



The Importance of Allergen Avoidance in High Risk Infants and Sensitized Patients: A Meta-analysis Study

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Purpose: At this time, there is uncertainty regarding whether allergen avoidance is the most appropriate strategy for managing or preventing allergies. The purpose of this study was to evaluate the effectiveness of allergen avoidance in the prevention of allergic symptoms in previously sensitized patients and newborns that have the potential to develop allergies.

Methods: We performed online searches of articles published from January 1980 to December 2012 in PubMed and The Cochrane Central Register of Controlled Trials, and selected articles involving randomized controlled trials (RCTs) and allergen avoidance. The parameters used to determine allergenic potential in newborns included the risk ratio (RR) of eczema, asthma, rhinitis, wheeze, and cough. The methods employed to evaluate previously sensitized patients were the standardized mean difference (SMD) of forced expiratory volume in 1 second (FEV1) and peak expiratory flow rate (PEFR). Data quality was assessed using the Jadad scale. **Results:** A total of 14 RCTs were identified. Meta-analysis demonstrated that allergen avoidance for newborns did not reduce the subsequent incidence of allergic diseases (eczema, $P=0.21$; rhinitis, $P=0.3$; cough, $P=0.1$) but significantly reduced the incidence of asthma and wheezing in high-risk infants (asthma, $P=0.03$; wheeze, $P=0.0004$). However, previously sensitized patients who reduced their exposure to known allergens did not show improvement in their lung functions (FEV1, $P=0.3$; PEFR morning, $P=0.53$; PEFR evening, $P=0.2$; PEFR, $P=0.29$). **Conclusions:** Allergen avoidance may not always be successful in preventing allergic symptoms. However, rigorous methodological studies are required to confirm this hypothesis.

Key Words: Meta-analysis; allergen avoidance; allergenic potential newborns; previously sensitized patients; allergic diseases

INTRODUCTION

Allergic diseases have been a global health problem that has increased to epidemic proportions in the last few decades.¹ Currently available treatments for allergic diseases generally include allergen avoidance, pharmacotherapy, and allergen-specific immunotherapy (SIT). Exposure to allergens contributes to the development of hypersensitivity, and until 2007, many allergy societies advocated allergen avoidance as part of allergy management.² After a diagnosis of allergic sensitivity has been established based on anamnesis, skin tests, and specific serum IgE antibodies, clinicians generally recommend that their patients avoid future contact with the specific allergen(s). However, allergen avoidance has not decreased the incidence of allergic disorders, but rather an increase in allergies has been observed.^{3,4} In recent years, several studies have noted the ineffec-

tiveness of allergen intervention in reducing the incidence of allergies. Previous studies have demonstrated that intervention using bed covers impermeable to house dust mite significantly decreases allergen exposure but does not ameliorate the pa-

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tient's asthma. Furthermore, extended delay in the introduction of foods known to cause allergic reactions actually increased the risk of developing food allergies in infants and children.^{5,6} In addition, stringent allergen avoidance is not always practical as an allergy treatment; however, desensitization through supervised exposure maybe a better and more feasible therapeutic option.⁷

Allergen avoidance is commonly used to reduce the incidence and degree of allergic symptoms, but there is still uncertainty and even controversy regarding whether allergen avoidance is the most appropriate strategy for managing or preventing allergies. Thus, to determine whether the practice of allergen avoidance is a reliable and effective method that should continue to be recommended by clinicians for the prevention of allergic symptoms, we analyzed recent randomized controlled trials (RCTs) that applied allergen avoidance to reduce the incidence of allergies.

MATERIALS AND METHODS

Search strategy

Literature searches were conducted for articles published from January 1980 to December 2012 in PubMed and The Cochrane Central Register of Controlled Trials. All databases were searched in English and the MeSH terms included were "allergen avoidance" OR "allergen intervention" OR "allergen abatement" OR "allergen free" (all referred to as "allergen avoidance" hereafter) plus at least one of the following words: "randomized", "controlled", or "blind." After carefully examining the content of the abstracts, we rejected some allergen avoidance trials not relevant to our study. We retrieved the full texts of the preselected abstracts to further assess whether they met our inclusion criteria.

Inclusion criteria

The qualifying studies included the following: (a) limited to human trials, (b) RCTs with allergen avoidance as research subjects, (c) control groups that included a placebo or no interference, (d) newborn participants that had either their parents, siblings or two or more members of their immediate family affected by an allergic disorder, and (e) previously sensitized patients that were diagnosed with allergies by a physician and verified by clinical examination, such as skin testing or serum specific IgE tests.

Exclusion criteria

Studies that contained at least one of the following were excluded: (a) trials that were in combination with other therapies in addition to allergen avoidance, (b) trials that did not report the required outcome measures, (c) trials of presensitized patients that did not have 6 months or more follow-up time, and (d) crossover trials or ongoing clinical trials.

Outcome measures

Trials of newborns with allergenic potential reported the incidence of at least one of the following diseases: (a) asthma, (b) eczema, (c) wheeze, (d) cough, or (e) rhinitis. Trials of presensitized patients included at least one of the following outcome measures: (a) forced expiratory volume in one second (FEV1), (b) peak expiratory flow rate (PEFR), (c) PEFR morning, or (d) PEFR evening.

Data extraction

Studies for analysis were selected by 2 reviewers according to the inclusion/exclusion criteria, and the following essential information was recorded: (a) author, year of publication, (b) participants (sample size, age), (c) intervention and control method, (d) duration, and (e) outcome measures and results. The data extraction process was repeated by 2 additional reviewers.

Trial quality assessment

The methodological quality of meta-analysis was independently assessed by 2 reviewers according to the Jadad scale.⁸ The scale consisted of 4 items: descriptions of randomization (0-2 points), allocation concealment (0-2 points), blinding (0-2 points), and withdrawals (0-1 points).^{9,10} The maximum number of points available was 7. Total scores of 4-7 represent high-quality trials, while 0-3 was considered low quality. If the reviewers disagreed on the quality scores, discrepancies were identified and a consensus was reached.

Statistical analysis

Meta-analysis was performed using the Revman 5.0 software from the Cochrane Collaboration. Dichotomous data were calculated as the risk ratios (RR) with 95% confidence intervals (CI). Continuous data were presented as the standardized mean difference (SMD) with 95% CI. The overall effect was represented using Z scores. A *P* value of <0.05 was considered to indicate statistical significance. Statistical heterogeneity of effect sizes was evaluated by the χ^2 and I^2 tests. A *P* value of <0.1 was taken as an indicator of statistically significant heterogeneity using the random-effects model. The fixed-effects model was used for meta-analysis in the absence of significant heterogeneity ($P \geq 0.1$). Sensitivity analysis was performed by excluding trials for which the Jadad score was low.

RESULTS

Study descriptions

Of 420 citations selected for broad screening, 79 were considered potentially relevant according to the inclusion criteria after scanning their titles and abstracts. After reviewing the 79 full texts, 65 trials were excluded and 14 trials (4,082 patients)¹¹⁻²⁴ were selected for meta-analysis (Fig. 1).

All 14 selected articles were RCTs, and 8 pertained to the aller-

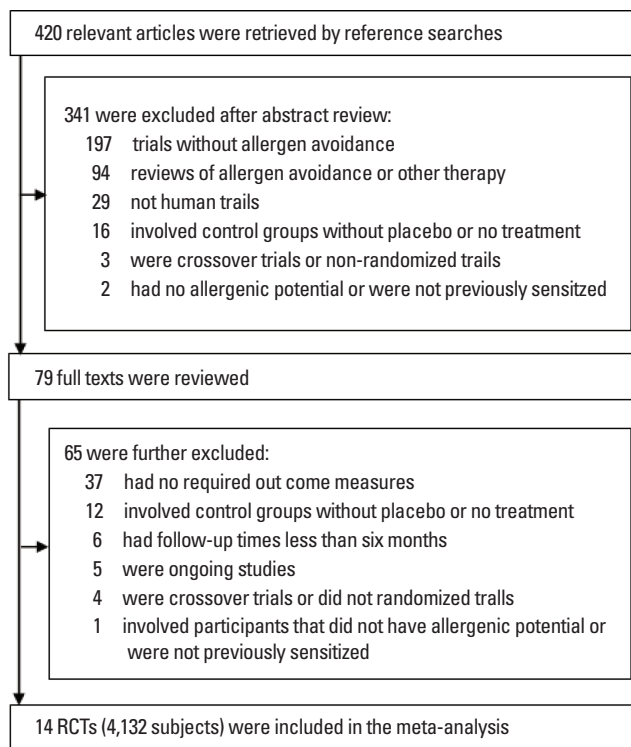


Fig. 1. Flow chart of the trial selection process. A total of 14 randomized controlled trials (RCTs) related to allergen avoidance were included in this study. In total, 4,132 subjects participated in these trials.

genic potential of infants. Study participants generally followed the environmental allergen intervention protocols in combination with early avoidance of dietary antigens. Six trials enrolled adult allergic patients but did not include any infants. Only studies related to environmental allergens were included. The details of the 14 trials are provided in Tables 1-1 and 1-2.

Data quality

Assessment of the data quality of the 14 trials is summarized in Table 2. All studies provided the number of patients who withdrew from the trials. Nine studies (64%) achieved or exceeded a Jadad score of 4 and were considered high quality. All eligible trials claimed to have randomly distributed subjects into the experiment and control groups; however, a substantial number of trials did not provide clear randomization or adequate concealment. Only one (7%) of the trials reported adequate double-blinded results because some allergen control measures are not possible to blind.

Effects of interventions

The fixed-effect models were also utilized for the analysis of eczema ($\chi^2=6.92$, $df=6$, $P=0.33$) (Fig. 2), rhinitis ($\chi^2=4.66$, $df=5$, $P=0.46$) (Fig. 3), and cough ($\chi^2=2.27$, $df=5$, $P=0.81$) (Fig. 4). Overall analysis of these 3 symptoms demonstrated that allergen avoidance, including reduction of exposure to environment allergens and early dietary antigen avoidance, did not re-

Table 1-1. Summary of eight trials of newborns with allergic potential

Study (reference)	Follow-up (months)	Study groups	Interference method	Subject No. (N = 2,920)	Types of symptoms (incidence/total)				
					Eczema	Asthma	Rhinitis	Wheeze	Cough
Arshad <i>et al.</i> 2007	96	Exp	IC+IFA+LMA	58	6/58	11/58	19/58	N/A	N/A
		Con	no interference	62	14/62	20/62	27/62	N/A	N/A
Becker <i>et al.</i> 2004	24	Exp	ECM+HF	246	N/A	40/246	N/A	2/246	18/246
		Con	no interference	230	N/A	53/230	N/A	8/230	25/230
Chan-Yeung <i>et al.</i> 2005	84	Exp	ECM+IC+IFA	202	25/202	30/202	64/202	35/202	40/202
		Con	no interference	178	24/178	41/178	49/178	52/178	37/178
Corver <i>et al.</i> 2006	60	Exp	IC	324	25/324	N/A	30/324	17/324	27/324
		Con	placebo	279	28/279	N/A	28/279	16/279	27/279
Custovic <i>et al.</i> 2001	12	Exp	IC+MVS	133	53/133	6/133	N/A	51/133	18/133
		Con	no interference	118	44/118	11/118	N/A	56/118	22/118
Horak <i>et al.</i> 2004	24	Exp	ECM+IC+IFA	291	36/275	13/291	45/290	6/289	28/252
		Con	no interference	272	29/263	6/270	56/272	9/269	27/247
Woodcock <i>et al.</i> 2004	36	Exp	ECM+IC	128	27/128	15/128	3/128	43/128	12/128
		Con	no interference	111	32/111	13/111	5/111	46/111	16/111
Zeiger <i>et al.</i> 1992	48	Exp	HF+IFA+PLMA	103	3/103	18/103	26/103	N/A	N/A
		Con	no interference	185	11/185	25/185	47/185	N/A	N/A

Exp, experimental group; Con, control group; N/A, not available; ECM, environmental control measures including sweeping furniture or bedding regularly or forbidding smoking or removing pets; HF, hydrolyzed formula; IC, impermeable cover; IFA, infant avoidance of hypersensitive food; LMA, maternal avoidance of hypersensitive foods while lactating; MVS, mechanical ventilation systems for accelerating air circulation; PLMA, maternal avoidance of hypersensitive foods during pregnancy and while lactating.

Table 1-2. Summary of 6 trials of previously sensitized patients

Study (reference)	Participant age (year)	Follow-up (months)	Study groups	Interference method	Subject No. (N = 1,162)	Types of measurements (M ± SD)			
						FEV1	mPEFR	ePEFR	PEFR
Eggleston et al. 2005	6-12	12	Exp	IC+MVS	50	94 ± 21	N/A	N/A	N/A
			Con	no interference	50	101 ± 20	N/A	N/A	N/A
Hayden et al. 1997	5-18	6	Exp	IC	11	N/A	N/A	N/A	328 ± 62
			Con	placebo	9	N/A	N/A	N/A	266 ± 102
Morgan et al. 2004	5-11	12	Exp	IC+MVS	444	87 ± 0.8	216.7 ± 3.1	N/A	N/A
			Con	no interference	425	87.4 ± 0.8	219.3 ± 3	N/A	N/A
Rijssenbeek et al. 2002	11-44	12	Exp	IC	16	N/A	434.6 ± 114.7	444.7 ± 113.5	N/A
			Con	placebo	14	N/A	440.2 ± 115	453.6 ± 134.4	N/A
Sheikh et al. 2002	5-14	6	Exp	IC	23	N/A	N/A	N/A	16.4 ± 25.6
			Con	placebo	20	N/A	N/A	N/A	13.7 ± 43.1
Wright et al. 2009	16-60	12	Exp	MVS	53	86.6 ± 18.1	419.2 ± 127.9	436.1 ± 124.7	N/A
			Con	placebo	47	82.5 ± 16.9	395.8 ± 96	405.9 ± 93.4	N/A

FEV1, forced expiratory volume in one second; mPEFR, peak expiratory flow rate in the morning; ePEFR, peak expiratory flow rate in the evening; PEFR, peak expiratory flow rate; Con, control group; Exp, experimental group; IC, impermeable cover; MVS, mechanical ventilation systems for accelerating air circulation; N/A, not available.

Table 2. Quality assessment of trials included in the meta-analysis

	Randomization (grades) ^a	Allocation concealment (grades) ^a	Blind method (grades) ^a	Withdrawal (grades) ^b	Total score
References for newborns with allergic potential					
Arshad et al. 2007	2	1	0	1	4
Becker et al. 2004	2	1	0	1	4
Chan-Yeung et al. 2005	2	1	0	1	4
Corver et al. 2006	1	1	1	1	4
Custovic et al. 2001	1	1	0	1	3
Horak et al. 2004	1	1	0	1	3
Woodcock et al. 2004	1	1	0	1	3
Zeiger et al. 1992	2	1	0	1	4
References for presensitized patients					
Eggleston et al. 2005	1	1	0	1	3
Hayden et al. 1997	1	1	0	1	3
Morgan et al. 2004	2	1	0	1	4
Rijssenbeek et al. 2002	1	1	1	1	4
Sheikh et al. 2002	2	2	2	1	7
Wright et al. 2009	1	1	1	1	4

^aScoring criteria of randomization/allocation concealment/blind method: 2=adequate with correct procedures; 1=unclear or without a description of methods; 0=inadequate procedures, methods, or information.

^bScoring criteria of withdrawal: 1=description of withdrawal reason and number; 0=unknown reason for withdrawal.

duce the risk of infants for the development of eczema (RR = 0.89, 95% CI = 0.74–1.07; Z = 1.24, P = 0.21) (Fig. 2), rhinitis (RR = 0.91, 95% CI = 0.77–1.09; Z = 1.03, P = 0.30) (Fig. 3), or cough (RR = 0.84, 95% CI = 0.68–1.04; Z = 1.64, P = 0.10) (Fig. 4). Similarly, no obvious heterogeneity was observed in the analysis of asthma ($\chi^2 = 10.20$, df = 6, P = 0.12) (Fig. 5) and wheezing ($\chi^2 = 4.71$, df = 5, P = 0.45) (Fig. 6), supporting the use of a fixed-effects mod-

el. The result of the overall analysis of asthma and wheezing was opposite to that of eczema, rhinitis, and cough, and demonstrated that allergen avoidance significantly reduced the incidence of asthma and wheezing in high-risk infants (asthma RR = 0.8, 95% CI = 0.65–0.98, Z = 2.15, P = 0.03; wheezing RR = 0.73, 95% CI = 0.61–0.87, Z = 3.51, P = 0.0004).

The results of stratified analysis of several other parameters of

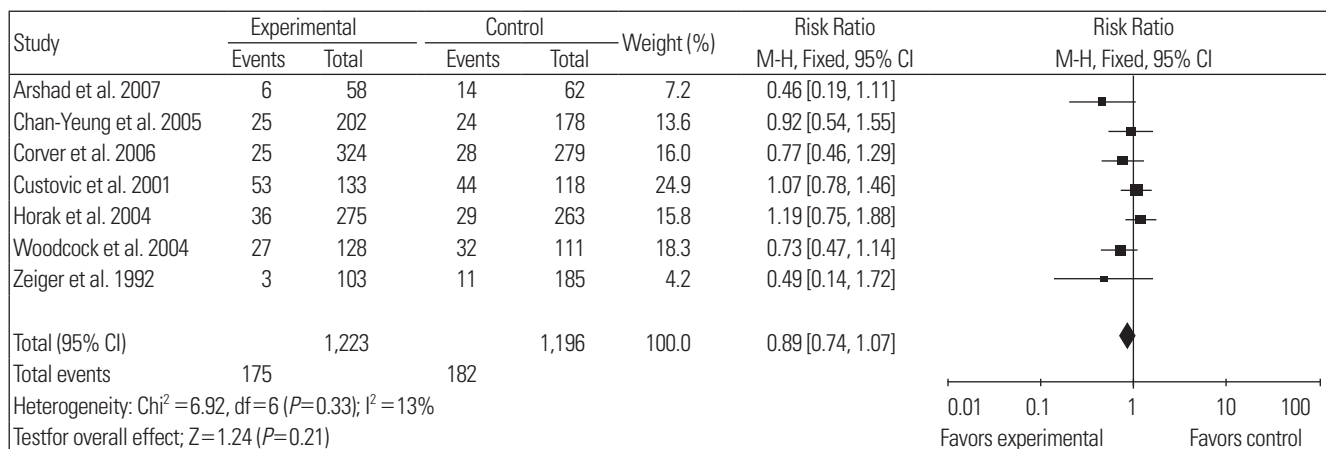


Fig. 2. Forest plot showing the risk ratio for the incidence of eczema comparing allergen avoidance to the control in newborns with the potential to develop allergies. There was no significant difference between the experimental and control groups ($P = 0.21$). Allergen avoidance did not improve the prevalence of eczema in high-risk infants.

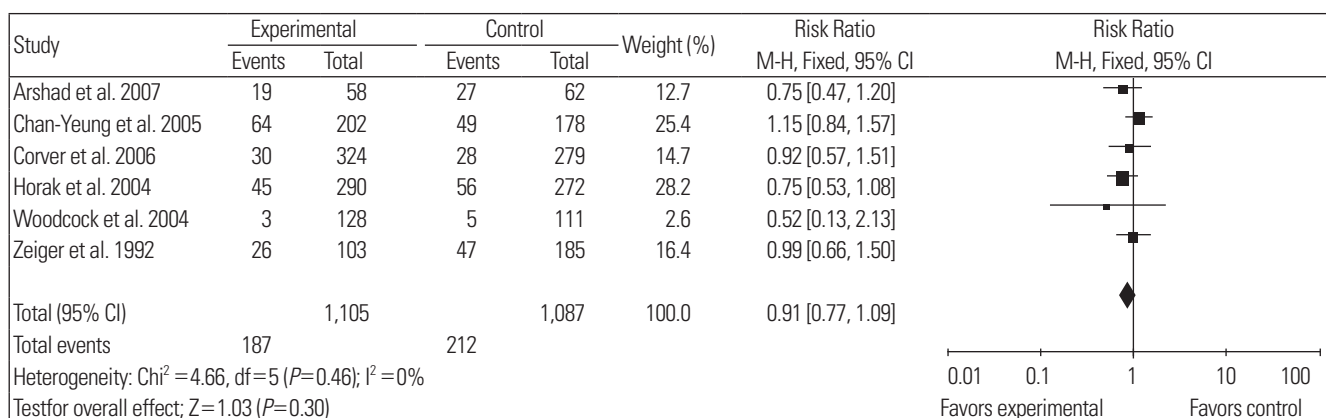


Fig. 3. Forest plot showing the risk ratio for the incidence of rhinitis comparing allergen avoidance to the control in newborns with the potential to develop allergies. There was no significant difference between the experimental and control groups ($P = 0.30$). Allergen avoidance did not improve the prevalence of rhinitis in high-risk infants.

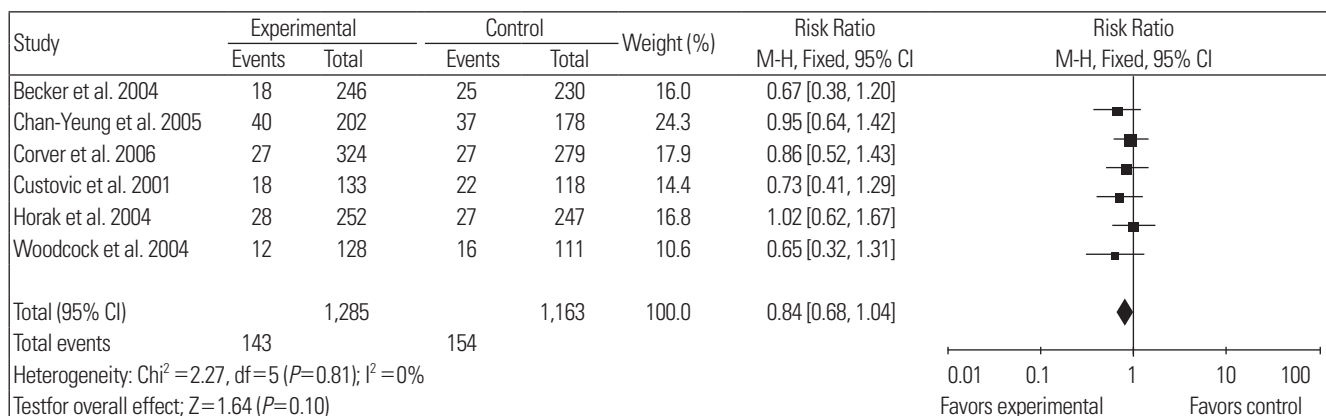


Fig. 4. Forest plot showing the risk ratio for the incidence of cough comparing allergen avoidance to the control in newborns with the potential to develop allergies. There was no significant difference between the experimental and control groups, demonstrating that allergen avoidance had no effect on the development of cough in infants with allergenic potential ($P = 0.10$).

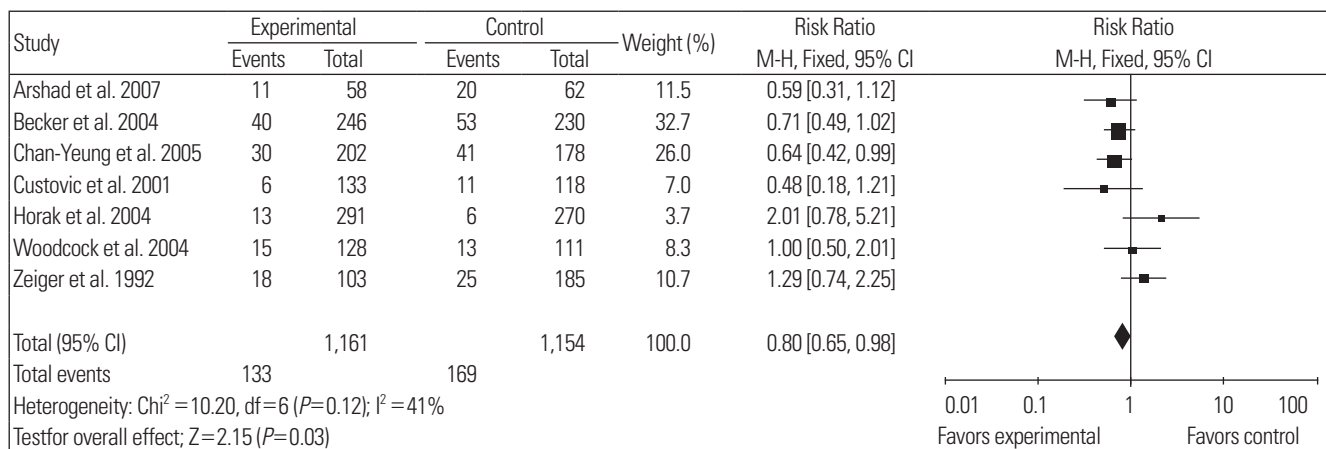


Fig. 5. Forest plot showing the risk ratio for the incidence of asthma comparing allergen avoidance to the control in newborns with the potential to develop allergies. There was a significant difference between the experimental and control groups ($P = 0.03$), indicating the effectiveness of allergen avoidance in high-risk infants.

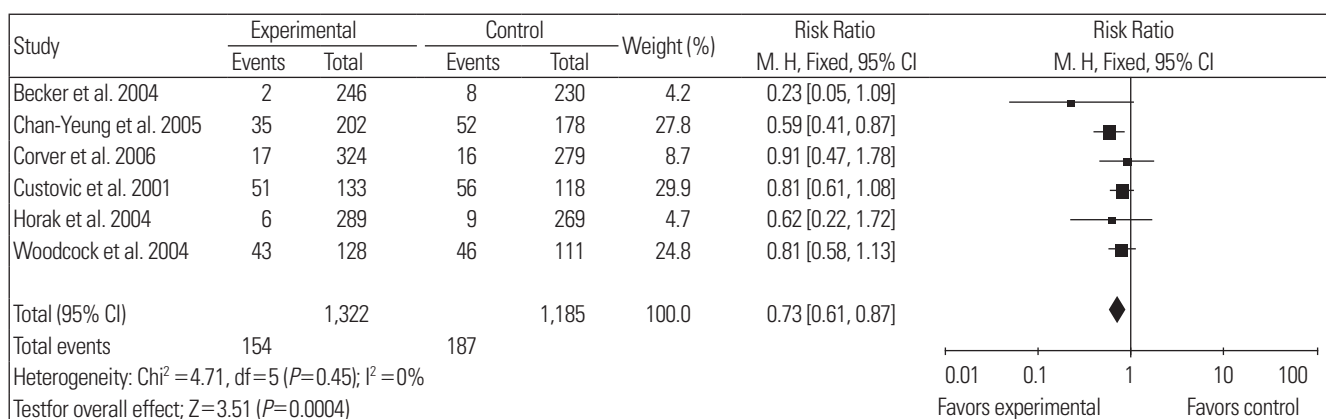


Fig. 6. Forest plot showing the risk ratio for the incidence of wheezing comparing allergen avoidance to control in newborns with the potential to develop allergies. Similar to the above asthma analyses, the overall analysis of the prevalence of wheezing in the experimental group when compared to control infants showed a significant improvement ($P = 0.0004$).

Table 3. Stratified analysis of lung function parameters

End point	Trials (references)	SMD (95% CI)	Z value	P value	Chi square (χ^2)	Heterogeneity (P)
FEV1	16, 19, 23	-0.23 (-0.66-0.20)	1.04	0.30	12.00	0.002
mPEFR ^a	19, 20, 23	-0.26 (-0.17-0.55)	0.63	0.53	28.22	<0.00001
ePEFR ^a	20, 23	0.22 (-0.12-0.57)	1.27	0.20	0.22	0.64
PEFR ^b	17, 21	0.27 (-0.23-0.77)	1.05	0.29	1.34	0.25

SMD, standardized mean difference; CI, confidence interval; FEV1, forced expiratory volume in one second; mPEFR, peak expiratory flow rate in the morning; ePEFR, peak expiratory flow rate in the evening; PEFR, peak expiratory flow rate.

lung functions are provided in Table 3. The results of FEV1 from the random-effects model analysis were similar in the experimental and control groups. There was obvious heterogeneity in the analysis of PEFR and PEFR evening; therefore, a fixed-effects model was used for the analysis of these parameters, but because the PEFR morning analysis did not show heterogeneity, a random-effects model was used in this case. Stratified

analysis based on the FEV1 and PEFR data (including morning and evening) suggested no protective effect of environmental allergen avoidance on previously sensitized patients (Table 4), which contradicted the results of asthma and wheezing.

Sensitivity analysis

Since inclusion of suboptimal trials could degrade the meta-

Table 4. Sensitivity analysis

End point	RCTs (references)	RR/SMD (95% CI)	<i>P</i> value	Heterogeneity (<i>P</i>)	Excluded trials (references)
Eczema	11, 13, 14, 24	0.74 (0.53-1.02)	0.06	0.53	15, 18, 22
Asthma	11-13, 24	0.75 (0.59-0.94)	0.01	0.18	15, 18, 22
Rhinitis	11, 13, 14, 24	0.99 (0.81-1.21)	0.94	0.51	18, 22
Wheeze	12-14	0.62 (0.45-0.86)	0.004	0.23	15, 18, 22
Cough	12-14	0.85 (0.64-1.12)	0.24	0.62	15, 18, 22
FEV1	19, 23	-0.16 (-0.87~-0.56)	0.66	0.0006	16
mPEFR ^a	/	/	/	/	/
ePEFR ^a	/	/	/	/	/
PEFR ^b	21	0.08 (-0.52~-0.68)	0.8	/	17

Sensitivity analysis was performed by removing low-quality trials, which were defined by having a total Jadad score <4. A *P* value <0.05 was considered as a statistically significant in the overall analysis. A Heterogeneity (*P*) value <0.1 was considered an indicator of statistically significant heterogeneity. After removing the low-quality trials, all adjusted results were the same as those found in the overall analysis of previously unadjusted trials.

^a Data regarding the peak expiratory flow rate in the morning (mPEFR) and peak expiratory flow rate in the evening (ePEFR) were not part of any low quality trial, and hence were not included in the sensitivity analysis.

^b After removing a low quality trial, PEFR data were obtained from only one RCT, so the heterogeneity (*P*) was not applicable.

RCTs, randomized controlled trials; RR, risk ratio; SMD, standardized mean difference; CI, confidence interval; FEV1, forced expiratory volume in one second; mPEFR, peak expiratory flow rate in the morning; ePERF, peak expiratory flow rate in the evening; PEFR, peak expiratory flow rate.

analysis, sensitivity analysis is commonly performed by excluding the suboptimal trials (such as those of low quality or with small sample sizes) to determine whether the same conclusion could be drawn, thus determining the reliability of meta-analysis. If the results from the adjusted meta-analysis are in accordance with those of the unadjusted meta-analysis, the results of the meta-analysis can be considered reliable. In this study, compared with the unadjusted analysis, identical heterogeneity statuses were indicated by the analyses adjusted by removing trials with Jadad scores of less than 4 (eczema: *P*=0.53, asthma: *P*=0.18; rhinitis: *P*=0.51; wheezing: *P*=0.23; cough: *P*=0.62; FEV1: *P*=0.0006). Thus, the same effects models were applied for the adjusted analyses. The sensitivity analysis results indicated that allergen avoidance did not improve the risk of infants for the development of eczema (*P*=0.06), rhinitis (*P*=0.94), or cough (*P*=0.24), but could reduce the incidence of asthma and wheezing in high-risk infants (asthma, *P*=0.01; wheezing, *P*=0.0004.), which was in agreement with the overall analysis of unadjusted trials (Table 4).

DISCUSSION

It is generally believed that allergen avoidance reduces the risk of—or prevents—allergic reactions and that greater allergen exposure increases the immune response. However, recent arguments challenge the effectiveness of this avoidance practice. To date, there has been no clear understanding of whether allergen avoidance alleviates or prevents the symptoms of allergies. Relevant reviews and guidelines do not acknowledge the fact that measures designed to reduce patient exposure to allergen(s) are ineffective, probably because these recommendations were not based on the results of RCTs.

Current analysis using the broader MeSH terms “allergen avoidance” or “allergen intervention” or “allergen abatement” or “allergen free” may allow inclusion of more allergen avoidance-related trials, which may account for multiple allergen interference approaches and allergy symptoms and improve the reliability and credibility of meta-analysis. However, we are not certain whether all relevant RCTs were retrieved in our search if the eligible trials did not use the above key words in their reports.

At this time, allergen avoidance can be classified into either the reduction of exposure to environmental allergens or avoidance of dietary antigens. Environmental allergen exposure reduction commonly pertains to the avoidance of indoor allergens, including the removal of pets, use of air filtration and vacuum cleaners, use of allergen-impermeable mattress and pillow covers, cockroach extermination, and measures to control mold growth in the home. Because patients sensitized to food allergens who are required to restrict their diets cannot be recruited into RCTs, dietary antigen avoidance in this analysis applies only to newborns and their mothers. Pregnant or lactating mothers followed a strict dietary regimen and/or used hydrolyzed formula instead of milk/breast-feeding.

Some trials recorded allergen (*i.e.*, cat dander, mite) counts by collecting allergen samples from the home or workplace. However, decreases in allergen concentrations at sampled sites did not always correspond to a similar reduction in the participant's exposure. Moreover, even very low allergen levels can lead to bronchial responsiveness.²⁵ Therefore, we did not consider allergen concentrations in the evaluation of the efficacy of allergen avoidance.

The practice of reducing exposure to environmental allergens did protect patients with moderate-to-severe asthma against

increased allergen sensitivity when they were evaluated after 1 month, but asthmatic symptoms had recurred by the time these patients were reviewed after 12 months.^{20,26} Thus, environmental allergen avoidance for a short duration may lead to an increased rate of false positive results. In general, allergen interference of more than 6 months did not alleviate patient symptoms.^{5,27-29} Therefore, only RCTs of previously sensitized patients who were followed up for 6 months or more were selected for meta-analysis in this study.

Although some trials included in this study were graded moderately, sensitivity analysis supported the reliability of our results. Nevertheless, factors, such as incomplete randomization, the absence of blinding, or inadequate allocation concealment, may pose a risk of potential bias in this analysis.

Data from the analyzed RCTs showed that the practice of allergen avoidance did not achieve a statistically significant reduction in the symptoms of allergic diseases, including eczema, cough, or rhinitis in high-risk infants. Moreover, even after 2 years of intervention, the incidence of eczema, rhinitis, and cough did not decrease. While the meta-analysis revealed that practicing allergen avoidance did not reduce the risk of eczema, rhinitis, or cough in high-risk infants, it did reduce the risk of asthma and wheezing. It is worth noting that dietary antigen avoidance may have an adverse effect on maternal and fetal nutritional status by restricting the consumption of foods, such as eggs, milk and nuts, which are sources of important nutrients.³⁰

Previously sensitized patients enrolled in the trials were asthmatics and were sensitized most frequently to house mites. FEV1 and PEFr (including morning and evening) are the most common parameters used for evaluating the severity of asthma.³¹ Asthma is a chronic condition characterized by ongoing inflammation of the airways. Therefore, the elimination of allergens should reduce inflammation and improve the symptoms of asthmatic patients. However, some asthmatic patients who were able to reduce their allergen (mite) exposure did not experience a positive effect. It is necessary to mention that mite-sensitized asthmatic patients are often cross-reactive to other allergens, such as food allergens, thus complicating achievement of a reduction in exposure to all allergens.^{32,33}

Considering that patients are unwilling to risk eating foods that they have allergies towards, performance of RCTs with food allergens is problematic. Additionally, cross-sensitization invalidates attempts to avoid all allergens. Some studies have demonstrated that pollen-sensitized patients frequently present allergic symptoms after ingestion of several types of plant-derived food³⁴⁻³⁶ or after exposure to other inhaled pollens.³⁷ The phylogenetic relationships between organisms are the cause of cross-sensitization; certain allergens are common to a variety of species and a high degree of homology in the primary antigenic structure can contribute to a loss of efficacy of allergen avoidance in terms of preventing allergic symptoms.

Strict allergen avoidance is not always suitable for treatment

due to difficulties in implementation. Patients must learn how to avoid cross-reactive and/or cross-contaminated allergens. Product labels can facilitate identification of known allergens, but some individuals cannot understand complex lists of ingredients, let alone unlabeled products. The lack of information regarding food allergens also restricts the avoidance process.³⁸ Avoidance of airborne allergens is even more difficult. As Morris Ling has reported,³⁹ adequate allergen avoidance is difficult because of the physical characteristics of airborne animal allergens and patient noncompliance. Low levels of indoor allergens may be achieved through reliable house cleaning, but outdoor pollens as well as molds are impossible to avoid completely. This might explain why lung functions of asthmatic patients, referenced by FEV1 and PEFr data (including morning and evening), showed no improvement after environmental allergen avoidance.

The rationale for practicing allergen avoidance is based on the assumption that exposure could result in dangerous or unpleasant allergic reactions and avoidance may prevent or accelerate recovery from allergic symptoms. However, this assumption does not agree with the "hygiene hypothesis."^{39,40} This hypothesis states that a lack of early childhood exposure to infectious agents, symbiotic microorganisms, and parasites increases susceptibility to allergic diseases by suppressing the natural development of the immune system. Many studies have expanded this hypothesis to non-infectious agents. For example, a previous study confirmed that food-allergic children on an elimination diet developed dysregulation of their Th1 and Th2 responses after exposure to food allergens.⁴¹ Another study suggested that early consumption of peanuts in infancy, rather than avoidance, will prevent peanut allergy.⁷

In conclusion, this study demonstrates that allergen avoidance aimed at reducing allergic sensitization is not always successful and may not be a suitable for the majority of patients. The diverse views on the practice of allergen avoidance may provide novel therapeutic perspectives in the prevention of allergic diseases. However, more rigorous methodological studies are required.

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