Original Article

Annals of Otology, Rhinology & Laryngology
2024, Vol. 133(6) 545–553

DOI: 10.1177/00034894241234593
journals.sagepub.com/home/aor
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Comparison of Allergen Immunotherapy Alone and in Conjunction With Turbinate Surgery for Nasal Obstruction in Perennial Allergic Rhinitis Patients

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Abstract

Background: Nasal obstruction, triggered by allergic rhinitis, often does not resolve with allergen-specific immunotherapy (AIT) alone, thus inferior turbinate reduction surgery (ITR) may be required. This study aims to investigate the impact of combined treatment on nasal obstruction, as evidence is currently limited.

Methodology/Principal: A retrospective cohort study of perennial allergic rhinitis patients experiencing nasal obstruction and undergoing ≥12 months AIT was conducted. Two groups were derived, those undergoing AIT—with or without an ITR. Patient reported nasal obstruction (evaluated with questionnaires) and nasal airway function (Nasal Peak Inspiratory Flow [NPIF] and Nasal Airflow Resistance [NAR]) were monitored. The change from baseline to 12 months post-treatment in each group were compared.

Results: A total of 118 patients (33.71 ± 14.43 years, 41.5% female) were recruited, 72% had AIT and 28% AIT&ITR. At baseline, the AIT&ITR group had a higher level of nasal obstruction (>moderate%; 63.6% vs 52.9%, $P = .048$). Post treatment, AIT&ITR group reported greater reduction in nasal obstruction (>1 category change: 75.8% vs 48.2%, $P = .002$). Similarly, the AIT&ITR group had greater improvement in nasal function by NPIF (−13.9 ± 110.3 L/minute vs −3.4 ± 78.1 L/minute, $P = .049$) and NAR (−0.120 ± 0.342 Pa/cm³/second vs −0.093 ± 0.224 Pa/cm³/second, $P = .050$).

Conclusions: Allergic rhinitis patients, with moderate to severe nasal obstruction, who undergo combined AIT&ITR have greater relief of nasal obstruction and improved airflow analysis compared to AIT alone.

Keywords

allergic rhinitis, nasal obstruction, patient reported outcomes, airway analysis, allergen immunotherapy, turbinate surgery

Introduction

Nasal obstruction is the commonest presentation of allergic rhinitis (AR), which is also the most prevalent respiratory disease in humans.[1] The prevalence of self-reported AR is up to 25% in children[2] and up to 40% in adults, depending on geographical setting.[3,4] Multiple environmental triggers, such as inhalant allergens (house dust mite, weed, grass and tree pollen, animal dander, and molds), can induce the abnormal immune response seen in AR. Patients often initially attempt to relieve nasal obstruction with pharmacotherapy including oral or intra-nasal antihistamines, intra-nasal steroids, and combined antihistamine/steroid sprays.[1] Although these medications help to target both the acute and delayed phase inflammation to help relieve nasal obstruction, they are not disease modifying and turbinate hypertrophy can still occur.

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Allergen immunotherapy (AIT) is a long-term treatment option which works by inducing immune tolerance, also known as desensitization. It is effective in minimizing allergic rhinitis symptoms and ultimately the IgE dominated response of allergic rhinitis, thus modifying the disease process or offering a long term "cure."[5] AIT is recommended by international guidelines for the treatment of moderate to severe AR.[6] While AIT in the form of sublingual immunotherapy can reduce total combined rhinitis scores in randomized double-blind, placebo-controlled phase 3 trials, there is often still a burden of patient reported nasal obstruction.[7-9]

Prolonged and repeated allergen exposure often results in chronic refractory nasal obstruction.[10] Beneath the respiratory epithelium of nasal turbinates contain erectile and vascular tissue which contribute to the regulation of nasal airflow and to the nasal cycle.[7,10] Persistent allergen exposure can result in dilatation of submucosal vessels due to inflammation, which contributes to turbinate enlargement. Although reversible at early stages, studies have shown that prolonged allergen challenge/exposure can result in a continuous upregulation of genes for inflammatory mediators,[7] which leads to permanent structural changes referred to as inferior turbinate hypertrophy.[11] Therefore, when turbinates are irreversibly hypertrophied, disease modifying interventions may not resolve nasal obstruction for allergic patients. Turbinate surgery, whereby the inferior turbinates are minimized in size to improve nasal airflow, may then be required.

Inferior turbinate reduction (ITR) is effective in reducing nasal congestion. A recent validation study has observed a very large decrease in Nasal Obstruction Symptom Evaluation (NOSE) scores after ITR from 96.7% to 8.8% at the 6- to 8-week follow-up.[12] This proves the high efficacy of ITR in reducing nasal obstruction rapidly. However, if the underlying allergic disease remains untreated without additional therapy it is likely that symptoms will return. In this same study, 55.3% of patients with AR still required at least once daily topical medication postoperatively to manage their AR symptoms.[12]

Thus, patients with allergic rhinitis seeking long-term relief of nasal obstruction should consider AIT and a subset of patient with established turbinate hypertrophy could benefit from additional ITR. Unfortunately, for the allergic patients, surgeons may perform ITR regularly but infrequently offer AIT and similarly, physicians who regularly provide AIT do not perform ITR, thus many patients miss out on the optimal combined approach. Currently, there is limited evidence available on the concurrent use of both treatment approaches as highlighted in a Cochrane review by Jose et al,[13] which aimed to assess the effectiveness of ITR on unrelieved or partially relieved nasal obstruction in patients after medical treatment. The current study was retrospectively performed to compare allergic rhinitis patients who elected to undergo a turbinate reduction as part of their AIT to those patients who remained on AIT alone. It was hypothesized that AIT&ITR provides patients with better nasal obstruction outcome than those who only had AIT-alone when measured by Patient Reported Outcome Measures (PROMs) and airway function analysis post treatment.

Materials and Methods

A retrospective cohort study was performed on patients presenting with allergic rhinitis. The primary objective of this study was to compare[1] patient reported nasal obstruction,[2] and nasal function of allergic rhinitis patients undergoing AIT with or without ITR surgery. The patients were recruited from a tertiary Rhinology practice. One treatment population consisted of those patients who had both AIT and a surgical reduction of the inferior turbinate as part of their care. The surgical technique used in this study was medial flap inferior turbinoplasty technique, which is the removal of turbinate bone with preserved mucosal flaps.

The comparative population remained surgically naïve and had AIT alone for their care. This study was approved by the local Human Research Ethics Committee (2019/PID13822 and 2021/PID02338). Informed consent was obtained.

Inclusion Criteria

Patients presenting with allergic rhinitis with varying degree of nasal obstruction and have commenced AIT.

Exclusion Criteria

Patients who had ITR or other sinonasal surgery prior to commencing AIT.

Timeline

Patients in the AIT group were followed up at 583 ± 223 days, whilst the patients in the AIT & ITR group were followed up at 669 ± 279 days. There is no significant difference in the duration of AIT between both groups (Table 2). The mean duration of patients undergoing ITR after initiating AIT is 350 ± 345 days (Figure 1). Patients who had ITR were followed up at a mean of 444 ± 286 days after surgery.

Patient Characteristics

Basic patient characteristics including age (years), gender (male or female), smoking status (current smoker or recent cessation of smoking <12 months), asthma status (based on current inhaled beta-agonist or corticosteroid use), and allergic status (skin prick test or serum specific IgE), were collected from patient medical records.

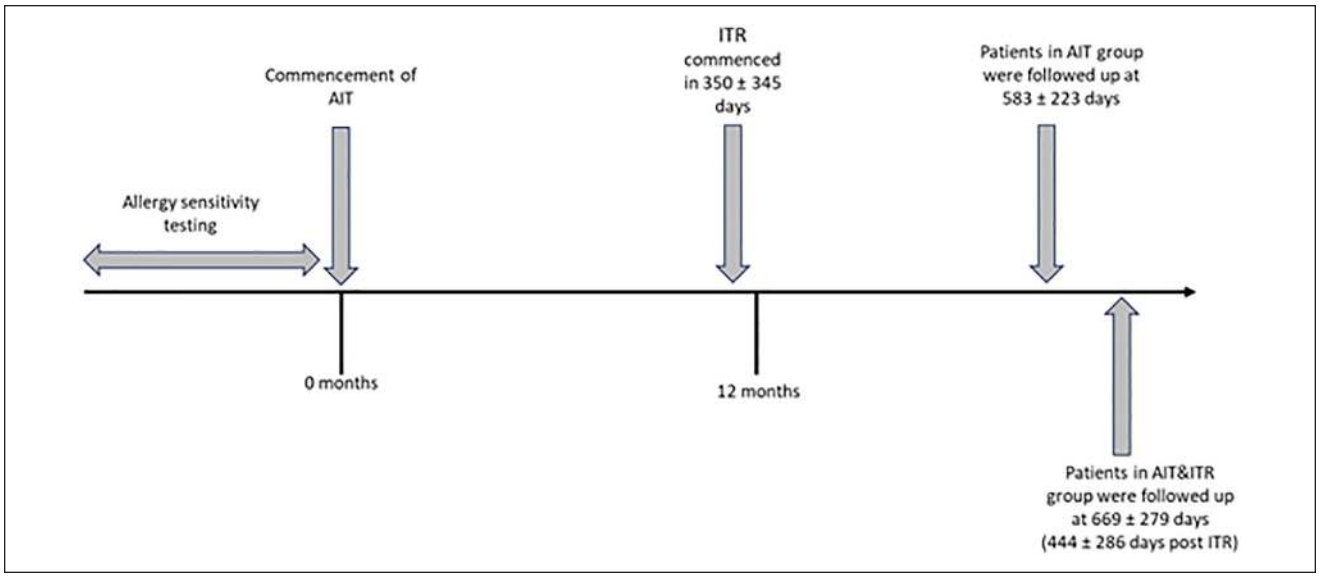

Figure 1. Timeline diagram depicting when patients commenced AIT and when patients in the AIT&ITR commenced ITR; and when both treatment groups were followed up.

Allergy Status

Allergen sensitization was based on either epicutaneous testing or serological assessment. Patients were instructed to abstain from antihistamines for at least 72 hours prior to epicutaneous testing. Epicutaneous testing was carried out using allergens in a 50% glycerin solution. Allergens were applied to the volar forearm with a Multi-test II device. The aeroallergen panel used comprised of dust mites (Dermatophagoides farinae and Dermatophagoides pteronyssinus), molds (penicillium and Cladosporium sp. Mix (Cladosporium cladosporioides and Cladosporium herbarum), Aspergillus sp. Mix (Aspergillus fumigatus, Aspergillus nidulans, Aspergillus niger, and Alternaria alternata), animal epithelium (cat and dog), and grass (7-grass mix [Kentucky Blue/June, meadow, rye, sweet vernal, cocksfoot, and timothy], Bermuda grass, Bahia grass, and rye grass). The negative control was glycerin and the positive control was histamine acid phosphate 10 mg/mL. After 15 minutes, the wheal size was recorded. A positive skin test result was defined as a wheal of ≥ 3 mm to any 1 of the allergens, with a non-reactive negative control. Serum-specific IgE, toward 4 allergen mixes that corresponded to the epicutaneous test panel (house dust, mold, animal, and grass), were evaluated by automated immunoassay. A serum specific IgE value of ≥0.35 KU/L for any of the mixed antigen mixes was recorded as positive. Patients' individual allergen sensitivity were recorded.

Patient Reported Outcome Measures (PROMs)

Patients' sense of nasal function was measured utilizing 4 tools.

(1) The Visual Analog Scale (VAS), a continuous linear scale where patients rated their sense of obstruction for each nostril from being not blocked (0 mm) to being totally blocked (100 mm) and compared with the same side post treatment. The more obstructed side at baseline was recorded and remained the same for each patient post treatment.
(2) Sino-nasal outcome test (SNOT22; 0-110) consisted of 22 questions with a 6-point Likert scale from 0 (no problem) to 5 (very severe problem) to each question. A recently validated model defined the following: no symptoms <8, "mild" 8 to 20; "moderate" >20 to 50; and "severe" >50.[14] There are 4 subdomains—sleep, nasal, otological/facial pain, and emotional symptoms.[14] Among them, nasal and sleep subdomains were the focus in this study as they are highly influenced by nasal obstruction. The SNOT-22 nasal (0-40) and sleep subdomains (0-40) scores were therefore also analyzed.[15] A 13-point Likert scale to evaluate overall nasal function from −6 (terrible) to +6 (excellent) was also used.
(3) Nasal obstruction was individually evaluated using a Visual Analog Scale (VAS), which is a 10-point Likert scale (from no problem –problem as bad as can be).[16] On this ordinal scale, an improvement of ≥1 from baseline to last follow-up was also assessed. The percentage of patients who reported an improvement of greater than equal to 1 in the Likert scale was calculated and compared between the 2 groups.
(4) The mini Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) is a validated questionnaire

which correlates the impact of AR on QOL such as how irritable patients felt because of their symptoms.[17] The questionnaire consists of 14 questions on a 7-point ordinal scale from 0 being not troubled to 6 being extremely troubled with a total score of 84.

Airflow Analysis

Nasal airflow analysis was conducted to analyze nasal peak inspiratory flow (NPIF), unilateral nasal airway resistance (NAR), and bilateral NAR. For both NPIF and NAR measurements, patients remained in a seated position for at least 20 minutes in a temperature-controlled environment (22°C). After which, measurements were recorded at baseline. NPIF was measured as L/minute with an anesthetic face mask which was attached to an In-Check flow meter (Clement Clarke International, Harlow, Essex, UK).[18] The mask provided an airtight seal while allowing full movements of the anterior nares. After a full expiration, patients were instructed to take a maximal inspiration through their nostrils with their mouth closed. The highest result of 3 attempts was recorded. A result of >120 L/minute for bilateral NPIF was considered normal. This cut-off was derived from the half standard deviation method where the minimal clinically important difference for bilateral NPIF is >20 L/minute.[19]

A 4-phase active anterior rhinomanometry (A6 Rhinomanometer; GM Instruments) was used to measure nasal airway resistance (NAR) as Pa/cm³/second at a fixed reference level of 150 Pa (in accordance with international standards) The patient was instructed to place an airtight anesthetic mask covering their nose and mouth, with the left nostril sealed with a nasal plug; to measure the NAR of the right nostril, patients then breathed normally through the open nostril with mouth closed. The steps were repeated on the contralateral side. Two readings of no more than 15% difference were recorded. The 2 values from both nostrils were inputs into the NARIS software (GM Instruments) to obtain the total NAR. A total NAR of ≤0.250 Pa/cm³/second was considered normal.[20] The side with the higher NAR was recorded as the obstructed side of each patient. This same side was compared with all future measurements.

PROMs and airway analysis outcomes were reported as mean ± SD.

Statistical Analysis

Statistical analysis was performed using SPSS version 27 (IBM; Armonk, New York USA). Chi-square tests were used to compare proportions of gender, smoking, asthma, and allergic status between both treatment groups. Age (years) was analyzed using Student's *t*-test. Kendall tau *B* test was used to compare the proportion of patients in ordinal scores. Paired *t* tests were used to compare unilateral VAS, mini-RQLQ, SNOT22, SNOT22 nasal and sleep subdomain, bilateral NPIF, unilateral, and total rhinomanometry (last follow up−baseline) across the entire population, while Student's *t*-tests were used to compare the change in these domains between the treatment groups. The obstructed side for each patient was defined by the nostril measuring a higher NAR score compared to the non-obstructed side. A *P*-value ≤.05 was considered statistically significant.

Results

The final population assessed included 118 patients (33.7 ± 14.4 years, 41.5% female). There were 85 (72%) participants who underwent AIT alone (Table 1). There were no significant differences in population demographics between both treatment groups.

Population Baseline Characteristics

The total duration patients were on AIT was 608.70 ± 242.27 days (Table 2). At baseline, a larger proportion of the patients in the AIT&ITR group reported having ≥moderate obstruction (SNOT22 nasal obstruction score ≥3) than those in the AIT group at baseline (% patients reporting ≥moderate obstruction: 63.6% vs 52.9 %, *P*=.048; Table 2).

Total Population Outcomes

The entire population reported a significant improvement of quality of life when assessed by mini RQLQ (0-6) after at least 12 months treatment compared to baseline (2.2 ± 1.2 vs 1.3 ± 1.0, *P*<.001; Table 3). Participants also reported improvement in the SNOT22 (36.8 ± 21.6 vs 25.6 ± 18.4, *P*<.001), and in the nasal (15.7 ± 9.1 vs 10.0 ± 7.3, *P*<.001); and sleep subdomains (16.9 ± 9.9 vs 12.5 ± 8.8, *P*<.001; Table 3). There was improvement in nasal airway parameters as measured by NPIF (130 ± 47 L/minute vs 144 ± 43 L/minute, *P*=.002) and NAR (0.259 ± 0.272 Pa/cm³/second vs 0.151 ± 0.098 Pa/cm³/second, *P*<.001). There were no other significant findings observed in outcome parameters measured (Table 3).

Outcome Comparison Between Study Groups

In patient reported measures, there were no differences in reported general allergy symptoms following treatment, however a significantly greater proportion of participants in the AIT&ITR group reported a ≥1 category improvement in nasal obstruction compared to the AIT-only group in the SNOT22 questionnaire (75.8% vs 48.2%, *P*=.002; Table 4).

Nasal airway analysis comparison between groups showed that patients in the AIT&ITR group had a significantly greater NPIF improvement compared with the AIT-only group (13.9 ± 110.3 L/minute vs 3.4 ± 78.1 L/minute,

Table 1. Population Demographics.

		Treatment group		
	Total	AIT	AIT&ITR	*P*-value
Number of participants	118	85	33	
Age (years; mean ± standard deviation)	33.7 ± 14.4	34.5 ± 14.2	31.7 ± 15.0	.801*
Gender (% Female)	41.5	43.5	36.4	.194#
Smoking status (% Yes)	11.0	8.2	18.2	.165#
Asthma status (% Yes)	35.6	37.7	30.3	.766#
Allergic status (%) percentage of patients who test positive for each of these				
Grass (temperate)	60.2	64.7	48.5	.242#
Grass (tropical)	45.8	49.4	36.4	.404#
Animal	48.3	48.2	48.5	.970#
Mold	17.8	17.7	18.2	.860#
HDM	83.9	83.5	84.9	.957#

Abbreviations: AIT: allergen immunotherapy; AIT&ITR: allergen immunotherapy and inferior turbinate surgery; HDM, House Dust Mite.
*Student's *t*-test.
#Chi-square test.

Table 2. Baseline Disease Factors (Allocation Table).

		Treatment group		
	Total	AIT	AIT&ITR	*P*-value
Number of participants	118	85	33	
Duration on AIT (days)	608.70 ± 242.27	583.11 ± 223.43	669.45 ± 279.80	.239*
Obstructed side nasal obstruction (VAS 0-100)	75.4 ± 21.1	63.1 ± 20.6	86.0 ± 15.2	.221*
Nasal obstruction (%≥3) moderate	55.9	52.9	63.6	.048#
RQLQ (0-6)	2.21 ± 1.28	2.1 ± 1.3	2.5 ± 1.2	.722*
SNOT22 (0-110)	35.9 ± 21.5	34.6 ± 22.2	39.3 ± 19.4	.239*
Nasal sub	15.2 ± 9.1	14.7 ± 9.2	16.6 ± 9.0	.618*
Sleep sub	16.3 ± 9.88	15.4 ± 10.0	18.7 ± 9.3	.566*
Nasal peak inspiratory flow (L/min)	130.72 ± 45.87	134.58 ± 45.09	120.79 ± 47.06	.855*
NAR (Pa/cm³/s)				
More obstructed side	0.818 ± 1.210	0.761 ± 1.231	0.966 ± 1.454	.183*
Total	0.258 ± 0.216	0.239 ± 0.236	0.309 ± 0.337	.144*

Note. Evaluation Scale: SNOT-22, 22-item Sinonasal Outcome Test.

Abbreviations: AIT, allergen immunotherapy; AIT&ITR, allergen immunotherapy and inferior turbinate surgery; NAR, nasal airway resistance; NPIF, nasal peak inspiratory flow; PROMs, patient-reported outcome measures; VAS, Visual Analog Scale; Sub, subdomain.
*Student's *t*-test.
#Kendall tau *B* test.

P = .049); and a lower n total airway resistance (−0.120 ± 0.342 Pa/cm³/second vs −0.093 ± 0.224 Pa/cm³/second, *P* = .050; Table 4). There were no other significant findings observed in outcome parameters measured (Table 4).

Discussion

The clinical rationale for combining AIT and ITR therapies as management for AR is so that nasal obstruction can be optimally resolved. This study demonstrated that AR patients who underwent both AIT and ITR had a greater improvement in nasal breathing both by patient-reported and objective airway analysis.

AIT is very effective in resolving the underlying inflammation driving AR.[7] However, in a significant number of patients nasal obstruction refractory to AIT occurs due to remodeling changes in the inferior turbinates. Therefore, this study demonstrates, using both PROMs and objective

Table 3. Outcome of the Entire Population.

	Entire population			
	Baseline (absolute)	Last follow-up (absolute)	Change	*P*-value
Number of participants	118	118	118	
Obstructed side nasal obstruction (VAS 0-100)	71.3 ± 23.0	32 ± 31.4	−39.3 ± 36.7	.684*
Nasal obstruction (%≥3) moderate	55.9 %	30.5 %	−25.4 %	.261#
RQLQ (0-6)	2.2 ± 1.2	1.3 ± 1.0	−0.9 ± 1.2	<.001*
SNOT22 (0-110)	36.8 ± 21.6	25.6 ± 18.4	−11.2 ± 20.0	<.001*
Nasal sub	15.7 ± 9.1	10.0 ± 7.3	−5.7 ± 9.0	<.001*
Sleep sub	16.9 ± 9.9	12.5 ± 8.8	−4.5 ± 1.1	<.001*
Nasal peak inspiratory flow (L/min)	130 ± 47	144 ± 43	14 ± 31	.002*
NAR (Pa/cm³/s)				
Obstructed side	0.815 ± 1.264	0.381 ± 0.406	−0.434 ± 1.289	.312*
Total	0.259 ± 0.272	0.151 ± 0.098	−0.312 ± 1.231	<.001*

Note. Last follow up-baseline ΔY = Y1−Y0. Unless stated otherwise, values are represented as means and standard deviation.
Abbreviations: AIT, allergen immunotherapy; AIT&ITR, allergen immunotherapy and inferior turbinate surgery; NAR, nasal airway resistance; NPIF, nasal peak inspiratory flow; PROMs, patient-reported outcome measures; VAS, Visual Analog Scale; Sub, subdomain. evaluation scale; SNOT-22, 22-item sinonasal outcome test.
*Student's *t*-test.
#Kendall tau *B* test.

Table 4. Outcome Comparison Between AIT and AIT&ITR.

	Treatment group		
	AIT	AIT&ITR	*P*-value
Number of participants	85	33	
Δ Obstructed side nasal Obstruction (VAS 0-100)	−42.7 ± 34.7	−60 ± 27.4	.422*
Nasal obstruction (% ≥1 score improvement in each treatment group)	48.2%	75.8%	.002#
ΔRQLQ (0-6)	−0.8 ± 1.2	−1.3 ± 1.1	.986*
ΔSNOT22 (0-110)	−9.9 ± 20.8	−17.5 ± 21.5	.655*
ΔNasal Sub (0-40)	−5.1 ± 9.0	−9.7 ± 9.5	.367*
ΔSleep Sub (0-40)	−4.0 ± 10.6	−7.0 ± 10.9	.912*
ΔNasal peak inspiratory flow (L/min)	3.4 ± 78.1	13.9 ± 110.3	.049*
ΔNAR (Pa/cm³/s)			
Obstructed side	−0.439 ± 1.28	−0.622 ± 1.55	.108*
Total	−0.093 ± 0.224	−0.120 ± 0.342	.050*

Note. Last follow up-baseline ΔY = Y1−Y0. Unless stated otherwise, values are represented as means and standard deviation.Symptom Evaluation Scale.
Abbreviations: AIT, allergen immunotherapy; AIT&ITR, allergen immunotherapy and inferior turbinate surgery; NAR, nasal airway resistance; NPIF, nasal peak inspiratory flow; PROMs, patient-reported outcome measures; VAS, Visual Analog Scale; Sub, subdomain.; SNOT-22, 22-item sinonasal outcome test.
*Student's *t*-test.
#Kendall Tau *B* test;Δ = change.

measures, that a combination of AIT and ITR provides better results than AIT alone in patients with significant nasal obstruction.[21]

A recent randomized trial investigating the efficacy of sublingual immunotherapy in patients allergic to HDM demonstrated a statistically significant reduction of nasal congestion in the 6 SQ-HDM group when assessed by PROMs.[7] However, it has also been reported that nasal obstruction caused by inferior turbinate hypertrophy refractory to AIT (minimum 3 months of persistent symptoms), often suggests that ITR intervention is required.[22] The current study supports this premise, as patients who presented with a higher burden of nasal obstruction when commencing AIT, progressed to undergoing ITR as part of their allergy treatment. Patients with symptomatic turbinate hypertrophy presenting with worse nasal obstruction despite AIT initiation should be promptly evaluated as potential ITR candidates. It is important to note that the key players driving the severity of AR symptoms are both allergic mucosa inflammation in the inferior turbinates as well as

increased turbinate size.[23] As such, symptom relief may require these 2 factors contributing to refractory nasal obstruction to be targeted.

Currently, patients with AR are often treated by only allergist or ENT surgeons, with minimal overlap, and therefore will be directed to AIT or ITR preferentially. However, this study had demonstrated that a combined approach offers the best outcomes for nasal obstruction, and thus might benefit from a combined medical and surgical approach. This is also in line with ASCIA's recent allergic rhinitis clinical update which advised the need to refer to an ENT surgeon for ITR if there is medically refractory nasal obstruction

ENT specialists often recommend ITR followed by pharmacotherapy as management of AR.[24] Prospective studies have demonstrated the gradual decline of ITR efficacy at follow up consults, from the probability of at least a 50% decrease in nasal blockage score to 27% at 2.5 years post-surgery.[25] This has demonstrated the ineffectiveness of relying on ITR alone in managing AR. That is because ITR alone has limited benefit in resolving the underlying allergic disease driving AR symptoms.

The results of our study indicate that using both AIT and ITR best improves nasal obstruction outcomes. This supports the significance of shifting the clinical approach to managing moderate to severe AR. That is, from symptom management to that of resolving the allergic disease and nasal obstruction. Studies have also shown that approximately 40% of AR patients rely on numerous drug regimens concurrently for AR treatment.[26,27] There is limited research on how the continuous reliance on pharmacotherapy to manage allergy symptoms can affect AR patients' quality of life (QoL), especially depending on them postoperatively.[28,29] A recent prospective observational study has highlighted the importance of counseling patients preoperatively regarding the need to continue allergy management postoperatively to achieve optimal control of their nasal symptoms.[30] Patients' expectations of turbinate surgery should be as an intervention that is complementary to and not a replacement for medical management of allergic rhinitis.

The prompt relief of AR symptoms can also improve patients' QoL, especially with resolution of the nasal obstruction.[31] A recent phase 3 trial has demonstrated that upon AIT commencement, AR symptoms were observed to reduce rapidly from as early as 14 weeks into treatment.[7] Therefore, patients who do not respond early to AIT, exhibiting ongoing nasal obstruction may benefit from a concurrent rapid reduction in nasal obstruction with ITR and the added disease-modifying effect of AIT in reducing AR flares. Early referral to an ENT specialist to consider AIT&ITR as a resolution to their nasal obstruction is recommended. Resolving nasal obstruction promptly improves patients' QoL, sleep, and work and ensures progression of symptom relief while on AIT.

A major strength of this study was the use of retrospectively collected validated tools that have been well published in previous studies.[14,32-34] Furthermore, this study adopted the use of PROMs to assess the patients' perception of nasal obstruction. The strengths of adopting PROMs is that they are simple to use, inexpensive, and have proven reliability, validity, and reproducibility.[35] In addition, all PROMs and airway analysis were collected by highly trained staffs of a tertiary Rhinologic lab, optimizing consistency of results.

A limitation to this study was the absence of an ITR only comparative group. Therefore, it was not possible to analyze the efficacy of ITR alone (without pharmacotherapy) in reducing nasal obstruction in AR patients. This is the focus of an active future project, with a control group and ITR treatment arm to establish if patients receiving AIT&ITR had better nasal obstruction outcomes. Furthermore, recruitment bias could arise due to all patients being consulted from a tertiary practice. Tertiary practice patients also often represent the more severe disease population of AR. According to the Allergic Rhinitis and its impact on Asthma (ARIA) guidelines, the more severe disease population of AR would include patients who experienced persistent ($\geq$4 days/week and $\geq$4 weeks) and moderate-severe symptoms affecting quality of life, which can be assessed by the mini-RQLQ used in our study.[3,36] Whether this significant improvement of the AIT&ITR group can be extended to the general population of allergic rhinitis patients with less severe nasal obstruction is uncertain. Another limitation is that this is a retrospective study and therefore there was limited control over confounders. Furthermore, this study did not exclude patients with other anatomical contributions to nasal obstruction, such as concha bullosa and septal deviations. It is important to acknowledge that this inclusion of patients with pre-existing anatomical variations may have influenced the degree of change observed post-treatment. Future research may consider stratifying or analyzing subgroups based on these anatomical variations to better understand their impact on treatment outcomes. Another challenge encountered in this study is comparing the degree of allergen sensitivity between the 2 groups, primarily due to the varied methods used to assess allergy levels within each group. The assessment techniques utilized in this study was skin prick tests and radioallergosorbent test (RAST). The diversity in these diagnostic tools used post a challenge in establishing a uniform baseline for allergen sensitivity across the study population. Lastly, the baseline nasal obstruction of the participants in AIT&ITR group was worse than those in the AIT group. This is due to real life patients of various comorbidities being recruited in this study. To minimize the skewed effects of the unequal baseline of a retrospective study, only the change ($\Delta Y = Y1 - Y0$) scores and measurements were compared at post treatment. Future studies

should involve a randomized controlled trial where patients are randomly allocated into treatment groups with similar baselines. Although limitations were present in this study, a recent Cochrane review has concluded there was insufficient literature of the combined treatment of AIT&ITR as management for moderate to severe allergic rhinitis,[13] hence the importance of our study to help bridge this gap.

Conclusion

Concomitant treatment of allergen immunotherapy and turbinate surgery in AR patients was found to reduce nasal obstruction more effectively than AIT alone, when assessed by PROMs and nasal airway analysis. Though it is important to note that global health-related quality of life measures (SNOT-22, RQLQ) did not show significant differences in this study, future prospective studies with controlled trials are needed to confirm significant differences in these measures. Therefore, this study supports 12 months of immunotherapy followed by turbinate surgery can significantly reduce nasal obstruction. This study also suggests that patients with a high burden of nasal obstruction when commencing immunotherapy should consider turbinate surgery as part of their overall AR treatment if expectations of symptom relief is not met on AIT-alone.

Author's Note

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Acknowledgments

Special thanks to the Sydney ENT clinic staffs for providing technical assistance in data collection.

Author Contributions

The first author of this study (A. X. J. Chong) declares that this submission is her original work with input from all contributors as acknowledged above. She was responsible for data collection from patients' consult records into excel spreadsheets, statistical analysis, interpretation, and authoring this manuscript. This study was designed by R. J. Harvey and R. Alvarado. Data used in this study were also collected by staff members of the Sydney ENT Clinic. Assistance with data collection, technical, and administrative support was provided by R. Alvarado. Statistical analysis assistance was provided by R. J. Harvey.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Richard J Harvey is a consultant/advisory board with Medtronic, Novartis, GSK and Meda pharmaceuticals and received research grant funding from Glaxo-Smith-Kline. He has been on the speakers' bureau for Glaxo-Smith-Kline, Astra-zeneca, Meda Pharmaceuticals, and Seqirus. Both Richard J Harvey and Raquel Alvarado have affiliations to the School of Clinical Medicine, St Vincent's Healthcare Clinical Campus, Faculty of Medicine and Health, UNSW Sydney, Australia. Janet Rimmer has honoraria with Sanofi Aventis, Novartis, Mundipharma, BioCSL, Stallergenes. Raewyn Campbell has honoraria with Medtronic, Seqirus, Viatris, and Novartis steering committee. Larry Kalish is on the speakers' bureau for Care Pharmaceuticals, Mylan, and Seqirus Pharmaceuticals.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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