

A Prospective Study to Evaluate the Effectiveness of Budesonide Nasal Irrigations Comparison with Saline Irrigations During Postoperative Care of Patients with Rhinosinusitis

Anshu Kumar¹, Pramod Kumar², Rana Pratap Thakur³

¹Assistant Professor, Department of ENT, ANMMCH, Gaya, Bihar, India

²Assistant Professor, Department of ENT, ANMMCH, Gaya, Bihar, India

³Associate Professor and HOD, Department of ENT, ANMMCH, Gaya, Bihar, India

Received: 10-11-2021 / Revised: 29-12-2021 / Accepted: 22-01-2022

Corresponding author: Dr. Pramod Kumar

Conflict of interest: Nil

Abstract

Aim: This study aimed to evaluate the effectiveness of budesonide nasal irrigations compared with saline irrigations during postoperative care of patients with rhinosinusitis.

Materials and Methods: A total of 200 patients who underwent functional Endoscopic Sinus Surgery (ESS) were randomly divided into two groups (A and B) of 100 participants each (normal saline [NS] + budesonide irrigation and NS irrigation alone, respectively). Pre- and post-operative evaluation was done with a 22-item sinonasal outcomes test (SNOT-22), and Lund Kennedy endoscopic (LKE scores) in second and sixth week.

Results: The condition of the patients significantly improved in both intervention arms related to SNOT-22 and LKE score at each postoperative visit (Group A: $p < 0.001$, Group B: $p < 0.001$). A Repeated measures ANOVA F- test shows that mean SNOT-22 score difference is statistically significant between Preoperative, Postoperative (6th week), ($p \leq 0.001$). The significant P value of ≤ 0.001 "between groups" comparison shows that the two groups are statistically significantly different concerning the LKE score. It indicates that, in general, the LKE score of category A had been different from category B.

Conclusion: Steroid nasal irrigation is a good option in postoperative EES patients. The difference of reduction of both SNOT 22 score and LKE score was statistically significant ($p < 0.05$ and $p < 0.01$ respectively) by repeated contrast test. This study is one of the few comparative studies evaluating budesonide and saline nasal irrigations in post-ESS patients.

Keywords: budesonide nasal irrigation, saline nasal irrigation, endoscopic sinus

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Chronic rhinosinusitis (CRS) with nasal polyp is a common inflammatory condition of the nasal mucosa carrying significant morbidity and detriment to quality of life (QOL). Many CRS patients

with nasal polyps require surgery. Along with the development of new equipment and technology, the resolution of the endoscope has increased resulting in a decrease in recurrence of the disease. Unfortunately, even after surgery the

patients with asthma are often difficult to manage because of the high recurrence rate and worse clinical course. We have to explain to patients with asthma before the surgery that endoscopic sinus surgery (ESS) is not intended to be curative but is rather directed towards long-term symptom control [1]. The current mainstay of medical therapy for CRS with asthma after surgery is saline irrigation, topical or systemic steroid or recurrent oral medication of some other kind. In severe cases of recurrence, revision surgery may be required.

Topical nasal steroid spray can be effective in patients with CRS: the nasal polyps may decrease in size and not recur [2]. But the effect is not constant especially in those with asthma, so systemic steroid is often used in such cases [1]. The side effect of long-term systemic steroid are of serious concern to physicians [3].

Endoscopic sinus surgery (ESS) is an essential part of the therapeutic management of medically refractory CRS. The idea of surgery is to increase access of inflamed mucosa to topical anti-inflammatory therapies [4]. The backbone of medical therapy is the nasal steroid and saline sprays delivered by various means [5]. Saline irrigations enhance mucociliary clearance, reduce the local concentration of pro-inflammatory mediators, and humidify nasal mucosa [6, 7].

Topical steroids are the preferred maintenance strategy due to the reduced risk of potential systemic side-effects with prolonged therapy and increased concentrations applied to the diseased tissue, especially after Endoscopic sinus surgery. Topical steroid sprays may not deliver an adequate dose of the drug to the entire postoperative nasal cavity the presence of mucosal secretions, edema, crusting, and scarring. Budesonide nasal irrigation can solve this problem by delivering drugs in a high-volume high-

pressure system. [8-10] However, normal saline nasal irrigation alone has been effective in few studies compared to budesonide nasal irrigation. [11-13]

The off-label use of budesonide nasal irrigation was introduced recently for postoperative management of patients with CRS. The safety and effectiveness of this procedure is becoming accepted by many physicians [14-16].

Therefore, this study aims to comparative studies evaluating budesonide and saline nasal irrigations for patients with polyposis/ rhinosinusitis are deficient in the current literature. This study aimed to evaluate the effectiveness of budesonide nasal irrigations compared with saline irrigations during postoperative care of patients with rhinosinusitis.

Material & Methods:

It is a prospective, single-blinded randomized controlled trial study. Those patients who underwent functional endoscopic sinus surgery in the Department of ENT, ANMMCH, Gaya, Bihar, India, over a period of one and a half year.

Inclusion criteria:

Patients between age 18 and 60 years, and those who undergo Endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps during the study period were included in the study.

Exclusion criteria:

Patients who were on concomitant use of oral steroids (patients with bronchial asthma, autoimmune disorders), patients with known hypersensitivity to corticosteroid, and Immunocompromised patients.

Methodology:

A sample size of 212 patients was enrolled in the study and divided into two categories. Randomization was done by a

computerized random number generator, at the time of his or her pre-operative visit. Twelve patients were lost during follow-up making it a total of 200 patients for the study participation. Each category had 100 patients.

Category A includes patients using Budesonide with normal saline for nasal irrigation postoperatively (2 respules of budesonide (2 mg) mixed in 500 ml normal saline given twice a day with 10 ml syringe, 10 ml on each side). Category B patients include normal saline for nasal irrigation postoperatively (10 ml of normal saline in each nasal cavity, twice daily). Each category's outcomes were assessed using SNOT 22 score and LKE score at the second week and sixth week.

Statistical analysis:

SNOT-22 score/LKE score was given in mean and standard deviation. The similarity of demographic distribution among category A and category B was tested using the chi-square test. Quantitative variables difference between Category A and Category B was assessed using an independent student t-test. Quantitative differences between Pretest, posttest 1 and posttest 2 were assessed using one-way repeated measures analysis of variance F-test/ two way repeated measures analysis of variance F-test and Posthoc multiple comparisons were conducted using Bonferroni t-test. Association between demographic variables and SNOT-22 score/LKE score was analyzed using one-way analysis of variance F-test and independent student t-test. A p-value of 0.05 was considered statistically significant, and two-tailed tests were used for testing significance. SPSS version 22(SPSS Inc, IL, USA) and STATA (version10) software were used for statistical analysis.

Results:

Major age group in both categories was between 21-30 years, which was observed

as 36.5% and 45.5% in group A and group B. Statistically age group wise there is no significant difference between the groups ($\chi^2=7.21$ $p=0.09$ (NS)). There were 61% and 39% in group A, and group B were males. The similarity of gender distribution between the groups is assessed, there is no significant difference between the groups ($\chi^2=1.12$ $p=0.29$ (NS)). There is no association between the Postoperative (6th week) SNOT-22 score and patient's age in the normal saline group ($F=0.24$ $P=0.90$). There is a significant association between the postoperative (6th week) SNOT-22 score and patients' gender in Budesonide with the normal saline group. Male patients are reduced more score than female patients ($t=3.87$ $P=0.04$)(one-way ANOVA F-test and student t-test).

SNOT-22 score preoperatively, there is no significant difference between category A and category B in post functional EES patients ($t=0.24$ $p=0.80$). Postoperative (2nd week) and postoperative (6th week) SNOT-22 score difference is statistically significant ($t=6.72$, $p=0.01$) (Table 1).

In the experiment group, Repeated measures one-way analysis of variance F-test shows that the mean overall SNOT-22 score is statistically significant between preoperative and posttest (6th week) ($F=1582.91$, $P\leq 0.001$). In preoperative, they have a 61.92 score, and in postoperative (6th week), they have a 17.01 score, so the difference is 49.0. This difference is statistically significant. Therefore, category A reduces more SNOT-22 score significantly. In the control group, Repeated measures ANOVA F-test shows that the mean overall SNOT-22 score is statistically significant between preoperative and posttest (6th week) ($F= 799.1$, $P\leq 0.001$). Therefore, category B reduces the SNOT-22 score significantly but less in category B (Table 2).

In category A, Repeated measures ANOVA F-test shows that mean SNOT-

22 score difference is statistically significant between Preoperative, Postoperative (6th week) ($F=1582.91$, $p \leq 0.001$). Posthoc multiple comparisons of Bonferroni t-test show the SNOT-22 reduction score from Preoperative to 2nd week (65.81 ± 8.87 vs. 37.01 ± 6.82), which was statistically significant ($p \leq .001$). After the 6th week, Budesonide with normal saline further reduces the SNOT-22 score (65.81 ± 8.87 vs. 18.19 ± 4.01 , respectively, mean difference is 49.02), which was statistically significant reduction from Pretest to posttest 6th-week score ($p \leq 0.001$). Therefore, we can conclude that category A reduces the SNOT-22 score significantly (Table 3). A Repeated measures ANOVA F- test shows that mean SNOT-22 score difference is statistically significant between Preoperative, Postoperative (6th week), ($p \leq 0.001$).

Post hoc multiple comparisons of Bonferroni t-test show the SNOT-22 reduction score from Preoperative to 2nd week (62.01 ± 6.92 vs. 39.73 ± 7.01 , which was statistically significant ($p \leq 0.001$). After the 6th week, normal saline further reduces the SNOT- 22 score (62.01 ± 6.92 vs. 25.01 ± 5.95) which was a statistically significant reduction from Pretest to posttest 6th week score ($p \leq .001$). Therefore, we can conclude that normal saline reduces the SNOT-22 score significantly but less than category B (Table 3).

To ascertain whether improvement in the two groups is statistically different at all the three assessments, a 2x3 ANOVA test with the last variable as the repeated measure was applied. The significant P value of ≤ 0.001 "between groups" comparison shows that the two groups are statistically significantly different concerning the SNOT-22. It indicates that, in general, SNOT-22 of category A had been different from the category B group (Table 4)

In category A, Repeated measures ANOVA F- test shows that mean LKEScore difference is statistically significant between Preoperative, Postoperative (6th week)($F = 872.82$, $p \leq 0.001$). Post hoc multiple comparisons of Bonferroni t test shows the LKE score reduction score from Preoperative to 2nd week (7.80 ± 0.62 vs. 5.25 ± 0.90 , respectively mean difference is 3.73), which was statistically significant ($p \leq .001$). After the 6th week, category A further reduces the LKE score (7.76 ± 0.62 vs. 3.81 ± 0.79 , respectively difference is 6.03), which was a statistically significant reduction from Pretest to posttest 6th-week score ($p \leq .001$). Therefore, we can conclude that category A reduces the LKE score significantly. category, repeated measures ANOVA F-test shows that mean LKE score difference is statistically significant between Preoperative, Postoperative (6thweek) ($F=p \leq 0.001$).

Post hoc multiple comparisons of Bonferroni t-test shows the LKE score reduction score from Preoperative to 2nd week (6.02 ± 0.79 vs. 5.02 ± 0.74 , respectively mean difference is 2.89), which was statistically significant ($p \leq .01$). After the 6th-week, category B further reduces the LKE score (6.02 ± 0.79 vs. 4.28 ± 0.41 , respectively mean difference is 3.91), which was a statistically significant reduction from Pretest to post-test 6th week score ($p \leq 0.001$). Therefore, we can conclude that category B reduces the LKE score significantly but less than category A

The ANOVA test results are shown in Table 6. The significant P value of ≤ 0.001 "between groups" comparison shows that the two groups are statistically significantly different concerning the LKE score. It indicates that, in general, the LKE score of category A had been different from category B (Table 6).

The reduction of LKE score was statistically significantly different for the

two groups. To understand which assessment, the changes differ between the two groups, the "Repeated Contrast test" was applied. The corresponding P value of the two comparisons between PreOP -2nd week and 2nd week -6th week shows that in

Category A, the LKE score Reduction score has been more compared to category B. The above finding indicates category A was more effective in reducing LKE score than category B.

Table 1: Pre-operative and post operative comparison of SNOT-22 Score

	Category A		Category B		p-value
	Mean	SD	Mean	SD	
Pre-operative	67.90	8.90	63.71	6.81	p=0.90 (NS)
Post op (2nd week)	35.71	6.77	37.01	7.92	p=0.01** (S)
Post op (6th Week)	18.90	4.09	27.61	6.88	p=0.001*** (S)

p \geq 0.05 not significant NS= not significant, S= significant **p \leq 0.01 highly significant, ***p \leq 0.001 very high significant

Table 2: Comparison of mean SNOT-22 score during Preoperative, Postoperative (2nd week) and Postoperative (6th week) among category A and category B by within- group analysis

	Preoperative		Postoperative (2nd week)		Postoperative (6 th week)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Budesonide with normal saline	61.92	8.28	35.02	5.91	17.01	5.99	0.001*** (S)
normal saline	61.80	6.61	39.61	6.90	25.71	4.20	0.001*** (S)

S= significant ***p \leq 0.001 very high significant

Table 3: Multiple comparison of SNOT-22 score between Preoperative, Postoperative (2nd week) and Postoperative (6th week) analysis using Bonferroni t-test

	Assessment	Score Mean SD		Bonferroni t- test Comparison MD		P value
Category A	Pretest	65.81 \pm 8.7	P=0.001***	Pretest vs. Post-1	30.81	0.001
	Post test-1	37.01 \pm 6.82				
	Post test-2	18.19 \pm 4.01		Pretest vs. Post-2	49.02	0.001
Category B	Pretest	62.02 \pm 6.92	P=0.001***	Pretest vs. post-1	28.89	0.001
	Post test-1	39.73 \pm 7.01				
	Post test-2	25.01 \pm 5.95		Pretest vs. Post-2	39.72	0.001

Discussion:

Functional outcome after ESS is entirely determined by preoperative, intraoperative, and postoperative management methods [18]. The management of CRSwNP is an onerous task. Despite excellent surgical techniques, 80% of patients experience recurrence, and around 37% still need revision surgery [19].

The studies investigating pharmacotherapy after ESS are notably lacking in the literature. A major obstacle is topical therapy's ability to reach the sinuses sufficiently to treat mucosal inflammation where high-volume sinonasal irrigations are found to be apt. [20]. Topical steroids are preferred owing to fewer systemic side effects [21]. However, literature analyzing the use of nasal steroid irrigations in post-ESS cases is limited, controversial, and somewhat ambiguous [22].

A recent meta-analysis showed that topical steroid is effective against sinonasal symptoms in patients with CRS without nasal polyps [23], and it decreases polyp size [24, 25] and prevents polyp recurrence in CRS with nasal polyps [24]. The literature contains a number of different findings concerning the use of nasal steroid spray after ESS. Dijkstra et al. [25] used a double-blinded randomized trial to assess the use of fluticasone propionate in reducing polyposis recurrence after ESS. The conclusion of the study was that the steroid did not have any beneficial effect on disease recurrence. Lavigne et al. [26] examined a similar situation in revision ESS patients, using delivery of the steroid through a maxillary antrostomy indwelling tube, and concluded that budesonide was superior to placebo.

Kosugi et al. in 2015, did a Prospective uncontrolled intervention trial. Participants were assessed before and three months after budesonide nasal irrigation. 75% improved Lund Kennedy scores after high-volume budesonide nasal irrigations. They

concluded that high-volume corticosteroid nasal irrigations are a good option in difficult-to-treat Chronic Rhinosinusitis control of the disease. [27]

In a study by Kang et al. [14] in 2016, the endoscopy score improved from 7.4_4.7 before irrigation to 2.2_2.7 after six months. Nasal irrigation with Budesonide is an effective postoperative treatment for chronic rhinosinusitis with asthma, which frequently recurs, reducing the oral steroid intake. [28]

A study by Huang et al. corresponds with our study as it concluded significant benefit in endoscopy scores in the budesonide group at, because the recovery of the mucosa is completed within this period. However, the prognosis of disease after ESS improved in both intervention arms. [29,30] This study claims monetary losses to patients as well as the presumption of HPAA suppression with continuous use of budesonide irrigations. However, studies with prolonged follow-up periods are required to assess the therapeutic benefit of steroids over saline irrigations because further worsening of the disease cannot be ruled out because of the heterogeneity of the disorder.[31]

Conclusion:

In conclusion, high-volume budesonide irrigation therapy has the edge over saline irrigations in the routine postoperative care of patients with CRS, especially with nasal polyposis. Owing to the heterogeneity of the disorder, current recommendations should not necessarily be applied to all patients with CRS, and clinical knowledge should be applied before recommending appropriate postoperative care for a particular patient.

References:

1. Rotenberg BW, Zhang I, Arra I, Payton KB. Postoperative care for Samter's triad patients undergoing endoscopic sinus surgery: a double-

- blinded, randomized controlled trial. *Laryngoscope*. 2011 Dec;121(12):2702-5.
2. Snidvongs K, Pratt E, Chin D, Sacks R, Earls P, Harvey RJ. Corticosteroid nasal irrigations after endoscopic sinus surgery in the management of chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2012 Sep-Oct;2(5):415-21.
 3. Poetker DM, Reh DD. A comprehensive review of the adverse effects of systemic corticosteroids. *Otolaryngol Clin North Am*. 2010 Aug;43(4):753-68.
 4. Snidvongs K, Pratt E, Chin D, Sacks R, Earls P, Harvey RJ. Corticosteroid nasal irrigations after endoscopic sinus surgery in the management of chronic rhinosinusitis. *Int Forum Allergy Rhinol* 2012; 2: 415-21. [CrossRef]
 5. Rotenberg BW, Zhang I, Arra I, Payton KB. Postoperative care for Samter's triad patients undergoing endoscopic sinus surgery: A double-blinded, randomized controlled trial. *Laryngoscope* 2011; 121: 2702-5. [CrossRef]
 6. Hermelingmeier KE, Weber RK, Hellmich M, Heubach CP, Mösges R. Nasal irrigation as an adjunctive treatment in allergic rhinitis: A systematic review and meta-analysis. *Am J Rhinol Allergy* 2012; 26: 119-25. [CrossRef]
 7. Tabary O, Muselet C, Miesch MC, Yvin JC, Clément A, Jacquot J. Reduction of chemokine IL-8 and RANTES expression in human bronchial epithelial cells by a seawater derived saline through inhibited nuclear factor-kappaB activation. *Biochem Biophys Res Commun* 2003; 309:310-6.
 8. Jang DW, Lachanas VA, Segel J, Kountakis SE. Budesonide nasal irrigations in the postoperative management of chronic rhinosinusitis. *Int forum allergy Rhinol*. 2013;3(9):708-11.
 9. Huang ZZ, Chen XZ, Huang JC, Wang ZY, Li X, Chen XH, et al. Budesonide nasal irrigation improved Lund-Kennedy endoscopic score of chronic rhinosinusitis patients after endoscopic sinus surgery. *Eur ArchOto-Rhino-Laryngology*. 2019;276(5):1397-403.
 10. Xu Z, Luo X, Xu L, Deng J, Gao W, Jiang L, et al. Effect of short-course glucocorticoid application on patients with chronic rhinosinusitis with nasal polyps. *World Allergy Organ J*. 2020;13(6):100131.
 11. Rawal RB, Deal AM, Ebert CS, Dhandha VH, Mitchell CA, Hang AX. Postoperative budesonide irrigations for patients with polyposis: a blinded, randomized controlled trial. *Rhinology*. 2015;53(3):227-34.
 12. Rotenberg BW, Zhang I, Arra I, Payton KB. Postoperative care for Samter's triad patients undergoing endoscopic sinus surgery: a double-blinded, randomized controlled trial. *Laryngoscope*. 2011;121(12):2702-7.
 13. Yoon HY, Lee HS, Kim IH, Hwang SH. Postoperative corticosteroid irrigation for chronic rhinosinusitis after endoscopic sinus surgery: A metaanalysis. *Clin Otolaryngol*. 2018;43(2):525-32.
 14. Welch KC, Thaler ER, Doghramji LL, Palmer JN, Chiu AG. The effects of serum and urinary cortisol levels of topical intranasal irrigations with budesonide added to saline in patients with recurrent polyposis after endoscopic sinus surgery. *Am J Rhinol Allergy*. 2010 Jan-Feb;24(1):26-8.
 15. Sachanandani NS, Piccirillo JF, Kramper MA, Thawley SE, Vlahiotis A. The effect of nasally administered budesonide respules on adrenal cortex function in patients with chronic rhinosinusitis. *Arch Otolaryngol Head Neck Surg*. 2009 Mar;135(3):303-7.
 16. Thamboo A, Manji J, Szeitz A, Santos RD, Hathorn I, Gan EC, et al. The safety and efficacy of short-term

- budesonide delivered via mucosal atomization device for chronic rhinosinusitis without nasal polyposis. *Int Forum Allergy Rhinol*. 2014 May;4(5):397-402.
17. Jang DW, Lachanas VA, Segel J, Kountakis SE. Budesonide nasal irrigations in the postoperative management of chronic rhinosinusitis. *Int Forum Allergy Rhinol*. 2013 Sep;3(9):708-11.
 18. Tysome J, Sharp H. Current trends in pre and postoperative management of functional endoscopic sinus surgery. *Int J Otorhinol* 2005; 5.
 19. Gevaert P, Calus L, Van Bruaene N, Van Zele T, Bachert C. Allergic sensitization, high local IL-5 and IgE predict surgical outcome 12 years after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. *J Allergy Clin Immunol* 2015; 135: AB238.
 20. Sanoussi M, N. ., Brahim, B. ., Derkaoui, A. ., Abdelkrim, S. ., & Mohammed, K. . (2022). Risk factors for sepsis in severe head trauma. *Journal of Medical Research and Health Sciences*, 5 (1), 1653–1657. <https://doi.org/10.52845/JMRHS/2022/5-1-3>
 21. Adappa ND, Wei CC, Palmer JN. Nasal irrigation with or without drugs: The evidence. *Curr Opin Otolaryngol Head Neck Surg* 2012; 20: 53-7.
 22. Rudmik L. High volume sinonasal budesonide irrigations for chronic rhinosinusitis: An update on the safety and effectiveness. *Adv Pharmacoepidemiol Drug Saf* 2014; 3: 148.
 23. Rotenberg BW, Zhang I, Arra I, Payton KB. Postoperative care for Samter's triad patients undergoing endoscopic sinus surgery: A double-blinded, randomized controlled trial. *Laryngoscope* 2011; 121: 2702-5.
 24. Kalish L, Snidvongs K, Sivasubramaniam R, Cope D, Harvey RJ. Topical steroids for nasal polyps. *Cochrane Database Syst Rev*. 2012 Dec;12:CD006549.
 25. Joe SA, Thambi R, Huang J. A systematic review of the use of intranasal steroids in the treatment of chronic rhinosinusitis. *Otolaryngol Head Neck Surg*. 2008 Sep;139(3):340-7.
 26. Khan, A. ., & Tidman, D. M. M. . . (2022). Causes of Medication Error in Nursing . *Journal of Medical Research and Health Sciences*, 5(1), 1753–1764. <https://doi.org/10.52845/JMRHS/2022-5-1-7>
 27. Dijkstra MD, Ebbens FA, Poublon RM, Fokkens WJ. Fluticasone propionate aqueous nasal spray does not influence the recurrence rate of chronic rhinosinusitis and nasal polyps 1 year after functional endoscopic sinus surgery. *Clin Exp Allergy*. 2004 Sep;34(9):1395-400.
 28. Lavigne F, Cameron L, Renzi PM, Planet JF, Christodoulouopoulos P, Lamkioued B, et al. Intranasal administration of topical budesonide to allergic patients with chronic rhinosinusitis following surgery. *Laryngoscope*. 2002 May;112(5):858-64.
 29. Kosugi EM, Moussalem GF, Simões JC, Rde PS, Chen VG, Neto S. Topical therapy with high-volume Budesonide nasal irrigations in difficult-to-treat chronic rhinosinusitis. *Braz J Otorhinolaryngol*. 2016;82(2):191–8.
 30. Kang TW, Chung JH, Cho SH, Lee SH, Kim KR, Jeong JH. The Effectiveness of Budesonide Nasal Irrigation After Endoscopic Sinus Surgery in Chronic Rhinosinusitis With Asthma. *Clin Exp Otorhinolaryngol*. 2017;10(1):91–6.
 31. Huang ZZ, Chen XZ, Huang JC, et al. Budesonide nasal irrigation improved Lund-Kennedy endoscopic score of chronic rhinosinusitis patients after endoscopic sinus surgery. *Eur Arch Otorhinolaryngol* 2019; 276: 1397-403.