


# Nasal mucosa healing after endoscopic sinus surgery in chronic rhinosinusitis of elderly patients: role of topic alpha-tocopherol acetate

Domenico Testa<sup>1</sup> · Giuseppina Marcuccio<sup>1</sup> · Giorgio Panin<sup>2</sup> · Andrea Bianco<sup>3</sup> ·  
Domenico Tafuri<sup>4</sup> · Francesco Zappoli Thyron<sup>1</sup> · Michele Nunziata<sup>1</sup> ·  
Pasquale Piombino<sup>1</sup> · Germano Guerra<sup>2</sup>  · Gaetano Motta<sup>1</sup>

Received: 18 September 2016 / Accepted: 12 October 2016  
© Springer International Publishing Switzerland 2016

## Abstract

**Background** Chronic rhinosinusitis (CRS) in European country ranges in elderly patients from 4.5 to 12% of population and has a significant effect on quality of life. In these patients, rhinosinusitis is linked to immune functions changes with age and to mucosal paraphysiological alterations such as crusting formations with atrophic epithelium, variations of nasal airflow and modifications of the mucociliary clearance. Failure of medical treatments leads to surgery in patients with persistent symptoms and radiographic signs of CRS. The choice of appropriate post-surgical topic treatments is important for healing time and for preventing mucosal complications such as synechiae, crusting formation and atrophy with secondary bacterial and fungal infections.

**Aims** Defining the effects of topic alpha-tocopherol acetate administration on nasal mucosa healing after endoscopic sinus surgery in CRS of elderly patients.

**Methods** In this study were included 32 patients, mean age 68.6, who underwent FESS because affected by CRS not

responsive to medical treatments. After surgical treatment, we distinguish two groups basing on local nasal therapy.

**Results** We investigated, in the postoperative time, the role of alpha-tocopherol acetate compared to gomenol oil. Follow-up was performed at 7–15 days and 1–3 months after surgery. We evaluated mucosal restoration using Rhinoscopy Sum Score and quality of life using Nasal Six Items Symptom Questionnaire. We observed a faster healing time and less recurrence of complications in patients who underwent topic treatment with alpha-tocopherol acetate.

**Discussion** In our research, we observed that alpha-tocopherol acetate has no contraindications and side effects.

**Conclusions** Our study showed the effectiveness of alpha-tocopherol acetate topic treatment in elderly patients affected by CRS after FESS, in improving and speeding up the process of restoring the sinonasal mucosa, compared to another topic medication.

**Keywords** Alpha-tocopherol acetate · Nasal mucosa · Chronic rhinosinusitis (CRS) · Rhinoscopy Sum Score (RSS) · Functional endoscopic sinonasal surgery (FESS)

✉ Germano Guerra  
germano.guerra@unimol.it

<sup>1</sup> Department of Anesthesiologic, Surgical and Emergency Sciences, Otolaryngology, Head and Neck Surgery Unit, Second University of Naples, Naples, Italy

<sup>2</sup> Department of Medicine and Health Sciences “V Tiberio”, University of Molise, Via F. De Santis, 86100 Campobasso, Italy

<sup>3</sup> Department of Cardiothoracic and Respiratory Sciences, Second University of Naples, A.O. Dei Colli - Monaldi Hospital, Naples, Italy

<sup>4</sup> Department of Sport Sciences and Wellness, University of Naples “Parthenope”, Naples, Italy

## Introduction

Chronic rhinosinusitis (CRS) ranges from 4.5 to 12% of all the European population [1–3]. Although not life threatening, it seriously interferes with the quality of life (QL) and represents a challenging problem to deal with it in terms of surgery and postoperative management [1–3]. Risk factors for developing CRS include allergy; sinonasal anatomic variations; compromised immune status; mucociliary disfunctions; lower airways involvement. [4, 5]. CRS is often associated to asthma with increasing

**Table 1** Diagnostic criteria of the American Academy of Otolaryngology-Head and Neck Surgery of Chronic Sinusitis in Adults (2015)

Chronic rhinosinusitis	Twelve weeks or longer of two or more of the following signs and symptoms Nasal obstruction (congestion) Mucopurulent drainage (anterior, posterior or both) Facial pain–pressure–fullness, or Decreased sense of smell and inflammation is documented by one or more of the following findings Purulent (not clear) mucus or edema in the middle meatus or ethmoid region Polyps in nasal cavity or the middle meatus, and/or Radiographic imaging showing inflammation of the paranasal sinuses
Recurrent acute rhinosinusitis	Four or more episodes per year of acute bacterial rhinosinusitis without signs or symptom of rhinosinusitis between episodes

morbidity and mortality in older patients: the death rate due to asthma is 14 times higher for people over than 65 years old [6]. Furthermore, in elderly patients CRS might lead to decreasing cognitive functions at the Mini-Mental State Examination [7]. CRS in old patients is also linked to immune functions changes with age, immunosenescence, depending on impaired cell-mediated immunity due to thymus involution [8, 9].

A lot of pathogenic mechanisms are proposed for CRC including oxidative stress and elevated ROS (reactive oxygen species) especially in old age [10, 11]. These factors are implicated in cancer, higher probability of complications, like cardiovascular illness, respiratory complications, and challenging management of physical and psychological conditions [12–14].

Medical treatments for chronic rhinosinusitis include topic and systemic drugs (steroids, nasal decongestionants, mucolytic agents and antibiotics) in order to reduce intranasal inflammation, to promote nasal and paranasal drainage and to treat possible bacterial infections [15]. Failure of medical treatments induces surgical indication in symptomatic patients with radiological and clinical evidence of CRS [16, 17]. Regardless of medical postsurgical treatment, sinonasal mucosa requires an average healing time, and even following a precise surgical technique, complications can arise both in the immediate and after weeks from the surgical procedure even if an appropriate surgical technique is performed [16]. To avoid these complications such as bleeding, excessive crusting, synechia formation or infections, it is necessary a specific postoperative treatment [17]. A constant cleaning of the nasal cavities can prevent the stagnation of blood and secretions and can promote a functional recovery after surgery and a proper tissue repair [16]. For this reason, a correct postoperative treatment of patients subjected to sinonasal surgery is a primary importance to ensure the success of the surgical treatment, making possible to prevent the risk of complications and guarantee a quick healing and an effective recovery of respiratory functions

[17]. Considering the actual medical treatments, in elderly patients decreased immune response and dehydration of nasal mucosa, due to paraphysiological histologic changes, cause a longer healing time [16, 17].

Alpha-tocopherol acetate,  $\alpha$  isoform of vitamin E discovered by Evans and Bishop in 1938, has anti-inflammatory, antioxidant and immunostimulatory functions widely documented in different anatomical regions, such as skin, oral, vaginal and gastric mucosa [18–26]. In this research study, we investigated the activity of alpha-tocopherol acetate in the postoperative treatment in elderly patients undergoing sinonasal surgery for Chronic rhinosinusitis.

## Methods

In this study were included 32 patients (19 M e 13 F) of age 65–76 years (mean age 68.6), who underwent functional endoscopic sinonasal surgery (FESS) in Head and Neck Surgery Unit of Second University of Naples, between November 2014 and April 2016. These patients received the diagnosis of Chronic rhinosinusitis using diagnostic criteria of the American Academy of Otolaryngology-Head and Neck Surgery [27, 28] (Table 1). The etiopathogenesis of CRS in these patients was allergic (14 patients, 9 M and 5 F), odontogenic (2 patients, 2 M) and related to paranasal anatomic anomalies (in 16 patients, 7 M and 9F). The first assessment was carried out through the use of nasal fiberoptic endoscopy (rigid endoscope, 2.7 mm diameter; angle views 0°, 30° and 45° degrees). We excluded patients with barotraumatic sinusitis, fungal sinusitis, nasal polyposis, mucocele, antrochoanal polyps, topic drugs abuse, uncontrollable arterial hypertension, diabetes mellitus, immune-depressed state and patients with less than 3 months of follow-up. All patients showed Chronic rhinosinusitis without nasal polyps (CRSsNP), with persisting facial pain and purulent rhinorrhea for at least 1 year and not responsive to topic and systemic medical treatments.

**Table 2** Nasal Six Items Questionnaire

Nasal symptoms	Score		
	0	1	2
Dry nose	Not observed	Sometimes	Always
Itching	Never	Sometimes	Always
Nasal obstruction	Not observed	Sometimes	Always
Hyposmia/anosmia	Not observed	Sometimes	Always
Cacosmia	Not observed	Sometimes	Always
Nasal crusting	Not observed	Sometimes	Always

**Table 3** Rhinoscopy Sum Score

	2 weeks	1 month	3 months
A	5.40	3.18	3.00
B	6.12	5.50	3.06

Individual rhinoscopic findings: dried nasal mucus, dryness, fibrin deposition, nasal obstruction; (Score: 0—none; 1—mild; 2—moderate; 3—severe)

These patients were evaluated with CT scan after 1 month of therapy, showing mucoperiosteal thickening and multiple paranasal sinuses opacification, and nasal endoscopy confirmed the diagnosis. For them, surgical treatment

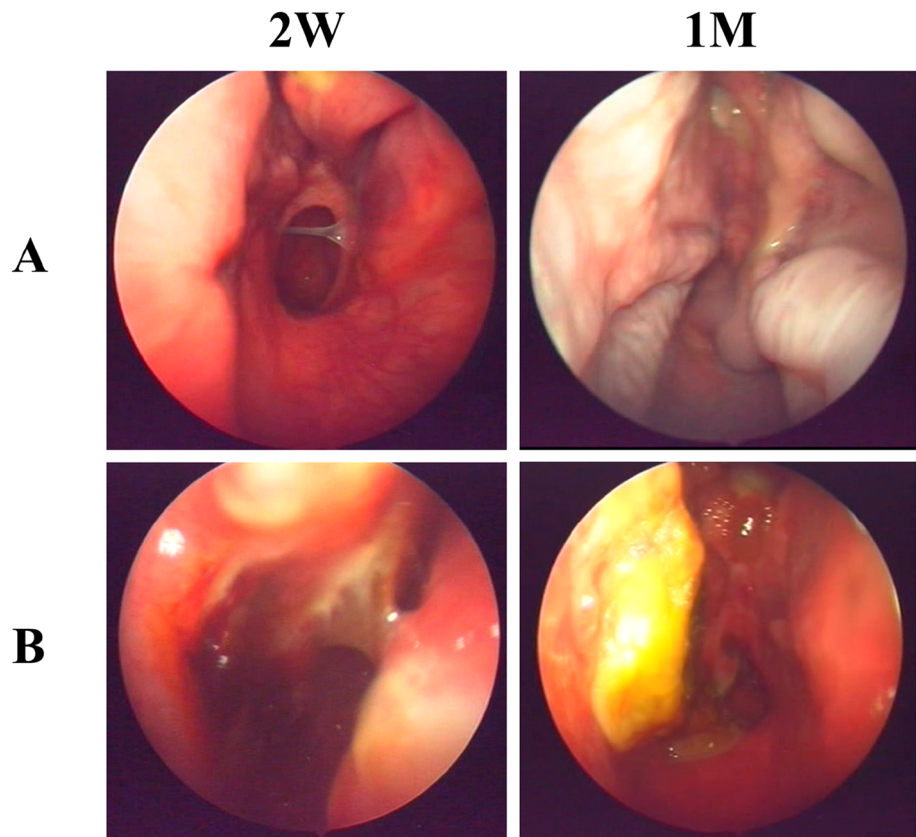
choice was functional endoscopic sinonasal surgery (FESS), in addition to septoturbinoplasty when needed.

Two groups were selected, randomly assigned: group A (study group) including 16 patients (10 M and 6 F) treated with nasal hypertonic saline solution (2 puff each nostril 8/10 times, daily for 15 days) associated with alpha-tocopherol acetate (2 puff each nostril 3 times, daily for 3 months) topical treatments after surgery, and group B, control group, including 16 patients (9 M and 9F) treated with nasal hypertonic saline solution (2 puff each nostril 8/10 times, daily for 15 days) and gomenol oil (2 applications each nostril 3 times, daily for 3 months) topical treatments after surgery. Follow-up was performed at 7–15 days, and 1–3 months after surgery. Clinical evaluation has provided nasal endoscopy, Rhinoscopy Sum Score (RSS) and quality of life evaluation using Nasal Six Items Questionnaire (Table 2).

## Results

The primary evaluation was performed through RSS (Table 3; Fig. 1), which was attained from the clinical, objectively recorded endoscopy findings: nasal dryness, dried nasal mucus, fibrin deposition and nasal obstruction.

**Fig. 1** Nasal endoscopic evaluation after 2 weeks and after 1 month of medical postsurgical treatment (**a** alpha-tocopherol acetate; **b**: gomenol oil)



**Table 4** Complications after ESS: 1 patient (group A) presented septoturbinal synechia; 3 patients (group B) presented septoturbinal synechia and 1 patient (group B) presented closure of maxillary meatoplasty

Tot.	N°	%
A	1	6.25
B	4	25

**Table 5** Results at Nasal Six Items Questionnaire before and after topic medical treatments in Group A (alpha-tocopherol acetate-treated patients) and in Group B (gomenol oil-treated patients)

	Before surgical treatment	1 month after surgery	3 months after surgery
Group A	8.9	1.7	1.3
Group B	9.1	3.6	1.5

All these parameters were evaluated using a 4-point scale as follows:

- absent = 0;
- mild = 1;
- moderate = 2;
- severe = 3.

In just 2 weeks of therapy, it was possible to demonstrate a lower score at RSS in the nasal cavities of group A, compared to B. In 1-month group A showed a complete healing of the nasal mucosa, with complete absence of crusts. Group B, in the same period, revealed nasal cavities still occupied by eschar and not well epithelialized. Nasal endoscopy demonstrates complete healing of sinonasal mucosa of Group B, only at the third month. At the end of the follow-up (third month) was possible to observe less recurrence of complications in the study group such as septoturbinal synechia (1 case in group A, 3 in group B) and partial closure of maxillary meatoplasty, with secondary infection of the sinus (1 case in Group B, after FESS + septoturbino-plasty) (Table 4). These complications required a second revision surgery under local anesthesia, and no complications needed further treatment or surgical procedure under general anesthesia. At Nasal Six Items Questionnaire, we observed the following: group A showed after 1 month of therapy a decreased mean value in patients treated with alpha-tocopherol acetate; instead patients of group B referred the persistence of symptoms 1 month after medical treatment (Table 5).

## Discussion

CRS in elderly has significant effects on quality of life, increasing in some cases morbidity and mortality for asthma and bronchopneumonia and causing a decrease in

cognitive functions [1–3]. Nasal mucosa in the geriatric population presents crusting with atrophic epithelium, variation of nasal airflow and alterations in mucociliary clearance; the same morphological and functional changes are observed in postmenopausal women [8, 29, 30]. These physiopathological conditions induce clinical evidence of cough, olfactory loss, postnasal drip and nasal dryness [8, 9]. When medical treatment fails, surgery is indicated and FESS has become the procedure of choice [15–17]. After surgical treatment, nasal mucosa needs to be restored in order to reduce healing time. Alpha-tocopherol acetate for its anti-inflammatory, antioxidant and immunostimulatory functions has been used in other anatomic district [22, 31–33]. In our study, we investigate the role of topic alpha-tocopherol acetate in nasal and sinusal mucosal restoration, after FESS by means of nasal endoscopy before and after 7–15 days and after 1–3 weeks from surgery. In just 2 weeks of medical treatment, we observed less formation of crusts in nasal cavities of patients treated with alpha-tocopherol acetate (group A), compared to patients treated with gomenol oil (group B). In 1 month, group A showed a complete healing of the nasal mucosa, with complete absence of crusts. Group B, in the same, period revealed nasal cavities still occupied by eschars with not epithelialized mucosa. Patients of group A presented recurrence of complications (septoturbinal synechia) in 6.25% of patients compared to group B patients (Table 4).

Our research showed the effectiveness of alpha-tocopherol acetate topic treatment in improving and speeding up the process of restoring the sinonasal mucosa, compared to other topical medications in which the presence of comorbidity often induce prudence in the administration. We believe that choice of alpha-tocopherol acetate treatment that has no side effects should be preferred in these patients. Endoscopy demonstrates a faster healing process, confirmed by symptoms referred by patients and less recurrence of complications.

## Conclusions

For all these above-mentioned reasons, we consider alpha-tocopherol acetate a valuable aid in postoperative treatment, and we propose it in the postoperative management of sinonasal surgery in elderly patients.

### Compliance with ethical standards

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Human and animal rights** The purpose of the study—that was approved by the local Human Investigation Committee—and complete information regarding it was clearly explained, after which a consent form was signed by all subjects enrolled.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References

- DeConde AS, Soler ZM (2016) Chronic rhinosinusitis: epidemiology and burden of disease. *Am J Rhinol Allergy* 30:134–139
- Smith KA, Orlandi RR, Rudmik L (2015) Cost of adult chronic rhinosinusitis: a systematic review. *Laryngoscope* 125:7–15
- Ryan NW, Brooks EG (2010) Rhinosinusitis and comorbidities. *Curr Allergy Asthma Rep* 10:188–193
- Cughey R, Jameson M, Gross CW et al (2005) Anatomic risk factors for sinus disease: fact of fiction. *Am J Rhinol* 19:334–339
- Vatrella A, Montagnani S, Calabrese C et al (2010) Neuropeptide expression in the airways of COPD patients and smokers with normal lung function. *J Biol Regul Homeost Agents* 24:425–432
- Diette G, Krishnan J, Dominici F et al (2002) Asthma in older patients: factors associated with hospitalization. *Arch Intern Med* 162:1123–1132
- Matsui T, Arai H, Nakajo M et al (2003) Role of chronic sinusitis in cognitive functioning in elderly. *J Am Geriatr Soc* 51:1818–1819
- Pinto JM, Jeswani S (2010) Rhinitis in the geriatric population. *Allergy Asthma Clin Immunol* 6:1–12
- Aspinall R, Andrew D (2000) Thymic involution in aging. *J Clin Immunol* 20:250–256
- Yu Z, Wang Y et al (2015) Expression of heme oxygenase-1 in eosinophilic and non-eosinophilic chronic rhinosinusitis with nasal polyps: modulation by cytokines. *Int Forum Allergy Rhinol* 5:734–740
- Cui H, Kong Y, Zhang H (2012) Oxidative stress, mitochondrial dysfunction, and aging. *J Signal Transduct* 2012:646354. doi:10.1155/2012/646354
- Testa D, Guerra G, Marcuccio G et al (2012) Oxidative stress in chronic otitis media with effusion. *Acta Otolaryngol* 132:834–837
- Cattaneo F, Iaccio A, Guerra G et al (2011) NADPH-oxidase-dependent reactive oxygen species mediate EGFR transactivation by FPRL1 in WKYMVm-stimulated human lung cancer cells. *Free Radic Biol Med* 51:1126–1136
- Conti V, Russomanno G, Corbi G et al (2013) Aerobic training workload affects human endothelial cells redox homeostasis. *Med Sci Sports Exerc* 45:644–653
- Ban JH, Kwon HJ, Lee KC (2010) Outcomes of endoscopic sinus surgery in an elderly population: comparison with those in an adult population. *Clin Otolaryngol* 35:300–306
- Haroon Y, Saleh HA, Abou-Issa AH (2013) Nasal soft tissue obstruction improvement after septoplasty without turbinectomy. *Eur Arch Otorhinolaryngol* 270:2649–2655
- Tan BK, Chandra RK (2010) Postoperative prevention and treatment of complications after sinus surgery. *Otolaryngol Clin North Am* 43:769–779
- Oliguín-Martínez M, Hernández-Espinosa DR, Hernández-Muñoz R (2013)  $\alpha$ -Tocopherol administration blocks adaptive changes in cell NADH/NAD<sup>+</sup> redox state and mitochondrial function leading to inhibition of gastric mucosa cell proliferation in rats. *Free Radic Biol Med* 65:1090–1100. doi:10.1016/j.freeradbiomed.2013.08.176
- Oliguín-Martínez M, Mendieta-Condado E, Contreras-Zentella M et al (2006) Rate of oxidant stress regulates balance between rat gastric mucosa proliferation and apoptosis. *Free Radic Biol Med* 41:1325–1337
- Ying W (2008) NAD<sup>+</sup>/NADH and NADP<sup>+</sup>/NADPH in cellular functions and cell death: regulation and biological consequences. *Antioxid Redox Signal* 10:179–206
- Galuppi A, Perrone AM, La Macchia M et al (2011) Local  $\alpha$ -tocopherol for acute short-term vaginal toxicity prevention in patients treated with radiotherapy for gynecologic tumors. *Int J Gynecol Cancer* 21:1708–1711
- Gambardella V, Sorrentino N, Ciotola A et al (2008) Utilizzo del tocoferolo acetato nella terapia delle vaginosi batteriche in gravidanza. *Giornale Italiano di Ostetricia e Ginecologia*. XXX:21–24
- Meydani M (1995) Vitamin E. *Lancet* 345:170–175
- Osnengo G, Massarenti I, Panin G et al (2007) Tocoferolo acetato in ovuli vaginali: nuovo trattamento topico dopo conizzazione cervicale. *La Colposcopia in Italia XXI*: 23–26
- Casella G, Di Prima T, Ferlito S et al (2007) Stomatite aftosa ricorrente: patologia multifattoriale dalle nuove possibilità terapeutiche. *Il Dentista Moderno XXV*:55–62
- Gastaldi G, Bardellini E, Flocchini P (2003) Topical alpha-tocopherol in the treatment of decubitus ulcers due to prothetic trauma in patients with oral lichen planus. *Doctor OS* 14:883–886
- Rosenfeld AM, Piccirillo JF, Chandrasekhar SS et al (2015) Clinical practice guidelines: adult sinusitis. *Otolaryngol Head Neck Surg* 152:598
- Tafari D, Testa D, Guerra G et al (2006) Barotraumatic sinusitis in underwater sporting activity: physiopathological and clinical evaluations. *Med Sport* 59:335–342
- Nappi C, Di Spiezio Sardo A, Guerra G et al (2003) Functional and Morphological evaluation of the nasal mucosa before and after hormone replacement therapy in postmenopausal women with nasal symptoms. *Fertil Steril* 80:669–671
- Nappi C, Di Spiezio Sardo A, Guerra G et al (2004) Comparison of intranasal and transdermal estradiol on nasal mucosa in postmenopausal women. *Menopause* 11:447–455
- Testa B, Mazzei F, Mesolella M et al (1989) Histamine 2 antagonists in allergic rhinitis relationship of clinical response and serum concentrations of total and specific IgE antibody levels. *Arch Otolaryngol Head Neck Surg* 115:950–953
- Testa B, Mesolella C, Filippini P et al (1993) The role of H<sub>2</sub> antagonists in perennial allergic rhinitis. *Laryngoscope* 103:1013–1019
- Testa D, Motta G, Galli V et al (2006) Outcome assessment in patients with chronic obstructive rhinitis CO<sub>2</sub> laser treated. *Acta Otorhinolaryngol Ital* 26:32