Sublingual immunotherapy for pollen allergic rhinitis: a systematic review and meta-analysis

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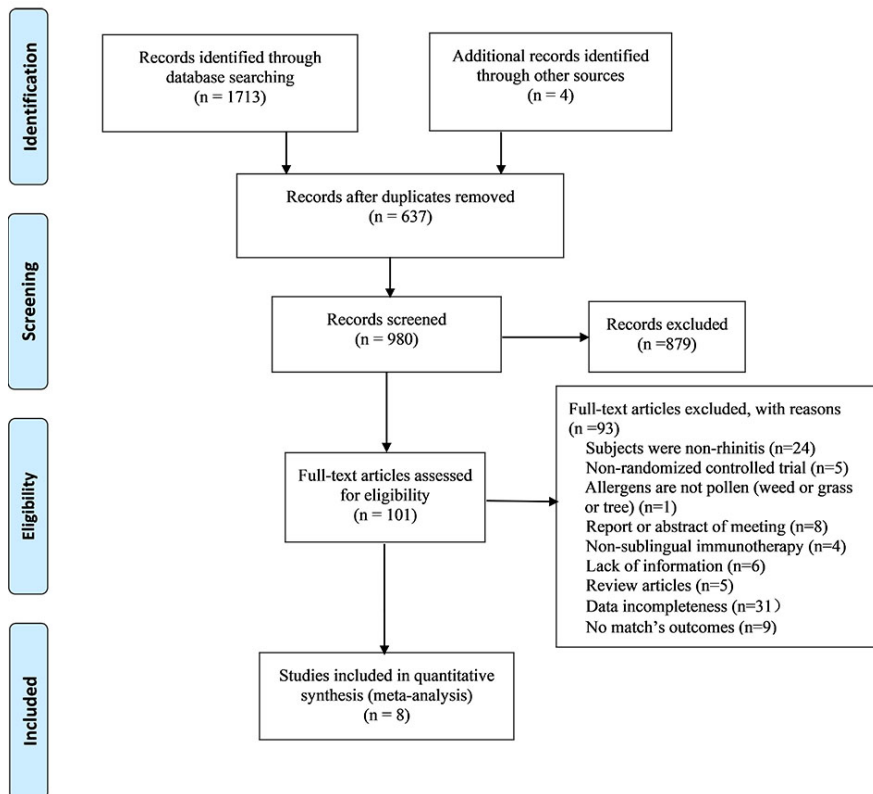
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Abstract

Intro Allergic rhinitis(AR) is a common condition which can significantly impair quality of life. This study aimed to illustrate the efficacy and safety of sublingual immunotherapy (SLIT) on pollen AR patients. Methods Four electronic databases (PubMed, EMBASE, Cochrane Library, and Web of Science) were searched from their inception until September 2019. Two reviewers (FLF and CLJ) independently extracted the data. The Cochrane's Risk of Bias tool was used to assess the quality of included studies. The outcomes of study were calculated by MD or SMD with 95%CI. A meta-analysis was performed using RevMan 5.3 software. Results In this systematic review, a total of 8 articles were included, involving 785 participants. The quality of the included studies ranged from low to moderate. The results of the meta-analysis showed that compared with placebo, a significant reduction of nasal symptoms were observed on SLIT (MD = -0.84, 95% CI = -1.47 to -0.22, P < 0.05), IgE (SMD =0.46, 95% CI = 0.16 to 0.76, P < 0.05); No significant effect on medication scores (MD = -0.41, 95% CI = -0.89 to 0.07, P =0.10). No serious adverse events were reported, and symptoms of adverse events were reported more frequently in the gastrointestinal symptoms. Conclusion SLIT can effectively relieve rhinitis symptoms and decrease the level of specific-IgE for pollen allergic rhinitis patients and the safety was verified. But due to the low quality of studies, more high-quality randomized trials are needed to provide stronger evidence of the conclusion.

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Identification

Records identified through database searching
(n = 1713)

Additional records identified through other sources
(n = 4)

Records after duplicates removed
(n = 637)

Screening

Records screened
(n = 980)

Records excluded
(n =879)

Eligibility

Full-text articles assessed for eligibility
(n = 101)

Full-text articles excluded, with reasons
(n =93)
    Subjects were non-rhinitis (n=24)
    Non-randomized controlled trial (n=5)
    Allergens are not pollen (weed or grass or tree) (n=1)
    Report or abstract of meeting (n=8)
    Non-sublingual immunotherapy (n=4)
    Lack of information (n=6)
    Review articles (n=5)
    Data incompleteness (n=31）
    No match's outcomes (n=9)

Included

Studies included in quantitative synthesis (meta-analysis)
(n = 8)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
A. Pradalier 1999	+	?	+	?	+	+	?
Akefeh Ahmadiafshar 2012	+	?	+	+	−	+	?
Alvaro Moreno-Ancillo 2007	+	?	+	?	+	+	+
Andrzej Bozek 2014	+	+	+	+	+	+	+
C. André 2003	+	?	+	+	+	+	+
Guy W.Scadding 2017	+	?	+	+	+	+	+
Helen Smith MSc 2004	+	?	+	+	+	+	+
Joanna Jerzynska 2016	+	+	+	?	+	+	?

Study or Subgroup	SLIT Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 < 60 years old								
A. Pradalier 1999	0.47	0.474	62	0.535	0.618	61	22.4%	-0.07 [-0.26, 0.13]
Alvaro Moreno-Ancillo 2007	-0.33	0.467	52	-0.18	0.426	53	22.5%	-0.15 [-0.32, 0.02]
C. André 2003	0.505	0.453	26	0.645	0.612	48	22.1%	-0.14 [-0.39, 0.11]
Guy W.Scadding 2017	-2.42	1.78	36	-1.43	2.3	34	14.8%	-0.99 [-1.96, -0.02]
Subtotal (95% CI)			176			196	81.7%	-0.13 [-0.26, -0.01]
Heterogeneity: Tau² = 0.00; Chi² = 3.52, df = 3 (P = 0.32); I² = 15%								
Test for overall effect: Z = 2.05 (P = 0.04)								
1.3.2 ≥ 60 years old								
Andrzej Bozek 2014	-3.705	1.7	41	-0.347	1.2	37	18.3%	-3.36 [-4.01, -2.71]
Subtotal (95% CI)			41			37	18.3%	-3.36 [-4.01, -2.71]
Heterogeneity: Not applicable								
Test for overall effect: Z = 10.15 (P < 0.00001)								
Total (95% CI)			217			233	100.0%	-0.84 [-1.47, -0.22]
Heterogeneity: Tau² = 0.44; Chi² = 95.91, df = 4 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 2.64 (P = 0.008)								
Test for subgroup differences: Chi² = 91.48, df = 1 (P < 0.00001), I² = 98.9%								

Mean Difference IV, Random, 95% CI — Favours [SLIT] Favours [Placebo] (-4, -2, 0, 2, 4)

Study or Subgroup	SLIT Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
A. Pradalier 1999	0.47	0.474	62	0.535	0.618	61	22.4%	-0.07 [-0.26, 0.13]
Alvaro Moreno-Ancillo 2007	-0.33	0.467	52	-0.18	0.426	53	22.5%	-0.15 [-0.32, 0.02]
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Guy W.Scadding 2017	-2.42	1.78	36	-1.43	2.3	34	14.8%	-0.99 [-1.96, -0.02]
Total (95% CI)			217			233	100.0%	-0.84 [-1.47, -0.22]
Heterogeneity: Tau² = 0.44; Chi² = 95.91, df = 4 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 2.64 (P = 0.008)								

Mean Difference IV, Random, 95% CI — Favours [SLIT] Favours [Placebo] (-4, -2, 0, 2, 4)

Study or Subgroup	SLIT Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 < 60 years old								
A. Pradalier 1999	1.77	2.27	62	2.13	2.74	61	19.0%	-0.36 [-1.25, 0.53]
Alvaro Moreno-Ancillo 2007	-0.76	2.78	52	-1	2.17	53	17.3%	0.24 [-0.72, 1.20]
C. André 2003	2.41	3.09	55	4	4.24	55	9.9%	-1.59 [-2.98, -0.20]
Guy W.Scadding 2017	111.2	309.719	36	6.28	329.439	32	0.0%	104.92 [-47.61, 257.45]
Subtotal (95% CI)			205			201	46.2%	-0.46 [-1.46, 0.53]
Heterogeneity: Tau² = 0.48; Chi² = 6.37, df = 3 (P = 0.09); I² = 53%								
Test for overall effect: Z = 0.91 (P = 0.36)								
1.1.2 ≥ 60 years old								
Andrzej Bozek 2014	-0.448	0.123	41	-0.027	0.201	37	53.8%	-0.42 [-0.50, -0.35]
Subtotal (95% CI)			41			37	53.8%	-0.42 [-0.50, -0.35]
Heterogeneity: Not applicable								
Test for overall effect: Z = 11.01 (P < 0.00001)								
Total (95% CI)			246			238	100.0%	-0.41 [-0.89, 0.07]
Heterogeneity: Tau² = 0.11; Chi² = 6.42, df = 4 (P = 0.17); I² = 38%								
Test for overall effect: Z = 1.67 (P = 0.10)								
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.93), I² = 0%								

Mean Difference IV, Random, 95% CI — Favours [SLIT] Favours [Placebo] (-2, -1, 0, 1, 2)