, which is close to the level reported in two studies of the US.[16,17] The incidence of olfactory disorders in the intervention group was 3.33% (see Fig. 2), which was significantly lower than the control group. By analyzing GEE results, this intervention reduced the probability of postoperative olfactory disorders. Although it does not completely solve the problem of olfactory disorders, reasonable nasal cavity irrigation techniques have been shown to effectively promote benign nasal mucosal lesion outcomes, thereby helping to improve postoperative olfactory function and prevent or reduce the occurrence of olfactory disorders. The ability to recognize surgical hazards has a very important impact on outcomes.

4.2. Sphenoid sinusitis

In this study, the statistical analyses showed that staged nasal irrigation after endoscopic transsphenoidal pituitary tumor resection did not reduce the incidence of sphenoid sinusitis. After a 3-month intervention, the control group had a few cases of sphenoid sinusitis, whereas the intervention group had no cases; however, no statistically significant difference was found between the groups. The incidence of sphenoid sinusitis between the two groups was lower than that seen in patients of a US-based study[18] (see Fig. 3). However, in this study, the surgical approach of 200 patients did not indicate clearly if an endoscopic or microscopic transsphenoidal approach was used. Both of these approaches are transsphenoidal-based, but the tissue injury to the patient is slightly distinct due to the various methods used. Nasal damage caused by the absence of a nasal spreader during the endoscopic transsphenoidal approach has been found to be relatively small. Additionally, in recent years, patient management after hospital discharge has been improved. In our study, control group patients adhered to regular follow-up visits and were instructed to clear their nasal cavities, greatly reducing or completely inhibiting (intervention group) the incidence of sphenoid sinusitis compared with other studies. We believe that reasonable nasal irrigation treatments clear nasal secretions over time, thus reducing residual inflammatory factors and the risk of nasal adhesions. In addition, timely nasal cleanings after discharge prevent the occurrence of sphenoid sinusitis. However, from the statistical analysis, the results of this study suggest that phased nasal irrigation is ineffective for the prevention and treatment of sphenoid sinusitis.

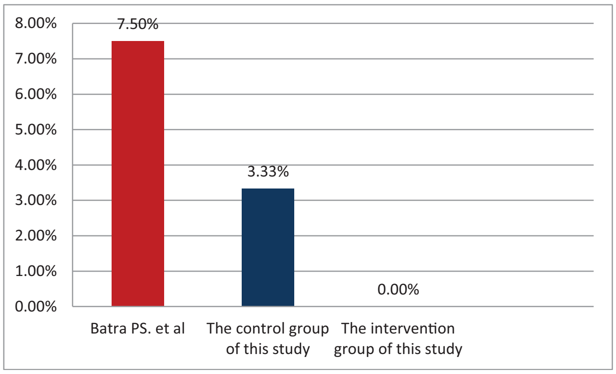

Figure 3. Comparison of the incidence of sphenoid sinusitis of different groups and studies.

4.3. Nasal adhesions

The transnasal approach causes nasal mucosal congestion, edema, increased nasal secretions, increased inflammatory factors and could induce nasal adhesions and atresia, which significantly reduces patient quality-of-life.[19] Nasal adhesions are often related to mucosal edema, nasal cavity stenosis, mucosal epithelial dysfunction, and scar contracture. In this study, we saw that 1 week and 1 month after the nasal interventions, the incidence of nasal adhesions in the intervention group was significantly different from that of the control group ($P < .05$); and over time, some patients with nasal adhesions were seen in the intervention group. However, there was a gradual decrease in the number of patients with nasal adhesions, demonstrating the full therapeutic effect of nasal cavity irrigation. In the intervention group, nasal cavities were irrigated with 50 mL of 2% saline at 37°C to 38°C within 1 week after the nasal gauze was drawn. A 2% saline solution is considered hypertonic. Hypertonic fluids can promote the transfer of intracellular fluid and reduce nasal edema and clean nasal cavity secretions, promoting nasal mucosal regeneration, preventing nasal adhesion formations, and reducing mucous membrane postoperative recovery times. In the control group, the nasal cavity was strengthened over time so that the difference between the two groups was not obvious after the 3-month intervention.

4.4. Epistaxis

In this study, epistaxis occurred in both groups. Epistaxis, due to sphenopalatine arterial bleeding and thought to be related to intraoperative injury, resolved in one patient after digital subtraction angiography (DSA) and vascular embolization. At the 1 week and 1 month intervention, epistaxis was significantly lower in the intervention group than in the control group. Nasal irrigation in the intervention group effectively reduced delayed nasal mucosal bleeding. Therefore, nasal irrigation with hypertonic saline should be considered to reduce nasal congestion and edema, increasing mucosal moisturization and reducing nasal mucosal adhesions.

The temperature of the saline should not be too cold or too hot as cold temperatures would cause mucosal irritation and patient discomfort and hot temperatures would cause blood vessel dilation and nasal bleeding. Thus, a temperature closer to normal human body temperatures is best, and in this study, we chose the temperature to be from 37°C to 38°C.[20] The number of epistaxis cases in the intervention group was significantly less than in the control group, further confirming the safety of staged nasal irrigation.

A main limitation of the study is the sample size. An opportunity to explore the incidence of sphenoid sinusitis would be useful with a larger sample size. We think that the deviation between the statistical analysis results and the intuitive data is related to the small number of cases. In the future, the sample size will be increased to explore the incidence of sphenoid sinusitis.

5. Conclusions

In this study, we proposed a simple, safe, and effective intervention strategy to prevent nasal complications in patients undergoing transsphenoidal pituitary tumor resections. This method is easy to operate, facilitating patient compliance. Patients undergoing endoscopic transnasal pituitary adenoma resection had a reduced incidence of postoperative olfactory dysosmia after nasal irrigation therapy was instituted after resections. In the early stages of treatment and rehabilitation, nasal irrigation can reduce epistaxis and nasal adhesions; however, it did not reduce the incidence of sphenoid sinusitis.

Supplemental Digital Content (R2-original data.xlsx): http://links.lww.com/MD/G543.

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Author contributions

Conceptualization: Peng Xu, Shuling Liu.
Data curation: Wei Liang.
Formal analysis: Yahong Dong.
Funding acquisition: Peng Xu.
Investigation: Shuling Liu, Yahong Dong, Wei Liang, Zijun Li, Fang Liu.
Methodology: Shuling Liu.
Project administration: Wei Liang, Zijun Li, Fang Liu.
Software: Yahong Dong.
Supervision: Peng Xu.
Writing – original draft: Shuling Liu.
Writing – review & editing: Peng Xu, Shuling Liu.

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