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Allergen Immunotherapy for a Year Can Effectively Reduce the Risk of Postoperative Recurrence of Adenoid Hypertrophy in Children with Concurrent Allergic Rhinitis (IMPROVEII)

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Background: Adenoid hypertrophy (AH) and allergic rhinitis (AR) are common pediatric diseases, seriously affecting the quality of life and growth of children. The recurrence rate of AH is higher for patients with than for those without concurrent AR. Allergen specific immunotherapy (AIT) is the only effective therapy for modifying the course of allergic diseases. This study sought to investigate the efficacy of AIT in preventing AH recurrence in patients with AR who underwent adenoidectomy.

Methods: This study included 134 children aged 5–12 years with concurrent AH and AR. They were separated into the subcutaneous immunotherapy (SCIT) group treated with a double-mite allergen preparation or the non-AIT group treated symptomatically with only medications. The adenoid/nasopharyngeal ratio at one year after adenoidectomy was used to assess AH recurrence. The Obstructive Sleep Apnoea Questionnaire (OSA-18), Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ), and Visual Analogue Scale (VAS) were used to assess the severity of the sleep disorders and AR.

Results: This study included 62 and 72 children with concurrent AH and AR in the SCIT and non-AIT groups, respectively. The rate of recurrence in the SCIT group was significantly lower than that in the non-AIT group (4.84% vs.16.67%; P=0.030). The OSA-18, PRQLQ, and VAS scores were significantly lower for the SCIT than ($P<0.001$) for the non-AIT group after one year of treatment.

Conclusion: The findings suggest that AIT should be considered the preferred therapy for reducing postoperative recurrence of AH in children with concurrent AR following adenoidectomy, but further research is needed to confirm these findings in a larger population.

Keywords: adenoid hypertrophy, allergic rhinitis, allergen specific immunotherapy, recurrence, adenoidectomy

Introduction

In paediatric otorhinolaryngology, adenoid hypertrophy (AH) is a common illness and a common cause of obstructive sleep apnoea in children, with an incidence of 34.6%.[1] It can easily result in nasal congestion, open-mouth breathing, snoring, waking, apnoea at night, and maxillofacial developmental disorders. It can also result in inflammation of nearby ear and nasal organs, leading to a diminished quality of life and impaired learning capabilities in children.[2] Moreover, AH may impact children's growth and development, potentially causing behavioural and cognitive issues like reduced attention span, hyperactivity, and irritability.[2–4]

Allergic Rhinitis (AR), a non-infectious inflammatory illness of the nasal mucosa, mainly caused by IgE-mediated mediators in individuals with atopy after exposure to allergens and involves allergic inflammatory response. It mainly presents as nasal obstruction, runny nose, nasal itching, paroxysmal sneezing, and other symptoms. Although the exact cause of AH is unknown, repeated exposure to different allergens and microorganisms has been implicated,[5–7] and AR and AH often co-occur. From the

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perspective of anatomical factors, when AR is combined with postnasal drip syndrome, aggravation of adenoid stimulation by secretions is more likely to cause AH. Adenoidectomy has shown effectiveness in treating AH;[8] however, approximately 8% of children with AH experience recurrence.[9] The recurrence rate is higher in children with AH and AR than in those with AH alone, owing to long-term chronic irritation caused by allergens.[10] Recurrence of AH requires additional surgery, amplifying both the physical and mental distress experienced by the child and imposing a greater economic burden on both the family and society. Unlike children with only AH, 80% of children with AH complicated by AR do not demonstrate appreciable benefits after adenoidectomy.[7] The high postoperative recurrence rate and low postoperative satisfaction suggest that adenoidectomy alone might not suffice for patients with AR.

Intranasal steroids and antihistamines have demonstrated some effects in alleviating AH and preventing postoperative recurrence,[11–13] but there is a risk of recurrence after withdrawal, and long-term medication is needed for control. Notwithstanding, allergen specific immunotherapy (AIT), as the current first-line treatment, can control AR over a long duration with a definite curative effect. AIT refers to a treatment method to control or reduce allergic symptoms by repeatedly exposing patients to gradually increasing doses of allergen extracts on the basis of identifying the major allergens that cause allergic diseases, so that the body's immune system can develop tolerance to such allergens.[14] It is also the only effective treatment for modifying the course of allergic diseases. Adenoidectomy is the primary treatment for AH, but adenoidectomy alone is not an effective treatment for AH patients with AR, and treatment of AR is essential to prevent unfavourable surgical outcomes and postoperative recurrence. Hence, we undertook a follow-up study to observe the postoperative recurrence of AH complicated by AR following AIT by subcutaneous immunotherapy (SCIT). The impact of AIT on postoperative recurrence was also investigated to offer insights into the treatment of AH complicated by AR. This innovative findings may provide novel therapeutic strategies for preventing postoperative recurrence in patients with AR and AH, influencing clinical practice or leading to new treatment guidelines.

Methods

Patients

This single-centre, prospective clinical trial with two parallel arms investigating the efficacy of AIT in preventing AH recurrence in children with AR was carried out at Renmin Hospital of Wuhan University between October 2022 and February 2024. The study protocol was approved by the Clinical Research Ethics Committee of Renmin Hospital of Wuhan University (protocol code: WDRY2022-K019) and registered in the Chinese clinical trial registry (ChiCTR2200063899). This study was conducted in accordance with the Declaration of Helsinki. The parents of the children provided written informed consent for their inclusion in the study. The inclusion criteria were as follows: (a) age of 5–12 years; (b) children diagnosed with AH and AR according to the Chinese guidelines for the diagnosis and treatment of childhood obstructive sleep apnoea (2020) and the 2018 AR and its Impact on Asthma guidelines;[15,16] allergens were *Dermatophagoides pteronyssinus* (Derp) and/or *Dermatophagoides farinae* (Derf); patients undergoing adenoid plasma ablation in our hospital; history of AR for more than one year; and agreement of parents of the children to their involvement in the study and signed the informed consent form. The exclusion criteria were as follows: severe hypersensitivity to allergens other than dust mites; severe or uncontrolled asthma; other immune diseases; interrupted SCIT; failure to undergo regular follow-up; history of sublingual immunotherapy; and usage of montelukast and/or corticosteroids within four weeks before the first evaluation. The flowchart of the participant selection is shown in Figure 1.

Initial Assessment and Evaluation

All patients underwent otorhinolaryngological examination, serum-specific IgE detection (ImmunoCAP 250), lateral cranial radiography, and nasal secretion tests. They also completed electronic questionnaires, including the Obstructive Sleep Apnoea Questionnaire (OSA-18),[17] Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ),[18] and the Visual Analogue Scale (VAS) for nasal symptoms[19] before surgery. Smears of nasal secretions were obtained for eosinophil cationic protein (ECP)- myeloperoxidase (MPO) test paper analysis. Lateral cranial radiographs were used to assess the adenoid size. The adenoidal/nasopharyngeal (A/N) ratio was determined according to the method described by Fujioka et al;[20] A represents the

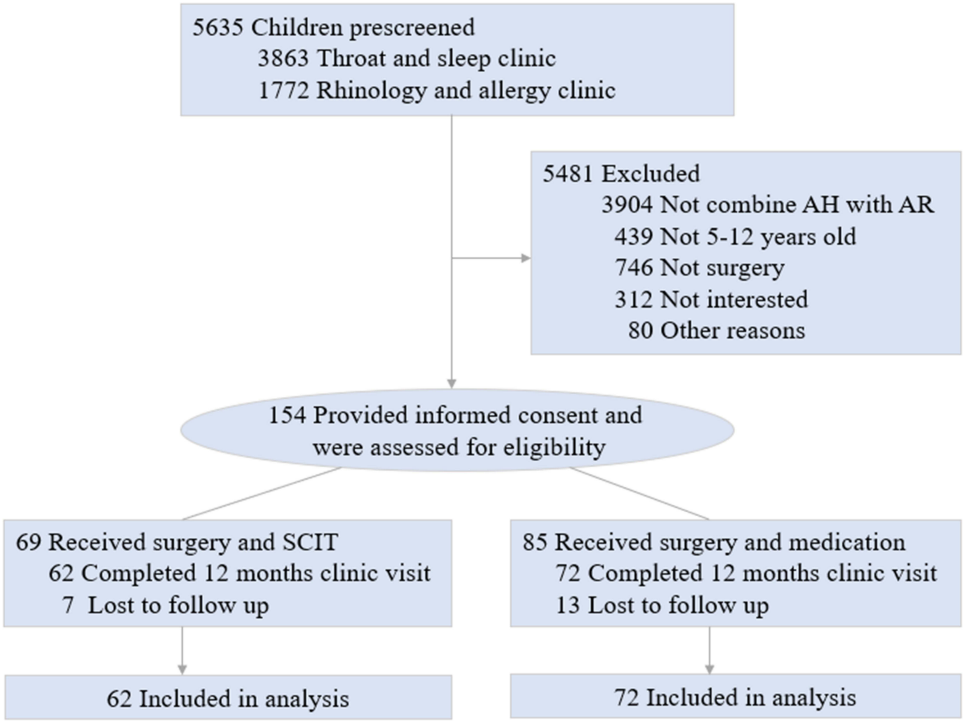

Figure 1 Patient screening flow chart.
Abbreviations: AH, adenoid hypertrophy; AR, allergic rhinitis; SCIT, subcutaneous immunotherapy.

distance between the outer tangential line of the occipital slope and the point of maximum convexity of the adenoid shadow, while N denotes the length from the anteroinferior edge of the sphenobasioccipital synchondrosis to the posterior border of the hard palate. AH was defined as an A/N ratio >0.60.

ECP-MPO test strips (Dabai Xiaobai Technology) were used to determine the expression of ECP and MPO in the nasal secretions of patients. The detailed procedure was described by Xi et al.[21] By comparing the colour depth of the control and detection lines, four levels were determined: level 0, where the detection line was not coloured; level 1, where the detection line was only slightly coloured; level 2, where the detection line was slightly lighter than the control line; and level 3, where the detection and control line colour intensities were similar.[21] Patient grouping information is hidden from data collectors and analysts.

Intervention

All the children underwent endoscopic low-temperature plasma radiofrequency ablation adenoidectomy or adenotonsillectomy. Depending on the proportion of tonsils in the pharynx and history of tonsillitis, the surgeon performed adenoidectomy or adenotonsillectomy in the children. The children were grouped into SCIT and non-AIT groups based on whether their parents were willing to undergo desensitisation therapy after surgery. Both groups began treatment within two weeks of surgery. The SCIT group was treated with SCIT of standardised allergens (Allergopharma) and symptomatic medications as needed. All patients in the SCIT group received the same AIT preparations. In the SCIT group, the corresponding dose and concentration of dust mite extract were injected subcutaneously on time during the dose accumulation and maintenance stage. When the interval between injections in the dose accumulation and maintenance stage was more than 4 weeks and 10 weeks, respectively, we considered the injection delay to be too long and classified patients as lost to follow-up. The non-AIT group was treated with symptomatic medications as required.

Follow-Up

All patients were examined every three months after treatment and were followed up for one year. The OSA-18, PRQLQ, and VAS were completed, and smears of nasal secretions were obtained every three months for the ECP-MPO test. Lateral head radiographs were obtained every 6 months to evaluate adenoid size.

Hypothesis and Outcomes

We hypothesised that AIT for one year would effectively reduce the risk of postoperative recurrence in children with AH and AR. The primary endpoint was the reduction of the risk of AH recurrence in patients with AR and AH after SCIT therapy for one year after surgery. The secondary endpoint was the trend of AH recurrence in both groups within one year of surgery. Recurrence was considered when the A/N ratio was >0.6. For patients with A/N ratios of >0.6, nasal endoscopy was performed to rule out tubal torus hyperplasia.

The proposed methodology has not yet been undertaken in any study involving AH. Therefore, we conducted a preliminary experiment before the study commenced. In the preliminary experiment, 15 children were recruited in the SCIT group, and 1 child recurred at 1 year of follow-up, while 12 children were recruited in the non-AIT group, and 4 children recurred at 1 year of follow-up. We estimated an effect size of 26.67% for between-groups differences in recurrence rate, with an α level of 0.05, 80% power, and 20% shedding rate. The sample size for each group was finally calculated to be 62. GPower 3.1 program (Düsseldorf, Germany) was used to calculate the sample size.

Statistical Analysis

SPSS 26.0 (IBM, Armonk, NY, USA) and R 4.0.3 (R Foundation, Vienna, Austria) were used for statistical analysis. Normally distributed measurement data were analyzed using an independent-sample *t*-test. Non-normally distributed measurement data for two groups were compared using the Mann–Whitney *U*-test, while for multiple groups, the Kruskal–Wallis *H*-test was employed. Counting data were assessed using the chi-square test, and multiple groups of rank data were compared using the Kruskal–Wallis rank-sum test. $P<0.05$ was regarded as statistically significant.

Results

Clinical Parameters

The clinical parameters of the study participants are listed in Table 1. After screening, 62 patients in the SCIT group and 72 in the non-AIT group met the inclusion criteria and completed the follow-up. There were no significant differences between the baseline data of the two groups ($P \geq 0.05$).

Table 1 Characteristics of the Study Participants

	SCIT group	Non-AIT group	Overall	P
N	62	72	134	
Age, years	6.710[5.830,8.000]	6.045[5.500,7.580]	6.420[5.648,7.690]	0.234
Sex: Male	62(37)	72(51)	134(88)	0.175
Adenoid size before surgery	0.715[0.670,0.780]	0.740[0.700,0.780]	0.740[0.680,0.780]	0.123
Tonsil volume				
I	13	12	25	0.408
II	35	40	75	
III	14	20	34	
Level of specific IgE to Derp and/or Derf				
1–2	4	12	16	0.199
3–4	25	27	52	
5–6	33	33	66	
Total IgE	407.000[193.750, 856.000]	269.000[151.250, 551.500]	316.500[168.500, 699.000]	0.101
Asthma (%)	14/62(22.581%)	11/72(15.278%)	134(25)	0.279
CRS (%)	30/62(48.387%)	38/72(52.778%)	134(68)	0.612

Abbreviations: IgE, Immunoglobulin E; Derp, Dermatophagoides pteronyssinus; Derf, Dermatophagoides farinae; CRS, chronic sinusitis.

Table 2 Comparison of AH Recurrence in the Two Groups at 6 and 12 Months After Surgery

	SCIT Group	Non-AIT Group	Overall	P
6 months	1/62(1.613%)	7/72(9.722%)	8/134(5.970%)	0.107
12 months	3/62(4.839%)	12/72(16.667%)	15/134(11.194%)	0.030

Postoperative Recurrence of the SCIT and Non-AIT Groups

Nasal endoscopy was performed in all patients with A/N >0.6 to rule out tubal torus hyperplasia. There was no significant difference in recurrence at 6 months postoperatively between the two groups (P=0.107). The recurrence in the SCIT group was lower than that in the non-AIT group (P=0.030) at 12 months postoperatively (Table 2). There was no significant difference in the preoperative A/N ratio between the two groups. The A/N ratio in the SCIT group was lower than that in the non-AIT group 6 and 12 months after surgery (P<0.05) (Figure 2a). Figure 2b and c show the lateral cranial radiographs of the patients in both groups before surgery and 6 and 12 months after surgery.

ECP-MPO Test of Nasal Secretions of the SCIT and Non-AIT Groups

There was no significant difference in ECP detection between the SCIT and non-AIT groups before surgery or 3 and 6 months after surgery (Figure 3a). ECP detection in the SCIT group was significantly better than that in the non-AIT group 9 and 12 months after surgery. There was no significant difference observed in MPO levels between the SCIT and non-AIT groups neither before surgery nor at 3, 6, and 9 months post-surgery. MPO detection in the SCIT group was significantly better than that in the non-AIT group 12 months after surgery (Figure 3b).

Questionnaire Findings of the SCIT and Non-AIT Groups

There were no significant differences in the OSA-18, VAS, and PRQLQ scores of the SCIT group before and three months after surgery. The OSA-18 scores in the SCIT group at 9 and 12 months after surgery were significantly lower

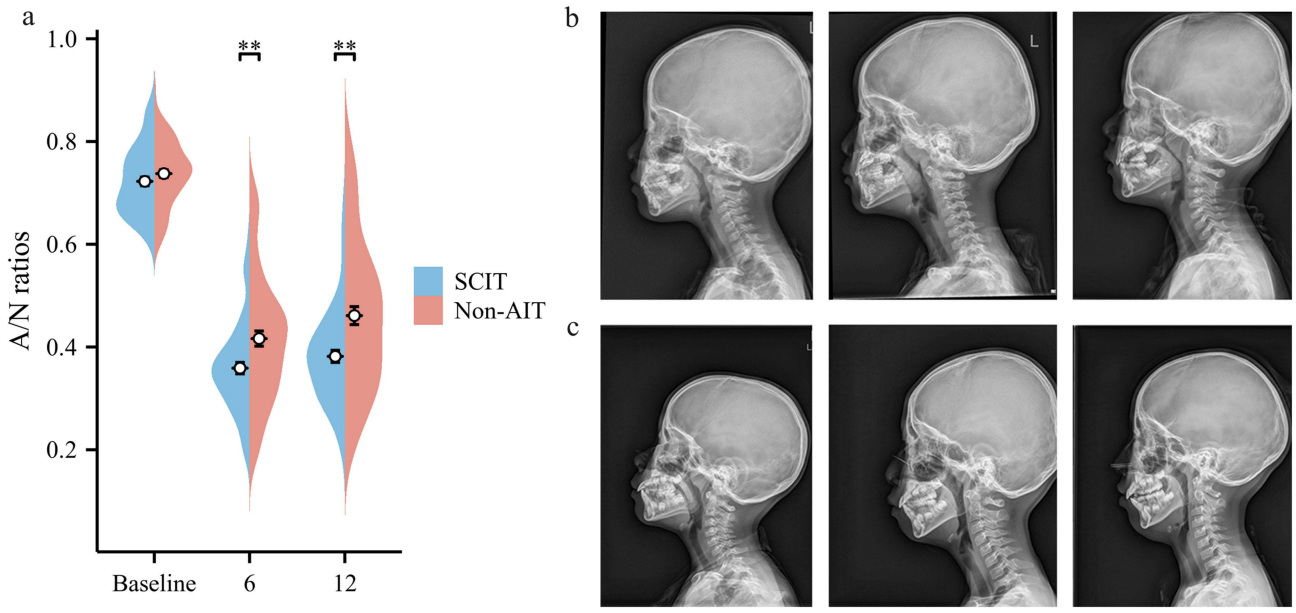

Figure 2 Adenoidal/nasopharyngeal (A/N) ratios and lateral cranial radiographs before and after treatment. (**a**) Comparison of the A/N ratios of the two groups before surgery and at 6 and 12 months after surgery. (**b**) Lateral cranial radiographs were obtained before and six months after, as well as one year after surgery in patients with postoperative recurrence in the non- allergen specific immunotherapy (non-AIT) group. (**c**) Lateral cranial radiographs were obtained before and six months after, as well as one year after surgery in patients without postoperative recurrence in the subcutaneous immunotherapy (SCIT) group. **P<0.01.

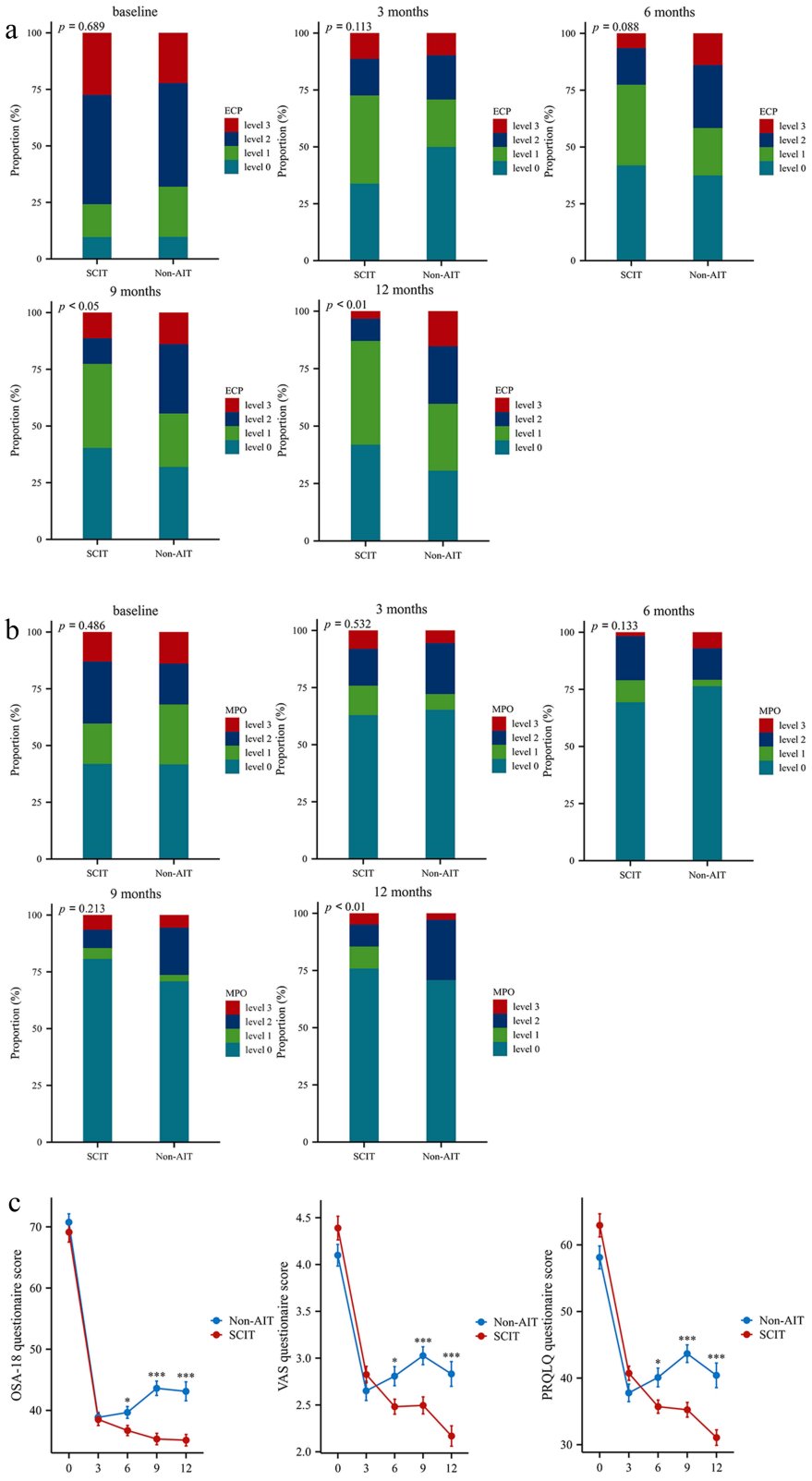

Figure 3 Eosinophil cationic protein (ECP) and myeloperoxidase (MPO) detection and questionnaire score curves for the subcutaneous immunotherapy (SCIT) and non-allergen specific immunotherapy (non-AIT) groups after one year of treatment. (**a**) ECP detection before and 3, 6, 9, and 12 months after surgery in the SCIT and non-AIT groups, respectively. (**b**) MPO detection before and 3, 6, 9, and 12 months after surgery in the SCIT and non-AIT groups, respectively. (**c**) Obstructive Sleep Apnoea Questionnaire (OSA-18), Visual Analogue Scale (VAS), and Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) score curves for the SCIT and non-AIT groups after one year of treatment. *P<0.05, ***P<0.001.

than those in the non-AIT group. The VAS and PRQLQ scores at 6, 9, and 12 months after surgery were significantly lower than those in the non-AIT group (Figure 3c).

Comparison of the Recurrence and Non-Recurrence Groups

There were no significant differences between the recurrence and non-recurrence groups before treatment, except for specific IgE concentration and tonsil volume (Table 3). The concentration of specific IgE in the non-recurrence group was lower than that in the recurrence group. The tonsil volume was higher in the non-recurrence group, and the proportion of children with normal tonsil volume in the non-recurrence group was significantly lower than that in the recurrence group ($P < 0.05$).

ECP detection before and after treatment was more severe in the recurrence group than in the non-recurrence group (Figure 4a). The VAS scores of the recurrence group before surgery and at 6, 9, and 12 months after surgery were higher than those of the non-recurrence group (Figure 4b). The PRQLQ score of the recurrence group was not significantly different from that of the non-recurrence group before surgery but was higher than that of the non-recurrence group after surgery.

Discussion

This study is a prospective clinical trial to explore whether SCIT could prevent postoperative recurrence in patients with AR and AH. We found that AIT for one year can effectively reduce the risk of postoperative recurrence in children with AH and AR and improve postoperative rhinitis symptoms and sleep disorders. Significant differences were observed as early as 6 or 9 months after treatment.

The primary reasons for postoperative AH recurrence include persistent inflammation mediated by allergic disease, residual adenoid tissue post-surgery, and local infection factors such as CRS. Conventional adenoidectomy and indirect nasopharyngoscopic adenoid curettage tend to retain adenoid tissue, leading to postoperative AH recurrence.[22] The extensive utilization of radiofrequency ablation with low-temperature plasma in clinical practice has progressively reduced the need for adenoidectomy and indirect nasopharyngoscopic adenoidectomy. Low-temperature plasma radiofrequency ablation has the advantages of less residual tissue and a lower postoperative recurrence rate. This effectively solves the problem of postoperative adenoid residue.[23] In children with sinusitis, inflammatory secretions from the nasal cavity and sinuses can reach the residual adenoids through normal anatomical channels. This leaves residual tissues in a state of chronic inflammation and immune activation, eventually leading to adenoid recurrence after surgery.[24] Adenoidectomy is an effective first-line surgical option for the treatment of chronic sinusitis in children under 12 years of age. Sinusitis in most children improves after adenoidectomy, especially in younger children.[25] However, allergic inflammation in patients with AR cannot improve after adenoidectomy, making it the main risk factor for

Table 3 Comparison of General Data in Recurrence and Non-Recurrence Groups Before Treatment

	Non-Recurrence Group	Recurrence Group	P
Age, years	6.580[5.670,7.670]	5.830[5.420,8.250]	0.463
Sex: Male	119(77)	15(11)	
Adenoid size	0.740[0.680,0.780]	0.740[0.700,0.780]	0.748
Tonsil volume			
I	19	6	0.042
II	68	7	
III	32	2	
Level of specific IgE to Derp and/ or Derf			
1–2	16	0	0.000
3–4	51	1	
5–6	52	14	
Total IgE	264.000[149.000, 660.000]	589.000[319.000, 1482.000]	0.002
Asthma (%)	21/119(17.647%)	4/15(26.667%)	0.622
CRS (%)	57/119(47.789%)	11/15(73.333%)	0.063

Abbreviations: IgE, Immunoglobulin E; Derp, Dermatophagoides pteronyssinus; Derf, Dermatophagoides farinae; CRS, chronic sinusitis.

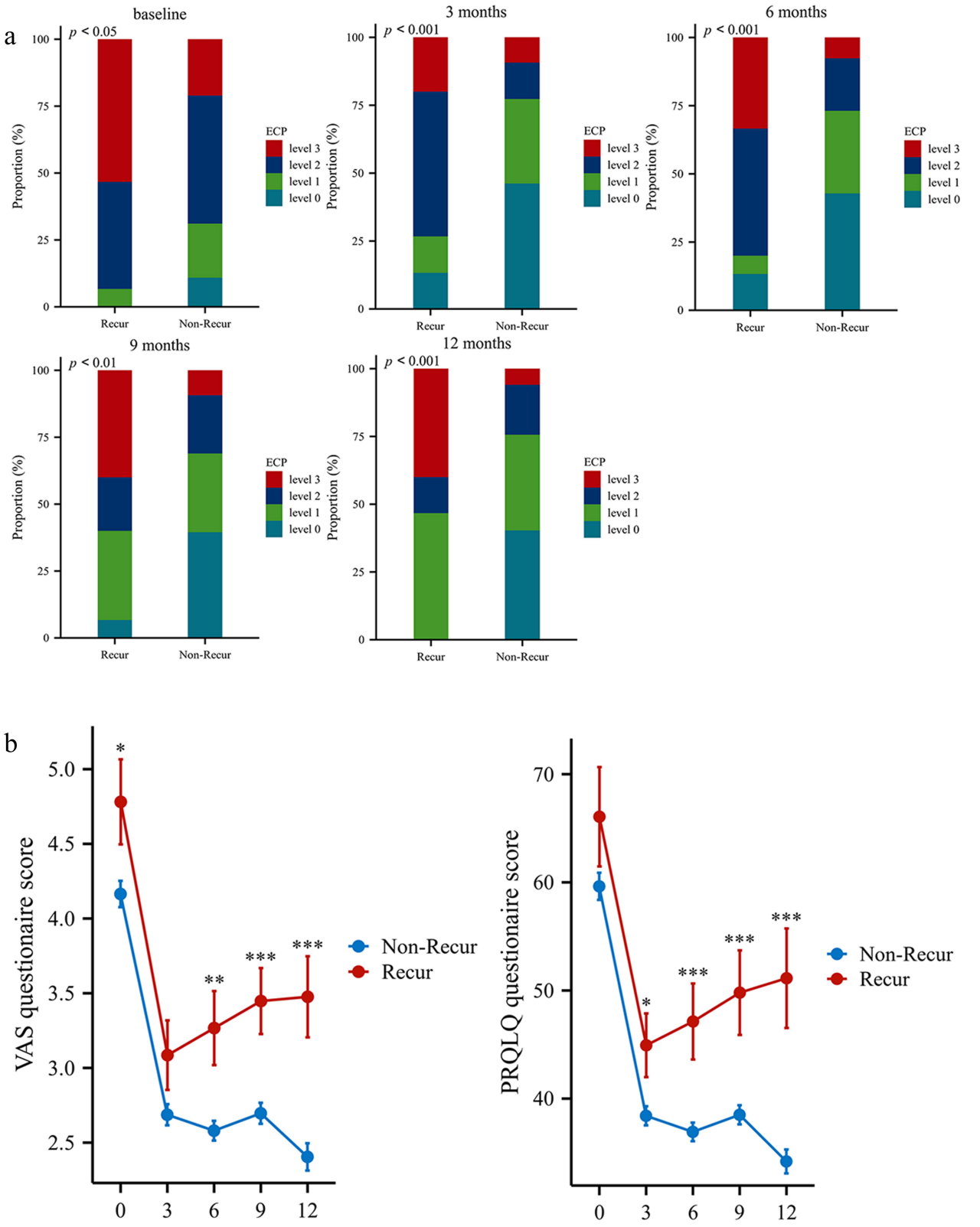

Figure 4 Eosinophil cationic protein (ECP) detection and questionnaire score curves in the recurrence and non-recurrence groups within one year of treatment. (**a**) ECP detection in the recurrence and non-recurrence groups before surgery and 3, 6, 9, and 12 months after surgery. (**b**) Visual Analogue Scale (VAS) and Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) score curves for the recurrence and non-recurrence groups within one year of treatment. Recur, recurrence; Non-Recur, non-recurrence; *P<0.05, **P<0.01, ***P<0.001.

postoperative recurrence after adenoidectomy.[26] Rhinitis symptoms persist in patients with AR, and sleep disorders are not effectively resolved even after adenoidectomy.[27–29] In this study, the recurrence rate of AH in the non-AIT group was as high as 16.67%, indicating that adenoidectomy cannot completely eradicate AH in patients with AR and that preventing AH recurrence in patients with AR after surgery is indispensable. The postoperative recurrence rate of 4.84% for the SCIT group was lower than that for the non-AIT group at 12 months postoperatively, suggesting that AIT is effective for preventing postoperative recurrence in patients with AR. The OSA-18, a validated survey assessing sleep-disordered breathing symptom burden, comprises 18 items, divided into 5 categories: sleep disturbance, physical suffering, emotional distress, daytime problems, and caregiver concerns, with higher scores indicating more severe symptoms and a greater association with quality of life.[30] The OSA-18 score was also significantly lower for the SCIT than for the non-AIT group, suggesting that AIT is effective in improving postoperative sleep disorders and maximizing the efficacy of adenoidectomy in AR patients.

PRQLQ and VAS are the most commonly used measures to evaluate efficacy in clinical trials and practice.[18,31] PRQLQ includes a quality of life assessment of nose symptoms, eye symptoms, practical problems, other symptoms, and activities. VAS score was a subjective evaluation of the severity of nasal symptoms in AR patients. ECP is considered a marker of eosinophils and can be used to monitor AR severity and therapeutic efficacy.[32,33] Test strips for ECP have been shown to reflect local ECP concentrations and AR severity in nasal secretions.[21] The VAS and PRQLQ scores and ECP detection in the nasal secretions of the SCIT group were also significantly lower than those of the non-AIT group one year after surgery, suggesting that SCIT treatment can effectively relieve AR. MPO is a biomarker of infectious rhinitis,[34,35] and MPO test strips sensitively reflect MPO concentrations and neutrophil counts in nasal secretions. The MPO levels of the two groups were different one year after surgery. This indicates that SCIT can reduce the incidence of sinusitis by reducing AH recurrence.

There were no significant differences between the various indicators in the two groups at the 3-month follow-up. At the 6-month follow-up, the A/N ratio and rhinitis-related questionnaire scores of the SCIT group were lower than those of the non-AIT group, although there was no significant difference between the recurrence rates of the two groups. The OSA-18 score of the SCIT group was also lower than that of the control group at the 9-month follow-up. This indicates that SCIT treatment can control rhinitis, relieve adenoid tissue hyperplasia after 6 months of treatment, and improve the sleep status of patients after 9 months of treatment.

This study revealed that SCIT therapy can effectively prevent postoperative recurrence in patients with AH. However, some patients hesitate to undergo SCIT in clinical practice due to economic and geographical constraints. Therefore, we need to screen patients with a high risk of recurrence, recommend more targeted treatments, and create awareness regarding AIT for high-risk patients. We compared the preoperative allergens, ECP test results, VAS scores, and PRQLQ scores between the recurrence and non-recurrence groups. Allergen allergy grade, ECP, and VAS scores were higher in the recurrence group than in the non-recurrence group, suggesting that patients with severe AR have a higher risk of recurrence after surgery. In addition, the ECP, VAS, and PRQLQ scores of the non-recurrence group were lower than those of the recurrence group, indicating that patients whose AR symptoms are not effectively controlled are more likely to experience AH recurrence. Therefore, AIT and regular postoperative follow-up are recommended for patients with severe AR, and timely AIT is recommended for patients with poorly controlled rhinitis to prevent postoperative recurrence. The pathogenesis of AH is unclear but is believed to be caused by repeated stimulation by allergens and various pathogens. Previous studies have suggested that tonsil hypertrophy is mainly related to infectious factors.[36] The tonsil volume in recurrence group was smaller than that in non-recurrence group, and the proportion of normal tonsil volume in recurrence group was also higher than that in non-recurrence group. It is reasonable to speculate that AH in patients without tonsil hypertrophy in recurrence group may be mainly due to allergic factors. This phenomenon indicates that AH patients associated with AR and normal tonsil volume should be vigilant about postoperative recurrence, and also suggests that AH induced by allergic factors may be more prone to postoperative recurrence.

In summary, these innovative findings provide a novel therapeutic strategy for preventing postoperative recurrence in AH patients with AR, which has significant theoretical and practical innovation. AIT combined with adenoidectomy effectively solves the problem of high recurrence rate and low satisfaction after traditional adenoidectomy in AH patients with AR, and also advances the current knowledge on preventing postoperative recurrence in these patients.

The strengths of this study include the prospective trial design, standardised measurements that included both subjective and objective indicators, blinding of key research personnel, and follow-ups conducted every 3 months for 12 months. However, this study also has some limitations. First, the patients were assessed using lateral cranial radiographs and sleep questionnaires, but

polysomnographic evaluation was not performed. Second, the medication score was not assessed, and it was not possible to assess differences in medication use between the two groups. Since polysomnographic and medication score are important for evaluating sleep disorders and medication use, these two tests should be performed in future studies.

Conclusion

In summary, AIT can not only effectively mitigate the risk of postoperative recurrence in children with AH and AR, but also improves the quality of life of patients by alleviating rhinitis symptoms and sleep disorders. This could serve as a promising sequential therapy for children with AH and AR undergoing surgery. It is recommended that AIT should be considered a preferred treatment option for children at high risk of recurrence, especially for those whose AR symptoms are not effectively controlled.

Abbreviations

AH, adenoid hypertrophy; AR, allergic rhinitis; AIT, Allergen specific immunotherapy; Derp, Dermatophagoides pteronyssinus; Derf, Dermatophagoides farinae; OSA-18, Obstructive Sleep Apnoea Questionnaire; PRQLQ, Paediatric Rhinoconjunctivitis Quality of Life Questionnaire; VAS, Visual Analogue Scale; ECP, eosinophil cationic protein; MPO, myeloperoxidase; A/N, adenoidal/nasopharyngeal; SCIT, subcutaneous immunotherapy; non-AIT, non-allergen specific immunotherapy.

Data Sharing Statement

The data underlying this article will be shared upon reasonable request to the corresponding author.

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Disclosure

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