European Archives of Oto-Rhino-Laryngology (2019) 276:1397–1403
https://doi.org/10.1007/s00405-019-05327-6

RHINOLOGY

Budesonide nasal irrigation improved Lund–Kennedy endoscopic score of chronic rhinosinusitis patients after endoscopic sinus surgery

Zi-zhen Huang[1] · Xian-zhen Chen[2] · Jian-cong Huang[1] · Zhi-yuan Wang[1] · Xia Li[1] · Xiao-hong Chen[1] · Xiao-ping Lai[1] · Li-hong Chang[1] · Ge-hua Zhang[1]

Received: 25 November 2018 / Accepted: 31 January 2019 / Published online: 20 February 2019

Abstract

Purpose Budesonide improves the prognosis of chronic rhinosinusitis (CRS). However, few reports have examined whether its use for nasal irrigation, compared to normal saline, improves the prognosis of patients after endoscopic sinus surgery (ESS). We compared the effects of nasal irrigation with budesonide and normal saline in CRS patients after ESS.

Methods Sixty CRS patients who had undergone ESS were randomly divided into an experimental group (30 patients), which used budesonide nasal irrigation, and a control group (30 patients), which used normal saline nasal irrigation. All patients received regular follow-up evaluations and were assessed via questionnaires, including the Lund–Kennedy endoscopic score (LKES), the symptom visual analog scale (VAS), the 22-item Sino-Nasal Outcome Test (SNOT-22), the Short-Form 36-Item Questionnaire (SF-36), the Self-Rating Anxiety Scale (SAS), the Self-Rating Depression Scale (SDS) and a side effects scale.

Results Scores of polyposis, mucosal edema, secretions and total score of LKES; VAS scores of nasal blockage, hyposmia and rhinorrhea; and SNOT-22 results in both groups were significantly improved 3 months after ESS. Scores of polyposis, mucosal edema, secretions and scarring and total score of LKES in experimental group were significantly better than in control group 3 months after ESS. No significant differences were observed in SF-36, SAS or SDS before or 3 months after ESS within or between the two groups. The side effects of the two groups were not significantly different.

Conclusions Nasal irrigation improved the prognosis of CRS patients after ESS. Budesonide nasal irrigation had a better effect than normal saline nasal irrigation.

Keywords Budesonide · Irrigation · Chronic rhinosinusitis · Prognosis · Endoscopy

Introduction

Chronic rhinosinusitis (CRS) is a chronic inflammation of the nose and the paranasal sinuses lasting 12 weeks or longer without complete resolution of symptoms [1]. It is a common health problem worldwide. In China, the overall prevalence of CRS is 8.0% [2], and in Europe and the USA, the overall prevalence is 10.9% [3] and 14% [4], respectively. CRS is strongly associated with asthma at all ages (adjusted OR: 11.85). In the absence of nasal allergies, CRS is positively associated with late-onset asthma [5].

As a severe health problem, CRS affects individual quality of life (QoL), societies and economies worldwide. The symptoms of CRS include nasal blockage, rhinorrhea, loss of smell, facial pain and symptoms derived from lower airway involvement; these symptoms significantly affect the QoL of patients and have negative effects on physical health,

Zi-zhen Huang and Xian-zhen Chen contributed equally to this article.

✉ Li-hong Chang
changlihong19840719@126.com

✉ Ge-hua Zhang
zhanggeh@mail.sysu.edu.cn

[1] Department of Otolaryngology-Head and Neck Surgery, The Third Affiliated Hospital of Sun Yat-sen University, No. 600, Tianhe Road, Guangzhou 510630, Guangdong, People's Republic of China

[2] Department of Otolaryngology-Head and Neck Surgery, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai 519020, Guangdong, People's Republic of China

sleep, social functioning, mental health and general health, leading to workplace absenteeism [6–8].

The goal of CRS treatment is to achieve and maintain clinical control after appropriate treatment (recommended medication and surgery). Although the majority of CRS patients can achieve control, some patients will not, and CRS has a high potential for recurrence even with maximal medical therapy and surgery [1]. This characteristic makes CRS a severe problem, and improving the prognosis of CRS patients is important and urgent.

We reviewed the literature and analyzed the effects of nasal irrigation with various solutions on the prognosis of patients with CRS after endoscopic sinus surgery (ESS). A total of 824 studies were included, and 5 were included in a systematic review. The effects of the following solutions for the treatment of the CRS patients (331 cases) after ESS were reviewed: lactated Ringer's solution-electrolyzed acid water, amphotericin B, hyaluronan plus saline and sulfurous–arsenical–ferruginous thermal water. Nasal irrigation with these five solutions was effective in CRS patients after ESS and significantly improved symptoms and nasal endoscopy scores. However, the results were not significantly different from those of normal saline use alone. Since normal saline is less expensive and safer, we concluded that normal saline was the first and best choice for nasal irrigation [9].

Nasal steroids play an important role in the postoperative management of patients with CRS. However, commercially available nasal steroid sprays may not deliver adequate amounts of medication to the entire postoperative nasal and sinus cavity because of polyposis, mucosal edema, secretions, scarring and crusting after ESS. Off-label use of budesonide nasal irrigation can theoretically deliver concentrated steroid solution to the entire postoperative nasal and sinus cavity through a high-pressure, high-volume system. Moreover, budesonide can remain in the sinus cavity for a long time and is the only topical corticosteroid that has been proven to improve the prognosis of CRS. Several studies have demonstrated the safety of budesonide nasal irrigation [10–14], but few reports have examined its efficacy and whether its use for nasal irrigation could improve the prognosis of CRS patients after ESS compared to normal saline.

We performed a study to compare the effects of nasal irrigation with budesonide and normal saline in CRS patients after ESS.

Materials and methods

This study was a prospective cohort analysis of prospectively collected data. All patients with or without polyps had undergone primary ESS for CRS by a single surgeon in our department between May 2017 and January 2018. CRS patients were divided into an experimental group and a control group via simple randomization according to a random number table. Surgery was unilateral or bilateral and consisted of removing all gross polyps and sufficiently widening the natural ostia of all affected sinuses to allow access for topical medications. The experimental group used topical corticosteroid (budesonide dissolved in normal saline) nasal irrigation and the control group used normal saline nasal irrigation. All patients were also prescribed conventional oral antibiotics, mucolytics, expectorants, nasal steroid sprays and antihistamines after ESS. Patients performed postoperative nasal irrigation once daily for 6 days postoperatively after the first cleaning of the nasal cavity and sinus, and each patient's medication records were reviewed. Only patients who used budesonide or normal saline nasal irrigation therapy for 3 months while complying with oral antibiotic, nasal steroid spray, mucolytic, expectorant and antihistamine use were included in the study. The Lund–Kennedy endoscopic score (LKES), visual analog scale (VAS) of CRS symptoms, 22-item SinoNasal Outcome Test (SNOT-22) results, Short-Form 36-Item Questionnaire (SF-36) results, Self-Rating Anxiety Scale (SAS) scores, Self-Rating Depression Scale (SDS) scores and reported CRS-related absenteeism were recorded pre- and postoperatively for all patients. All patients underwent regular follow-up evaluations after ESS and provided VAS scores of CRS symptoms, LKES and scale assessments. In addition, we recorded the side effects, including a nasal burning sensation, nasal itching, nasal pain, epistaxis, headache, ear pain, cough, nausea and vomiting, postnasal drip, aural fullness and dizziness. We performed a paired parametric statistical analysis (Student's *t* test) to compare outcomes for all visits. Any visit in which a patient reported no use of budesonide nasal irrigation or normal saline nasal irrigation was categorized as "without nasal irrigation" and was not included in the analysis. This prospective cohort study was approved by the Medical Ethics Committee at the Third Affiliated Hospital of Sun Yat-sen University. In our practice, most CRS patients are prescribed short-term conventional oral antibiotics, mucolytics and expectorants and a long-term regimen consisting of nasal saline irrigation, nasal steroid sprays and antihistamines.

Statistical analysis

Statistical analysis was performed with IBM® SPSS Statistics version 20.0 (IBM SPSS, Armonk, NY). Demographic and clinical data are expressed as the means and SDs, and other data are expressed as the means and SEMs. Student's *t* test, the rank-sum test and the Mann–Whitney *U* test were used to compare groups. Significance was defined at the $P < 0.05$ level.

Results

There were 30 patients in the experimental group and 30 patients in the control group.

Demographic and clinical data

No differences were observed between the groups regarding gender, age, allergic history, lateral or bilateral surgery and eosinophil percentage and count in peripheral blood (Table 1).

Lund–Kennedy endoscopic score (LKES)

Scores for polyposis, mucosal edema, secretions, scarring and the total score (except crusting) of LKES in the experimental group were significantly different before and after ESS (Table 2).

Scores of polyposis, mucosal edema and secretions and the total score (except crusting and scarring) of LKES were also significantly different before and after surgery in the control group (Table 2).

No significant differences were observed in the LKES between the experimental and control groups before ESS.

Scores of polyposis, mucosal edema, secretions and scarring and the total score (except crusting) of LKES were significantly better in the experimental group than in the control group at 3 months after ESS (Table 3).

VAS scores of symptoms

In the experimental group, the postoperative VAS scores for nasal blockage, hyposmia and rhinorrhea were significantly better than their preoperative VAS scores (Table 4); however, the VAS score for facial pain was not significantly different.

In the control group, the postoperative VAS scores for nasal blockage, hyposmia, rhinorrhea and facial pain were significantly better than the preoperative VAS scores (Table 4).

No significant differences were found in the VAS scores for nasal blockage, hyposmia, rhinorrhea or facial pain between the two groups before or after ESS (Table 5).

SNOT-22 scores

The SNOT-22 scores of the experimental and control groups were both significantly improved after ESS compared to the preoperative values (Table 6).

The SNOT-22 scores were not significantly different between the two groups before or after ESS (Table 6).

SF-36, SAS and SDS

No significant differences were observed in the SF-36, SAS or SDS scores before or 3 months after ESS within or between the experimental and control groups.

Side effects

The side effects were not significantly different between the two groups (Fig. 1).

Discussion

Corticosteroids are mainstays of treatment and the most effective drugs for treating CRS [15]. A meta-analysis concluded that compared to the control treatment, intranasal corticosteroids significantly reduced the size of nasal polyps. Long-term treatment with intranasal corticosteroids was recommended for patients with mild-to-severe disease both before and after ESS [16]. In our practice, most CRS patients are prescribed long-term nasal steroid sprays.

The effects of topical therapy on the sinus mucosa rely on the delivery technique, delivery device, fluid dynamics (volume, pressure, position) and surgical state of the nasal and sinus cavity. Distribution of topical solution to the sinus cavity is limited before ESS [17], and in the setting of CRS with mucosal edema, the distribution of topical solution is probably less than 2% of the total irrigation volume [18].

Table 1 Demographic and clinical data of the experimental and control groups

	Experimental group ($n=30$)	Control group ($n=30$)	P value
Gender (male), N (%)	21 (70%)	18 (60%)	0.589
Age (years, $\bar{x}\pm s$)	37.15 ± 8.623	38.10 ± 15.579	0.929
Allergic history (yes, %)	1 (3.33%)	2 (6.66%)	1.000
Percentage of eosinophils in the peripheral blood (%, $\bar{x}\pm s$)	0.05 ± 0.037	0.03 ± 0.026	0.172
Eosinophil count in peripheral blood ($\times10^6$, $\bar{x}\pm s$)	286 ± 153.770	256 ± 166.725	0.472
Lateral or bilateral surgery (lateral, %)	7 (23.3%)	9 (30%)	0.771

Table 2 Lund–Kennedy endoscopic score of the control and experimental groups before and 3 months after endoscopic sinus surgery(ESS) ($\bar{x}\pm s$)

	Control group						Experimental group					
	Polyposis	Mucosal edema	Secretions	Scarring	Crusting	Total	Polyposis	Mucosal edema	Secretions	Scarring	Crusting	Total
Before ESS	1.40 ± 1.566	2.26 ± 1.014	2.16 ± 1.053	0.06 ± 0.365	0.00 ± 0.000	5.90 ± 2.975	1.80 ± 1.323	2.36 ± 0.850	2.10 ± 1.295	0.00 ± 0.00	0.06 ± 0.365	6.33 ± 2.324
After ESS	0.26 ± 0.827	0.83 ± 1.176	0.46 ± 1.008	0.23 ± 0.626	0.16 ± 0.530	1.96 ± 2.822	0.10 ± 0.402	1.26 ± 1.048	0.96 ± 1.129	0.36 ± 0.764	0.13 ± 0.434	2.83 ± 1.782
t value	3.659	5.487	6.353	− 1.223	− 1.720	6.388	6.353	4.469	5.321	− 2.626	− 0.812	7.273
P value	0.001	0.000	0.000	0.231	0.096	0.000	0.000	0.000	0.000	0.040	0.313	0.000

With sinus penetration of no more than 3%, nebulization is also ineffective [19]. ESS has been proven essential to and can improve the effective delivery of topical medications into the sinus cavity [20, 21]. Nebulizers poorly penetrate the sinuses even after maximal ESS [22]; however, large-volume spray bottles and passive flow devices appear to have the best efficacy after ESS [17, 20–22].Pre-ESS, the distribution to the sinuses is extremely limited regardless of the device [17, 18, 23], and sprays are the least effective method [17]. Simple low-volume sprays and drops have very poor distribution and should be considered for nasal cavity treatment only, especially before ESS [17]. Less than 50% of most low-volume applications reach even the middle meatus, although multiple devices and head positions have been examined [24]. There are limited data on the exact volume required to allow complete distribution. The post-ESS distribution is superior due to the use of high-volume and high positive-pressure devices [17, 18, 23]. In recent years, topical nasal steroids have been increasingly delivered via high-volume saline irrigations (typically 240 mL), specifically in the post-ESS patient group.[11] High-volume and positive-pressure irrigation are likely to result in optimal distribution, according to current research. High volumes appeared to penetrate both the maxillary and frontal sinuses with good coverage starting at approximately 100 mL [25]. The frontal and sphenoid sinuses are not accessed well by pressurized sprays, as opposed to high-volume devices such as squeeze bottles or neti pots [17].

Several formulations of concentrated nasal irrigations consisting of budesonide repulse mixed with normal saline that can be delivered in high volumes through a high-pressure system after ESS have been reported, and they have shown no significant effect on the hypothalamic–pituitary–adrenal axis (HPAA), even with long-term use [12–14]. However, Neubauer et al. had proved patients treated with budesonide(received budesonide respules via a mucosal atomization device twice daily) after ESS for CRSwNP had greater improvement in SNOT-22 and LKES compared to fluticasone [26]. Studies on the effects of the addition of budesonide nasal irrigation to the postoperative management of patients with CRS are rare and controversial. A randomized placebo-controlled trial by Rotenberg et al. [27] that used budesonide nasal irrigation in 60 Samter's triad patients after surgery found no advantage over a placebo at 1 year. In contrast, a large case series by Snidvongs et al. [28] reported great improvement of QoL and endoscopy outcomes in 111 patients who used budesonide or betamethasone nasal irrigations postoperatively. Unlike the study by Rotenberg et al., Snidvongs et al., prescribed high-volume (240 mL) nasal irrigations delivered into large, unobstructed nasal and sinus cavities. Jang et al. [10] also showed that the use of budesonide nasal irrigation after ESS may help to improve both subjective and objective outcomes in patients with CRS.

Table 3 Lund–Kennedy endoscopic score of the experimental and control groups 3 months after endoscopic sinus surgery ($\bar{x} \pm s$)

	Polyposis	Mucosal edema	Secretions	Scarring	Crusting	Total
Experimental group	0.10 ± 0.402	1.26 ± 1.048	0.96 ± 1.129	0.36 ± 0.764	0.13 ± 0.434	2.83 ± 1.782
Control group	0.26 ± 0.827	0.83 ± 1.176	0.46 ± 1.008	0.23 ± 0.626	0.16 ± 0.530	1.96 ± 2.822
Z value	− 4.867	− 4.691	− 4.706	− 2.025	− 1.009	− 2.599
P value	0.000	0.000	0.000	0.040	0.313	0.009

Table 4 VAS scores of symptoms of the control and experimental groups before and 3 months after endoscopic sinus surgery(ESS) ($\bar{x} \pm s$)

	Control group				Experimental group			
	Nasal blockage	Hyposmia	Rhinorrhea	Facial pain	Nasal blockage	Hyposmia	Rhinorrhea	Facial pain
Before ESS	5.73 ± 3.947	4.60 ± 4.039	3.06 ± 3.759	1.46 ± 2.445	5.60 ± 3.489	3.63 ± 3.605	3.13 ± 2.873	1.16 ± 2.018
After ESS	1.23 ± 1.546	2.30 ± 3.405	1.00 ± 1.893	0.40 ± 1.037	1.46 ± 1.995	1.30 ± 2.451	1.13 ± 1.455	0.50 ± 1.224
t value	6.796	2.968	3.509	2.587	6.194	3.034	5.022	1.670
P value	0.000	0.006	0.001	0.015	0.000	0.005	0.000	0.106

Table 5 VAS scores of symptoms of the experimental and control groups before and after endoscopic sinus surgery (ESS) (Mann–Whitney *U* test)

Group	Before ESS				After ESS			
	Nasal blockage	Hyposmia	Rhinorrhea	Facial pain	Nasal blockage	Hyposmia	Rhinorrhea	Facial pain
Experimental	5.60 ± 3.489	3.63 ± 3.605	3.13 ± 2.873	1.16 ± 2.018	1.46 ± 1.995	1.30 ± 2.451	1.13 ± 1.455	0.50 ± 1.224
Control	5.73 ± 3.947	4.60 ± 4.039	3.06 ± 3.759	1.46 ± 2.445	1.23 ± 1.546	2.30 ± 3.405	1.00 ± 1.893	0.40 ± 1.037
Z value	− 0.194	− 0.840	− 0.785	− 0.313	− 0.322	− 1.186	− 1.181	− 0.074
P value	0.846	0.401	0.432	0.754	0.748	0.235	0.238	0.941

Table 6 SNOT-22 scores of the experimental and control groups before and after endoscopic sinus surgery (ESS) ($\bar{x} \pm s$)

Group	Before ESS	After ESS	*t* value	*P* value
Experimental	31.16 ± 19.142	13.26 ± 12.108	5.719	0.000
Control	34.16 ± 20.671	13.53 ± 8.889	6.669	0.000
t value	− 0.583	− 0.097	–	–
P value	0.562	0.923	–	–

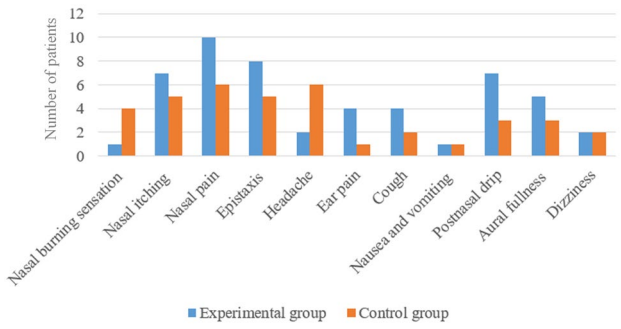

Fig. 1 Side effects in the experimental and control groups

A meta-analysis studied by Yoon et al. [29] revealed that although steroid nasal irrigation would not induce adverse effects related to systemic steroid absorption, the beneficial effects of additional steroids in saline irrigation were ambiguous in regard to endoscopic score and CRS-related QOL improvement compared with saline alone irrigation and they concluded that further clinical trials with robust research methodologies should be conducted to confirm the results of their study. We found that nasal irrigation with budesonide and normal saline improved the prognoses of patients with CRS after ESS. Scores of polyposis, mucosal edema, secretions and scarring and the total score of LKES in the budesonide nasal irrigation group were significantly decreased after ESS. Budesonide nasal irrigation, which significantly improved LKES, had a better therapeutic effect than nasal irrigation with normal saline.

Long-term use of budesonide nasal irrigations (with a mean duration of 22 months) was generally safe, but asymptomatic HPAA suppression may occur in selected patients. Concomitant use of nasal steroid sprays and pulmonary steroid inhalers with daily budesonide nasal irrigations was associated with an increased risk of HPAA suppression, and rhinologists should be alerted to this finding [11].

The nasal mucosa will mostly recover within 3 months after ESS in most patients, which will decrease the burden of polyposis, mucosal edema, secretions, scarring and crusting of the nasal cavity and sinus, improving the efficacy of topical nasal steroid sprays. Moreover, use of topical nasal steroid sprays is simpler and more convenient for patients, leading to better compliance. Therefore, the patients in our study used budesonide nasal irrigation for only 3 months after ESS, and this short-term use likely did not cause HPAA suppression. Nasal irrigation may cause side effects because of the high delivery volume and pressure, incorrect delivery technique and position, and the surgical state of the nasal and sinus cavity. During this study, we recorded side effects, including nasal burning sensations, nasal itching, nasal pain, epistaxis, headache, ear pain, cough, nausea and vomiting, postnasal drip, aural fullness and dizziness, but there were no differences in the side effects of the two groups.

Both budesonide and normal saline nasal irrigation improved the prognoses of patients with CRS after ESS. Nasal irrigation with budesonide significantly improved LKES and had a better therapeutic effect than nasal irrigation with normal saline. However, budesonide nasal irrigation increased the financial burden of patients, and its long-term use may cause HPAA suppression.

Acknowledgements We thank Xi-fu Wu, Luo-ying Yang and Shuai-xiang Li for their help in collecting and processing clinical specimens.

Funding This study was supported by the Program of the National Natural Science Foundation of China (NSFC 81371073, 81670913), the Science and Technology Planning Project of Tianhe District, Guangzhou, Guangdong Province, China (201409KW027), and Medical Scientific Research Foundation of Guangdong Province (A2015312).

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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