Sinonasal Irrigation using Ceftriaxone-Saline Solution ameliorates Chronic Rhinosinusitis Clinical Severity and Improves Patients' Quality of Life

Mohamed F. Shindy and Bkr E Ras

Otorhrinolaryngology Department, Faculty of Medicine, Benha University, Egypt.
M_Shindy@yahoo.com

Abstract: Objectives: To evaluate the therapeutic yield of sinonasal irrigation (SNI) using ceftriaxone solution in saline and its impact on quality of life (QoL) scores. Patients & Methods: This multicenter study was assigned to include all patients attending the outpatient clinic with symptoms suggestive of chronic rhinosinusitis (CRS). Patients were diagnosed according to criteria defined by the Rhinosinusitis Task Force. All patients underwent rigid endoscopy and endoscopic findings were graded according to Lund-Kennedy scoring. All patients were asked to complete two quality of life questionnaires: the Rhinosinusitis Disability Index (RSDI) and the chronic sinusitis score (CSS). All patients received bilateral nasal and sinus irrigation using ceftriaxone sodium 1 gm/200 ml normal saline. Then, all patients were allowed to use the same fluid for twice daily nasal irrigation for 6 weeks and reevaluated. Study outcome included clinical evaluation of presenting symptoms, evaluation of QoL questionnaires and endoscopic scoring at the end of 6 weeks of domiciliary irrigation. Results: The study included 700 CRS patients; 450 in Emirate and 250 Egyptian patients. After 6-weeks of irrigation; 220 patients had only minor symptoms (Responders) and 480 patients had varied distribution among other symptoms severity grades (Non-responders). There was significant difference of the frequency of patients among symptom severity grades between both evaluation sessions. After 6-weeks follow-up, mean Lund-Kennedy scores, total and subscales of RSDI were significantly lower with significantly higher CSS compared to baseline scores of responders. Moreover, responders showed significantly lower Lund-Kennedy scores and RSDI with significantly higher CSS at the end of follow-up compared to non-responders. Conclusion: SNI has a significant role as a therapeutic modality for CRS patients which could be implemented wherein bacterial resistance to systemic antibiotics was encountered or to postpone surgery or in patients who are unfit or refusing surgery. SNI with ceftriaxone-saline solution allowed minimization of clinical manifestations with improvement of QoL scores.

[Mohamed F. Shindy and Bkr E Ras. **Sinonasal Irrigation using Ceftriaxone-Saline Solution ameliorates Chronic Rhinosinusitis Clinical Severity and Improves Patients' Quality of Life.** *Nat Sci* 2013;11(5):126-132]. (ISSN: 1545-0740). http://www.sciencepub.net. 19

Key Words: Chronic rhinosinusitis, Irrigation, Ceftriaxone, Quality of Life.

1. Introduction

Chronic rhinosinusitis (CRS) is a chronic disease that involves long-term inflammation of the nasal and paranasal sinus mucosa. Although commonly known as 'chronic sinusitis', the term 'chronic rhinosinusitis' is now being used more frequently, due to the involvement of the entire nasal and sinus passages seen with this condition. CRS causes not only physical suffering, but also impacts psychological wellbeing and daily functioning. CRS is estimated to result in an annual 18 to 22 million physician office visits in the US **(Benninger *et al.*, 2003, Daines & Orlandi, 2012, Hytönen & Suvilehto, 2012)**.

Rhinosinusitis is a common, expensive disorder that has a significant impact on patients' quality-of-life (QOL). In a subset of patients, sinus symptoms can become chronic and are epidemiologically associated with asthma, allergic rhinitis, and nasal polyposis, though the etiological relationships are not well understood. Each condition is associated with significant morbidity, cost, and impact on QOL. Allergic rhinitis affects 20-40 million persons annually in the US, is responsible for 3.5 million lost work days, 2 million missed school days each year, and an estimated 28 million days of restricted activity or reduced productivity. Overall health care costs for allergic rhinitis are rising at a rate of 12% per year and its treatment is expensive and has significant side effects **(Kirtsreesakul & Naclerio, 2003, Guilemany *et al.*, 2010, Meltzer & Hamilos, 2011)**.

Nasal irrigation is a simple, inexpensive procedure that has been used to treat sinus and nasal conditions for many years. It is still recommended routinely by otolaryngologists. The procedure involves flushing the nasal cavity with saline solution, which promotes improved mucociliary clearance by moisturizing the nasal cavity and removing encrusted material. Evidence shows that pulsating saline lavage can remove bacteria also **(Kassel *et al.*, 2010, Jeffe *et al.*, 2012)**.

2.Patients and Methods

The current multicenter study was conducted at Departments of Otorhinolaryngology at FMC, Abu Dhabi, Emirate and Benha University Hospital, Egypt since June 2010 till Aug 2012. All patients attending the outpatient clinic of both hospitals and complaining symptoms suggestive of chronic rhinosinusitis were included in the study.

Patients were diagnosed according to criteria defined by the Rhinosinusitis Task Force **(RSTF, 1997)** and were established by the American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) where CRS is probable if the patient has two or more major factors or one major and two or more minor factors (Table 1) for more than 12 weeks **(Benninger *et al.*, 2003)**.

Table (1): Factors associated with diagnosis of rhinosinusitis (Benninger *et al.*, 2003)

	Minor Factors
Facial pain/pressure	Headache
Nasal obstruction/blockage	Fever (all non-acute rhinosinusitis)
Nasal discharge/purulence/discolored postnatal drainage	Halitosis
	Fatigue
Hyposmia/anosmia	Dental pain
Purulence in nasal cavity on examination	Cough
Fever (acute rhinosinusitis only)	Ear pain/pressure/fullness

Data are presented as numbers; percentages are in parenthesis

All patients underwent rigid endoscopy and endoscopic findings were graded according to Lund-Kennedy scoring system to assess the following parameters: nasal mucosa edema (absent=0, mild-moderate=1 or polypoid degeneration=2), presence of secretion (absent=0, hyaline=1 or thick &/or mucopurulent=2) and presence of polyps (absent=0, limited to the middle meatus=1 or extended to the nasal cavity=2). The assessment was performed bilaterally, with the total points corresponding to the sum of values obtained in both sides. Thus, the score ranged from 0-12 and the endoscopic result was considered positive for CRS if Lund-Kennedy score was >2, **(Lund & Kennedy, 1995)**.

All patients were asked to complete two quality of life questionnaires: the Rhinosinusitis Disability Index (RSDI) and the chronic sinusitis score (CSS). Patients were asked to complete each questionnaire at time of enrollment and after 3-months of start of conservative treatment. The RSDI contains 30 questions (score range: 0–120) and consists of three subscales that measure disease-specific patient status in the physical, functional, and emotional domains **(Benninger & Senior, 1997)**. The physical subscale contains 11 questions (score range: 0–44), the functional subscale contains 9 questions (score range: 0–36), and the emotional subscale contains 10 questions (score range: 0–40). Lower RSDI total and subscale scores represent a lower impact of sinus disease. The CSS is a six-item questionnaire used to measure sinusitis-specific symptom and medication use during the preceding 8-week period **(Gliklich & Metson, 1995)**. The aggregate and subscale scores each range from 0 to 100 with lower scores representing a greater impact of sinus disease.

All patients received bilateral sinonasal irrigation using ceftriaxone sodium 1 gm (Rocephin, Co; USA) dissolved in 200 ml normal saline. Under local topical anesthesia sinus lavage was performed by flushing the maxillary sinus through an 18-gauge spinal needle attached to a collection trap via a 2-way stop. This design allows flushing with instantaneous sample collection if indicated. Needle flushing was performed under the inferior turbinate for each side in all patients and before endoscopic sinus surgery, if indicated. Then, all patients were allowed to use the same fluid for twice daily nasal irrigation for 6 weeks and reevaluated.

Outcome of the study

1. Clinical evaluation of presenting symptoms as shown in table 1.
2. Evaluation of quality of life using Patients assigned for surgery
3. Endoscopic scoring

3.Results

This multi-center study included 700 CRS patients; 450 in Emirate and 250 Egyptian patients. Collectively, there were 415 males (59.3%) and 285 were females (40.7%). Mean age of enrolled patients was 37.8±7.5; range: 25-53 years. There were 95 patients younger than 30 years, 322 patients were in range of 30-40 years, 244 patients were in range of 40-50 and 39 patients were older than 50 years (Table 2).

Table (2): Patients' enrolment data

Data			Findings	
Age (years)	Strata	<30	95 (13.6%)	27.4±1.2 (25-29)
		30-<40	322 (46%)	33.7±2.4 (30-39)
		≥40-<50	244 (34.8%)	44.9±2.1 (41-49)
		≥50	39 (5.6%)	51.9±0.8 (51-53)
	Total		700 (100%)	37.8±0.7 (25-53)
Gender	Males		415 (59.3%)	
	Females		285 (40.7%)	

Data are presented as numbers; percentages are in parenthesis

At time of enrollment; 362 patients (51.7%) had one major and two minor symptoms of CRS, 113 patients (16.1%) had two major symptoms, 107 patients (15.3%) had one major and three minor symptoms, 65 patients (9.3%) had three major symptoms and 53 patients (7.6%) had one major and 4 minor symptom. After 6-weeks of irrigation; 220 patients had only minor symptoms and were considered as responders for applied policy and the remaining 480 patients had varied distribution among other symptoms categorized according to severity, where 41 patients (5.8%) still had three major symptoms, 97 patients (13.9%) still had two major symptoms, 234 patients (33.4%) still had one major and two minor symptoms, 79 patients (11.3%) still had one major and three minor symptoms and 29 patients (4.1%) still had one major and four minor symptoms. There was significant difference (X^2=9.344, p<0.01) of the frequency of patients among symptom severity grade between both evaluation sessions, (Table 3, Fig. 1).

Table (3): Patients' distribution among CRS symptom grades determined at time of enrolment and 6-weeks thereafter

Number of factors	At enrolment	After 6-w Follow-up
Three major symptoms	65 (9.3%)	41 (5.8%)
Two major symptoms	113 (16.1%)	97 (13.9%)
One major and 2 minor symptoms	362 (51.7%)	234 (33.4%)
One major and 3 minor symptoms	107 (15.3%)	79 (11.3%)
One major and 4 minor symptoms	53 (7.6%)	29 (4.1%)
Only minor symptoms	0	220 (31.5%)

Data are presented as numbers; percentages are in parenthesis

Mean Lund-Kennedy scores determined at time of enrollment were non-significantly (p>0.05) different between responders and non-responders. After 6-weeks follow-up, mean Lund-Kennedy scores were significantly (Z=2.254, p =0.024) lower compared to at enrolment scores of responders, while were non-significantly (Z=0.686, p >0.05). Moreover, responders showed significantly lower (Z=2.532, p <0.05) Lund-Kennedy scores at the end of follow-up compared to non-responders, (Table 4, Fig. 2).

Table (4): Patients' total Lund-Kennedy score determined at time of enrolment and 6-weeks thereafter

		Responders	Non-responders	Total
At enrolment		5.06±1.75 (2-8)	5.16±1.28 (3-8)	5.13±1.43 (2-8)
At 6-w follow-up		3.84±1.25 (2-5)	5.07±1.19 (3-8)	4.68±1.25 (2-8)
Statistical significance	Z	2.254	0.686	1.947
	p	=0.024	>0.05	>0.05

Data are presented as mean±SD; ranges are in parenthesis

Mean total and subscales of RSDI determined at time of enrollment were non-significantly (p >0.05) different between responders and non-responders. After 6-weeks follow-up, mean total and subscales of RSDI were significantly (p <0.05) lower compared to at enrolment scores of responders, while were non-significantly (p >0.05) lower in non-responders. Moreover, responders showed significantly lower (p <0.05) total and subscales of RSDI at the end of follow-up compared

to non-responders, (Fig. 3). Similarly, mean CSS scores determined at time of enrollment were non-significantly (p >0.05) different between responders and non-responders. After 6-weeks follow-up, mean CSS scores were significantly (p <0.05) higher compared to at enrolment scores of responders, while were non-significantly (p >0.05) higher in non-responders. Moreover, responders showed significantly higher (p <0.05) SCC at the end of follow-up compared to non-responders, (Table 5, Fig. 4).

Table (5): Patients' RSDI subscales and total score and CSS determined at time of enrolment and 6-weeks thereafter

			Responders	Non-responders	Total
RSDI	At enrolment	Physical	31.9±2.39	32.2±2.85	32.4±2.7
		Functional	26.32±4.39	25.55±4.7	25.79±4.6
		Emotional	26.6±2.17	26.71±2.62	26.68±2.48
		Total	84.83±5.28	84.88±5.7	84.87±5.54
	At 6-w follow-up	Physical	28.71±2.15*†	31.84±3.3	30.87±3.32
		Functional	23.69±3.95*†	24.84±4.9	24.48±4.64
		Emotional	23.95±1.95*†	25.88±2.86	25.28±2.75
		Total	76.35±4.75*†	82.56±6.24	80.64±6.48
CSS	At enrolment		50.87±11	50.71±10.67	50.76±10.71
	At 6-w follow-up		58.26±12.9*†	51.55±11.2	53.63±12.1

Data are presented as mean±SD

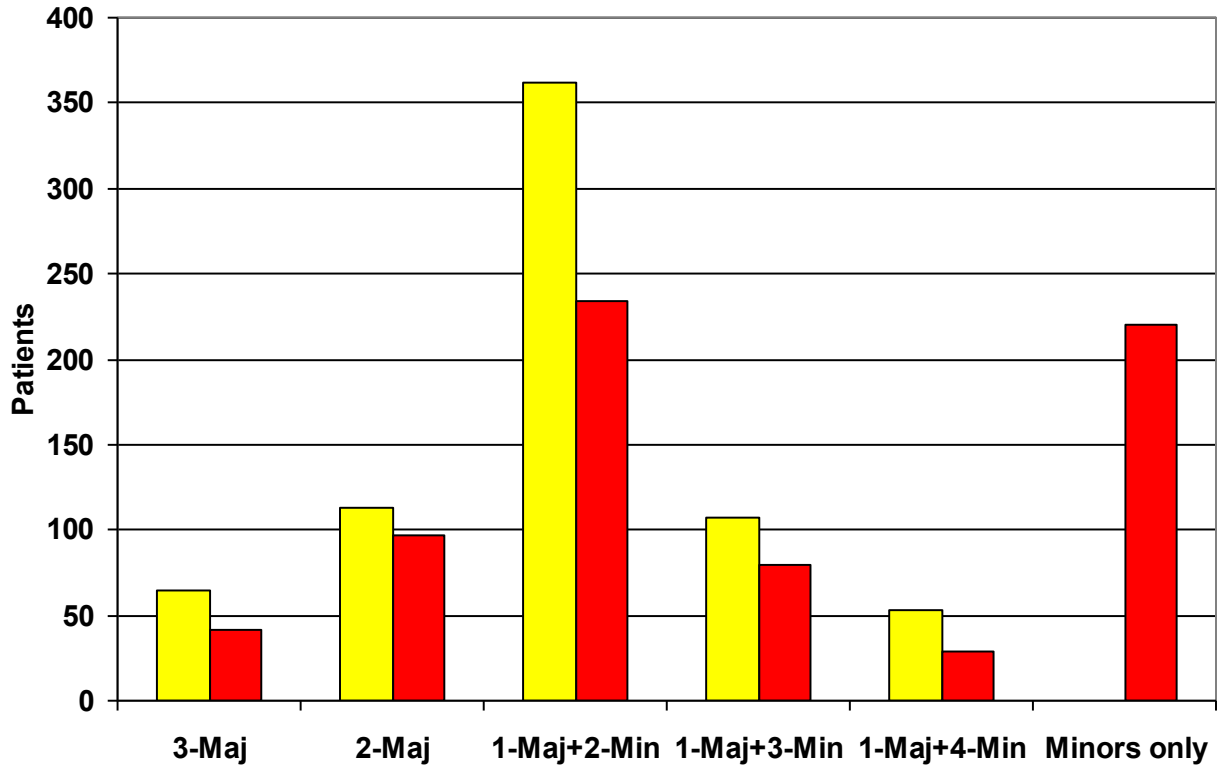

Fig. (1): Patients' distribution among CRS severity grades determined at time of enrolment and 12-wk later

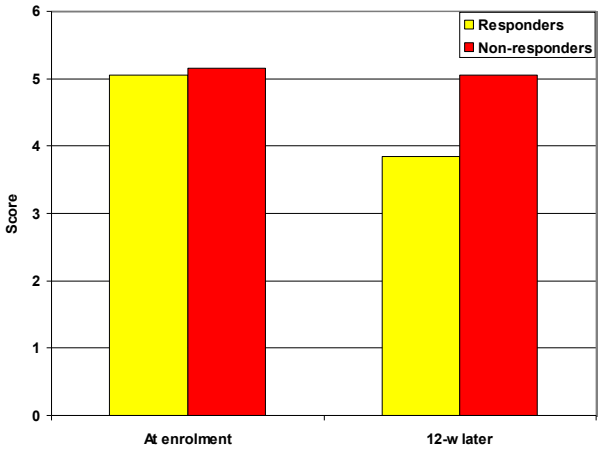

Fig. (2): Mean total endoscopic scores determined at enrolment and 12-w later

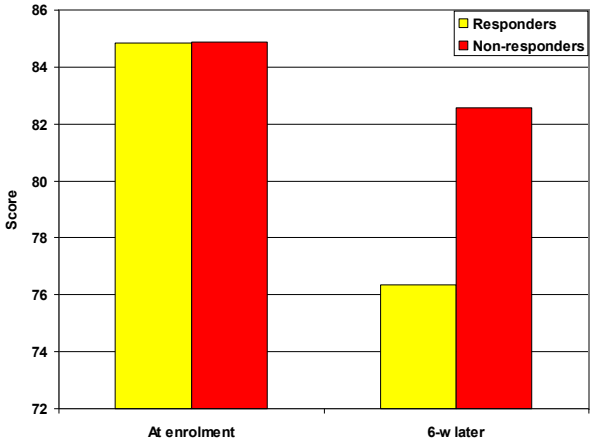

Fig. (3): Mean total RSDI score determined at enrolment and 6-w later

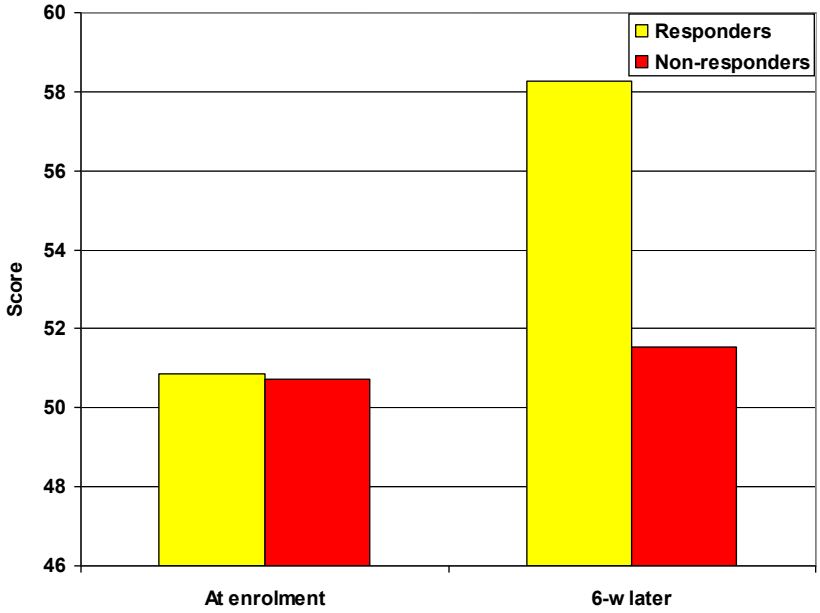

Fig. (4): Mean total CSS score determined at enrolment and 6-w later

4.Discussion

The current study reported response rate of about 30% manifested as significant improvement of presenting symptoms with concomitant significant improvement of quality of life. This subjective improvement was documented endoscopically at 6-weeks of irrigation and showed significant improvement of endoscopic scores.

These findings indicated a significant role for irrigation as a therapeutic policy for CRS patients and supported that previously reported by **Liang *et al.* (2008)** who evaluated the efficacy of nasal irrigation on the management of radiotherapy(RT)-induced rhinosinusitis and found that patients in the irrigation group had significantly lower endoscopic and questionnaire scores than patients in the non-irrigation group from pre-RT to 6 months after RT and the between-group differences were most obvious at the post-RT second and third months. **Gelardi *et al.* (2009)** found that nasal irrigation with the Lavonase system was effective in reducing symptoms, as all significantly diminished and significantly decreased nasal resistances.

One concern of the current study is the use of an antibiotic solution not plan saline for irrigation; the reported improvement indicated a role for

antibiotic and that this therapeutic policy was not dependent only on the mechanical effect for bacterial eradication but also on the antibacterial effect of antibiotic. In support of the use of antibiotic solution for sinus wash and nasal irrigation, multiple studies tried solutions of various medications for the use as continuous nasal irrigate; **Videler *et al.* (2008)** tried nasal irrigation with bacitracin/colimycin or placebo using the RhinoFlow nebulizer twice daily in patients with recalcitrant CRS and found that most VAS items and Disease-Specific Symptom Scores showed a reduction in severity of symptoms in both the bacitracin/colimycin and the placebo group, but with non-significant difference between groups despite being in favor of bacitracin/ colimycin group. **Bhalla *et al.* (2008)** tried topical budesonide in saline for nasal irrigation for 8 weeks for treatment of refractory cases of CRS with nasal polypi (CRSwNP) and reported improvement of clinical manifestations without causing hypothalamo-pituitary axis suppression. **Jervis-Bardy *et al.* (2012)** found mupirocin sinonasal rinses are an effective short-term anti-S aureus treatment in surgically recalcitrant CRS as assessed by microbiological and selected rhinological outcomes.

Multiple recent work assigned plane for treating CRS included SNI as a non-specific effective therapeutic modality; **Alobid & Mullol, (2012)** documented that among the objectives of CRSwNP management are to eradicate nasal polyps from nasal and sinus cavities, eliminate symptoms, and prevent recurrences; corticosteroids are the mainstay of treatment and are the most effective drugs for treating CRSwNP and other potential treatments are nasal saline irrigation and antihistamines (in allergic conditions), but endoscopic sinus surgery is recommended when medical treatment fails. **Adappa *et al.* (2012)** reviewed recent literature of nasal irrigations with or without drugs and found physiologic saline irrigation is beneficial in the treatment of symptoms of CRS, low-level evidence supports the effectiveness of topical antibiotics in the treatment of CRS, the use of topical antifungals is not supported by the majority of studies and intranasal steroids are beneficial in the treatment of CRSwNP. **Rudmik *et al.*(2012)** performed systematic review of the literature and documented that based on the available evidence, sinonasal saline irrigation and standard topical nasal steroid therapy are recommended in the topical treatment of CRS.

Achilles & Mösges (2013) documented that to conclusive proof of the efficacy of SNI in the treatment of acute rhinosinusitis is still pending, while in CRS, SNI is one of the cornerstones of treatment. **Huang & Govindaraj (2013)** concluded that topical saline and corticosteroids should be considered as the first line of therapy; additional studies are required to evaluate the efficacy of topical antibiotics with improved delivery methods. **Chusakul *et al.* (2013)** reported that buffered isotonic saline with some degree of alkalinity may improve nasal symptoms.

As another support for the efficacy of SNI for treatment of rhinosinusitis; **Wang *et al.*(2012)** documented that nasal irrigation is an effective adjunctive treatment for acute sinusitis in atopic children

It could be concluded that sinonasal irrigation has a significant role as a therapeutic modality for CRS patients which could be implemented wherein bacterial resistance to systemic antibiotics was encountered or to postpone surgery or in patients unfit or refusing surgery. SNI with ceftriaxone allowed minimization of clinical manifestations with improvement of quality of life scores.

References

1. Achilles N, Mösges R: Nasal saline irrigations for the symptoms of acute and chronic rhinosinusitis. Curr Allergy Asthma Rep. 2013;13(2):229-35.
2. Adappa ND, Wei CC, Palmer JN: Nasal irrigation with or without drugs: the evidence. Curr Opin Otolaryngol Head Neck Surg. 2012; 20(1):53-7.
3. Alobid I, Mullol J: Role of medical therapy in the management of nasal polyps. Curr Allergy Asthma Rep. 2012;12(2):144-53.
4. Benninger MS, Senior BA. The development of the rhinosinusitis disability index. Otolaryngol. Head Neck Surg 1997;123:1175–9.
5. Benninger MS, Ferguson BJ, Hadley JA: Adult chronic rhinosinusitis: definitions, diagnosis, epidemiology, and patho-physiology. Otolaryngol Head Neck Surg, 2003; 129 (3Suppl):S1-32.
6. Bhalla RK, Payton K, Wright ED: Safety of budesonide in saline sinonasal irrigations in the management of chronic rhinosinusitis with polyposis: lack of significant adrenal suppression. J Otolaryngol Head Neck Surg. 2008; 37(6):821-5.
7. Chusakul S, Warathanasin S, Suksangpanya N, Phannaso C, Ruxrungtham S, Snidvongs K, Aeumjaturapat S: Comparison of buffered and nonbuffered nasal saline irrigations in treating allergic rhinitis. Laryngoscope. 2013;123(1):53-6.
8. Daines SM, Orlandi RR: Chronic rhinosinusitis. Facial Plast Surg Clin North Am. 2012; 20(1):1-10.

9. Gelardi M, Mezzoli A, Fiorella ML, Carbonara M, Di Gioacchino M, Ciprandi G: Nasal irrigation with lavonase as ancillary treatment of acute rhinosinusitis: a pilot study. J Biol Regul Homeost Agents. 2009; 23(2):79-84.
10. Gliklich RE, Metson R. Techniques for outcomes research in chronic sinusitis. Laryngoscope, 1995; 105:387–90.
11. Guilemany JM, Alobid I, Mullol J: Controversies in the treatment of chronic rhinosinusitis. Expert Rev Respir Med. 2010; 4(4):463-77.
12. Huang A, Govindaraj S: Topical therapy in the management of chronic rhinosinusitis. Curr Opin Otolaryngol Head Neck Surg. 2013; 21(1):31-8.
13. Hytönen M, Suvilehto J: Sinusitis or rhinosinusitis?. Duodecim. 2012; 128(2):230-1.
14. Jeffe JS, Bhushan B, Schroeder JW Jr: Nasal saline irrigation in children: a study of compliance and tolerance. Int J Pediatr Otorhinolaryngol. 2012;76(3):409-13.
15. Jervis-Bardy J, Boase S, Psaltis A, Foreman A, Wormald PJ: A randomized trial of mupirocin sinonasal rinses versus saline in surgically recalcitrant staphylococcal chronic rhinosinusitis. Laryngoscope. 2012 Oct; 122(10):2148-53.
16. Kassel JC, King D, Spurling GK: Saline nasal irrigation for acute upper respiratory tract infections. Cochrane Database Syst Rev. 2010; (3):CD006821.
17. Kirtsreesakul V, Naclerio RM. Role of allergy in rhinosinusitis. Curr Opin Allergy Clin Immunol 2004;4(17):17–23.
18. Liang KL, Kao TC, Lin JC, Tseng HC, Su MC, Hsin CH, Shiao JY, Jiang RS: Nasal irrigation reduces postirradiation rhinosinusitis in patients with nasopharyngeal carcinoma. Am J Rhinol. 2008; 22(3):258-62.
19. Lund VJ, Kennedy DW: Quantification for staging sinusitis. International Conference on Sinus Disease: Terminology, Staging, Therapy. Ann Otol Rhinol Laryngol Suppl, 1995; 104 (suppl): 17-21.
20. Meltzer EO, Hamilos DL: Rhinosinusitis diagnosis and management for the clinician: a synopsis of recent consensus guidelines. Mayo Clin Proc. 2011; 86(5):427-43.
21. Report of the Rhinosinusitis Task Force Committee Meeting. Alexandria, Virginia, August 17, 1996. Otolaryngol Head Neck Surg 1997;117(3 Pt 2):S1-68.
22. Rudmik L, Hoy M, Schlosser RJ, Harvey RJ, Welch KC, Lund V, Smith TL: Topical therapies in the management of chronic rhinosinusitis: an evidence-based review with recommendations. Int Forum Allergy Rhinol.; Epub ahead of print.
23. Videler WJ, van Drunen CM, Reitsma JB, Fokkens WJ: Nebulized bacitracin/colimycin: a treatment option in recalcitrant chronic rhinosinusitis with Staphylococcus aureus? A double-blind, randomized, placebo-controlled, cross-over pilot study. Rhinology. 2008; 46(2):92-8.
24. Wang YH, Ku MS, Sun HL, Lue KH: Efficacy of nasal irrigation in the treatment of acute sinusitis in atopic children. J Microbiol Immunol Infect. 2012: S1684-1182(12)00179-X.

3/15/2013