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ORIGINAL ARTICLE

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Effectiveness and safety of immunotherapy with a mixture of polymerized allergen extracts of *Alternaria alternata* and *olea europaea* in children

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Abstract
Background: In southern Europe, allergy to *Alternaria alternata* (*A. alternata*) and *Olea europaea* (*O. europaea*) pollen are prevalent, significantly contributing to allergic conditions like asthma and rhinitis. This study investigates the effectiveness and safety of immunotherapy in pediatric patients utilizing a glutaraldehyde-polymerized allergen extract mixture of *A. alternata* and *O. europaea*.
Methods: This real-world, retrospective, observational study included pediatric patients diagnosed with rhinitis with or without asthma, co-sensitized to *A. alternata* and *O. europaea*. Patients received immunotherapy with a mixture of individually polymerized allergen extracts of *A. alternata* and *O. europaea*, each at a concentration of 10,000 TU/mL. Effectiveness was assessed by comparing rhinitis and asthma severity and medication requirements before and after at least 6 months of treatment. Safety was evaluated by documenting local and systemic adverse reactions.
Results: A total of 49 patients were included, with a median treatment duration of 9 months. Prior to treatment, 84% (41/49) of patients had moderate-severe rhinitis, which significantly decreased to 49% (24/49) posttreatment (p=0.001). Asthma severity also improved considerably, with the proportion of patients experiencing intermittent-mild asthma rising from 8% pretreatment to 61% posttreatment. The use of medication for both rhinitis and asthma also declined. Out of 424 injections, only two local reactions were reported (0.47%), with no systemic reactions.
Conclusion: Immunotherapy using a mixture of glutaraldehyde-polymerized *A. alternata* and *O. europaea* extract is both safe and effective in reducing the severity of rhinitis and asthma in children. This treatment exhibits a high safety profile, with a very low incidence of adverse reactions, making it a promising therapeutic option for pediatric patients with coexisting sensitivities to these common allergens.

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Key Message

Allergic respiratory diseases, particularly those triggered by *Alternaria alternata (A. alternata*) and *Olea europaea* (*O. europaea*), represent a significant health burden in pediatric population in Southern Spain. While allergen-specific immunotherapy (AIT) is a cornerstone of treatment, data on the use of polymerized extracts containing both allergens in children remain limited. A key innovation of this study lies in addressing this gap by evaluating the effectiveness and safety of a novel immunotherapy approach by using a mixture of polymerized *A. alternata* and *O. europaea* allergen extracts in a group of pediatric patients. The polymerization ensures the stability of the allergen extracts and, critically, overcomes the challenge of mixing these two components. Native *A. alternata* extracts possess significant enzymatic and proteolytic activity that would degrade native *O. europaea* extracts, making a stable combined native formulation unfeasible. This is a key technical advantage that offers a robust and effective solution for co-sensitized patients.

Our findings demonstrate a favorable safety profile with good tolerability. We believe that these results contribute valuable insights into the potential of this combined immunotherapy approach for children suffering from allergies to *A. alternata* and *O. europaea*, offering a promising therapeutic path.

Introduction

Alternaria alternata (*A. alternata*) is the most common allergenic mold,[1] particularly associated with severe asthma, including emergency visits, hospitalizations, and deaths from asthma.[2] Sensitization is higher in children,[3-5] showing a decreasing trend with age,[6] which could reflect the acquisition of tolerance naturally or after immunotherapy. *A. alternata* acts as both an indoor and outdoor allergen, especially in agricultural areas.[7] Depending on geography, 3–10% of the general population, 12–42% of atopic individuals, and over 66% of severe asthmatics are mold-sensitized, being more prevalent in hot, dry inland regions.[8,9] Notably, most patients are sensitized to other aeroallergens,[4,8] so *A. alternata* is also proposed to induce co-sensitization to them.[10]

Olea europaea (*O. europaea*) (olive) pollen is, after grass, the second most significant cause of pollinosis in southern Spain, being the main cause of respiratory allergy in some Andalusian regions, with high sensitization rates, up to 80% in seasonal asthma/rhinoconjunctivitis patients, reaching 84% in areas with high exposure.[11,12]

Coexisting sensitization to *A. alternata* and *O. europaea* is common in southern Spain, necessitating treatment for both allergies. Historically, mixing fungal extracts with other allergens in immunotherapy was not recommended[13] because of mold proteases degrading pollens. The European Medicines Agency (EMA), in 2008, recommended avoiding mixtures of allergen native extracts from nonhomologous groups and extracts with high enzymatic activity.[14]

However, glutaraldehyde polymerization significantly reduces this enzymatic activity, allowing for stable mixtures.[15,16] For polyallergic patients, combined polymerized extracts at optimal concentrations are an option, avoiding the dilution effect by doubling the concentration of each extract before mixing. This ensures that each allergen's concentration maintained in the final product is the same as it would be if each allergen were administered separately. The safety of mixtures containing polymerized allergen extracts of *A. alternata* with other polymerized allergen extracts without dilution has been reported in an observational real-world study.[17]

This study addresses the need for effective joint immunotherapy for *A. alternata* and olive pollen allergies in children, considering previous uncertainties about mixture stability and limited data on effectiveness and safety. This real-life retrospective study aims to analyze the effectiveness and safety of a combined polymerized *Alternaria* plus *Olea* allergen extract in pediatric patients.

Materials and Methods

This is a real-world, retrospective study, approved by the Ethics Committee of Andalucia, CEIM/CEI of Granada, Spain. Data from the patients' medical records, related to the severity of RC and asthma before starting treatment with immunotherapy and at the first review (more than 6 months from the initiation of treatment) were collected by the investigators.

Methods

Patient population

After signature of parents' inform consent, patient data were collected from medical records of pediatric subjects diagnosed with asthma and rhinitis, where both *A. alternata* and *O. europaea* sensitizations were clinically relevant.

Allergen Immunotherapy (AIT)

Subjects were treated with a mixture of two individually glutaraldehyde-polymerized extracts (*A. alternata* and *O. europaea*), adsorbed onto aluminum hydroxide (Clustoid Max® Inmunotek SL, Alcalá de Henares. Spain). Each polymerized allergen extract in the mixture was at a concentration of 10,000 TU/mL, containing all relevant allergens.

Two administration schedules were employed: a short regimen (0.2 mL on day 1; 0.5 mL after 1 week, then monthly 0.5 mL) and a rush schedule (0.2 mL plus 0.3 mL in the contralateral arm 30 minutes later, followed by monthly 0.5 mL).

Effectiveness

Effectiveness was evaluated by comparing the severity of rhinitis and asthma before and after at least 6 months of treatment. Rhinitis was classified using ARIA guidelines:[18] (1) mild intermittent; (2) moderate intermittent; (3) severe intermittent; (4) mild persistent; (5) moderate persistent; and (6) severe persistent, and asthma severity followed GEMA 5.4,[19] based on medication needed to maintain control and prevent exacerbations: (1) Intermittent (step 1 of treatment); (2) mild persistent (step 2); (3) moderate persistent (Steps 3–4); and (4) severe persistent (Steps 5–6).

The medication for rhinitis was scored as described in the EAACI position paper[20] with slight modifications: occasional antihistamines (H1A)-1 point-; regular H1A-2 points-; and intranasal glucocorticosteroids (INGCS) with/without H1A-3 points-. In the case of asthma, the medication was scored as described in GEMA 5.4 report for the asthma treatment steps for children.[21]

Safety

Safety was assessed by recording immediate (<30 minute) and delayed (>30 minute) adverse reactions, classified as local (wheal/redness diameter) or systemic.[19] Systemic reactions were graded per EAACI Position Paper (Grade I: Mild, Grade II: Moderate, Grade III: Severe, and Grade IV: Anaphylactic shock).

Statistics

Statistical analyses used Excel (Microsoft; Richmond, VA, USA) with XLSTAT AddIn (Addinsoft; New York, USA) and GraphPad Prism 9 (v 9.5.1). Shapiro–Wilk test confirmed nonnormal data distribution. Descriptive statistics used median with IQR or frequency (%). Fisher's exact test compared rhinitis and asthma control grading scores, with Phi Coefficient for effect size. All subjects contributed data to both effectiveness and safety analyses.

Results

All 49 enrolled patients had been diagnosed with respiratory allergy to both *A. alternata* and *O. europaea*, confirmed by specific IgE and/or skin prick test (SPT) and presented with rhinitis with or without asthma. The median age at diagnosis was 9 years (IQR: 6–11), 67% were male, 24% had a personal history of atopic dermatitis, 9% had food allergy, and 63% were sensitized to other aeroallergens deemed not clinically relevant. Twelve patients had previously been treated with IT with nonpolymerized allergens (six with olive extract, one with a mixture of *Olea* and grass pollen, three with *A. alternata,* and two with other mixtures of *A. alternata-Olea)*. Forty-nine percent of the children had a family history of allergy. Table 1 shows the demographic and epidemiological data, including other nonrelevant clinical sensitizations.

Regarding olive tree pollen allergy, 47/49 subjects had positive skin tests to native allergen extracts. The two subjects who were not tested had positive specific IgE against this pollen. The median value of specific IgE to pollen extract was 29.8 kU/L (IQR 20–100). Table 2 shows the median values of total and specific IgE.

For *A. alternata*, 45/49 patients had a positive skin test. The four subjects who had not been tested by SPT had specific IgE to *A. alternata* and to Alt a1. The median of these values of IgE to *A. alternata* was 10 kU/L (IQR 4.6–31.1).

The median period of treatment to evaluate the clinical response was 9 months (IQR 6–12). Ten patients followed the short administration regimen, while the rest followed the rush schedule. Before starting treatment, 84% of the subjects were in the ARIA rhinitis Steps 3–5. After the AIT period, this percentage significantly dropped to 49% (p = 0.001). At baseline, 80% were availing the rhinitis treatment classified in medication Steps 2–3. After a median of 6 months of AIT, the percentage of patients dropped to 17% (Table 3 and Figures 1A and 1B).

Regarding asthma, 92% of patients were in severity grades 3–4 at baseline, decreasing to 39% after AIT. The percentage of patients using drugs included in asthma treatment Steps 3–5 at baseline was 96%, decreasing to 22%

Table 1 Demographic and epidemiological data of patients.

Gender	n (%)
Male	33 (67%)
Female	16 (33%)
Age (years)	Median (IQR)
	9.0 (6.0, 11.0)
Other allergic pathologies	n (%)
Atopic dermatitis	12 (24%)
Food allergy	9 (18%)
Other allergen sensitizations	n (%)
All	31 (63%)
Grass pollen	16 (33%)
English plantain pollen	10 (20%)
House dust mites	4 (8%)
Cat dander	12 (24%)
Dog dander	8 (16%)

Table 2 Values (kU/L) of total and specific IgE.

Total IgE	419.5 (105.1–1088.2)
Specific IgE	
O. europaea pollen	42.8 (20.4–100.0)
Ole e1	32.5 (4.8–83.5)
A. alternata	10.0 (4.6–40.0)
Alt a1	11.0 (7.3–20.7)

Table 3 Pre- and post-AIT classification and medication for rhinitis.

Grade rhinitis			Medication control rhinitis		
Steps	Pre	Post	Steps	Pre	Post
1-2	16%	51%	1	20%	83%
3-5	84%	49%	2-3	80%	17%
Fisher's exact p-value		<0.001	Fisher's exact p-value		<0.001
Effect size (Phi)		0.367	Effect size (Phi)		0.628
Interpretation effect size		Moderate	Interpretation effect size		Strong

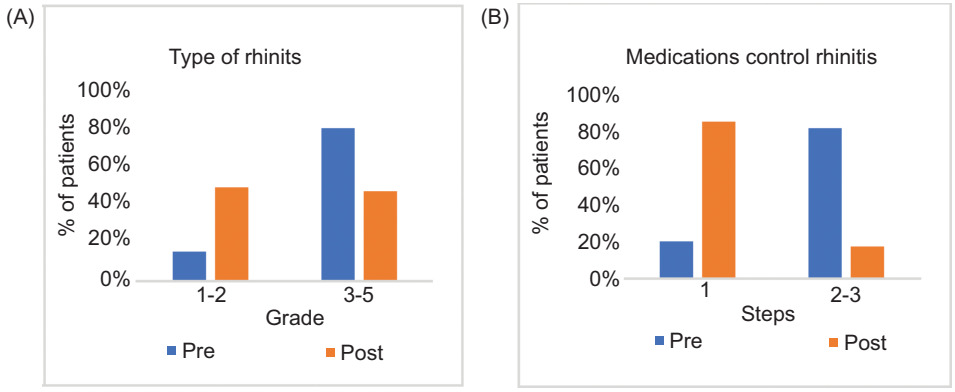

Figure 1 (A) pre- and post-AIT classification of rhinitis according to ARIA (1. Mild intermittent, 2. moderate intermittent, 3. severe intermittent, 4. mild persistent, and 5. moderate-severe persistent). (B) Pre- and post-AIT medication control rhinitis. Step (1) Occasional antihistamines. Step (2) Regular use of antihistamines. Step (3) Local nasal corticosteroids.

Table 4 Pre- and post-AIT classification and medication for asthma.

Grade asthma			Medication control asthma		
Steps	Pre	Post	Steps	Pre	Post
1-2	8%	61%	1-2	4%	78%
3-4	92%	39%	3-5	96%	22%
Fisher's exact p-value		<0.001	Fisher's exact p-value		<0.001
Effect size (Phi)		0.557	Effect size (Phi)		0.747
Interpretation effect size		Strong	Interpretation effect size		Very strong

after the evaluation period of AIT (Table 4 and Figures 2A and 2B).

A total of 424 injections were administered. Only two local reactions (0.47% of administrations) were reported from the start of AIT until the first follow-up visit. One reaction occurred 5 minutes post-administration and was managed with local cold application. The other was a delayed reaction, resolving with a single dose of oral antihistamine. The first reaction happened during the maintenance period, and the second during the build-up phase. Importantly, no systemic reactions were recorded.

Discussion

Allergic diseases, particularly those triggered by *A. alternata* and *O. europaea*, represent a significant health burden in pediatric populations, particularly in Southern Spain. While AIT is a cornerstone of treatment, data on the combined use of polymerized extracts of these specific allergens in children remain limited.

Our study addresses this gap by evaluating the effectiveness and safety of an immunotherapy approach using a modified (glutaraldehyde-polymerized) AIT combining A. *alternata* and *O.* europaea extracts, each at 10,000 TU/mL in a group of pediatric patients. After at least 6 months of AIT, children and adolescents demonstrated significant improvement, showing lower grades of clinical severity and reduced pharmacological treatment requirements for both rhinitis and asthma compared to pre-AIT. A key innovation of our study lies in the use of polymerized extracts for both *A. alternata* and *O. europaea*. This polymerization ensures the stability of the allergen extracts and, critically, overcomes the challenge of mixing these two components. Native *A. alternata* extracts possess significant enzymatic and proteolytic activity that would degrade native *O. europaea* extracts, making a stable combined native formulation unfeasible. This is a key technical advantage that offers a robust and effective solution for co-sensitized patients.

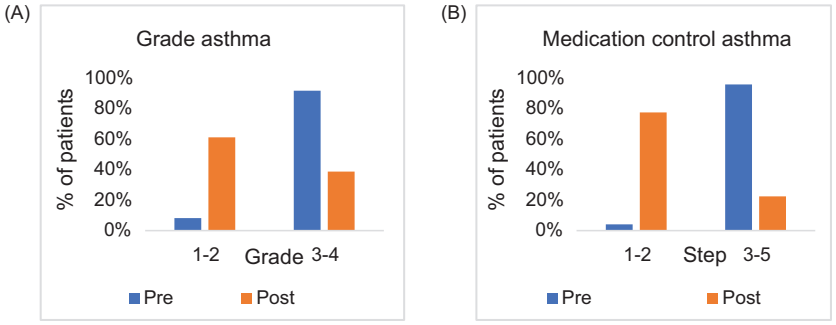

Figure 2 (A) Pre- and post-AIT grade asthma (according to GEMA 5.4). (B) Pre- and post-AIT asthma maintenance medication.

Fungal allergy is a well-known risk factor for severe and fatal asthma (3,8,20,21), with mold allergens often affecting the lower respiratory tract more than pollens. *A. alternata* is associated with greater bronchial inflammation and worse lung function,[22] and a higher risk of developing asthma attacks,[23] hospitalizations,[24] and death from asthma.[25] As with pollens, the concentration of specific allergens is better associated with respiratory allergy symptoms than the concentration of spores.[26] Given *A. alternata*´s association with severe asthma, early diagnosis and treatment are crucial to prevent such adverse outcomes. Allergen Immunotherapy is unique in its ability to modify allergic disease progression, prevent asthma development in rhinitis patients, and new sensitizations.[27] Therefore, particularly when allergen avoidance is impossible, initiating AIT early in childhood for clinically significant asthma and/or rhinitis is vital. In spite of fungi's importance because of their link with severe asthma, there are few efficacy studies on specific immunotherapy with these allergens.[28] In spite of this fact, *A. alternata* immunotherapy has shown efficacy in various studies.[20,29–32]

To our knowledge, this is the first real-life, proof-of-concept study assessing the effectiveness and safety of subcutaneous immunotherapy with the Clustoid® Max *A. alternata* plus *O. europaea* mixture. It demonstrates that this treatment is safe and significantly improves rhinitis and asthma severity and control. Studies on fungal immunotherapy are scarce,[33,34] and even fewer studies examine a mixture of molds with another allergen.

The proteolytic activity of molds traditionally discouraged from mixing them in native extracts with other allergens because of concerns about mixture stability. Polymerized allergoids substantially reduce this proteolytic activity, ensuring stability.[15,16] Importantly, when mixing different modified extracts, the optimal concentration of each component must be guaranteed. This study confirms that this combined treatment is highly effective for both asthma and rhinitis in children allergic to these two aeroallergens, reducing the number of injections (compared to the use of two native AIT products). Significant improvements in severity and control for both conditions were observed after a median of 9 months of treatment. This highlights the treatment's potential to prevent progression to severe or poorly controlled asthma in children with *A. alternata* and *O. europaea* respiratory allergy. The effectiveness also suggests optimal allergen concentrations, indicating that even in a mixture of nonhomologous extracts, therapeutic doses of each component are not reduced and are adequate to reach clinical improvement.

The safety profile of this combined treatment, especially given the presence of *A. alternata*, could be a concern. However, its safety profile is excellent, with a very low rate (0.47%) of local reactions and no systemic reactions recorded. These safety results align with those from a large real-world observational study (738 patients, including 435 children) using polymerized *A. alternata* extract alone or in combination.[17] This safety profile is superior to those reported in older studies with native *A. alternata* extracts in children. A Spanish study with native *A. alternata* extract reported a 1.95% reaction rate,[35] mostly systemic with respiratory involvement, noting higher risk in children and asthmatics, with 7 of 38 children discontinuing because of Grade III systemic reactions. A 2005 study by the Spanish pediatric allergology society showed a lower, but still higher (0.95%), incidence of adverse reactions with native *A. alternata* extract.[31]

Limitations of this real-world retrospective observational study include the small sample size and lack of randomization. In spite of these, a significant reduction in severity and medication need for rhinitis and asthma was observed. The strengths and novelty of this work lie in the characteristics of the studied population (polysensitized children) and the according of personalized immunotherapy composition.

In conclusion, this real-world study unequivocally demonstrates that immunotherapy using a mixture of polymerized *A. alternata* and *O. europaea* extracts is a key technical advantage that assures safety and significantly improves the severity and control of rhinitis and asthma in co-sensitized children.

Author's Contribution

All authors contributed equally to this article.

Conflict of Interest

JTB has received honoraria for participation in advisory boards and lectureship from Astra Zeneca, Leti, GSK, and Diater. AMCB has received honoraria for participation in advisory boards and lectureship from Leti and Diater. LPML and RCM have no conflict of interest to declare. The authors declare that they have no relationship with Inmunotek and have not received any fees from this company.

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References

1. Arbes Jr. SJ, Gergen PJ, Elliott L, Zeldin DC. Prevalences of positive skin test responses to 10 common allergens in the US population: results from the Third National Health and Nutrition Examination Survey. J. Allergy Clin. Immunol. 2005 Aug;116(2):377–83. https://doi.org/10.1016/j.jaci.2005.05.017
2. Barnes C. Fungi and atopy. Clin. Rev. Allergy Immunol. 2019 Dec 19;57(3):439–48. https://doi.org/10.1007/s12016-019-08750-z
3. Mahmoud Z., Catherine N., Bénédicte L., Renata L., Jean B., Françoise N., et al. Sensitisation to airborne moulds and severity of asthma: cross sectional study from European community respiratory health survey. BMJ. 2002 Aug 24;325(7361):411-7. https://doi.org/10.1136/bmj.325.7361.411
4. López Couso VP, Tortajada-Girbés M, Rodriguez Gil D, Martínez Quesada J, Palacios Pelaez R. Fungi sensitization in Spain: importance of the Alternaria alternata species and its major allergen Alt a 1 in the allergenicity. J. Fungi. 2021 Aug 3;7(8):631. https://doi.org/10.3390/jof7080631
5. Gabriel MF, Postigo I, Tomaz CT, Martínez J. Alternaria alternata allergens: markers of exposure, phylogeny and risk of fungi-induced respiratory allergy. Environ. Int. 2016 Apr;89–90:71–80. https://doi.org/10.1016/j.envint.2016.01.003

6. Fukutomi Y, Taniguchi M. Sensitization to fungal allergens: resolved and unresolved issues. Allergol. Int. 2015 Oct;64(4):321–31. https://doi.org/10.1016/j.alit.2015.05.007
7. Torres-Borrego J, Sánchez-Solís M. Dissecting airborne allergens. J. Clin. Med. 2023 Sep 8;12(18):5856. https://doi.org/10.3390/jcm12185856
8. Rick E, Woolnough K, Pashley C, Wardlaw A. Allergic fungal airway disease. J. Investig. Allergol. Clin. Immunol. 2016 Dec 19;26(6):344–54. https://doi.org/10.18176/jiaci.0122
9. Salo P, Arbes jr. S, Sever M, Jaramillo R, Cohn R, London S, et al. Exposure to Alternaria alternata in US homes is associated with asthma symptoms. J. Allergy Clin. Immunol. 2006 Oct;118(4):892–8. https://doi.org/10.1016/j.jaci.2006.07.037
10. Hernandez-Ramirez G, Barber D, Tome-Amat J, Garrido-Arandia M, Diaz-Perales A. Alternaria as an Inducer of allergic sensitization. J. Fungi. 2021 Oct 7;7(10):838. https://doi.org/10.3390/jof7100838
11. Fernández-Rodríguez S, Maya-Manzano JM, Colín AM, Pecero-Casimiro R, Buters J, Oteros J. Understanding hourly patterns of Olea pollen concentrations as tool for the environmental impact assessment. Sci. Total Environ. 2020 Sep;736:139363. https://doi.org/10.1016/j.scitotenv.2020.139363
12. Plaza MP, Alcázar P, Galán C. Correlation between airborne Olea europaea pollen concentrations and levels of the major allergen Ole e 1 in Córdoba, Spain, 2012-2014. Int. J. Biometeorol. 2016 Dec 19;60(12):1841-7. https://doi.org/10.1007/s00484-016-1171-6
13. Esch RE. Allergen immunotherapy: what can and cannot be mixed? J. Allergy Clin. Immunol. 2008 Sep;122(3):659–60. https://doi.org/10.1016/j.jaci.2008.07.018
14. European Medicines Agency. Committee for Medicinal Products for Human Use (CHMP). Note for Guidance on Allergen Products: Production and Quality Issues. https://www.ema.europa.eu/en/allergen-products-production-quality-issues-scientific-guideline. 2009.
15. Abel-Fernández E, Fernández-Caldas E, Iborra S. Characterisation of Alternaria alternata allergoids: evaluation of the stability of grass pollen allergen extracts mixed with Alternaria alternata allergoids. J. Fungi. 2025 Feb 25;11(3):181. https://doi.org/10.3390/jof11030181
16. Tudela JI, Soria I, Abel-Fernández E, Cantillo JF, Fernández-Caldas E, Subiza JL, et al. Polymerised mite allergoids with glutaraldehyde reduce proteolytic activity and enhance the stability of allergen mixtures: a proof of concept with grass mixtures. Front. Allergy. 2025 Feb 25;6. https://doi.org/10.3389/falgy.2025.1557650
17. Caballero R, Javaloyes G, Romero M, Ángel Rojas M, Del Pozo S, Lara B, et al. Safety of immunotherapy with Alternaria alternata glutaraldehyde-polymerized allergen extract in adults and children. Allergol. Immunopathol. (Madr). 2024 Nov 1;52(6):9–14. https://doi.org/10.15586/aei.v52i6.1166
18. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic rhinitis and its Impact on Asthma (ARIA) 2008*. Allergy. 2008 Apr 7;63(s86):8–160.
19. Alvarez-Cuesta E, Bousquet J, Canonica GW, Durham SR, Malling H -J., Valovirta E. Standards for practical allergen-specific immunotherapy. Allergy. 2006 Oct 24;61(s82):1–3. https://doi.org/10.1111/j.1398-9995.2006.01219_1.x
20. Bozek A, Pyrkosz K. Immunotherapy of mold allergy: a review. Hum. Vaccin. Immunother. 2017 Oct 3;13(10):2397-401. https://doi.org/10.1080/21645515.2017.1314404
21. Salo PM, Arbes SJ, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. J. Allergy Clin. Immunol. 2014 Aug;134(2):350–9. https://doi.org/10.1016/j.jaci.2013.12.1071
22. Tham R, Erbas B, Dharmage SC, Tang MLK, Aldakheel F, Lodge CJ, et al. Outdoor fungal spores and acute respiratory effects in vulnerable individuals. Environ. Res. 2019 Nov;178:108675. https://doi.org/10.1016/j.envres.2019.108675
23. Pongracic JA, O'Connor GT, Muilenberg ML, Vaughn B, Gold DR, Kattan M, et al. Differential effects of outdoor versus indoor fungal spores on asthma morbidity in inner-city children. J. Allergy Clin. Immunol. 2010 Mar;125(3):593–9. https://doi.org/10.1016/j.jaci.2009.10.036
24. Hughes KM, Price D, Torriero AAJ, Symonds MRE, Suphioglu C. Impact of fungal spores on asthma prevalence and hospitalization. Int. J. Mol. Sci. 2022 Apr 13;23(8):4313. https://doi.org/10.3390/ijms23084313
25. Targonski P, Persy V, Ramekrishnan V. Effect of environmental molds on risk of death from asthma during the pollen season. J. Allergy Clin. Immunol. 1995 May;95(5):955–61. https://doi.org/10.1016/S0091-6749(95)70095-1
26. Feo Brito F, Mur Gimeno P, Carnés J, Fernández-Caldas E, Lara P, Alonso AM, et al. Grass pollen, aeroallergens, and clinical symptoms in Ciudad Real, Spain. J. Investig. Allergol. Clin. Immunol. 2010;20(4):295–302.
27. Bousquet J, Lockey R, Malling H. Allergen immunotherapy: therapeutic vaccines for allergic diseases A WHO position paper. J. Allergy Clin. Immunol. 1998 Oct;102(4):558–62. https://doi.org/10.1016/S0091-6749(98)70271-4
28. Di Bona D, Frisenda F, Albanesi M, Di Lorenzo G, Caiaffa MF, Macchia L. Efficacy and safety of allergen immunotherapy in patients with allergy to molds: a systematic review. Clin. Exp. Allergy. 2018 Nov 4;48(11):1391–401. https://doi.org/10.1111/cea.13242
29. Zapatero L, Martínez-Cañavate A, Lucas JM, Guallar I, Torres J, Guardia P, et al. Clinical evolution of patients with respiratory allergic disease due to sensitisation to Alternaria alternata being treated with subcutaneous immunotherapy. Allergol. Immunopathol. (Madr). 2011 Mar;39(2):79–84. https://doi.org/10.1016/j.aller.2010.03.011
30. Kiliç M, Altintaş DU, Yilmaz M, Bingöl-Karakoç G, Burgut R, Güneşer-Kendirli S. Evaluation of efficacy of immunotherapy in children with asthma monosensitized to Alternaria. Turk. J. Pediatr. 2011;53(3):285–94.
31. Martínez-Cañavate A, Eseverri JL, Ródenas R, Tabar AI, Garde J, Torres J, et al. Evaluation of paediatric tolerance to an extract of Alternaria alternata under two treatment regimes. A multicentre study. Allergol. Immunopathol. (Madr). 2005 Jan;33(3):138–41. https://doi.org/10.1157/13075696
32. Tabar AI, Lizaso MT, García BE, Gómez B, Echechipía S, Aldunate MT, et al. Double-blind, placebo-controlled study of Alternaria alternata immunotherapy: clinical efficacy and safety. Pediatr. Allergy Immunol. 2008 Feb 10;19(1):67-75. https://doi.org/10.1111/j.1399-3038.2007.00589.x
33. Brehler R, Rabe U. Allergen-specific immunotherapy for mold allergies. Allergo. J. Int. 2024 Apr 23;33(4):101–5. https://doi.org/10.1007/s40629-024-00293-w
34. Nelson HS. Allergy immunotherapy for allergic fungal respiratory diseases. Allergy Asthma Proc. 2023 Nov 1;44(6):395-401. https://doi.org/10.2500/aap.2023.44.230058
35. Tabar AI, Lizaso MT, García BE, Echechipía S, Olaguibel JM, Rodríguez A. Tolerance of immunotherapy with a standardized extract of Alternaria tenuis in patients with rhinitis and bronchial asthma. J. Investig. Allergol. Clin. Immunol. 2000;10(6):327–33.