American Journal of Otolaryngology–Head and Neck Medicine and Surgery 39 (2018) 10–13

Contents lists available at ScienceDirect

American Journal of Otolaryngology–Head and Neck Medicine and Surgery

journal homepage: www.elsevier.com/locate/amjoto

Outcome of spray cryotherapy plus functional endoscopic sinus surgery on management of healing in nasal polyposis

Ahmad Rezaeian *

Department of Otorhinolaryngology, head and neck surgery, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

ARTICLE INFO

Article history:
Received 2 September 2017

Keywords:
Nasal polyposis
Functional endoscopic sinus surgery
Spray cryotherapy

ABSTRACT

Background: Nasal Polyposis is a benign tumor in nasal or paranasal mucosa, which confronts difficulties in management of healing after treatments with surgery. The aim of this study was to evaluate the effects of Spray Cryotherapy (SCT) on management of healing in patients with nasal polyposis who undergone functional endoscopic sinus surgery.

Methods: In this prospective, clinical trial study, we investigated on 40 patients with nasal polyposis that had indication for functional endoscopic sinus surgery. Patients were divided randomly into two parallel group; cryotherapy (with SCT) and placebo (without SCT). Evaluation of healing after surgery was evaluated with Lund-Mackay and The Sino-nasal outcome test (SNOT-22)-22 scores.

Result: Postoperatively, Lund-Mackay and SNOT-22 scores were significantly decreased in both groups, however these scores were significantly lower in cryotherapy group in comparison with placebo group. Also there were no reported serious side effects in both groups.

Conclusion: In this paper, we concluded that usage of SCT is an effective and safe method on management of healing and develops recovery rates in patients with nasal polyposis undergoing functional endoscopic sinus surgery.

1. Introduction

Nasal polyposis (NP) is a subgroup of chronic rhino sinusitis family which is defined as swellings, inflammation and discharge of nasal or paranasal mucosa. The exact etiology of this problem still remains unknown however it has been proven that eosinophils play a pivotal role in pathogenesis of the disease [1]. The prevalence rate of NP has been reported 0.2% to 4% in different studies which has been also reported to be more common in male population [2]. NP is divided into two types; symptomatic and asymptomatic NP, the symptoms of NP include, but no limited to, nasal packing or obstruction, sneezing, post-nasal drip, congestion, anosomia/hyposmia and facial pressure and pain [3,4]. Middle meatus and osteomeatal complex are the most common places for NP. Based on site of involvement, NP is divided into 3 grades: 1 which occurs in middle meatus, 2 that takes place middle turbinate and 3 that causes total obstruction. It is also noteworthy to mention that this inflammation is concomitant with allergy and infections such as fungal infection. The topical nasal steroid drops and oral antihistamine or short term of systemic steroids are often good choices of treatments for controlling the symptoms, however based on studies, surgery is a better choice that causes restoration of quality of life in recurrent or chronic NP [5]. Cryotherapy is a new modality and a novel method used to healing of wounds and normalization of mucosa in aerodigestive tract [6]. Spray cryotherapy (SCT) includes a cryoprobe and gas cryogen (nitrogen or carbon dioxide), utilized based on Joule-Thompson which affects on contact tissue ablation by cooling and freezing in temperature of −40 to −90 °C [7]. Recently SCT has been widely used for management of malignant and nonmalignant tumors in oncology, ophthalmology, and gastroenterology [8,9]. Other usages of SCT include ablation of tumors, treating infections, pain suppression, performing bronchoscopic biopsies, and also cosmetic surgery [10]. Additionally SCT can also be utilized by noncontact spray of liquid nitrogen with low-pressure (2 to 4 psi), which is a safe and effective method in managing benign diseases of airway system [11]. Although, there are limited number of studies about effects of SCT in management of tumors in ear, nose, and throat (ENT), this method has been proven effective in rabbit models of rhinosinusitis [12]. SCT can be also used to improve voice qualities of patients who had been underwent transoral resection of early glottic cancers [13]. Based on prior studies about the effectiveness of SCT, in this study I hypothesized that SCT can be also effective in management of NP, so the aim of current study was to evaluate the outcomes of SCT usage in management of postoperative healing in the patients undergoing surgical resection of NP.

* Corresponding author at: Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail address: dr.ahmadrezaeian@gmail.com.

https://doi.org/10.1016/j.amjoto.2017.10.007
0196-0709/

2. Methods and materials

2.1. Study design

In this prospective, controlled, randomized clinical trial that has been approved in Iranian registry of clinical trial (IRCT), 54 consecutive adult patients with NP were referred to Amin Hospital-Isfahan- Iran in 2015–2017. So 40 of 54 patients were enrolled to the study according to inclusion and exclusion criteria (18 males and 22 females). In this context, patients were diagnosed with clinical, preclinical and imaging finding such as CT scan (scored with Lund-McKay) and endoscopic evaluation. The mean age of patients was 43.22 ± 15.04 years. The inclusions criteria were: 1) patients with bilateral nasal polyposis (grade 2 or 3) who had indication for functional endoscopic sinus surgery (FESS), 2) age of 18 to 70 years 3) absence of any cardiovascular, neurological, respiratory and kidney diseases and malignant tumors, 4) Lund-McKay score > 10, 5) having informed consent in order to participate in the study. It should be also noted that patients with a history of pervious surgeries on nasal polyposis or FESS were not meeting inclusion criteria. Furthermore, patients who faced severe side effects were excluded from the study.

Before operations, the Lund-Mackay Score and Sino nasal outcome test or SNOT-22 were performed for all patients by an ENT surgeon who was blinded about type of groups (Cryotherapy or placebo groups). The Land-Mackay score is a CT scan evaluation in coronal and axial view. In the Land-Mackay, sinuses are divided into 12 parts of left and right sinuses which include anterior and posterior ethmoid sinuses, sphenoid sinus, frontal sinus, maxillary sinus and ostiomeatal complex. So the Land-Mackay is according to the fluid accumulation or mucosal inflammation severity of each sinus and is scored as 0 (complete lucency or mucosal thickening without fluid collection), 1 (partial lucency or mucosal thickening with fluid collection or moderate to severe mucosal thickness) and 2 (complete opacity) and also ostiomeatal complex is scored 0 (without obstruction) or 2 (with obstruction). In this regard, the scoring in the Land-Mackay is between 0 (complete lucency in all sinuses) to 24 (complete opacity in all sinuses) [14]. The SNOT-22 is an outcome measurement-test in rhino sinusitis patients, that includes 22 questions and is scored 0 to 110 [15]. Pre-operatively, the patients were allocated randomly into two parallel groups, the application for randomization was OxMAR software and this method was concealment. First group or cryotherapy group was undergoing FESS with SCT and second group or placebo group was undergoing FESS with normal saline.

2.2. Surgical technique and post-operative management

The surgical technique of this study was according to our institute [16]. All patients were administered with standard general anesthesia and Functional endoscopic sinus surgery; all operations were performed by an ENT surgeon. 10 min before surgery lidocaine and adrenaline were administered as decongestion, prevention of bleeding and local anesthesia, then 1 mL of lidocaine (10 mg/mL) and (5 μg/mL) adrenaline was injected in submucosal of medial infundibular wall. For induction of sedation, 1 mg midazolam and 0.05 mg fentanyl were performed. 4-mm rigid endoscopes with deflection angles of 0° and 30° were used according with standard procedure (Karl-Storz, Tuttlingen, Germany). Ostium forceps and a 4-mm microdebrider were used to uncinectomy. Microdebrider or nonpowered instruments were used to clear maxillary ostium. Infundibulectomy, middle meatal antrostomy, frontal sinusotomy, sphenoidotomy and total ethmoidectomy were performed to all patients. Also duration (minute) of operative was recorded for each patient. At the end of operation, sinus cavity was treated with

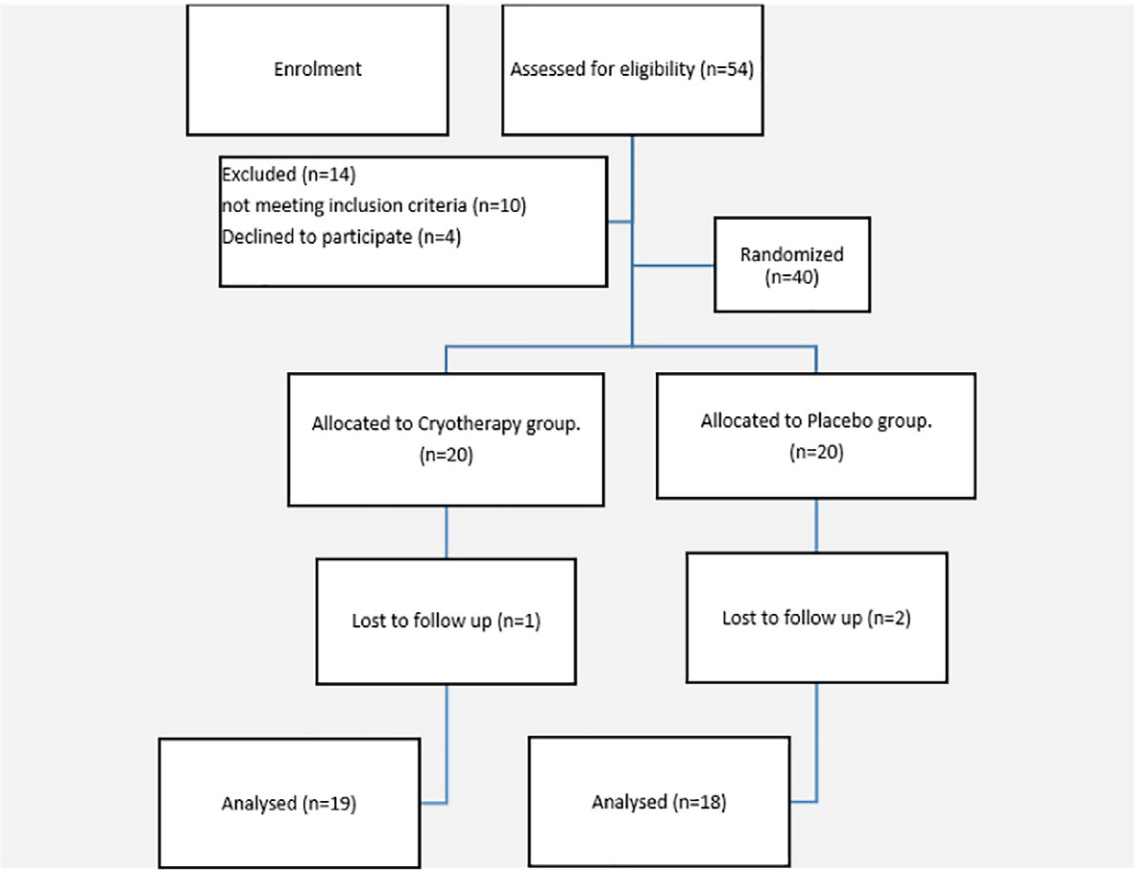

Fig. 1. Diagram of consort in following of patients.

Table 1
Demographic information of patients in both groups.

Characteristic		Cryotherapy group	Placebo group	P-value
Number		20	20	–
Gender	Male	10 (50%)	8 (40%)	0.52[a]
	Female	10 (50%)	12 (60%)	
Age (mean ± SD) (years)		42.80 ± 16.13	43.65 ± 14.27	0.33[b]
Grade of nasal polyposis	2	6 (30%)	5 (25%)	0.72[a]
	3	14 (70%)	15 (75%)	
Duration of operation (mean ± SD) (minute)		85.20 ± 15.04	95.85 ± 19.29	0.39[b]

[a] Chi squire test.
[b] Independent t-test.

cryotherapy in first group and was flushed with normal saline in second group. The suggested protocol in cryotherapy was according to previous studies [17], so SCT was done in 4 cycles with 5 s interval. The SCT device was Brymill (Ellington, CT) CRY-AC-3 Cryogenic System. Afterward nasal packing was performed with hemostasis (Merocel; Medtronic Xomed Surgical Products) and was removed after 2 days. Antibiotic such as co-amoxiclav 50 mg/kg TDS for 5 days and prednisolone 1 mg/kg/24 h for 5 days, and nasal steroids thrice daily for 1 month were administered as postoperative care. Postoperatively, patients were visited in 1, 2, 4, 8, and 12 weeks, and nasal cavities were debrided with sinus endoscope. Additionally, CT scan was performed for patients in 8 and 12 weeks after operation, so the Lund-Mackay Score and SNOT-22 were recorded in 8 and 12 weeks after operation and this recording was blinded. In this follow up, 1 patients of cryotherapy group and 2 patients of placebo group didn't continue study in during of follow up (Fig. 1).

2.3. Statistics

The sample size was according to previous studies [17], in the other similar study the standard division of Lund-McKay score was 4.01, respectively. The statistical power and significance level were considered 80% and 5%, respectively. The significant difference between the mean of two groups was considered 2.51, and the sample size was estimated at 20 patients in each group (40 patients for all). All data were analyzed with Statistical Package for the Social Sciences (SPSS) software (Version 24). Chi-Square test, Independent *t*-test and Man-Whitney test were used to compare both groups, also Paired Samples Correlation was used to compare Lund-McKay score and SNOT-22 in pre and post intervention. In addition, number (Percent) and mean ± Standard Division were showed in all data. Also *P*-value <0.05 was considered a significant threshold.

3. Results

In this current study, 40 patients with NP participated and were randomly divided into cryotherapy (10 males and 10 females) and placebo groups (8 males and 12 females), the mean age in cryotherapy and placebo groups were 42.80 ± 16.13 and 43.65 ± 14.27 years, respectively. Therefore, there were no significant relationships between both groups regarding to gender and age (P-values were 0.52 and 0.33, respectively). According to inclusion criteria, we enrolled patients with grade 2 or 3 of NP, so 70% of patients in cryotherapy group and 75% of patients in placebo group had grade 3 of NP. The mean duration of operation in the cryotherapy and placebo groups were 85.20 ± 15.04 and 95.85 ± 19.29 min, with no significant correlation between two groups according to grade of NP and duration of operation ($P = 0.72$ and 0.39, respectively) (Table 1). Preoperatively, Lund-McKay and SNOT-22 scores were recorded by a blinded surgeon, also there were no significant differences between two groups regarding to Lund-McKay and SNOT-22 scores (*P*-values were 0.23 and 0.83, respectively). Postoperatively, Lund-McKay and SNOT-22 scores were recorded again, therefore, Lund-McKay and SNOT-22 scores in cryotherapy group were significantly lower in placebo group after 12 and 36 weeks ($P < 0.0001$, for both). According to Paired Samples Correlation, Lund-McKay and SNOT-22 scores were decreased significantly in both group in after operation ($P < 0.0001$) (Table 2). Also there were no adverse effects in two groups and no osteitis was reported in following up performances.

4. Discussion

Here in this study, we to evaluate the outcomes of SCT usage in management of postoperative healing in 40 patients undergoing surgical resection of NP. Our assessments were Lund-McKay and SNOT-22 scores; therefore we showed that Lund-McKay and SNOT-22 scores in SCT group were significantly lower than placebo group, meaning a better outcome of the surgery. In this regard, our study is similar to the study, performed by Albu [17]. Albu and colleagues evaluated the effect of SCT on wound healing in chronic rhino sinusitis patients. It should also be noted that the assessment in the mentioned study was Lund-Kennedy and Perioperative Sinus Endoscopy (POSE) scores. There, they concluded that these scores were significantly different after operations suggesting SCT as an enhancing method for wound healing. Another study evaluated cryotherapy as Maxillary Antrostomy Patency in a Rabbit Model of Chronic Rhinosinusitis, in this study authors reported enhanced maxillary antrostomy area in the group that was under administration with cryotherapy 4 weeks after surgery. Also the authors didn't report any side effects postoperatively [12]. In another recent intervention, endoscopic spray was used to access genitourinary malignancies in porcine models, therefore the results of this intervention indicated cryotherapy to be able to raise safety and modality of treatment [18]. Other usage of cryotherapy was to treat Glottic and Subglottic Stenosis in a case report study, which was safe and promoted treating effect in subglottic and glottic narrowing as well as SCT usage [19]. Finley et al. [11] also evaluated the effects of SCT on management of airway diseases. They report that SCT is highly effective on vascular tumors as it reduces some complications such as bleeding. Also another study suggested SCT is an effective and safe adjuvant modality on benign tracheal stenosis [20]. There are of course limited number of studies about the usage of cryotherapy in otorhinolaryngology but they approved our conclusion that SCT had more effects in promotion of healing. Other usage of SCT was in benign airway strictures, reporting

Table 2
Result of Lund-McKay and SNOT-22 scores in baseline and after 12 and 36 weeks.

Variable		Cryotherapy group, number	Placebo group, number	P-value[a]
Lund-McKay score (Mean ± SD)	Baseline	18.35 ± 2.45, 20	17.40 ± 1.90, 20	0.23
	After 12 weeks	3.15 ± 1.53, 19	7.21 ± 1.51, 19	<0.0001
	After 36 weeks	2.63 ± 1.16, 19	6.88 ± 1.74, 18	<0.0001
SNOT-22 score (Mean ± SD)	Baseline	84.80 ± 12.21, 20	83.85 ± 10.37, 20	0.83
	After 12 weeks	8.57 ± 1.57, 19	18.63 ± 4.28, 19	<0.0001
	After 36 weeks	7.63 ± 1.57, 19	18.27 ± 12.81, 18	<0.0001

[a] Man Whitney Test, SNOT-22: The sino-nasal outcome test-22.

that SCT along with balloon dilation had more effects on improvement of symptoms and decreased severity of airway narrowing [21]. Also in esophageal cancer, SCT had more effects after tumor eradication and there was no reported serious side effects in this method [22]. In the management of xanthelasma palpebrarum, SCT was used for 4 patients with xanthelasma which indicated better effects and fewer side effects [23]. Other usages of SCT were in Barrett's esophagus [24], adenocarcinoma in the parietal pleura [25], airway injury [26] and bronchial stenosis [27].

As a conclusion, based on results gathered from our study, along with previous studies, SCT is an effective method with fewer or no reported side effects in management of benign and malignant tumors and injuries, especially with a better effect in mucosal tissue. In this paper, I conclude that SCT are more effects on management of NP after functional endoscopic surgery. There were also no serious adverse effects in this technique. So as a suggestion, usage of SCT might be an effective and safe method in healing management of NP after surgeries.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjoto.2017.10.007.

References

[1] Bachert C, Gevaert P, Holtappels G, et al. Nasal polyposis: from cytokines to growth. Am J Rhinol 2000;14(5):279–90.
[2] Lange B, Holst R, Thilsing T, et al. Quality of life and associated factors in persons with chronic rhinosinusitis in the general population: a prospective questionnaire and clinical cross-sectional study. Clin Otolaryngol 2013;38(6):474–80.
[3] Rimmer J, Fokkens W, Chong LY, et al. Surgical versus medical interventions for chronic rhinosinusitis with nasal polyps. Cochrane Database Syst Rev 2014;12.
[4] Radenne F, Lamblin C, Vandezande L-M, et al. Quality of life in nasal polyposis. J Allergy Clin Immunol 1999;104(1):79–84.
[5] Gohar MS, Niazi SA, Niazi SB. Functional endoscopic sinus surgery as a primary modality of treatment for primary and recurrent nasal polyposis. Pakistan Journal of Medical Sciences 2017;33(2):380.
[6] Dumot JA, Vargo JJ, Zuccaro G, et al. Results of cryospray ablation for esophageal high grade dysplasia (HGD) and intramucosal cancer (Imca) in high risk non-surgical patients. Gastrointest Endosc 2008;67(5):AB176.
[7] Bruley M. A study of safety and performance requirements for cryosurgical devices. Springfield (VA): FDA/BMDDP, National Technical Information Service; 1980.
[8] Baust J, Gage A. Progress toward optimization of cryosurgery. Technol Cancer Res Treat 2004;3(2):95–101.
[9] Johnston MH, Eastone JA, Horwhat J, et al. Cryoablation of Barrett's esophagus: a pilot study. Gastrointest Endosc 2005;62(6):842–8.
[10] Moore RF, Lile DJ, Abbas AE. Current status of spray cryotherapy for airway disease. J Thorac Dis 2017;9(Suppl. 2):S122.
[11] Finley DJ, Dycoco J, Sarkar S, et al. Airway spray cryotherapy: initial outcomes from a multiinstitutional registry. Ann Thorac Surg 2012;94(1):199–204.
[12] Gocea A, Taulescu M, Trombitas V, et al. Effects of cryotherapy on the maxillary antrostomy patency in a rabbit model of chronic rhinosinusitis. Biomed Res Int 2013;2013.
[13] Knott PD, Milstein CF, Hicks DM, et al. Vocal outcomes after laser resection of early-stage glottic cancer with adjuvant cryotherapy. Archives of Otolaryngology–Head & Neck Surgery 2006;132(11):1226–30.
[14] Chen JJ, Chen D-L, Chen C-J. The Lund-Mackay score for adult head and neck computed tomography. J Radiol Sci 2011;36(4):203–8.
[15] Hopkins C, Browne JP, Slack R, et al. The Lund-Mackay staging system for chronic rhinosinusitis: how is it used and what does it predict? Otolaryngology-Head and Neck Surgery 2007;137(4):555–61.
[16] Rezaeian A. Administering of pregabalin and acetaminophen on management of postoperative pain in patients with nasal polyposis undergoing functional endoscopic sinus surgery. Acta Otolaryngol 2017:1–4.
[17] Albu S, Trombitas V, Vlad D, et al. The influence of spray cryotherapy on wound healing following endoscopic sinus surgery in chronic rhinosinusitis. Laryngoscope 2016;126(1):25–32.
[18] Power NE, Silberstein JL, Tarin T, et al. Endoscopic spray cryotherapy for genitourinary malignancies: safety and efficacy in a porcine model. Ther Adv Urol 2013;5(3):135–41.
[19] Krimsky WS, Rodrigues MP, Malayaman N, et al. Spray cryotherapy for the treatment of glottic and subglottic stenosis. Laryngoscope 2010;120(3):473–7.
[20] Bhora FY, Ayub A, Forleiter CM, et al. Treatment of benign tracheal stenosis using endoluminal spray cryotherapy. JAMA Otolaryngology–Head & Neck Surgery 2016;142(11):1082–7.
[21] Fernando HC, Dekeratry D, Downie G, et al. Feasibility of spray cryotherapy and balloon dilation for non-malignant strictures of the airway. Eur J Cardiothorac Surg 2011;40(5):1177–80.
[22] Greenwald BD, Dumot JA, Abrams JA, et al. Endoscopic spray cryotherapy for esophageal cancer: safety and efficacy. Gastrointest Endosc 2010;71(4):686–93.
[23] Labandeira J, Vázquez-Osorio I, Figueroa-Silva O, et al. Tolerability and effectiveness of liquid nitrogen spray cryotherapy with very short freeze times in the treatment of xanthelasma palpebrarum. Dermatol Ther 2015;28(6):346–50.
[24] Xue H, Tan H, Liu W, et al. A pilot study of endoscopic spray cryotherapy by pressurized carbon dioxide gas for Barrett's esophagus. Endoscopy 2011;43(05):379–85.
[25] Downie G, Krimsky W. Response to spray cryotherapy in a patient with adenocarcinoma in the parietal pleura. Respiration 2010;80(1):73–7.
[26] Krimsky WS, Broussard JN, Sarkar SA, et al. Bronchoscopic spray cryotherapy: assessment of safety and depth of airway injury. J Thorac Cardiovasc Surg 2010;139(3):781–2.
[27] Janke KJ, Abbas AE-S, Ambur V, et al. The application of liquid nitrogen spray cryotherapy in treatment of bronchial stenosis. Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery 2016;11(5):349–54.