Respecting nasal mucosa during turbinate surgery: end of the dogma?*

G. Neri[1], V. Mastronardi[2], T. Traini[3], F. D'Orazio[2], M. Pugliese[2], F. Cazzato[1]

[1] Department of Neuroscience and Imaging, Faculty of Medicine, University "G. d'Annunzio" of Chieti-Pescara, Italy

[2] Graduate School of Medicine, Department of Otorhinolaryngology, Faculty of Medicine, University "G. d'Annunzio" of Chieti-Pescara, Italy

[3] Department of Oral Sciences, Nano and Biotechnology, Faculty of Medicine, University "G. d'Annunzio" of Chieti-Pescara, Italy

Rhinology 51: 0-0, 2013

DOI:10.4193/Rhino12.124

***Received for publication:**

July 19, 2012

Accepted: June 13, 2013

Summary

Background: Chronic rhinitis with inferior turbinate hypertrophy is the most common cause of chronic nasal obstruction. Pharmacological treatment, mainly consisting of corticosteroids, is largely inadequate and, therefore, in the last few years several surgical techniques have been proposed (emptying, radiofrequency, cryotherapy, etc...). The aim of our work is to demonstrate that surgical removal of the inferior turbinate mucosa with the microdebrider, along with the submucosal chorion, results in a full restoration of mucosal physiological structure and function.

Methodology: Thirteen symptomatic adult patients were subjected to bilateral inferior partial turbinoplasty with the microdebrider. All patients underwent endoscopic examination, functional nasal tests and nasal mucosa biopsy before and after surgery.

Results: The sensitivity in open airspaces improved after nasal surgery, and the results of functional tests returned to within a normal range. SEM examination confirmed that complete mucosal regeneration was within 4 months.

Conclusion: Total removal of the inferior turbinate mucosa with the microdebrider in patients suffering from hypertrophic chronic rhinitis allows the perfect regeneration of physiological respiratory tissue and doesn't have a negative impact on healing time and offsets any adverse postoperative event.

Key words: rhinitis, nasal surgical procedures, electron microscopy, nasal obstruction, mucociliary clearance

Introduction

Chronic nasal obstruction is one of the most common respiratory disorders in the rhinological practice. Epidemiological studies estimate that more than 20% of the general population presents chronic nasal obstruction caused by inferior turbinate hypertrophy [(1)].

The general term "chronic hypertrophic rhinitis" is used to describe turbinate enlargement and impaired nasal function resulting in histological changes in conchal mucosa, such as squamous metaplasia with loss of cilia, and/or sub-mucosa alterations, such as fibrosis, goblet cell hyperplasia and dilation of venous sinuses, due to vascular congestion [(2,3)].

Vasomotor or persistent allergic or pseudo-allergic rhinitis and compensatory hypertrophy of the contralateral side to the convexity of nasal septum deviation are the main non-infectious causes of mucosal swelling of the inferior turbinates [(4,5)]. What's more, drug-induced rhinitis due to abuse of decongestant medications, nasal trauma, and hormonal imbalances can lead to turbinate enlargement [(6,7)].

In particular, vasomotor rhinitis, which is part of the non-allergic strain [(8)], is mainly characterized by prominent symptoms of nasal obstruction, rhinorrhea and congestion, aggravated by strong smells, alcohol, spicy foods, emotions, environmental factors such as temperature, barometric pressure changes and light stimuli [(9)].

Patients with vasomotor rhinitis can be divided into two subgroups: the "runners", manifesting "wet" rhinorrhea, and "dry" patients, who exhibit nasal obstruction, airflow resistance with

minimal rhinorrhea [8]. "Runners" rhinorrea is due to increased cholinergic gland secretory activity, because autonomic stimulation results in predominance of parasympathetic function against a sympathetic one [10]. A pathogenesis related to nociceptive hyperexcitability with increased sensitivity to normally subliminal stimuli has been hypothesized for "dry" patients' nasal obstruction [8].

In vasomotor rhinitis, the nasal mucosa epithelium is severely damaged. In literature, a reduction in epithelial thickness and disappearance of ciliated and goblet cells, the absence of tight junctions, nasal mucus overproduction, inflammatory infiltration in lamina propria [3], marked disruption of the intercellular spaces and frequent basement membrane interruption [2] can be observed. The lack of mucociliary clearance, absence of tight junctions, widening of intercellular spaces and discontinuity of the basement membrane induce a reduction in epithelial defense functions, so that environmental factors may directly act on subepithelial structures. As a result, in the nasal respiratory mucosa an increased responsiveness of trigeminal afferent fibers and secretory and vascular reflexes might occur representing the basis of symptoms [11].

In literature, the therapy of hypertrophic forms is both medical or surgical. A stepwise pharmacologic treatment with topical corticosteroids is normally employed, basing it on the patient's predominant symptoms [12].
When conservative treatment fails, surgical reduction of the inferior turbinate could be attempted. Various reduction techniques have been applied, but each of them has possible complications. The Empty Nose Syndrome with, paradoxically, nasal obstruction could occur after total turbinectomy. Whereas mono- or bipolar electrocautery, laser cauterization or cryotherapy could create mucous necrosis, subsequent scarring, and therefore, histological and functional nasal alterations. The minimally-invasive techniques, such as turbinate bone sub-mucosal excision, sub-mucosal diathermy, radiofrequency coblation and high-frequency surgery have been recently proposed. After creating a sub-mucosal access, they directly act by reducing the thickness of turbinate stromal tissue, without damaging the surface epithelium [13]. Microdebrider treatment has been mainly employed so far in turbinate sub-mucosal depletion, saving the mucous layer as much as possible [14-17].
Each of these techniques was created with the intent of preserving the turbinate mucosa in an attempt to not modify the muco-ciliary function [18-24]. However, preserving an histologically altered mucosa translates into maintaining an impaired nasal function. However, the aim of surgery should instead be to improve nasal function and simultaneously to expand nasal breathing space.

This study describes our experience with microdebrider treatment extending the resection to the mucous layer degenerated by rhinopathy, assessing clinical outcomes, monitoring the healing process in terms of both ultra-structural and functional study and recording any adverse events arising from the newly-changed procedure. The aim of this paper was not to compare various surgical techniques to decide the best one, but to establish whether mechanical damage on the nasal mucosa, such as that carried out by microdebrider (or any other cutting tool), is followed by a more or less complete anatomical and functional recovery.

Materials and methods

Study design

A prospective clinical study was conducted on 16 adult volunteers (7 males and 9 females) from 16 to 56 years old (mean age 33 years) with inferior turbinate hypertrophy associated to nasal obstruction and breathlessness. All patients were provided information about the study, which adhered to the Declaration of Helsinki and to the ICH-GCP, GU 184/2003. Written informed consent was obtained from all patients.
The required inclusion criteria to recruit these patients were: a severe inferior turbinate hypertrophy, refractory to drug treatment with or without clinical complications due to nasal blockage (otitis, sinusitis, pharyngitis, tracheitis, recurrent rhino-bronchial syndrome, OSAS) and significant reduction in turbinate volume after decongestion test with naphazoline hydrochloride 0.1%.
Excluded from the study were patients with a negative decongestion test, stenosing septal deviations, ciliary dyskinesia caused by genetic diseases (i.e. cystic fibrosis, Kartagener's Syndrome), nasal polyps, previous nasal and paranasal sinuses surgery, active hypertrophic rhinitis. As a result, 3 patients were excluded.

Pre-surgery treatment

In preoperative time (T0) and after a follow-up of 4 months (T1) all 13 patients were subjected to:

- Ear, Nose and Throat (ENT) history and ENT clinical examination.
- Nasal endoscopy with Rigid 0 °fiberscope STORZ of 2.7 mm caliber and 13 cm in length without using local anesthetics and vasoconstrictors.
- Subjective assessment of respiratory obstruction by a visual analogue scale (VAS) graduated 10 cm as proposed by Eccles [25]. A score of 0 represents a constant nasal patency, without episodes of nasal obstruction; while a score of 10 indicates a complete, constant, unremitting subjective perception of airway obstruction.
- Muco-ciliary transport time (MCT), was performed by

placing 1,5 grams of 2% sodium saccharin behind the anterior edge of the inferior turbinate head. Each patient was trained to keep their head tilted at 10°, to swallow every 30 seconds and to breathe through the nose. The test was considered completed when they perceived a sweet taste in the oropharynx.

- Anterior Active Rhinomanometry (AAR) using ATMOS® 300 rhinomanometer was carried out after about 15-30 minutes of rest, to minimize variations due to the mucosal vascular autonomic influences of exercise, requiring everyone to carry out 5 deep breaths into the mask to allow the recording. The total nasal resistance and the inspiratory / expiratory airflow were measured in each nasal cavitity separately. These results were then evaluated at a 150 Pa transnasal pressure.
- A decongestion test with a topical vasoconstrictor nasal administration (0.1% naphazoline hydrochloride) was applied for 10 minutes and subsequent revaluation with AAR.
- Bilateral debrider turbinoplasty procedure by using the Xomed Power System 2000 microdebrider was used on outpatients under endoscopic guidance.

Surgical intervention

Local anesthesia was performed with 2 strips soaked in Xilocaina hydrochloride 5% and naphazoline 0.02% placed on nasal floor and turbinate medial wall in each nasal cavity. After getting loss of sensitivity in the upper dental arch (about 10 minutes), the mucosa and the hypertrophic cavernous tissue was shaved to the bone surface of the medial and inferior surfaces and partially of the inferior turbinate head by the microdebrider above the periosteum. It is a powered rotary shaving device, consisting of a small rotating blade protected by a blunt end, which can resect tissue that is suctioned into the opening. A 4 mm straight blade was moved along the turbinate length, at 2300-3000 rev/sec speed of oscillation with posterior-anterior direction and continuous suction, enabling the surgeon to maintain a bloodless field while operating. The surgical removal time was 1-2 minutes on average per side. At the end of the procedure, a post-surgery anterior packing was performed with packs made of a biocompatible synthetic polymer of esterified polyvinyl derivates with hyaluronic acid of 8 or 10 cm in length, left in place for 72 hours. After removal of buffers, local instillation of nose drops containing vitamin A and vaseline oil was recommended for about 1 month.

After local anesthesia, biopsy samples of about 2 mm were taken from the medial surface of the inferior concha mucosa and 1.5 cm behind the anterior inferior edge. We observed biopsy specimens at Zeiss EVO 50 SEM with a LaB6 XVP (SMY Carl Zeiss Ltd., Cambridge, United Kingdom) with a BSE detector tetra-solid state.

Statistical analysis

Statistical analysis was performed with the paired t-test.

Results

All patients tolerated the surgical procedure. Only in one case, we had a mild postoperative bleeding 15 days after surgery, which required a new anterior nasal packing. A significant breathing space expansion with morphological preservation of nasal conchal mucosa was revealed during anterior rhinoscopy, with no other complications such as mucosal erosion, crusting, synechiae, or recurrent bleeding. The healing phase was nearly completed at 4 months after surgery: the mucosa appeared pink, without submucosal oedema and limited secretions as compared to pre-surgical clinical evaluation.

Subjective valuation of nasal obstruction with VAS

Mean values of the subjective respiratory symptom assessment

Table 1. Comparison of VAS scores before and after turbinoplasty.

VAS	Pre-surgery (T0)	Post-surgery (T1)
0-3	0	10
4-6	0	3
7-10	13	0
Mean value	8,69*	1,77*

* $p < 0,001$ (by t-paired test)

Table 2. Comparision of mean values of MCT and AAR before and after turbinoplasty.

	Pre-surgery (T0)	Post-surgery (T1)
Mucociliary Transport Time	17,5 min*	11,3 min*
Total Nasal Resistance (150 Pa)	0,65 Pa/cm^3/s *	0,31 Pa/cm^3/s *

* $p < 0,001$ (by t-paired test)

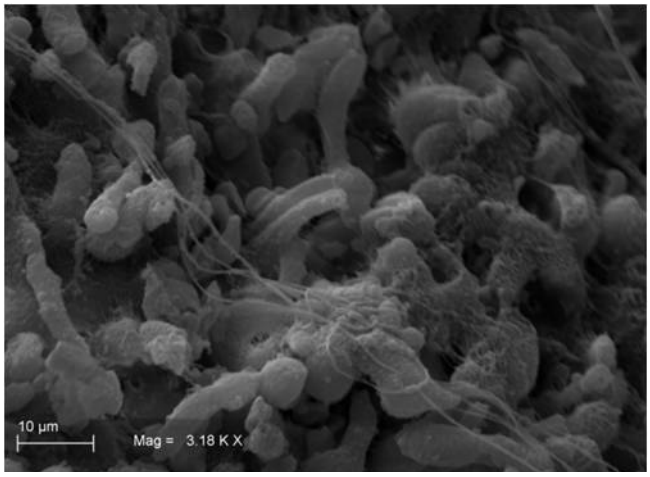

Figure 1. SEM observation of an inferior turbinate head section after 4 months post-operation, disclosing mucin filaments in addition to well-developed cilia.

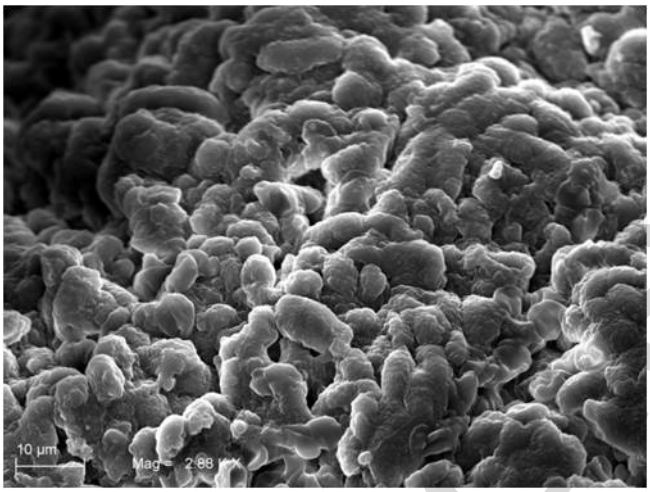

Figure 2. SEM observation of biopsy specimen taken from the inferior turbinate head after 4 months postoperation, demonstrating the nasal cilia of normal appearance.

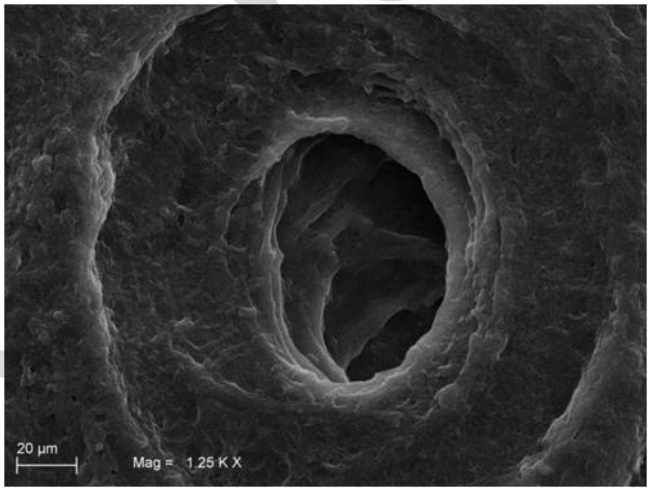

Figure 3. SEM observation of an inferior turbinate head section from a patient with chronic hypertrophic rhinitis during surgery, displaying dilated and engorged venous sinusoids.

at VAS decreased from an initial average of 8.69 in the preoperative period, at 1.77 after 4 months from the microdebrider turbinoplasty (Table 1). Data analysis showed that this decrease is statistically significant ($p < 0.001$).

Muco-ciliary transport time

The mucociliary transport time, which initially had a mean value of 17.5 minutes, had reached a final average of 11.3 minutes at T1, coming into the normal range (13 ± 3 minutes) (Table 2). Paired t-test showed a statistically significant decrease ($p < 0.001$).

Anterior active rhinomanometry (AAR)

The AAR data analysis shows that the mean value of the total nasal resistance before surgery, estimated at 150 Pa, was 0.65 Pa/cm^3/s, while at 4 months of follow-up, it was 0.31 Pa/cm^3/s, demonstrating a statistically significant reduction ($p < 0.001$) by the paired t-test (Table 2). However, during the nasal decongestion test, the total resistance decreased to 0.11 Pa/cm^3/s. The mean total inspiratory flow was 489.3 cm^3/s and after local vasoconstrictor treatment it became 1,308 cm^3/s.

SEM observation of biopsy specimens

In most patients, the biopsy electron microscopy analysis showed many respiratory epithelium areas with several degrees of differentiation after a 4 month follow-up. The regenerated respiratory epithelium was generally represented by physiological columnar cell with a variable representation of goblet and ciliated cells, with a ratio in favour of the second group (Figure 1). The ciliated columnar cells appeared numerous, with thickly scattered, well-developed cilia on the cell surface, estimating 24 µm of ciliary length and 3 µm in diameter (Figure 2). The glandular elements and superficial glandular openings were reduced in number. Giant cells or other typical parameters of a foreign body reaction have not been identified.

Discussion

The nasal mucosa is actively involved in physiological processes as nasal mucociliary transport, that is effective only when both the appropriate ciliary movement with an adequate mucous blanket secreted by Goblet cells, and the IgE-mediated immune-regulatory response in nasal mucosa are present. These properties led many authors to establish the dogma that surgical nasal mucosa removal could produce an irreversible functional damage over time.

In fact, the same chronic inflammatory processes create mucosal damage, with underlying molecular mechanisms at the base of the nasal disease, involving proteins such as p53 homologues (p63 and p73) that play a key role in orchestrating the epithelial development and repair processes in the nasal mucosa.

These alterations result in goblet cell hyperplasia, squamous metaplasia, fibrosis, dilation of venous sinuses, and reduction of

gap junctions [26].
It is not clear if the minimally invasive surgery leads to only a functional or also a structural nasal recovery, because in the literature only a few studies reported on this matter.

A variety of animal models demonstrate that in response to airway epithelium injury, the basal cells (BC) spread and migrate from the basement membrane at the wound edge to the denuded area. This occurs because of extracellular matrix-stem cell interactions, mainly through the glycoproteins fibronectin and vitronectin secreted after inflammatory TGF-β and TNF-α stimulation and components of the basement membrane such as laminin and type IV collagen. Cell migration is also regulated by matrix metalloproteinases (MMP7, MMP9) and β1-integrins [27]. After migration, BC daughters in the repairing area start to proliferate. The repairing epithelium then forms a transitory squamous metaplasia followed by a progressive re-differentiation with a final step of ciliogenesis and goblet cell differentiation, representative of the complete regeneration of a functional mucociliary epithelium [27].
The micro-environment undoubtedly influences the airway BC behaviour with paracrine signals secretion from neighboring epithelial cells and mesenchyme –Wnt, EGF, TGF-β and BMP [28-30]. This mucociliary regeneration model has also shown in human nasal turbinate [29].

Based on these concepts, we think that the thermal necrosis occurs in the electrode introduction site during minimally invasive surgical techniques [31], and represents an obstacle for the mucosal regeneration. Thus to obtain a physiological mucosal regeneration, a mechanical injury is necessary. A healing histological study of nasal mucosa in sheep assessed gradual recovery of the ciliated epithelium in the first 4 weeks after endoscopic partial mucosa removal. In the mucosa, 68.35% of cilia were present on day 84, as compared with 32,96% of cilia after full-thickness surgery [32]. These data demonstrate a greater efficiency of the microdebrider rather than total turbinectomy.
In humans, to avoid an empty nose syndrome, the resection must be limited and cannot reach the supporting bone or cartilaginous structure [33]. In fact, in this study we have used the microdebrider to evaluate whether the total removal of the mucosa and submucosa above the periosteum could lead to a structural, as well as functional, mucosal recovery. Our study confirms the effectiveness of the mucosa and sub-mucosa excision with a microdebrider in improving nasal dyspnea caused by turbinate hypertrophy, documented by a marked improvement of all tests administered. Post-surgery mucociliary transport time (MCT) returns to the normal range (13 ± 3 minutes) in 100% of the cases. These data underline the functional recovery of ciliated epithelium, which is evidently repaired, and subsequently confirmed by ultra-structural SEM analysis (Figures 1 and 2). Comparing these results with those proposed by Salzano et al. [34], we can confirm a clear predominance of microdebrider effectiveness over the other procedures taken into consideration. These methods lead to even higher MCT values than the pre-surgical ones, which stabilized at 2 months of follow-up, on average values of 15.95 minutes, which are at the limit of the normal range [34]. These results drove Salzano to suppose that even if these techniques are defined minimally invasive, because of the nasal mucosa preservation, the thermal energy used can cause damage to the surrounding tissue, like the ciliated epithelial cell surface, inducing chronic inflammation [34]. We also think that the thermal energy, even though spatially limited, generates tissue damage, while debridement mucosa excision enables removal of rhinopathy damaged mucosa without burning the edges, allowing easy tissue regeneration from the periphery of the wounded area.

At AAR, the mean total nasal resistance and the total inspiration flow strongly improve 4 months post-surgery (Table 2). To avoid dubious rhinomanometric assessments, we considered total nasal resistance as the main parameter. It is less variable than the unilateral one, because it is not affected by the nasal cycle and, therefore, it is a better indicator of the presence/absence of nasal obstruction in the nasal airflow. The local instillation of naphazoline hydrochloride results in a further airflow increase. It indicates a marked vasoreactivity, which persists despite the hypertrophic mucosa removal with the microdebrider, in contrast to results of other procedures.
The recovery of vasomotor reactivity, documented with AAR after surgery, highlights another advantage of the mechanical debridment compared to other methods [35]. It shows that the residual cavernous tissue maintains its thermoregulatory ability that, if operating synergistically to mucociliary function, allows the treatment regardless of the climate in which the patient lives. On the contrary, blood vessels and nervous destruction with the submucosal fibrosis that thermal techniques generate, leads a nasal mucosa hyporeactivity to stimuli by altering the normal physiology [34] while according to Leong et al., the submucosal fibrosis might cause a subjective sensation of nasal patency and a post-operative sensation of airflow because of surgical damage to sensory nerves and therefore to cold receptors despite an improvement in nasal conductance of airflow [35].

As with the nasal functional tests, the subjective evaluation of nasal obstruction at VAS scale also show an intense and progressive symptom relief after 4 months, a sufficient period to establish the failure of surgical treatment on turbinates [35]. By dividing the VAS values into 3 ranges (0-3, 4-6, 7-10), corresponding, respectively, to the mild, moderate and severe categories of nasal obstruction, we observed a gradual transition from a severe disease before surgery (VAS = 7-10), to a mild/no obstruction (VAS = 0-3) at 4 months after the surgical procedure (Table 1). These results are in accordance with those

reported in literature and nasal obstruction severity improved significantly after our procedure compared to others. Salzano et al., for example, has performed a study comparing 4 minimally invasive mucosal sparing procedures currently in use, i.e. the RF, HF, electro-cautery and the lower partial turbinotomia, and they certified lower baseline values (mean VAS = 7.8) and higher final values (mean VAS = 5.52) [34]. The early restoration of near normal nasal function using our technique represents another benefit compared to the radiofrequency turbinoplasty in which the desired effects appear much later (a period lasting from days to weeks) in comparison to the use of the microdebrider [14]. This phenomenon seems to be due both to the post-surgical turbinate swelling and to the time required for submucosal fibrosis [14], reducing patients' satisfaction in the long-term. These events were absent or decreased in the microdebrider technique, where to the contrary, produced an immediate relief of symptoms caused by the mechanical debridement of excess soft tissue after packing removal.
The endoscopic studies of our patients demonstrated the post-surgery preservation of the inferior turbinate form, that led to more physiologic airflow within nasal-sinus cavities. There was also a marked reduction in nasal allergic symptoms (sneezing, rhinorrhea, obstruction, hyposmia) in patients with a preoperative history of allergopathy.

We subjected the patients to follow-up for 4 months, an adequate time to establish the effectiveness of surgical treatment on the turbinate [35]; but the best assessment of the long-term treatment efficacy is the observation with SEM, that showed a perfect reepithelialization in all patients 4 months after surgery. The choice of the 4 month period was established because a longer follow-up would mainly evaluate the natural evolution of the disease itself, rather than the effects of our instruments [36].
The scanning electron microscope (SEM) observations provided by the literature revealed numerous changes in nasal mucosa during inferior turbinate chronic hypertrophic rhinitis. They are represented by: a severe metaplasia of the nasal epithelium, characterized by areas of hyperplasia and epithelial stratification, epithelial cell degeneration with loss of cilia and disruption of intercellular connections, an increased thickness of basement membrane and lamina propria in allergic patients, attributed to fibrosis, infiltration in lamina propria of various inflammatory cells and the increased number of blood vessels. The latter probably related to the formation of new blood vessels that dilated and congested venous sinusoids (Figure 3) with very thin-walled, fine oedema and over-production of nasal secretions due to increase in number of goblet cells, submucosal glands and superficial glandular outlets [3,37-39].

In a previous study, Wexler et al. [40] performed histological analyses on samples taken from patients undergoing microdebrider inferior turbinoplasty, highlighting the deep residual nasal mucosa characteristics. Their observations showed a well-organized basal cell layer, a less prominent and not so defined basement membrane compared to the usual structure of 15 to 20 µm thickness seen in conventional nasal mucosa specimens, a markedly changed lamina propria due to fibrosis with loss or reduction of subepithelial glandular elements and venous sinusoids, which could also suggest chances of recurrence [40].
Our study completes the Wexler's research, because it demonstrates that the improvements of the deep portion nasal mucosa after debridement also correspond to mucosa surface improvements: ultra-structural and physiological restoration of the mucosal surface cellular organization with many ciliated columnar cells coated with well-developed cilia of 24 µm of ciliary length and 3 µm in diameter, fewer glandular elements and superficial glandular openings. In conclusion, the mechanical removal of the degenerated nasal turbinate mucosa with a microdebrider not only does not cause any damage to the respiratory epithelium but stimulates the regeneration of a healthy and functionally active mucosal epithelium. For this reason, we believe the dogma of the nasal mucosa preservation during turbinate surgery can no longer be accepted, because the nasal mucosa possesses regenerative properties that exceed the surgical damage if mechanically generated.

In our opinion, the nasal packing does not change the functional recovery of the mucosa, because on the one hand it remains for a short time in the nasal cavities, later replaced with medical therapy, on the other hand, the quality of the mucosal healing is related to the regenerative capacity of the tissue that can only be accelerated by post-surgical medical therapy.
The surgical procedure with a microdebrider is a fast and precise method for the inferior-medial nasal airway expansion through controlled inferior-medial stroma excision from inferior turbinate, and does not increase the time required for mucosal healing. It can be performed as an outpatient treatment under local anesthesia with simultaneous endoscopic visualization and its lasts a few minutes. It has minimal invasiveness and simplicity in its execution.

Our experience has shown that the inferior turbinate endoscopic mucosal turbinoplasty with debrider not only improves nasal obstruction, but also rhinorrhea, hyposmia, headache, sneezing and post nasaldrip. It is neither associated with negative consequences such as dryness, crusting or nasal irritation, nor with alterations in mucosal function. It is easily performed, implies low costs, function respect, physiological airflow distribution and full restoration of nasal mucosa structures. The microdebrider technique in our opinion is the gold standard for the inferior turbinate hypertrophy treatment.

Acknowledgements

The authors thank Roberta Di Pietro and Lucia Centurione, Department of Medicine and Aging Science (DMSI)-Section of Human Morphology, University "G. d'Annunzio" of Chieti-Pescara, for for their valuable support.

Authorship contribution

GN: Senior author, conception manuscript, finalization supervision
VM: collecting patients and tissues, writing the manuscript
TT: electron microscopy analysis
FD'O: surgical collaboration
MP: translating and writing the manuscript
FC: collecting instrumental data

Conflict of interest

The authors have declared that they have no conflict of interest.

References

1. Passali D, Bellussi L, Damiani V, Passali GC, Passali FM, Celestino D. Allergic rhinitis in Italy: epidemiology and definition of most commonly used diagnostic and therapeutic modalities. Acta Otorhinolaryngol Ital. 2003; 23: 257-264.
2. Berger G, Gass S, Ophir D. The histopathology of the hypertrophic inferior turbinate. Arch Otolaryngol Head Neck Surg. 2006; 132: 588–594.
3. Gindros G, Kantas I, Balatsouras G, Kandiloros D, Manthos AK, Kaidoglou A. Mucosal changes in chronic hypertrophic rhinitis after surgical turbinate reduction. Eur Arch Otorhinolaryngol. 2009; 266: 1409-1416.
4. Farmer SE, Eccles R. Chronic inferior turbinate enlargement and the implications for surgical intervention. Rhinology, 2006; 44: 234–238.
5. Passali D, Passali FM, Damiani V, Passali GC, Bellussi L. Treatment of inferior turbinate hypertrophy: a randomized clinical trial. Ann OtolRhinolLaryngol. 2003; 112: 683–688.
6. Elwany SS, Stephanos WM. Rhinitis medicamentosa. An experimental histopathological and histochemical study. ORL J Otorhinolaryngol Relat Spec. 1983; 45: 187–194.
7. Toppozada H, Toppozada M, El-Ghazzawi I, Elwany S. The human respiratory nasal mucosa in females using contraceptive pills. An ultramicroscopic and histochemical study. J Laryngol Otol. 1984; 98: 43–51.
8. Dykewicz MS, Fineman S, Skoner DP, Nicklas R, Lee R, Blessing-Moore J, et al. Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on Practice Parameters in Allergy. Asthma and Immunology. American Academy of Allergy, Asthma and Immunology. Ann Allergy Asthma Immunol. 1998; 81(5 pt 2): 478-518.
9. Druce HM. Allergic and non-allergic rhinitis. In: Middleton E Jr, Ellis EF, Yunginger JW, Reed CE, Adkinson NF, Busse WW, eds. Allergy principles and practice. 5th ed. St. Louis: Mosby. 1998, 1005-1016.
10. Jaradeh SS, Smith TL, Torrico L, Prieto TE, Loehrl TA, Darling RJ, et al. Autonomic nervous system evaluation of patients with vasomotor rhinitis. Laryngoscope. 2000; 110: 1828-1831.
11. Giannessi F, Fattori B, Ursino F, Giambelluca A, Soldani P, Scavuzzo MC, Ruffoli R. Ultrastructural and ultracytochemical study of the human nasal respiratory epithelium in vasomotor rhinitis. ActaOtolaryngol. 2003; 123: 943-949.
12. Patricia W, Wheeler MD, Stephen F, Wheeler MD. Vasomotor Rhinitis. Am Fam Physician. 2005; 72: 1057-1062.
13. Passàli D, Lauriello M, Anselmi M, Bellussi L. Treatment of hypertrophy of the inferior turbinate: long-term results in 382 patients randomly assigned to therapy. Ann Otol Rhinol Laryngol. 1999; 108: 569-575.
14. Cingi C, Ure B, CakliH, Ozudogru E. Microdebrider-assisted versus radiofrequency assisted inferior turbinoplasty: a prospective study with objective and subjective outcome measures. Acta Otorynolaryngol Ita. 2010; 30: 138-143.
15. Friedman M, Tanyeri H, Lim J, et al. A safe, alternative technique for inferior turbinate reduction. Laryngoscope. 1999; 109: 1834-1837.
16. Lee CF, Chen TA. Power microdebrider-assisted modification of endoscopic inferior turbinoplasty: a preliminary report. Chang Gung Med J. 2004; 27: 359-365.
17. Gupta A, Mercurio E, Bielamowicz S. Endoscopic inferior turbinate reduction: an outcomes analysis, Laryngoscope, 2001; 111: 1957-1959.
18. Di Rienzo Businco L. Nuove tecniche nel trattamento delle sindromi ostruttive delle prime vie aeree. Scuola Medica Ospedaliera. 2009; 32: 3-6.
19. Celestino D. La patologia flogistica del naso, Argomenti di Otorinolaringoiatria Moderna (AIOLP). 2003; 2: 18-23.
20. Toppozada H, Toppozada M, El-Ghazzawi I, Elwany S. The human respiratory nasal mucosa in females using contraceptive pills. An ultramicroscopic and histochemical study. J Laryngol Otol. 1984; 98: 43–51.
21. Mullarkey MF, Hill JS, Webb DR. Allergic and non-allergic rhinitis: their characterization with attention to the meaning of nasal eosinophilia. J Allergy ClinImmunol. 1980; 65: 122-126.
22. Biackmore JT. Vasomotor rhinitis: an update. Laryngoscope. 1981; 91: 1600-1605.
23. Rossmann C, Lee RMKW, Newhouse MT. Nasal cilia in normal man, primary ciliary dyskinesia and other respiratory diseases: analysis of motility and ultrastructure. Eur J Respir Dis.1983; 64 (suppl 127): 64.
24. Nappi G, Carrubba IG, De Luca S. Influenze della crenoterapia sulla clearance mucociliare in pz affetti da sindrome rinosinusitica. Med Clin Term. 2002; 49: 305- 313.
25. Eccles R. Nasal airway resistance and nasal sensation of airflow. Rhinol Suppl.1992; 14: 86-90.
26. Li CW, Shi L, Zhang KK ,et al. Role of p63/p73 in epithelial remodeling and their response to steroid treatment in nasal polyposis. J Allergy ClinImmunol. 2011; 127: 765-772.
27. Coraux C, Roux J, Jolly T, Birembaut P. Epithelial Cell–Extracellular Matrix Interactions and Stem Cells in Airway Epithelial Regeneration. Proc Am Thorac Soc. 2008; 5: 689–694.
28. Masterson JC, Molloy EL, Gilbert JL, McCormack N, Adams A, O'Dea S. Bone morphogenetic protein signaling in airway epithelial cells during regeneration. Cellular Signalling, 2011; 23: 398–406.
29. Rock JR, Randell SH, Hogan BL. Airway basal stem cells: a perspective on their roles in epithelial homeostasis and remodeling. Dis Model Mech. 2010; 3: 545-556.
30. Kobayashi K, Kashima K, Higuchi K, Arakawa T. The mechanisms of gastrointestinal mucosal injury and repair, Nihon Rinsho. 998; 56: 2215-2222.
31. Pomukhina AN, Lokshina LS, Panchenko SN. Morphological changes in the nasal mucosa after diathermocoagulation in chronic hypertrophic rhinitis. VestnOtorinolaringol.1990; 1: 34-38.
32. Shaw CK, Cowin A, Wormald PJ. A study of the normal temporal healing pattern and the mucociliary transport after endoscopic partial and full-thickness removal of nasal mucosa in sheep. Immunol Cell Biol. 2001; 79: 145–148.
33. Nousia C, Gouveris H, Giatromanolaki A, et al. Ultrasound submucosal inferior nasal turbinatereduction technique: histological study of wound healing in a sheep model. Rhinology. 2010; 48-2: 169-173.
34. Salzano FA, Mora R, Dellepiane M, et al. Radiofrequncy, High-Frequency, and Electrocautery Treatments vs Partial Inferior Turbinotomy. Arch Otolaryngol Head Neck Surg. 2009; 135: 752-758.
35. Leong SC, Farmer SEJ, Eccles R. Coblation

for inferior turbinate reduction: a long-term follow-up with subjective and objective assessment. Rhinology. 2010; 48-1: 108-112.
36. Cornet ME, ReinartzSM, Georgalas C, van Spronsen E, Fokkens WJ. Themicrodebrider, a step forward or an expensive gadget? Rhinology. 2012; 50: 191-198.
37. Schmidt J, Zalewski P, Olszewski J, Olszewska-Ziaber A. Histopathological verification of clinical indications to partial inferior turbinectomy. Rhinology. 2001; 39: 147–150.
38. Berger G, Gass S, Ophir D. The histopathology of the hypertrophic inferior turbinate. Arch Otolaryngol Head Neck Surg. 2006; 132: 588–594.
39. Sanai A, Nagata H, Konno A. Extensive interstitial collagen deposition on the basement membrane zone in allergic nasal mucosa. ActaOtolaryngol. 1999; 119: 473–478.
40. Wexler DB, Berger G, Derowe A, Ophir D. Long-term histologic effects of inferior turbinate laser surgery. Otolaryngol Head Neck Surg. 2001; 124: 459-463.

Dr. Giampiero Neri
Strada Collemarino, 136
65125 Pescara (PE)
Italy

Tel: +34-95 627 591
E-mail: neri@unich.it