Turbinoplasty with quantic molecular resonance in the treatment of persistent moderate-severe allergic rhinitis: Comparative analysis of efficacy

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ABSTRACT

Background: *Allergic rhinitis (AR) presents as the main and most invasive symptom in the blocking of the nose. This condition is almost always related to hypertrophy of the inferior turbinates. When the medical treatments are found to be insufficient to solve the obstructive symptom of the patient, the quality of life is considerably impaired and it is often necessary to submit the patient to a surgical approach. In the present study we aimed to establish the efficacy and safety of a new technique recently introduced for the shrinkage of hypertrophic turbinates using a specific device, based on a new radiofrequency energy that does not produce thermal mucosal damage,* viz., *quantic molecular resonance (QMR) in a group of patients with persistent moderate–severe allergic rhinitis, in addition to standard medical treatment (nasal steroid and oral antihistamine).*

Methods: *All patients were randomly assigned to two homogeneous groups (group A, control subjects; group B, treated patients); each group included 145 individuals. During the study, both groups received standard medications (ebastine, 10-mg tablet, and budesonide nasal spray at 100 micrograms/nostril per day) for 90 days. Before the medical treatment, patients in group B underwent inferior endoscopic turbinoplasty using QMR. All of the patients enrolled in this study were submitted to a complete otorhinolaryngologic evaluation with objective clinical examination (basal rhinomanometry, nasal provocation test rhinomanometry, and mucociliary transport time), endoscopy, and questionnaires (22-item Sino-Nasal Outcome Test and visual analog scale for nasal symptoms).*

Results: *Greater efficacy has been achieved using a combined approach with the association of medical and QMR treatment, compared with medical treatment alone, in the control of AR associated with hypertrophy of the inferior turbinates, in particular in the reduction of turbinate volume at rhinoendoscopy.*

Conclusion: *QMR inferior turbinoplasty, in conjunction with medical therapy, improves the nasal flow, without any thermal mucosal damage, more effectively when compared with medical treatment alone in persistent moderate-to-severe AR. In particular, local reactivity, as measured with nasal provocation test, was noticeably reduced.*

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Allergic rhinitis (AR) presents as the main and most invasive symptom in the blocking of the nose. This condition is almost always related to hypertrophy of the inferior turbinates, area of the immunophlogosis, which leads to persistent inflammation with edema and prolapse of the mucosa obstructing the nasal fossa. Hypertrophy of the inferior turbinate may become irreversible when the vascular dilatation leads to prolapse of the submucosal venous sinusoids, which no longer respond to the sympathetic system and to medical treatment.[1,2] Several studies have revealed that a percentage (between 10 and 25%) of the population present nasal obstructive symptoms with hypertrophy of the inferior turbinates, correlated with the allergy.[3] When the medical treatments (antihistamines, steroids, and specific immunotherapy) are found to be insufficient to solve the obstructive symptom of the patient, the quality of life (QoL) is considerably impaired and it is often necessary to submit the patient to a surgical approach to improve the nasal airflow.[4] Surgery of the turbinates is, in fact, very common and represents the eighth procedure, in order of frequency, performed in otorhinolaryngologic surgery. Over the years, numerous surgical techniques have been proposed for the treatment of the inferior turbinate hypertrophy: the main problem was to increase the nasal airflow while maintaining the function of the mucosa, area of important protective actions, and of the absorption of medications useful in the long-term postoperative treatment of the allergic phlogosis (turbinectomy, submucosal emptying, cryocoagulation, electrocaustication, laser, radiofrequencies, and coblator).[2,5,6] Many of these techniques (in particular those performed at high temperatures and extremely destructive, with almost complete amputation of the turbinate, despite the guarantee of an increase in the nasal airflow) were accompanied by the loss of nasal sensitivity and by the formation of such air vortex to the so-called "empty nose" syndromes with the formation of crusts, bleeding, and synechia, resulting in an extremely negative impact on the QoL of the patients.[2,7–9]

In the present study we aimed to establish the efficacy and safety of a new technique recently introduced for the shrinkage of hypertrophic turbinates using a specific device, based on a new radiofrequency energy that does not produce thermal damage, *viz.*, quantic molecular resonance (QMR), in a group of patients with persistent moderate–severe AR, in addition to standard medical treatment (nasal steroid and oral antihistamine).[10]

The aim of this study was to compare the variation in the clinical–instrumental parameters and symptoms at the beginning and end of treatment. The patients were, therefore, divided into two study groups, the first treated with pharmacologic treatment and the second with both medical and endoscopic treatment with QMR of the hypertrophic inferior turbinates.

MATERIALS AND METHODS

Study Population

A total of 290 patients (162 male subjects), >18 years old, were consecutively enrolled in the present study (Table 1), all of whom submitted to complete ear, nose, and throat evaluation with objective clinical examination, endoscopy, and 22-item Sino-Nasal Outcome

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Table 1 **Patient demographics**

	Group A (n = 145)	Group B (n = 145)	p Value
Age (yr)	38.4 ± 3.12	40.5 ± 2.09	>0.05
Sex			
Male	85 (58.6%)	77 (53.1%)	>0.05
Female	60 (41.4%)	68 (46.9%)	

Test (SNOT-22) questionnaire presented with persistent moderate–severe AR, based on the ARIA/EAACI criteria (Allergic Rhinitis and Its Impact of Asthma document and the European Academy of Allergology and Clinical Immunology) with hypertrophy of the inferior turbinates. All patients presented skin allergenic positivity to the skin-prick tests for dust mites (*Dermatophagoides pteronyssinus* or *Dermatophagoides farinae*) or plant allergens (*Graminacee*, *Cupressus*, or *Parietaria*) and had specific IgE for the major allergen 3–4 class (RastCAP System EIA method; Pharmacia, Uppsala, Sweden). These patients should not have undergone any form of medical treatment for 4 months before inclusion in the study (maximum of six antihistamine tablets and/or 10 puffs in each nostril).

The criteria used for enrolling the patients in the study were nasal symptoms (nasal obstruction, hydrorhinorrhea, sneezing, and itching) with a score of >5 on a visual analog scale (VAS) of 0–10; nasal resistance values of >0.25 (measured at rhinomanometry in basal conditions and after nasal provocation test NPT); and a clinical endoscopic score of >2 (1 = small turbinate not in contact with septum or nasal floor; 2 = mild hypertrophic turbinate in contact with septum; 3 = moderate hypertrophic turbinate in contact with septum and nasal floor; 4 = severe hypertrophic turbinate in contact with septum, nasal floor, and superior compartment with complete nasal blockage). Patients with non-AR turbinate hypertrophy or nasal obstruction due to other reasons, such as significant septal deviations, previous turbinates or nasal surgery, nasal polyposis, or recurrent sinusitis, as well as, those with coagulopathy disorders, severe systemic disease, infection, and oncological conditions were excluded from this study. All patients signed the informed consent form and the study was officially approved by the local Hospital Ethics Committee.

Study Design

All patients were randomly assigned to two homogeneous groups (group A, control subjects, and group B, treated patients); each group included 145 individuals. Simple randomization was achieved with a sequence of random numbers from a computer-generated sequence. During the study, both groups received standard medications (ebastine, 10-mg tablet and budesonide nasal spray at 100 μg/nostril per day) for 90 days. Before the medical treatment, patients in group B underwent inferior turbinate endoscopic surgery using QMR. Both groups were requested to report eventual side effects during the study noting them on a paper or call for medical consultation if needed.

Procedure Group B

Patients receiving treatment with QMR were prepared 15 minutes before surgery with contact local anesthesia with lidocaine on surgical patties placed on the entire length of the turbinate.

Submucosal decongestion of the turbinate was performed by means of insertion with a handpiece, needle shaped, activated by a QMR machine, so-called Quantum (Telea, Sandrigo-Vicenza, Italy), for a total of 20–30 seconds, at an intensity force of 3.5, with immediate shrinkage of the mucosa and a reduction in the prolapse of the mucosal hypertrophy. A 3-mm nasal endoscope 0° (Karl Storz, Tuttlingen, Germany) was used to access and view the nasal cavity, and the wand was inserted in the anterior portion of the inferior turbinate. The wand was activated and moved through the medial, superior, and inferior compartments, toward the posterior compartment of the turbinates. Care was taken to avoid the superficial portion of the turbinates because of their important physiological role. The wand was inserted only once to reduce mucosal damage (single insertion site technique) as described elsewhere.[2]

In 39 patients in the treatment group, the surgical procedure was performed, at their request, under i.v. anesthesia.

With regard to concerns the anesthesia, the target-controlled infusion technique was used not only to induce, but also to maintain, the anesthetic effect. The pharmaceutical products used for this purpose were remifentanil and propofol. No anesthetic premedication was administered. Airway ventilation was guaranteed by means of the pressure-controlled mode and with the use of a laryngeal mask with a 90° curve. The patient woke up easily and immediately without postoperative pain. It was not necessary to administer antiemetic drugs, in the postoperative phase, in any of these patients.

The procedure did not cause bleeding and did not require insertion of nasal tampons in any of the patients in the treatment group.

Clinical Outcomes

At the beginning of the study (time T0), participants were asked to score the severity of the subjective outcomes (nasal obstruction, hydrorhinorrea, sneezing, and itching), from 0 to 10, on a VAS.

Before and after treatment, all patients were invited to answer an SNOT-22 questionnaire and, thereafter, the results regarding the five most important items were compared. Objective outcomes (basal rhinomanometry and NPT rhinomanometry) were assessed to determine nasal passage resistance. Rhinomanometry measures nasal airflow and pressure during respiration. The nasal resistance episodes were evaluated by means of active anterior rhinomanometry (AAR) (Rhinomanometer Labat srl, Venice, Italy) performed during the day.

AAR is a rapidly performed test during which the patient has to maintain an airflow, breathing autonomously through the nose. In accordance with the International Committee for Standardization of Rhinomanometry, the resistance episodes to nasal airflow were measured at a standard pressure (150 Pa) and the total nasal resistance episodes were calculated by means of the monolateral rhinomanometric recordings.[7,11,12] AAR measurements were not performed if the patient was in a symptomatic phase of an acute common cold or nasal allergy crisis, thus delaying measurement until the acute phase was resolved, while those patients presenting severe obstruction with regard to concerns breathing through the nose, for whom it was, therefore, impossible to record the rhinomanometric values, were excluded from the study. The AAR measurements were performed in the sitting position, after an acclimatizing period of 15 minutes in the room, at standard temperature conditions and humidity. The NPT is performed by administering the offending antigen in the nasal cavity and measuring the mucosal response according to clinical score and rhinomanometry parameters. It is an extremely reliable test for evaluating the change in nasal reactivity to antigens.[8,13,14] A rhinoendoscopic clinical score was determined for each participant, at the beginning of the study, by evaluating the obstruction based on the contact of the inferior turbinate with the nasal septum (one for minimum obstruction and four maximum obstruction).

To obtain functional data regarding the state of the nasal mucosa in the two study groups, the mucociliary transport time (MCTt) was calculated before and after treatment. All patients underwent nasal MCTt evaluation, using a mixture of vegetable carbon powder and 3% saccharine. The MCTt was calculated as the interval of time elapsing from the moment in which the powder was placed on the head of the lower turbinate (anterior compartment) until a smear of the same powder appeared on the oropharynx during direct pharyngoscopic examination, together when the patient reported a sweet taste in the throat.[15]

All of these questionnaires and tests were repeated 3 months later (time T1).

Table 2 **Baseline values for each study group**

Group	Group A Controls ($n = 145$)	Group B Treated Patients ($n = 145$)	p Value
Nasal obstruction (mean ± SD)	9.11 ± 0.85	9.63 ± 0.61	$p > 0.05$
Itching	8.89 ± 1.10	9.11 ± 0.91	>0.05
Rhinorrhea	9.12 ± 1.00	9.40 ± 0.83	>0.05
Sneezing	8.20 ± 1.11	8.40 ± 1.31	>0.05
Rhinoendoscopy clinical score			
1	0	0	>0.05
2	0	0	
3	55 (37.9%)	61 (42.1%)	
4	90 (62.1%)	84 (57.9%)	

Table 3 **Comparison of results between groups A and B after treatment**

Group	Control A ($n = 145$)	Treatment B ($n = 145$)	p Value
Nasal obstruction (mean ± SD)	6.11 ± 0.55	3.23 ± 0.51	<0.05
Itching	7.19 ± 1.4	4.1 ± 0.81	<0.05
Rhinorrhea	8.2 ± 1.10	5.20 ± 0.73	<0.05
Sneezing	7.21 ± 1.12	5.20 ± 1.21	<0.05
Rhinoendoscopy clinical score			
1	0	51 (35.2%)	
2	32 (22.1%)	60 (41.4%)	<0.05
3	81 (55.8%)	34 (23.4%)	
4	32 (22.1%)	0	

In four patients in group B, it was possible to collect a sample of the inferior turbinate mucosa for histological examination in the site where QMR reduction had been performed. The biopsy was taken, after informed consent, during another operation not related to nasal surgery, performed >1 year after the surgical procedure on the turbinate.

The turbinate mucosa sections were prepared according to a routine procedure for histological and immunohistochemical evaluation, by means of a paraffin inclusion and de-wax steps, to provide 5-μm slices. These were stained with hematoxylin and eosin (H&E) and fluorescence microscopy observation of the H&E slides was performed (original magnification, ×400).

The outcome assessors were blinded to the assigned treatment group.

Statistical Analysis

For all subjective and objective outcomes the p value of improvement between groups was calculated and chi-square was used.

The significance score was set at 0.05 to test the null hypothesis that there was no significant difference in reduction of objective and subjective nasal symptoms between control and treatment groups.

Statistical analyses were performed using SPSS (software package used for statistical analysis) Statistics Version 17.0 (SPSS, Inc., Chicago, IL).

RESULTS

The study focused on 290 patients (age range, 18–68 years; Table 1). At baseline, the differences between the groups were not significant (Table 2).

Table 4 **Comparison of AAR values and time results at MCTt before and after treatment**

	Group A	Group B
Before treatment		
AAR	0.33 ± 0.02 Pa/cc^3 per s	0.40 ± 0.06 Pa/cc^3 per s
MCTt	16.9 ± 2 minutes	17.55 ± 2 min
After treatment ($p < 0.05$)		
AAR	0.28 ± 0.03 Pa/cc^3 per s	0.17 ± 0.02 Pa/cc^3 per s
MCTt	14.1 ± 2 min	14.9 ± 2 min

AAR = active anterior rhinomanometry; MCTt = mucociliary transport time.

Table 5 **Comparison of AAR nasal resistance values after NPT before and after treatment**

	Group A	Group B
Before treatment		
AAR	0.41 ± 0.03 Pa/cc^3 per s	0.43 ± 0.05 Pa/cc^3 per s
After treatment ($p < 0.05$)		
AAR	0.37 ± 0.02 Pa/cc^3 per s	0.21 ± 0.03 Pa/cc^3 per s

NPT = nasal provocation test; AAR = active anterior rhinomanometry.

Patients in group B reported no pain during the procedure. Paracetamol (500 mg) was prescribed for postprocedure pain on an "as-needed" basis. A few participants reported slight itching at the site of the procedure. None of the participants experienced any major side effects during or after the procedure, such as, *e.g.*, bleeding, synechia formation, and rhinitis sicca. Only a small crust, at the site of insertion of the device, was observed in 27 patients on days 5–7.

For subjective complaints (nasal obstruction, sneezing, rhinorrhea, and itching), the improvement was significant within each group, with more significant improvements in the treatment group. When QMR treatment was compared with medical therapy treatment only, greater efficacy was observed in group B with regard to concerns reduction of nasal symptoms and nasal endoscopic findings (Table 3).

Concerning objective findings (rhinomanometric assessments with and without NPT), similar trends, such as subjective findings, were observed within each group (Tables 4 and 5). The improvements within each treatment group were significant with no report of significant side effects (none required of medication or medical consultation).

Among treatment groups, the group receiving QMR as part of the treatment therapeutic approach showed a significantly greater improvement when compared with the control group A.

The rhinoendoscopy clinical score (Table 3) showed significant improvements in both groups, but these were significantly higher in treatment group B ($p < 0.05$).

Results of the MCT did not reveal, in the comparison between pre- and posttreatment values, statistically significant differences between the two groups, thus indicating a substantial similarity between medical and surgical treatment with regard to concerns the mucociliary function (Table 4).

Comparison between groups A and B, before and after treatment, with the SNOT-22 questionnaire regarding the five most important questions (five most important items) showed an improvement in both study groups but with better results, concerning efficacy, in group B (Table 6).

The samples of turbinate mucosa sections, stained with H&E medium power, at long-term control show respiratory mucosa with focal

Table 6 **Comparison of results of questionnaire SNOT-22 for the five most important questions before and after treatment in the two groups (mean values)**

	Group A	Group B
Before treatment		
Five most important items (mean values)	23.2	20.3
After treatment ($p < 0.05$)		
Five most important items (mean values)	15.1	5.9

SNOT-22 = 22-item Sino-Nasal Outcome Test.

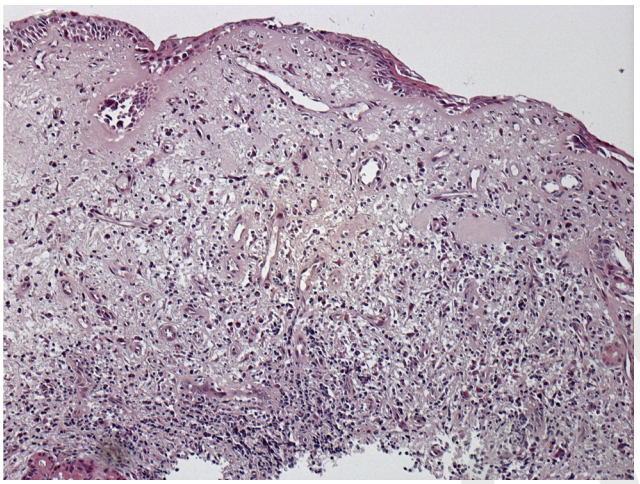

Figure 1. *No evidence of significant mucosal damage at long-term control of turbinate treated with quantic molecular resonance (QMR) turbinoplasty (hematoxylin and eosin [H&E], medium power).*

epithelial squamous metaplasia, mild edema, and inflammatory changes of the lamina propria, without necrosis or damage of the delicate superficial lining (Fig. 1).

DISCUSSION

From the results obtained, greater efficacy would appear to be achieved using a combined approach, *viz.*, the association of medical and QMR treatment, compared with medical treatment alone, in the control of AR associated with hypertrophy of the inferior turbinates. Symptoms evaluated by means of VAS showed greater efficacy in their control in those patients in treatment B group, in particular, those patients who had undergone treatment with QMR presented better objective parameters (AAR and endoscopic score) and at SNOT-22 compared with the group receiving only medical treatment. The combination of different frequencies (ranging between 4 and 16 MHz) produced by the QMR generator has, in fact, a particular effect: interrupting the molecular cell binding results in a break in the tissues involved with extreme selectivity and respect for the surrounding healthy tissue.[10] The mechanism of action is based on, in fact, the molecular bounds breaking, which enter in resonance with the frequency of the QMR keeping the surrounding tissues at a low temperature (<45°C). In this way, it is possible with the use of a handle inserted in the turbinate, through the submucosal tissue, to obtain a reduction in tissue volume without causing any burning effect leading to a *restitutio ad integrum* for primary intention with no significant edema and/or scars on the mucosa, as well as healing, as confirmed on histological samples similar to results observed with other radiofrequency.[16] Shrinkage obtained with QMR on the inferior hypertrophic turbinates is caused by evaporation of the contents of the soft tissues and submucosal fibrosis. This condition leads to a stable and long-lasting action caused by the disorder in the submucosal layers of the turbinate, which lack some of the cavernosal venous vessels and glands, resulting in a new and reduced volumetric configuration. Also, the lower mucosal response to the allergenic stimulation with NPT is caused by the interruption of the neurosensorial fibers and the receptors of the turbinate, together with the reduction in the amount of inflammatory cells. Decreasing the allergen responsiveness is a major goal of therapy for AR. To better establish the decreased responsiveness of the turbinate tissue to allergens after treatment, rhinomanometry was adopted after the NPT. In rhinomanometry, higher test results are indicative of more severe obstruction. The baseline values, in Table 2, clearly show higher rhinomanometric values after NPT when compared with those without NPT, in both allergen groups; the differences between treatment groups for corresponding tests are not significant. After 2 months, all rhinomanometry scores improved significantly in all allergen and treatment groups, but improvement was significantly better in the group submitted to surgery. These results are worthy of further examination. The improvement observed, after NPT, was found to be greater in group B than in group A. This would appear to suggest an action caused by the combined efficacy of the control of the allergic responsiveness to the treatment with QMR together with medical treatment, encouraging making the most of the synergy. An important issue in the treatment group is the wand's entry point. In the present study, the wand was introduced into the submucosa only once and treated all turbinate compartments (head, superior, medial, inferior, and posterior), thus reducing mucosal irritation. In our opinion, this technique is crucial when treating AR patients suffering from mucosal hyperreactivity. Results of the MCTt reveal that the function of the mucosal surface of the turbinate, also after surgery, is preserved and is a very important characteristic in a category of patients, such as those suffering from AR who have to undergo local medical treatment of the nose for prolonged periods while running the risk of mucosal atrophy.

CONCLUSIONS

QMR inferior turbinoplasty, in conjunction with medical therapy, improves the nasal flow more effectively when compared with medical treatment alone in persistent moderate-to-severe AR. In particular, local reactivity, as measured with NPTs, was noticeably reduced.

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