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CLINICAL TRIAL REPORT

Clinical Observation of Hydrogen-Rich Saline for Nasal Irrigation After Surgery for Chronic sinusitis: A Randomized, Double-Blind, Controlled Trial

Ling Jin[1,2,*], Kai Fan[1,2,*], Chunyan Yao[1,*], Yongjun Chang[1], Yang Wang[1], Jiawei Lu[1], Shaoqing Yu[1,2]

[1]Department of Otolaryngology, Tongji Hospital, School of Medicine, Tongji University, Shanghai, 200065, People's Republic of China; [2]Department of Allergy,Tongji Hospital, School of Medicine, Tongji University, Shanghai, 200065, People's Republic of China

*These authors contributed equally to this work

Correspondence: Shaoqing Yu, Department of Otolaryngology, Tongji Hospital, School of Medicine, Tongji University, 389 Xincun Road, Putuo District, Shanghai, 200065, People's Republic of China, Tel/Fax +8602166111042, Email yu_shaoqing@163.com

Purpose: The treatment of chronic rhinosinusitis (CRS) is often a difficult and long-term behavior, so it is necessary to seek a local treatment method that can be used for a long time, and is safe and effective. Nasal saline irrigation after functional endoscopic sinus surgery (FESS) is currently recognized as a local treatment method, but it has no anti-inflammatory, anti-damage, and healing-promoting functions. To investigate the efficacy and safety of hydrogen-rich saline (HRS) for nasal irrigation after CRS surgery.

Patients and Methods: A total of 61 patients after CRS completed the study. Subjects were randomly assigned to rinse the nasal cavity with HRS or normal saline (NS) after CRS. Participants were followed up once a week for 12 times, and were evaluated with visual analogue score (VAS), 22-item Sinonasal Outcomes Test (SNOT-22), and Lund-Kennedy endoscopy scores (LKES). The primary outcome was the VAS score of patients.

Results: After 12 weeks of follow-up, the VAS scores of both groups decreased, and the HRS group (0.52±0.85) was lower than the NS group (1.47±1.55), P=0.005. The total number of cases with complete control (clinical cure) in the short-term efficacy evaluation was more in the HRS group (20/31) than in the NS group (11/30), P=0.03<0.05. No obvious adverse reactions occurred in the two groups during the follow-up.

Conclusion: This study found that HRS was more effective than NS alone in nasal irrigation after CRS surgery, and could shorten the time of nasal mucosal healing and epithelialization, with a higher rate of recent complete control.

Keywords: physiological saline, hydrogen -rich saline, nasal irrigation, chronic rhinosinusitis, endoscopic sinus surgery

Introduction

Chronic rhinosinusitis (CRS) is a prevalent and refractory disease in otorhinolaryngology head and neck surgery, significantly impacting patients' daily life and health. It is a heterogeneous disease with a prevalence of 6%-27.1%,[1] negatively affecting patients' quality of life. Recent epidemiological data show that the incidence of CRS is increasing.[2] Although nasal endoscopic surgery is currently recognized as effective treatment for CRS, clinical practice has shown that surgery is only the beginning of the overall process of treating CRS. Clinical practice has shown that it only removes lesions, restores nasal ventilation and sinus drainage, while chronic inflammation cannot be immediately improved without surgery, leading to inflammatory secretions still being produced. Nasal mucosal injury caused by surgery can form cellulose pseudomembrane and blood scab, resulting in postoperative reactive mucosal edema, granulation growth, vesicles and mucociliary dysfunction causing inflammatory secretion retention. Failure to remove secretions, pseudo-membrane, blood scab or postoperative nasal packings will affect nasal ventilation, sinus drainage and nasal mucosal repair leading to surgical cavity adhesion or even disease recurrence over time. Therefore good follow-up treatment after

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surgery is key to cure; however long systemic treatment cycles after sinus surgery coupled with patient discomfort from endoscopic local treatments during follow-up lead to poor patient compliance which affects final efficacy.

Nasal irrigation has been recognized as a simple and easy treatment method in the guidelines for the diagnosis and treatment of CRS,[1,3,4] which can be applied both non-surgically and post-operatively. Timely and effective postoperative nasal irrigation is beneficial to the clean and moist of the nasal cavity, the ejection of secretions, the regression of mucosal edema, and the improvement of the function of the nasal and sinonasal mucociliary system, so as to improve the function of the sinuses and nasal cavity.[5–7] However, the common postoperative nasal irrigation solution is hypertonic and isotonic saline,[1] which mainly cleans secretions and scabs through physical action, without good anti-inflammatory effect, and lacks help for the physiological function recovery of nasal mucosa. In addition, the irrigation solution mixed with hormones, antibiotics or other various components,[8–13] their effective components have a very limited time of retention in the nasal cavity, resulting in insufficient absorption. Local use of antibiotics is easy to cultivate bacterial resistance, and long-term use of corticosteroid has the risk of systemic side effects and other disadvantages. Therefore, local treatment of postoperative anti-inflammation and conducive to the recovery of mucosal function is still an important direction of clinical CRS treatment research.

Medical research around hydrogen has become a hot spot of international research. Many studies have confirmed that hydrogen has rich biological effects. Hydrogen molecule is the smallest and simplest molecule in nature, with strong dispersion, which can easily penetrate the skin and mucosa and enter the cells, nucleus and mitochondria, and is easy to be absorbed and utilized by the human body. Hydrogen has the effects of antioxidant, anti-inflammatory and anti-damage, and can selectively remove oxygen free radicals, maintain the balance of internal environment inside and outside the cell, maintain the body's good immunity and enhance the self-repair ability, so as to improve symptoms and improve allergic physique.[14–20] In recent years, our team has carried out related research on irrigating the nasal cavity with hydrogen-rich saline. Basic and clinical studies in this field have achieved some results.[21–24] It has been confirmed that irrigating the nasal cavity with hydrogen-rich water is effective and safe for allergic rhinitis and chronic rhinitis in both rhinitis mice and rhinitis subjects. Based on the inseparable link between chronic sinusitis and chronic rhinitis in pathogenesis and pathological changes, We hypothesize to promote nasal irrigation with hydrogen-rich saline to the local treatment of CRS and observe whether it is also effective and safe. This study used HRS for nasal irrigation in patients with CRS after surgery, compared with irrigation with NS alone, to observe whether it is more beneficial to the postoperative management of CRS.

Material and Methods

Study Design and Eligibility Criteria

This is a randomized double-blind controlled clinical trial. Recruitment and follow-up work was conducted from January 17, 2022 to March 7, 2024. The follow-up time of this study was 12 weeks. According to the sample size estimate results of the study protocol, a total of 64 CRS patients who needed nasal endoscopic surgery in the Department of Otolaryngology of our hospital were selected and divided into two groups according to the random number table method, with 32 cases in each group. The experimental group was treated with HRS postoperatively, while the control group was treated with NS postoperatively (Figure 1). The inclusion criteria were in accordance with the guidelines:[1] patients diagnosed with chronic sinusitis (with or without nasal polyps) and requiring surgical treatment, aged over 18 years, male or female. The enrolled patients had good compliance and could cooperate with follow-up examinations and treatments. Patients with previous sinus surgery, fungal sinusitis, nasal sinus tumors, and severe heart, liver, kidney, and other diseases were excluded from this study. This study was registered and approved by the Chinese Clinical Trial Registry on February 3, 2020 (ChiCTR2000029538). The study was approved by the hospital ethics committee (2021-KYSB-188), and all patients signed informed consent.

Randomization and Blinding

The study adopted a randomized double-blind parallel controlled method. Statistical experts used SAS8.2 professional statistical software to generate group random numbers, which were divided into two groups. According to the group

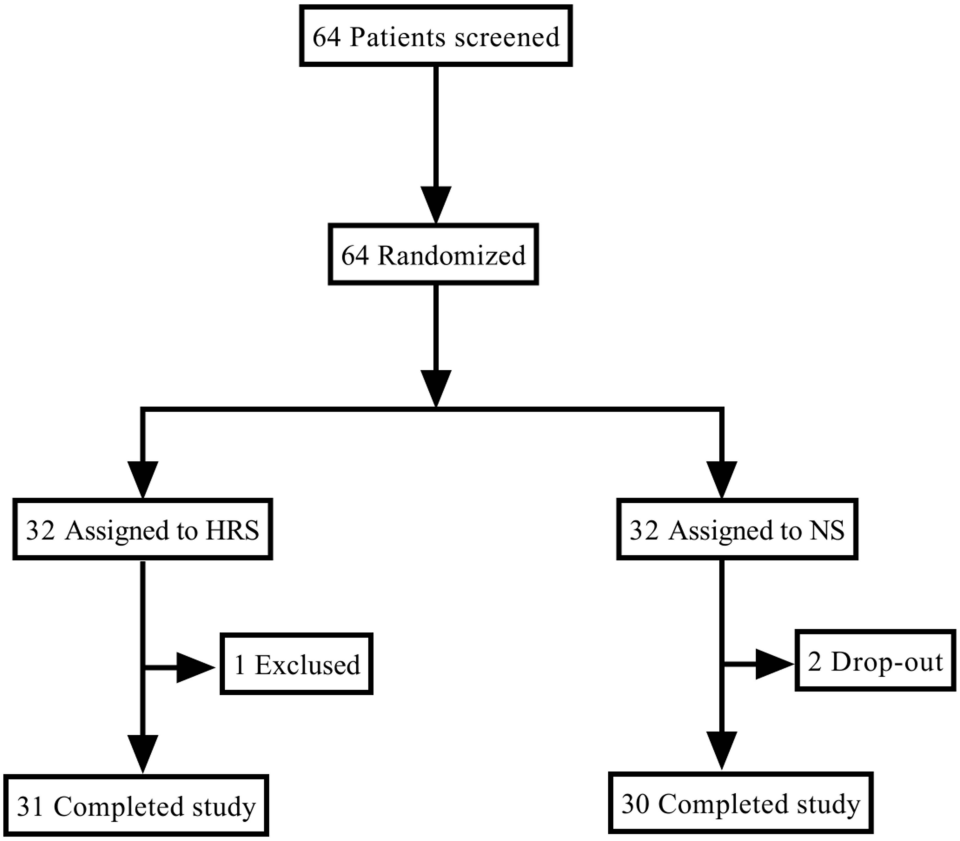

Figure 1 Flow Diagram for Randomized, Double-blind, Controlled Trial.

random numbers, the blinding of drugs (two kinds of irrigating fluids) was completed, and the random number was the drug number. The ratio of cases in the experimental group and the control group was 1:1. The enrolled subjects were randomly assigned according to the random number table, and the clinical study group was treated first. The preparation and distribution of irrigating fluids were performed by specialized nurses, and the outer packaging of irrigating fluids was the same. The doctors responsible for follow-up observation after surgery and the subjects did not know which irrigating fluids were used (were blinded).

Study Intervention

All patients were operated by the same group of doctors in strict accordance with the principles of functional nasal endoscopic surgery, open the diseased sinuses, remove polyps and irreversible diseased mucosa, and drain smoothly, try to retain normal mucosa, middle turbinate and other normal tissue structures, and for those with severe nasal septum deviation, vesicular middle turbinate, inferior turbinate hypertrophy and other abnormalities causing nasal stenosis and poor ventilation, corresponding surgery was also performed at the same time. The absorbable hemostatic materials filled in the nasal cavity were cleaned daily with negative pressure from the third day after surgery, and the nasal cavity was washed from the first week after surgery.

One week after the operation, the rinse solution was distributed by a special person (nurse) according to a random number table to ensure the double blindness of patients and observation doctors. The experimental group used HRS, 100mL sterile saline bag filled with pure hydrogen to reach saturation state (hydrogen concentration > 0. 6 mmol/L),[25,26] sealed and stored at 4 °C refrigerator. The control group used NS, 100mL sterile saline bag. The patients were asked to place the rinse solution at room temperature and pour it into the nasal washing pot every day, rinse 1 time in the morning and evening each day, and 100mL of rinse solution was used in each surgical side of the nasal cavity every time. During the rinse, the body was inclined forward by 30°, the head was bowed, the mouth was opened, and the rinse process was

not swallowed. Gently squeezed the rinse pot (pay attention to prevent excessive pressure causing ear discomfort), so that the liquid was slowly flushed through the nasal cavity and sinuses, and finally spit out from the mouth.

The combined medication of the two groups was unified after operation: intravenous cephalosporin antibiotics and dexamethasone were given within one week after operation; macrolide antibiotics and mucus-dissolving discharge agents were given orally for 4 weeks after discharge;medications for other chronic diseases (such as antihypertensive drugs and hypoglycemic drugs) were recorded.

The nasal endoscopic examination was performed by two fixed doctors weekly from the first week after surgery to observe the nasal mucosal vesicles, edema and opening of the sinus, and to clean the secretions, residual hemostatic materials, blood scabs, vesicles and granulations in the surgical cavity, and to separate the adhesive band.

Research Follow-Up Process

Two groups of patients initiated nasal irrigation one week after the surgery and were followed up once a week for a total of 12 weeks. The patients were evaluated by the observing physician based on the assessment indicators. The primary endpoints were the overall assessment of the disease condition and the evaluation of the main nasal symptoms. The secondary endpoints were the nasal endoscopy examination score, the nasal outcome scale score, the epithelialization time of the surgical cavity, and the short-term complete remission rate. (Figure 2).

Clinical Assessment

The Primary End Points

The visual analogue scale (VAS) score was used to evaluate the degree of distress of nasal congestion, runny nose, head and face pain, and hyposmia on a VAS (Score scale10cm), as well as the overall VAS score of the disease. Patients were assessed before surgery and at weekly follow-up after surgery.

The Secondary End Point

(1) Lund–Kennedy endoscopic score (LKES):Nasal endoscopic examination was performed preoperatively and weekly after one week, and the Lund-Kennedy nasal endoscopic examination quantitative score was used to evaluate the mucosal morphology and lesions in the nasal cavity,[1,27] such as the size of polyps, mucosal edema, scars, and nasal scabs preoperatively and postoperatively. Specific scoring method: polyps (no polyps score 0, polyps only in the middle nasal passage score 1, polyps beyond the middle nasal passage score 2), edema (no edema score 0, mild score 1, severe score 2), nasal leakage (no nasal leakage score 0, clear and thin nasal leakage score 1, thick and purulent nasal leakage score 2), scar (no scar score 0, mild score 1, severe score 2), scab (no scab score 0, mild score 1, severe score 2), each side score 0~10, take the sum of bilateral scores as the final score, total score 0~20.

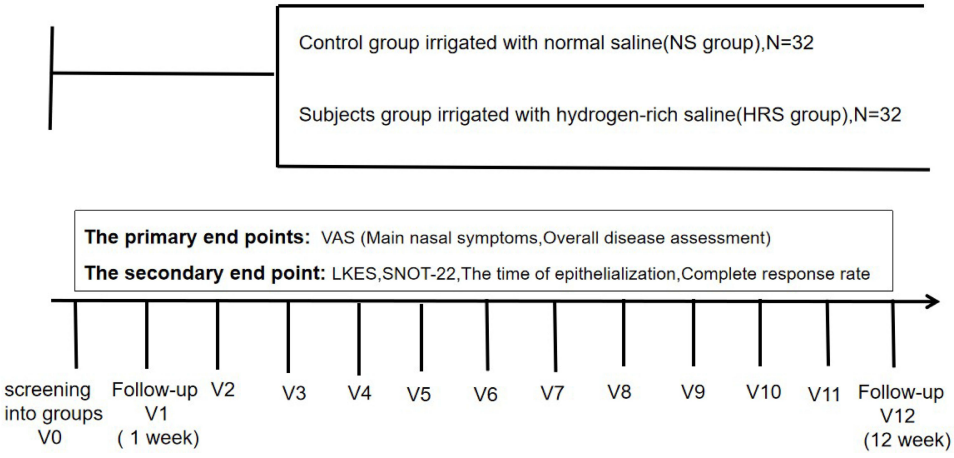

Figure 2 The flowchart for the research follow-up process.

(2) 22-item Sino-Nasal Outcome Test (SNOT-22)[28,29]: It is a validated and highly specific outcome measure for chronic sinusitis that covers sinus symptoms and related quality of life scores. The questionnaire is completed preoperatively and at the final follow-up visit. It includes 22 quality-of-life items, each with a score of 0 to 5, and the total score ranges from 0 to 110, with higher total scores indicating greater symptom severity.
(3) Evaluation of surgical cavity epithelial repair: The time required for complete epithelialization of the surgical cavity (weeks) was observed after the operation.
(4) Short-term efficacy evaluation: The number of patients in the two groups who achieved the "complete control criteria" in the guideline for efficacy evaluation during the observation period was recorded. The complete control criteria were: symptoms disappeared, VAS total score was 0, LKES score was no more than 1, sinus opening was well opened, no obvious secretion, sinus mucosal edema subsided, and epithelialization was well.1

Safety Indicators

The main observation was the adverse reactions after irrigation, such as nasal symptoms and other discomforts, and the correlation with irrigation was evaluated.

Statistical Analysis

SAS9.4 statistical software was used to process the data. The measurement data were expressed as mean ± standard deviation (x-±s), and the two independent sample *t* test (normal and homogeneous variance), corrected *t* test (normal but heterogeneous variance) or two independent sample rank sum test (skewed distribution) were used for comparison between groups; the frequency and percentage of counting data were expressed as chi-square test, corrected chi-square test or exact probability method were used for comparison between groups. Repeated measurement data could be analyzed by covariance analysis. $P<0.05$ was considered statistically significant.

Results

Baseline Comparison of the Two Groups

A total of 64 patients with chronic sinusitis were enrolled in this study (32 cases in each group), and 61 patients completed the trial, with 3 patients dropping out or quitting (1 case in HRS group and 2 cases in NS group). One patient was excluded due to nasal septum infection 1 week after the operation (before nasal irrigation), and the other two patients were lost to follow-up due to personal reasons, with an overall dropout rate of 4.69%. The grouping process and completion of the study are shown in Figure 1. There were no significant differences in baseline indicators between the two groups, including gender, age, disease duration, affected side, polyps, preoperative VAS score of general feeling (including VAS score of four nasal symptoms), preoperative SNOTT-22 score, and LKES ($P>0.05$), as shown in Table 1. Both groups were operated on by the same group of physicians, and the postoperative medications were unified.

Table 1 Baseline Demographic and Disease Characteristics of Randomized Participants

	HRS group (n=31)	NS group (n=30)	Statistic	P	Method
Age (years)	53.65(14.42)	57.33(16.74)	−0.923	0.360	*T* test
Sex					
Male	21(67.7%)	18(60.0%)	0.396	0.529	Chi-square test
Female	10(32.3%)	12(40.0%)			
Side					
Left	4(12.9%)	6(20.0%)	0.621	0.733	Likelihood-ratio chi-square
Right	4(12.9%)	3(10.0%)			
Bilateral	23(74.2%)	21(70.0%)			
With polyps					
Yes	19(61.3%)	17(56.7%)	0.135	0.714	Chi-square test
No	12(38.7%)	13(43.3%)			

(*Continued*)

Table 1 (Continued).

	HRS group (n=31)	NS group (n=30)	Statistic	P	Method
Course of disease (month)	59.81(91.34)	72.80(105.67)	−0.514	0.609	*T* test
VAS					
Overall feeling of illness	7.68(1.25)	7.37(1.63)	0.838	0.406	
Nasal obstruction	7.84(1.24)	7.20(1.75)	1.649	0.105	
Nasal discharge	7.10(1.56)	6.40(1.96)	1.541	0.129	
Head and face pain	4.43(2.60)	4.43(2.60)	0.265	0.792	
Hyposmia	4.45(3.11)	4.90(2.64)	−0.606	0.547	
SNOTT-22 score	26.71(11.58)	27.57(13.15)	−0.270	0.788	
LKES	6.74(2.54)	7.17(3.08)	−0.589	0.558	

Abbreviations: HRS, Hydrogen-rich saline; NS,normal saline; VAS, visual analogue score; SNOT-22-22, tem Sinonasal Outcomes Test; LKES,Lund-Kennedy endoscopy scores.

Primary Outcome

VAS Score of Overall Feeling of Illness

After 12 weeks of nasal irrigation treatment, the scores of the two groups decreased from baseline, from 7.68 (1.25) to 0.52 (0.85) in the HRS group, and from 7.37 (1.63) to 1.47 (1.55) in the NS group, with a more significant decrease in the HRS group (P=0.005<0.05), as shown in Figure 3A. Furthermore, a dynamic comparison of the scores of the two groups was conducted during the 12-week follow-up. Since the second week, the weekly VAS scores of the HRS group were lower than those of the NS group, with a statistically significant difference (P<0.001), as shown in Figure 3B.

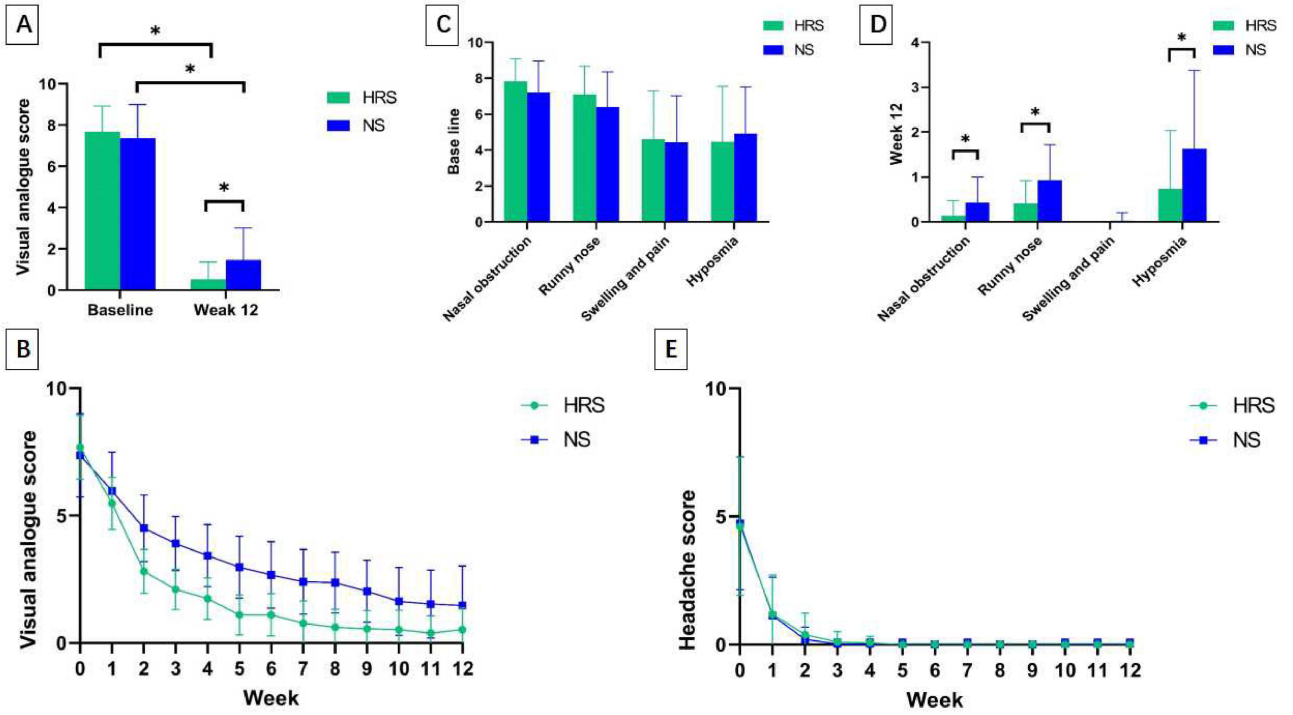

Figure 3 Comparison of the main evaluation indicators between the two groups. (**A**) The VAS score of the overall feeling of the disease decreased significantly in the HRS group after 12 weeks, (**B**) and from the dynamic analysis of 12 weeks, it was obvious that the HRS group decreased significantly compared with the NS group since the second week; (**C**) there was no difference in the VAS of the four nasal symptoms between the two groups before treatment; (**D**) after 12 weeks, except for the head and face swelling pain, there was no significant difference between the two groups, and the other three were significantly decreased in the HRS group, all P<0.05*; (**E**) the dynamic analysis of the change of headache in 10 weeks showed that the two groups decreased significantly since the first week after the operation, and there was no significant difference in 12 weeks.

Single VAS Score of Nasal Symptoms in the Two Groups

After treatment, the scores of both groups decreased, except for head and face swelling pain (P=0.326>0.05), the other three symptom scores of HRS group decreased significantly, with significant differences (all P<0.05), as shown in Figure 3C and D. Further dynamic analysis of headache symptoms showed that the scores of both groups decreased significantly since the first week after treatment, with no significant differences (all P>0.05), as shown in Figure 3E.

Secondary Outcomes

SNOTT-22 and LKES

After 12 weeks of irrigation treatment, the SNOTT-22 scores of the two groups decreased from baseline, and the HRS group decreased from 26.71 (11.58) to 0.97 (1.38), which was significantly lower than that of the NS group (P<0.001), as shown in Figure 4A. The LKES score of the HRS group also decreased significantly compared with that of the NS group (P=0.015<0.05), as shown in Figure 4B. Further dynamic analysis of the 12-week period showed that the score of the HRS group was significantly lower than that of the NS group from the second week (P<0.001), as shown in Figure 4C.

Comparison of postoperative epithelial repair time and clinical recovery (complete control of the disease) rate within 3 months after surgery between the two groups

The epithelialization time of the two groups was 6.61 (2.00) weeks in the HRS group and 9.97 (1.59) weeks in the NS group, which was shorter in the HRS group than in the NS group, with a statistically significant difference (P<0.001), as shown in Figure 4D. The number of cases reaching clinical recovery within 3 months was higher in the HRS group than in the NS group, indicating a statistically significant difference in the complete control rate of the disease within 3 months between the two groups (P=0.03 <0.05), as shown in Table 2.

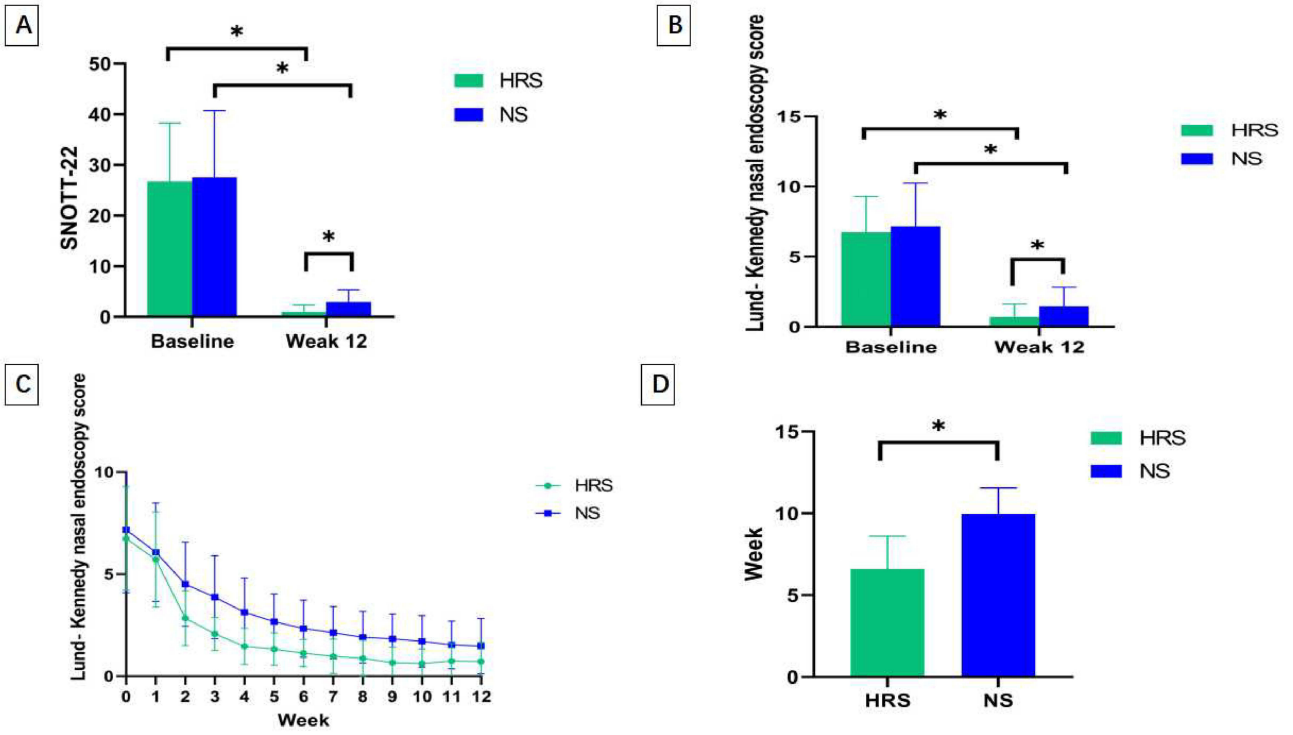

Figure 4 Comparison of secondary evaluation indicators between two groups. (**A** and **B**) After 12 weeks of treatment, the secondary indicators SNOT-22 and LKES were significantly improved in both groups. (**C**) The dynamic analysis of LKES at 12 weeks showed that the HRS group had a significant decrease compared with the NS group since the second week, and the difference was significant. (**D**) The time for complete epithelialization of the surgical cavity was shorter in the HRS group, P<0.001*.

Table 2 Comparison of Operative Cavity Epithelialization Time After Nasal Irrigation and Clinical Recovery Rate Within 3 Months

Group	Number of cases with complete disease control within 3 months (Number)	
	Yes	No
HRS group (n=31)	20(64.5%)	11(35.5%)
NS group (n=30)	11(36.7%)	19(63.3%)
Statistic	4.731	
P	0.030	
Methods	Chi-square test	

Abbreviations: HRS,Hydrogen-rich saline; NS,normal saline.

Adverse Reactions

Of the 61 patients who completed the follow-up in the two groups, 3 (1 in the HRS group and 2 in the NS group) had nasal hemorrhage at 2–3 weeks of follow-up, and 1 more in the NS group, and nasal packing was performed to stop the bleeding. No other adverse reactions occurred.

Discussion

The pathological essence of CRS is chronic inflammation of nasal mucosa, which is mediated by nasal cavity and sinus mucosal epithelial cells and T cells. The outcome of CRS after surgery is currently summarized as the cleaning stage of the surgical cavity, the competitive stage of mucosal outcome, and the epithelialization stage of the surgical cavity.[30–32] Postoperative wound exudation of fibrous tissue, leukocytes, and tissue fluid increases, and the sinus mucosa shows inflammatory hyperplasia, edema, and multiple inflammatory cell infiltration. Therefore, timely control of postoperative inflammation can shorten the time for the surgical cavity to reach epithelialization and reduce or delay the recurrence of polyps.

Hydrogen has shown anti-inflammatory effects in various animal models, such as reducing the levels of inflammatory mediators such as TNF-α, IL-6, IL-1, IL-4, and IL-13.[15,33–35] Hydrogen can improve nasal mucosal inflammation by increasing the number and function of Treg cells, increasing the release of anti-inflammatory factors (TGF-β and IL-10),[9,13] or by inhibiting the secretion of inflammatory factors (IL-4, IL-13, etc) by Th2 cells.[9,15] CRS is a chronic inflammation of nasal mucosa, surgery only removes obstructive lesions, and further drug therapy is needed to reverse the chronic inflammation of nasal mucosa. Our team has pioneered the use of hydrogen's anti-inflammatory and antioxidant mechanisms in clinical research on allergic rhinitis and chronic rhinitis, and has achieved positive results.[24] We will further promote it in clinical research on chronic sinusitis, and so far no other similar reports have been seen.

The results of this randomized double-blind controlled clinical study showed that subjects after FESS were treated with NS or HRS for nasal irrigation. After 12 weeks of follow-up, the VAS score, SNOTT-22 score and LKES of the HRS group were lower than those of the NS group ($P<0.05$), suggesting that the local irrigation treatment of HRS was better than that of saline irrigation alone, which may be due to the anti-inflammatory and antioxidant properties of hydrogen.

The VAS scores of nasal symptoms before and after treatment were compared. The VAS scores of nasal obstruction, runny nose and hyposmia also decreased significantly in the HRS group ($P<0.05$), but there was no significant difference in the head and face pain scores between the two groups ($P=0.326>0.05$). Considering that the head and face pain was mainly caused by sinus obstruction, this symptom would be significantly improved after the operation. We analyzed the VAS scores of headache separately (Figure 3E). The scores of the two groups were significantly lower than those before the operation in the first week after the operation (before irrigation), and there was no significant difference between the two groups ($P=0.877>0.05$). There was no difference in the 12-week score between the two groups, suggesting that surgery was the mainstay of relief.

There is also a process of wound healing after CRS in the nasal cavity and paranasal sinuses. Wound healing is a dynamic, complex, and orderly biological process. The process includes hemostasis, inflammation, proliferation, and remodeling. A series of exuberant cellular activities (such as cell migration, movement and secretion) occur during wound healing, which require a significant increase in oxygen consumption of cells to provide additional energy, and more reactive oxygen species (ROS) are produced.[36,37] Oxidative stress can activate macrophages and neutrophils, releasing inflammatory mediators such as interleukin (IL) and tumor necrosis factor (TNF).[38] On the one hand, they can interact with inflammatory cells, leading to capillary expansion, congestion, increased permeability and tissue edema, aggravating local inflammatory response; on the other hand, they can also activate cytokine cascades, hindering the wound healing process.[39] In addition, oxidative stress can mediate apoptosis through mitochondrial pathways, endoplasmic reticulum stress pathways and death receptor pathways.[40] Therefore, appropriate regulation of oxidative stress in the wound microenvironment may play a positive role in promoting wound healing. The Nrf-2 signaling pathway is involved in regulating the expression of antioxidant genes, thereby improving cell protection,[41] and Nrf-2 plays an important role in mitigating oxidative stress and promoting wound healing.[42,43]

Current studies have found that H2 molecules are more easily able to enter cells and subcellular organelles, including mitochondria,[15] and play a protective role through its strong penetration ability, and then activate the Keap1-Nrf2 antioxidant defense system, inhibit oxidative damage, and improve mitochondrial function. H2 has been shown to significantly activate the Keap1-Nrf2 system, regulate the activity of endogenous antioxidants, and enhance the ability of cells to resist injury.[15] Animal experiments have found that local HRS treatment of wounds shortens the wound closure time,[44] reduces the levels of pro-inflammatory cytokines and lipid peroxidation, reduces the apoptosis index, and increases the expression of Nrf-2. Therefore, it is believed that HRS promotes wound healing through antioxidant, anti-inflammatory and anti-apoptotic effects, and alleviates oxidative stress in the wound microenvironment through the Nrf-2/HO-1 signaling pathway. Other studies have found that hydrogen alone can improve wound healing rate without the combination of any specific drugs, and its advantages include but are not limited to promoting extracellular matrix (ECM) deposition, early proliferation of autonomous stem cells, angiogenesis, cell viability and natural wet healing mode.[45]

In this study, the dynamic observation of the total VAS score and the score of nasal endoscopy showed that the score of the HRS group was significantly lower than that of the NS group since the second week after irrigation. The epithelialization time was 6.61 (2.00) weeks in the HRS group and 9.97 (1.59) weeks in the saline group, which was significantly shorter in the HRS group than in the NS group ($P<0.05$). Accordingly, it is speculated that hydrogen may also play an antioxidant and anti-damage role in the nasal cavity and sinus mucosa after CRS, better reducing the edema of the surgical cavity, promoting the repair of nasal mucosa, reducing inflammatory reactions, and then shortening the time of epithelialization, and restoring the protection and defense function of nasal mucosa as soon as possible. Many other animal experiments have also found that hydrogen can promote wound healing,[46,47] and the results of our clinical study also confirm this benefit of hydrogen.

Patients with CRS seem to require a long-term treatment strategy, and there is increasing consensus that the main treatment goal of CRS is to maintain clinical control.[48,49] In this study, the number of cases reaching the guidelines of complete control (clinical cure) within 3 months in group A was more than that in group B ($P<0.05$), suggesting that hydrogen-rich saline plays its anti-inflammatory, antioxidant and anti-damage effects, thus improving the clinical control rate.

In this study, there were 3 cases of epistaxis in the two groups, 2 cases were less, and 1 case was more, and the bleeding was stopped by nasal packing. It is considered that the improper irrigation force may be related, but it can not exclude that some cases belong to delayed epistaxis after FESS.[50,51] Some authors reviewed and analyzed nasal irrigation as a local treatment method for allergic rhinitis with nasal bleeding as the main outcome indicator, and found no adverse reactions such as nasal bleeding,[52] which is for non-wound nasal surface. The particularity of this study is that the patients have just undergone surgery and have incompletely healed wounds, so improper irrigation has the risk of bleeding. This study shows that HRS irrigation of nasal cavity does not increase the risk of bleeding and is safe.

The limitation of this study is the small sample size, and the results of long-term efficacy evaluation were not statistically analyzed. Because it was a short-term efficacy evaluation, and considering the interference of blood clots in the sinus cavity, patients were not willing to be exposed to radiation again in a short time, so postoperative sinus imaging evaluation was not performed on patients.

Conclusions

Our research was conducted by implementing interventions with different irrigation fluids under similar baselines (not only including general information but also the same surgical physicians and unified postoperative medications, etc). If there were differences in the results, they could be attributed to the variations in the irrigation fluids. This study suggests that hydrogen-rich saline irrigation for postoperative CRS is safe and effective, and has certain advantages over simple saline irrigation. It can significantly improve nasal symptoms, shorten the time of nasal mucosal healing and epithelialization, and has a high recent complete control rate, hoping to provide help for the personalized treatment strategy of CRS in the future.

Data Sharing Statement

Related data and materials are available upon request to Ling Jin, Kai Fan, and Shaoqing Yu.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Clinical Research of Tongji hospital (Permit Number: 2021-KYSB-188).

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Disclosure

The authors report no conflicts of interest in this work.

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