CLINICAL STUDY

COMPARISON OF SALINE, HYALURONIC ACID AND XYLITOL NASAL IRRIGATION SOLUTIONS AFTER ENDOSCOPIC SINUS SURGERY: A PROSPECTIVE RANDOMIZED STUDY

Osman ERDOĞAN[1], MD; Onur İSMİ[2], MD; Yusuf VAYISOĞLU[2], MD; Kemal GÖRÜR[2], MD; Cengiz ÖZCAN[2], MD;

[1]Şanlıurfa Eğitim ve Araştırma Hastanesi, Kulak Burun Boğaz Hastalıkları, Şanlıurfa, Turkey [2]Mersin Üniversitesi Tıp Fakültesi, Kulak Burun Boğaz Hastalıkları, Mersin, Turkey

SUMMARY

Objective: To evaluate the effectiveness of saline, xylitol and hyaluronic acid nasal irrigation solutions after endoscopic sinus surgery (ESS) on edema, discharge, crusting, and mucociliary clearance.

Methods: Thirty-four patients who were undergone ESS for chronic sinusitis with or without nasal polyps were prospectively included. Patients were randomly divided into three groups according to the nasal irrigation solutions they used: saline group, hyaluronic acid group, and xylitol group. Nasal obstruction was measured with visual analog scale (VAS). Edema, discharge and crusting levels were scored by nasal endoscopic examination in the first week and first month. Mucociliary clearance was evaluated by applying the saccharin clearance test in the first month.

Results: While there was no difference in crusting between the three groups in the first month, it was observed that there was less crusting in xylitol group than in saline group in the first week (p=0.025). In the saline, hyaluronic acid and xylitol groups, less crusting was observed in the first month compared to the first week (p=0.006, p=0.008 and p=0.014, respectively).

Conclusion: Saline, hyaluronic acid, and xylitol irrigation solutions reduced crusting in patients underwent ESS. Xylitol solution showed this effect in the early period. After ESS, saline, hyaluronic acid, and xylitol solutions can be effectively used for nasal irrigation. Xylitol solutions can be recommended to patients with a history of crusting or prone to crusting in dry climates.

Keywords: Nasal irrigation, saline, hyaluronic acid, xylitol, mucociliary clearance, endoscopic sinus surgery

ENDOSKOPİK SİNÜS CERRAHİSİ SONRASI SALIN, HYALURONİK ASİT VE KSİLİTOL NAZAL İRRİGASYON SOLÜSYONLARININ KARŞILAŞTIRILMASI: PROSPEKTİF, RANDOMİZE BİR ÇALIŞMA

ÖZET

Amaç: Endoskopik sinüs cerrahisi (ESC) sonrası salin, ksilitol ve hyaluronik asit nazal yıkama solüsyonlarının ödem, akıntı, kabuklanma ve mukosiliyer klirens üzerindeki etkinliğini değerlendirmek.

Yöntemler: Nazal polipli veya polipsiz kronik sinüzit nedeniyle ESC uygulanan 34 hasta prospektif olarak çalışmaya dahil edildi. Hastalar kullandıkları nazal yıkama solüsyonlarına göre rastgele üç gruba ayrıldı: salin grubu, hyaluronik asit grubu ve ksilitol grubu. Burun tıkanıklığı görsel analog skala ile ölçüldü. Birinci hafta ve birinci ayda nazal endoskopik muayene ile ödem, akıntı ve kabuklanma düzeyleri ölçüldü. Birinci ayda sakkarin klirens testi uygulanarak mukosiliyer klirens değerlendirildi.

Bulgular: Birinci ayda üç grup arasında kabuklanma açısından fark yokken, birinci hafta ksilitol grubunda salin grubuna göre daha az kabuklanma olduğu görüldü (p=0,025). Salin, hyaluronik asit ve ksilitol gruplarında 1. ayda 1. haftaya göre daha az kabuklanma gözlendi (sırasıyla p=0.006, p=0.008 ve p=0.014).

Sonuç: Salin, hyaluronik asit ve ksilitol yıkama solüsyonları ESC uygulanan hastalarda kabuklanmayı azaltmıştır. Xylitol solüsyonu bu etkiyi erken dönemde göstermiştir. ESC'den sonra burun yıkama için salin, hyaluronik asit ve ksilitol solüsyonları etkili bir şekilde kullanılabilir. Ksilitol solüsyonları kuru iklimlerde kabuklanma öyküsü olan veya kabuklanmaya eğilimli hastalara önerilebilir.

Anahtar Sözcükler: Nazal yıkama, salin, hyaluronik asit, ksilitol, mukosiliyer klirens, endoskopik sinüs cerrahisi

INTRODUCTION

Chronic rhinosinusitis is one of the most important health problems because it significantly increases health expenditures and has a significant effect on lower respiratory tract diseases and general health[1]. Chronic rhinosinusitis without nasal polyps was reported as the most common chronic disease in the USA in 1997, according to the basic data of the National Institute of Allergy and Infectious Diseases, 16.3% of the entire population was affected by this disease[2]. Nasal irrigation is recommended after endoscopic sinus surgery (ESS) in chronic rhinosinusitis with or without nasal polyps. Postoperative nasal irrigation aims to remove infected debris and crusts, reduce synechia formation, accelerate mucosal healing, increase sinonasal drainage, and mucociliary clearance[3,4]. In the first article on the importance

Corresponding Author: Osman ERDOĞAN MD Şanlıurfa Eğitim ve Araştırma Hastanesi, Kulak Burun Boğaz Hastalıkları, Şanlıurfa, Turkey, E-mail: osman_erdogan@outlook.com

Received: 07 January 2023, revised for: 04 March 2023, accepted for publication: 04 March 2023

Cite this article: Erdoğan O., İsmi O., Vayısoğlu Y., Görür K., Özcan C., Comparison Of Saline, Hyaluronic Acid And Xylitol Nasal Irrigation Solutions After Endoscopic Sinus Surgery: A Prospective Randomized Study. KBB-Forum 2023;22(1):057-062

of nasal irrigation, published in 1902 by Wingrave[5], various solutions were used for the removal of dense secretions, deposits, and foreign bodies in the nasal cavity, for antisepsis and for diagnostic purposes.

To date, normal saline (0.9% sodium chloride) solution has been most commonly used for nasal irrigation. Many nasal irrigation solutions with different contents have been compared in the literature. These solutions include tap water, normal saline, hypertonic saline, solution containing xylitol, solution containing hyaluronic acid, hypertonic seawater, lactated Ringer's solution, saline containing sodium bicarbonate, solution containing surfactant, and solution containing budesonide[6-12].

Changes in salt concentrations in the airway surface liquid (ASL) affect antimicrobial factors. Xylitol, a five-carbon sugar-alcohol, is non-ionic and has low transepithelial permeability, thus increasing the antimicrobial activity by reducing ASL salt concentration.[13]. In addition, it causes less crust formation by reducing mucus viscosity with its humectant feature[14].

Hyaluronic acid is a non-sulfated, major glycosaminoglycan. It is one of the most important extracellular matrix components in the nasal and tracheobronchial mucosa. It plays an important role in epithelial mucociliary clearance, repair of the mucosal surface, wound healing process, and viscoelasticity of structures during speech[15].

In this study, the efficacy of solutions such as saline, hyaluronic acid and xylitol used for nasal irrigation after ESS for chronic rhinosinusitis with or without nasal polyps were evaluated. Considering the nasal mucosal protective effects of hyaluronic acid and xylitol solutions, it has been hypothesized that they will be more effective than saline solution on postoperative nasal congestion, edema, discharge, crusting, and mucociliary clearance.

MATERIAL and METHODS

Study design

This prospective and randomized study was approved by the Clinical Research Ethics Committee. Informed consent was obtained from the patients.

Study population

Thirty-four patients who underwent ESS for chronic sinusitis with or without polyps were included in the study. The inclusion criteria of the patients were defined as chronic sinusitis with or without polyps and bilateral localization of the disease. Patients with a history of immunosuppression, cystic fibrosis, primary ciliary dyskinesia, active smoking, antifungal medical therapy, radiation to the head and neck region, pregnancy, and granulomatous disease were excluded from the study.

Treatment

All patients underwent ESS with the Messerklinger approach. In line with the approach, maxillary antrostomy, anterior and posterior ethmoidectomy were performed, but the frontal and sphenoid sinuses were not intervened. Merocel nasal packing was applied for 2 days after the surgery. Patients used nasal decongestant spray for 5 days after nasal packing removal. Patients were randomly divided into three groups according to the nasal irrigation solutions they used: saline group (0.9% sodium chloride), hyaluronic acid group (0.9% sodium chloride + sodium bicarbonate + hyaluronic acid) and xylitol group (0.9% sodium chloride + sodium bicarbonate + xylitol). They performed nasal irrigation with these solutions three times a day for a period of one month postoperatively. They were instructed to douche each nasal cavity with 100 ml of solution with a squeeze bottle. During nasal douching, they were asked to adjust their head position by leaning their face 45 degrees forward.

Examination

Edema, discharge and crusting levels were determined by nasal endoscopic examination without the use of nasal decongestants and local anesthetics in the first week and first month follow-ups of the patients. In endoscopic nasal scoring, edema (0: absent, 1: mild-moderate, 2: moderate-severe), discharge (0: absent, 1: thin and clear, 2: thick and purulent) and crusting (0: absent, 1: mild-moderate, 2: moderate-severe) rated according to severity[16]. Before the nasal endoscopic examination, patients were asked to record perceived nasal obstruction on a scale of 0% to 100% (no obstruction to worst obstruction) via 10 cm visual analogue scale (VAS). In the first

month follow-up examination, the mucociliary activity was evaluated by applying the saccharin clearance test. In this test, a saccharin tablet was placed in the anteroinferior of the left inferior turbinate and the time elapsed until the taste of sugar in the patient's mouth was noted.

Statistical analysis

The data of the groups were shown as mean ± standard deviation. The continuous data were tested for normality with the Shapiro Wilk test. Independent nasal irrigation groups were compared with the Kruskal Wallis test. Pairwise comparisons of the nasal irrigation groups were made with Mann-Whitney U-test with Bonferroni correction. Wilcoxon signed rank test was used to compare the nasal endoscopic scores in the first week and the first month. Statistical significance level was accepted as <0.05.

RESULTS

The mean age of thirty-four patients included in the study was 43.47 ± 15.48 (range 16-70). The female to male ratio is 12:22. Demographic data of the patients were given in Table 1.

There was no difference between the groups in VAS scores of the first week and first month, in which nasal obstruction was measured. In endoscopic nasal scoring, there was no difference between the three groups in edema and discharge scores at the first week and the first month. While there was no difference in the crusting between the three groups in the first month, there was a statistically significant difference between them in the first week (p=0.029). In the pairwise comparison, it was observed that there was less crusting in the xylitol group than in the saline group (p=0.025). There was no difference between the three groups in the saccharin clearance test. The nasal endoscopic scores of the three groups were presented in Table 2.

When comparing the nasal endoscopic scores of each group between the first week and the first month, no significant difference was found in the nasal obstruction, edema, and discharge. In the saline, hyaluronic acid and xylitol groups, less crusting was observed in the first month compared to the first week (p=0.006, p=0.008 and p=0.014, respectively). First week and first month nasal endoscopic scores were shown in Table 3.

Table 1: Demographic data of the patients are presented as n (%)

	Total (n=34)	Salin group (n=13)	Hyaluronic acid group (n=10)	Xylitol group (n=11)
Gender, female	12 (35.3)	4 (30.8)	4 (40)	4 (36.4)
Family history of atopy	8 (23.5)	3 (23.1)	3 (30)	2 (18.2)
Allergy	5 (14.7)	2 (15.4)	2 (20)	1 (9.1)
Asthma	7 (20.6)	3 (23.1)	2 (20)	2 (18.2)

Table 2: Nasal endoscopic scores and saccharine clearance test results of salin, hyaluronic acid, and xylitol groups were compared

		Salin group (n=13)	Hyaluronic acid group (n=10)	Xylitol group (n=11)	p
Age (yr)		42.92±18.54	41.10±13.67	46.27±13.86	0.593
Nasal obstruction	1st week	6.77±2.32	8.60±1.43	6.91±2.98	0.128
	1st month	8.54±2.33	9.20±1.03	8.45±1.21	0.401
Edema	1st week	0.83±0.72	0.80±0.79	0.73±0.65	0.947
	1st month	1.08±0.76	0.70±0.48	0.82±0.87	0.466
Nasal discharge	1st week	0.83±0.84	0.40±0.52	1.00±0.45	0.088
	1st month	1.00±0.58	0.60±0.52	0.64±0.51	0.176
Crusting	1st week	1.58±0.67	1.20±0.42	0.82±0.75	0.029*
	1st month	0.38±0.51	0.20±0.42	0.00±0.00	0.073
Saccharine clearance test (second)	1st month	621.92±269.53	1063.00±930.97	1147.82±823.95	0.216

*: statistically significant

Table 3: Comparison of first week and first month nasal endoscopic scores of salin, hyaluronic acid, and xylitol groups

		1st week	1st month	p
Nasal obstruction	Salin group	6.77±2.32	8.54±2.33	0.076
	Hyaluronic acid group	8.60±1.43	9.20±1.03	0.141
	Xylitol group	6.91±2.98	8.45±1.21	0.078
Edema	Salin group	0.83±0.72	1.08±0.76	0.257
	Hyaluronic acid group	0.80±0.79	0.70±0.48	0.655
	Xylitol group	0.73±0.65	0.82±0.87	0.739
Nasal discharge	Salin group	0.83±0.84	1.00±0.58	0.527
	Hyaluronic acid group	0.40±0.52	0.60±0.52	0.157
	Xylitol group	1.00±0.45	0.64±0.51	0.102
Crusting	Salin group	1.58±0.67	0.38±0.51	0.006*
	Hyaluronic acid group	1.20±0.42	0.20±0.42	0.008*
	Xylitol group	0.82±0.75	0.00±0.00	0.014*

*: statistically significant

DISCUSSION

The present study showed that while the xylitol group eliminated crusting more than the saline group in the first week, both solutions reduced crusting by the similar amount in the first month. After ESS, there was a decrease in crusting in all three solution types in the first month compared to the first week. According to the hypothesis of the present study, the expected positive effect on nasal obstruction, edema, discharge, crusting, and mucosal clearance in hyaluronic acid and xylitol solutions compared to saline solution was observed only in xylitol solution on crusting in the early period.

Weissman et al. reported that xylitol solution provided improvement in sinonasal symptoms by reducing the SNOT-20 score compared to saline solution, but did not create a difference in well-being VAS score[11]. Kim et al. reported greater improvement in SNOT-20 and snoring, headache and facial pain VAS scores after ESS and/or septoplasty in the xylitol group compared to the saline group[17]. The present study revealed that xylitol solution was not superior to the other solutions, except for its effect on crusting in the early period.

In chronic rhinosinusitis, wet viscoelastic mucus is usually seen in the nasal cavity before surgery, while thick mucus and crusting are seen after surgery[18,19]. The crusting can cause postoperative scar formation, increased bacterial activity, and recalcitrant diseases[20]. While nasal irrigation solutions such as hypertrophic saline or normal saline significantly reduce postoperative crusting, they are not superior to each other[21]. Hardcastle et al. reported in their in vitro study that xylitol was more effective in dissolving crusting than saline solution. They proposed that xylitol causes water retention within the crust to dissolve it. In addition, they suggest that the symptoms of chronic rhinosinusitis can be alleviated by providing hydration of the nasal mucosa with water retention[22]. In the present study, the superiority of xylitol solution in reducing crusting in the early period can be explained by the water retention and nasal mucosa hydration effect.

Hyaluronic acid plays an important role in mucociliary clearance, wound healing, and repair of mucosal surfaces[23,24]. Gelardi et al. reported that after FESS, less nasal discharge and nasal congestion were observed with hyaluronic acid used for nasal irrigation compared to saline solution[15]. In a study by Casale et al. in which they evaluated turbinate edema, secretion, and crusting after inferior turbinate radiofrequency treatment, they achieved better scores, especially in crusting, in patients who performed nasal irrigation with hyaluronic acid compared to the saline group[25]. In the present study, hyaluronic acid was not superior to saline and xylitol solutions on edema, discharge, nasal congestion and mucociliary clearance. Although all solutions have a positive effect on crusting in the first month compared to the first week, there is no difference between the solutions.

Studies on mucociliary clearance have reported that ringer-lactate, hyaluronic acid, buffered hypertrophic saline solutions increase mucociliary clearance more than saline solutions in the postoperative period[4,9,15,26]. On the contrary, a study by Boek et al. reported that saline solution may have a negative effect on mucociliary activity[27]. In the present study, xylitol and hyaluronic acid solutions were not superior to saline solution in terms of mucociliary clearance.

CONCLUSION

While all three solutions evaluated in the present study reduced crusting, xylitol was the solution that showed this effect in the early period. After ESS, saline, hyaluronic acid, and xylitol solutions can be effectively used for nasal irrigation. In order to reduce crusting in the early postoperative period, xylitol solutions can be recommended to patients with a history of crusting or prone to crusting in dry climates.

REFERENCES

1. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, Toppila-Salmi S, Bernal-Sprekelsen M, Mullol J. Executive Summary of EPOS 2020 Including Integrated Care Pathways. Rhinology 2020; 58(2):82-111. https://doi.org/10.4193/rhin20.601

2. Bachert C, Van Bruaene N, Toskala E, Zhang N, Olze H, Scadding G, Van Drunen CM, Mullol J, Cardell L, Gevaert P, Van Zele T, Claeys S, Halldén C, Kostamo K, Foerster U, Kowalski M, Bieniek K, Olszewska-Ziaber A, Nizankowska-Mogilnicka E, Szczeklik A, Swierczynska M, Arcimowicz M, Lund V, Fokkens W, Zuberbier T, Akdis C, Canonica G,

Van Cauwenberge P, Burney P, Bousquet J. Important research questions in allergy and related diseases: 3-chronic rhinosinusitis and nasal polyposis - a GA2LEN study. Allergy 2009; 64(4):520-533. https://doi.org/10.1111/j.1398-9995.2009.01964.x

3. Keojampa BK, Nguyen MH, Ryan MW. Effects of buffered saline solution on nasal mucociliary clearance and nasal airway patency. Otolaryngology - Head Neck Surg 2004; 131(5):679-682. https://doi.org/10.1016/j.otohns.2004.05.026

4. Talbot AR, Herr TM, Parsons DS. Mucociliary Clearance and Buffered Hypertonic Saline Solution. Laryngoscope 1997; 107(4):500-503. https://doi.org/10.1097/00005537-199704000-00013

5. Wingrave W. A clinical lecture on the nature of discharges and douches. Lancet 1902; 159(4107):1373-1375. https://doi.org/10.1016/s0140-6736(01)83808-3

6. Kurtaran H, Ugur KS, Yilmaz CS, Kaya M, Yuksel A, Ark N, Gunduz M. The effect of different nasal irrigation solutions following septoplasty and concha radiofrequency: a prospective randomized study. Braz J Otorhinolar 2018; 84(2):185-190. https://doi.org/10.1016/j.bjorl.2017.01.005

7. Low TH, Woods CM, Ullah S, Carney AS. A double-blind randomized controlled trial of normal saline, lactated Ringer"s, and hypertonic saline nasal irrigation solution after endoscopic sinus surgery. Am J Rhinol Allergy 2014; 28(3):225-231. https://doi.org/10.2500/ajra.2014.28.4031

8. Salib RJ, Talpallikar S, Uppal S, Nair SB. A prospective randomised single-blinded clinical trial comparing the efficacy and tolerability of the nasal douching products SterimarTM and Sinus RinseTM following functional endoscopic sinus surgery. Clin Otolaryngol 2013; 38(4):297-305. https://doi.org/10.1111/coa.12132

9. Macchi A, Terranova P, Digilio E, Castelnuovo P. Hyaluronan Plus Saline Nasal Washes in the Treatment of Rhino-Sinusal Symptoms in Patients Undergoing Functional Endoscopic Sinus Surgery for Rhino-Sinusal Remodeling. Int J Immunopath Ph 2013; 26(1):137-145. https://doi.org/10.1177/039463201302600113

10. Farag AA, Deal AM, McKinney KA, Thorp BD, Senior BA, Ebert CS Jr, Zanation AM. Single-blind randomized controlled trial of surfactant vs hypertonic saline irrigation following endoscopic endonasal surgery. Int Forum Allergy Rh 2013; 3(4):276-280. https://doi.org/10.1002/alr.21116

11. Weissman JD, Fernandez F, Hwang PH. Xylitol nasal irrigation in the management of chronic rhinosinusitis: A pilot study. Laryngoscope 2011; 121(11):2468-2472. https://doi.org/10.1002/lary.22176

12. Kang TW, Chung JH, Cho SH, Lee SH, Kim KR, Jeong JH. The Effectiveness of Budesonide Nasal Irrigation After Endoscopic Sinus Surgery in Chronic Rhinosinusitis With Asthma. Clin Exp Otorhinolar 2016; 10(1):91-96. https://doi.org/10.21053/ceo.2016.00220

13. Brown CL, Graham SM, Cable BB, Ozer EA, Taft PJ, Zabner J. Xylitol Enhances Bacterial Killing in the Rabbit Maxillary Sinus. Laryngoscope 2004; 114(11):2021-2024. https://doi.org/10.1097/01.mlg.0000147939.90249.47

14. Cohen S, Marcus Y, Migron Y, Dikstein S, Shafran A. Water sorption, binding and solubility of polyols. J Chem Soc Faraday Trans 1993; 89(17):3271-3275. https://doi.org/10.1039/ft9938903271

15. Gelardi M, Guglielmi AVN, Candia ND, Maffezzoni E, Berardi P, Quaranta N. Effect of sodium hyaluronate on mucociliary clearance after functional endoscopic sinus surgery. European Ann Allergy Clin Immunol 2013; 45(3):103-108.

16. Lund VJ, Kennedy DW. Quantification for staging sinusitis. The Staging and Therapy Group. Ann Otology Rhinology Laryngology Suppl 1995; 167:17-21

17. Kim DH, Kim Y, Lim IG, Cho JH, Park YJ, Kim SW, Kim SW. Effect of Postoperative Xylitol Nasal Irrigation on Patients with Sinonasal Diseases. Otolaryngology Head Neck Surg 2018; 160(3):550-555. https://doi.org/10.1177/0194599818802815

18. Pigret D, Jankowski R. Management of post-ethmoidectomy crust formation: randomized single-blind clinical trial comparing pressurized seawater versus antiseptic/mucolytic saline. Rhinology 1996; 34(1):38-40.

19. Benninger M, Anon J, Mabry R. The medical management of rhinosinusitis. Otolaryngol Head Neck Surg 1997; 117(3):S41-49. https://doi.org/10.1016/s0194-5998(97)70006-8

20. Thaler ER. Postoperative Care After Endoscopic Sinus Surgery. Archives Otolaryngology Head Neck Surg 2002; 128(10):1204-1206. https://doi.org/10.1001/archotol.128.10.1204

21. Vakil AJ, Ojha T, Prasad S, Singh P. Comparison of Hypertonic Saline with Normal Saline in Nasal Irrigation Post Endoscopic Sinus Surgery. Indian J Otolaryngol 2022; 74(Suppl 2):1518-1522. https://doi.org/10.1007/s12070-021-02620-x

22. Hardcastle T, Jain R, Radcliff F, Waldvogel-Thurlow S, Zoing M, Biswas K, Douglas R. The in vitro mucolytic effect of xylitol and dornase alfa on chronic rhinosinusitis mucus. Int Forum Allergy Rh 2017; 7(9):889-896. https://doi.org/10.1002/alr.21970

23. Manzanares D, Monzon M-E, Savani RC, Salathe M. Apical Oxidative Hyaluronan Degradation Stimulates Airway Ciliary Beating via RHAMM and RON. Am J Resp Cell Mol 2007; 37(2):160-168. https://doi.org/10.1165/rcmb.2006-0413oc

24. Forteza R, Lieb T, Aoki T, Savani RC, Conner GE, Salathe M. Hyaluronan serves a novel role in airway mucosal host defense. Faseb J 2001; 15(12):2179-2186. https://doi.org/10.1096/fj.01-0036com

25. Casale M, Ciglia G, Frari V, Incammisa A, Mazzola F, Baptista P, Mladina R, Salvinelli F. The potential role of hyaluronic acid in postoperative radiofrequency surgery for chronic inferior turbinate hypertrophy. Am J Rhinol Allergy 2013; 27(3):234-236. https://doi.org/10.2500/ajra.2013.27.3869

26. Ünal M, Görür K, Özcan C. Ringer-Lactate solution versus isotonic saline solution on mucociliary function after nasal septal surgery. J Laryngology Otology 2001; 115(10):796-797. https://doi.org/10.1258/0022215011909288

27. Boek WM, Keles N, Graamans K, Huizing EH. Physiological and hypertonic saline solutions impair ciliary activity in vitro. Clin Otolaryngology Allied Sci 2000; 25(4):331-332. https://doi.org/10.1046/j.1365-2273.2000.00358-33.x