

# Efficacy of endonasal phototherapy for relieving the symptoms of allergic rhinitis: Meta-analysis

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## ABSTRACT

**Background:** Endonasal phototherapy can relieve the symptoms of allergic rhinitis (AR) for the patient. However, there is no consensus on whether or not endonasal phototherapy is effective in reducing the symptoms of AR.

**Objective:** The goal of this meta-analysis was to perform a systematic review of the available literature on the effects of endonasal phototherapy on symptoms of AR.

**Methods:** Two authors independently searched medical literature databases from their inception of article collection to July 2014. Studies that scored the nasal symptoms of AR and quality of life related to AR before and after endonasal phototherapy, and that compared the effects of phototherapy (treatment groups) with sham treatment (sham group) or antihistamine administration (antihistamine group) were included in the analysis. The outcomes of interest were total nasal symptom scores, disease-specific quality of life questionnaire assessments, and endoscopic findings (discharge and turbinate hypertrophy). Overall, a total of 13 trials met the inclusion criteria of this study, with a total sample size of 679 patients.

**Results:** Phototherapy significantly reduced nasal symptoms compared with pretreatment values and improved quality of life. The endoscopic findings also significantly improved after phototherapy. In addition, the symptom score and disease-specific quality of life after treatment were significantly lower in the treatment group versus the sham group, and were similar to those in the antihistamine group.

**Conclusions:** Phototherapy could provide nasal symptom relief and improve quality of life related to AR. However, when considering the insufficient evaluation of the efficacy of phototherapy according to the treatment methods and the high heterogeneity apparent in some parameters, further clinical trials with robust research methodologies should be conducted to confirm the results of this study.

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Allergic rhinitis (AR) is one of the most common allergic diseases, caused by the inhalation of allergens, which can affect both children and adults.<sup>1,2</sup> The worldwide prevalence of physician-diagnosed AR is 7–14%, which makes it a considerable global health problem.<sup>2</sup> Although AR has been regarded as a nuisance rather than a significant health problem, a number of studies have indicated that AR can be associated with significant morbidity, not only limited to its physical symptoms but including significant impact on learning, performance, and productivity at work and school as well as a patient's quality of life (QOL).<sup>3,4</sup> However, because current therapeutic options, such as allergen avoidance, medication, and immunotherapy, are far from ideal, a large number of patients with AR failed to achieve satisfactory improvement of symptoms through medication. As a result, the need for effective treatment modalities for the established indications of AR is patently clear.<sup>5</sup>

Complementary and alternative medicines (CAM) are used frequently worldwide to treat AR.<sup>6</sup> One type of CAM treatment is phototherapy, which is defined as the application of light to a pathologic area to promote tissue regeneration, reduce inflammation, and relieve pain. Several types of phototherapeutic devices that deliver selected wavelengths and a controlled dosage of irradiation are currently used for medical treatment. Further, significant suppression of clinical AR symptoms after phototherapy treatment with ultraviolet (UV) and visible light has been reported.<sup>7,8</sup> In addition, marked improvement in the clinical symptoms of AR was found after narrow-band red-light phototherapy as well as a low-level energy laser and

far infrared ray.<sup>3,9,10</sup> Although recent results from several studies for the treatment of AR demonstrated the effects of phototherapy on allergic symptoms, the evidence available in the literature is not sufficient to substantiate the use of phototherapy to treat AR. Therefore, this study aimed to assess evidence of the efficacy of phototherapy for improving outcomes for patients with AR. (Fig. 1).

## MATERIALS AND METHODS

### Search Strategy and Selection of Studies

Clinical studies, published in English, up to July 2014 were identified from MEDLINE, SCOPUS, and the Cochrane Register of Controlled Trials. The following search terms were used: "phototherapy," "rhinitis," "allergy," "light," and "complementary therapies." Only studies published in English were selected for inclusion. Reference lists of identified studies were also checked to ensure that no relevant studies were missed.

Two literature reviewers (H.K.C., S.H.H.) independently screened the abstracts and titles of all candidate studies, and discarded studies that were not related to phototherapy for the treatment of AR. Criteria for considering studies for this review were the following: randomized or case-controlled trials of the effect of any method of endonasal phototherapy, such as UV and visible light, narrow-band red light, low-level energy laser, or far infrared ray, on AR-related symptoms or QOL were included. Children or adults with a history of moderate-to-severe AR that was not controlled by conventional antiallergic treatment were included. Studies with more than eight patients per treatment group were included, which compared the effect of phototherapy before and after treatment or with a control (sham or antihistamine). Studies were not eligible for inclusion if (1) patients underwent additional procedures, such as turbinateplasty or vidian neurectomy; (2) patients with significant nasal structural abnormalities, bronchial asthma, upper respiratory tract infection within the past 2 weeks, or a lower respiratory infection within 4 weeks before the start of the study; (3) patients were treated with systemic

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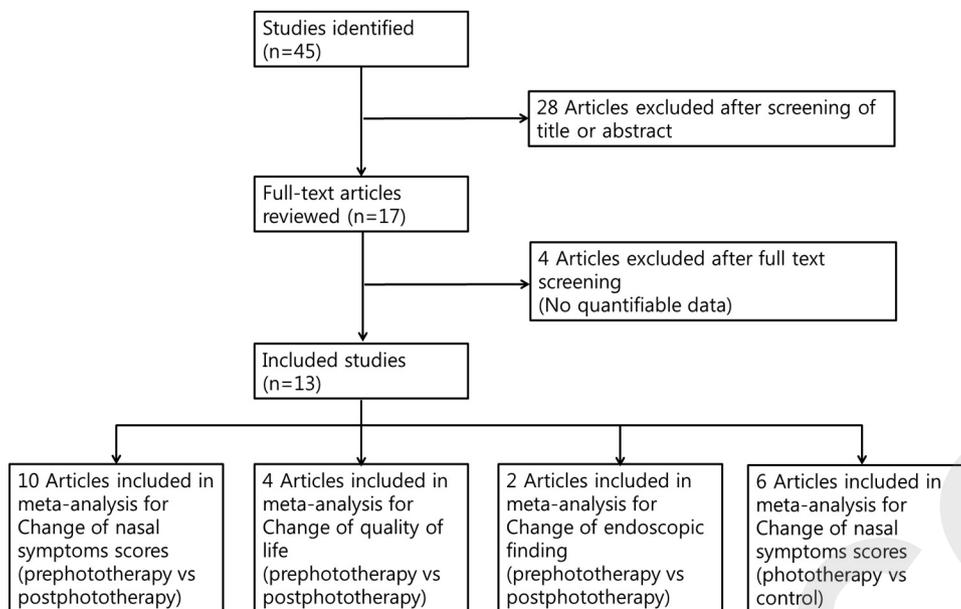


Figure 1. Diagram of the study selection.

Table 1 Summary of studies included in the meta-analysis

Study, y	Sample Size	Comparison	Outcome Measurement Analyzed	Judgment of Risk of Bias	Type of AR
Lee, <sup>3</sup> 2013	42	Before vs. after treatment	Total symptom score and life quality	High	Perennial
Moustafa <i>et al.</i> , <sup>16</sup> 2013	60	Before vs. after treatment	Total symptom score and endoscopic finding	High	Perennial
Yildirim <i>et al.</i> , <sup>15</sup> 2013	31	Before vs. after treatment	Total symptom score	High	Perennial
Brehmer and Schon, <sup>11</sup> 2011	10	Before vs. after treatment	Total symptom score	High	Seasonal
Csoma <i>et al.</i> , <sup>12</sup> 2004	8	Before vs. after treatment	Total symptom score	High	Seasonal
Garaczi <i>et al.</i> , <sup>13</sup> 2011	18	Before vs. after treatment	Total symptom score	Low	Seasonal
Albu and Baschir, <sup>14</sup> 2013	31	Phototherapy vs. antihistamine	Total symptom score and life quality	Low	Seasonal
Neuman, <sup>9</sup> 2007	77	Before vs. after treatment	Total symptom score and endoscopic finding	Low	Perennial
Cingi <i>et al.</i> , <sup>5</sup> 2010	78	Phototherapy vs. sham	Total symptom score	Low	Seasonal
Emberli, <sup>26</sup> 2009	41	Before vs. after treatment	Total symptom score	Unclear risk	Seasonal
Csoma <i>et al.</i> , <sup>7</sup> 2006	79	Phototherapy vs. sham	Total symptom score	High	Seasonal
Koreck, <sup>8</sup> 2011	13	Before vs. after treatment	Total symptom score	Low	Seasonal
Cingi <i>et al.</i> , <sup>17</sup> 2009	25	Before vs. after treatment	Total symptom score	High	Seasonal
	49	Phototherapy vs. sham			
	100	Before vs. after treatment	Total symptom score		

corticosteroids within the previous 4 weeks, topical corticosteroids or cromolyn sodium within 2 weeks, antihistamines and decongestants within 1 week before the beginning of the study, or immunotherapy in the past 2 years; or (4) multiple reports were based on the same trial data. In addition, studies were excluded from the analysis if clinical outcomes of interest were not clearly reported with quantifiable data or if it was not possible to extract and calculate the appropriate data from the published results.

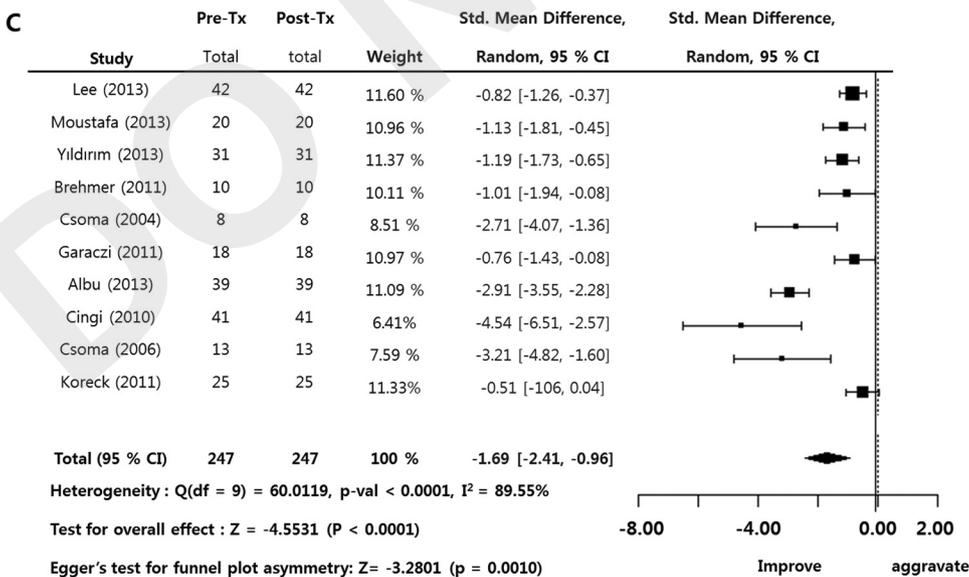
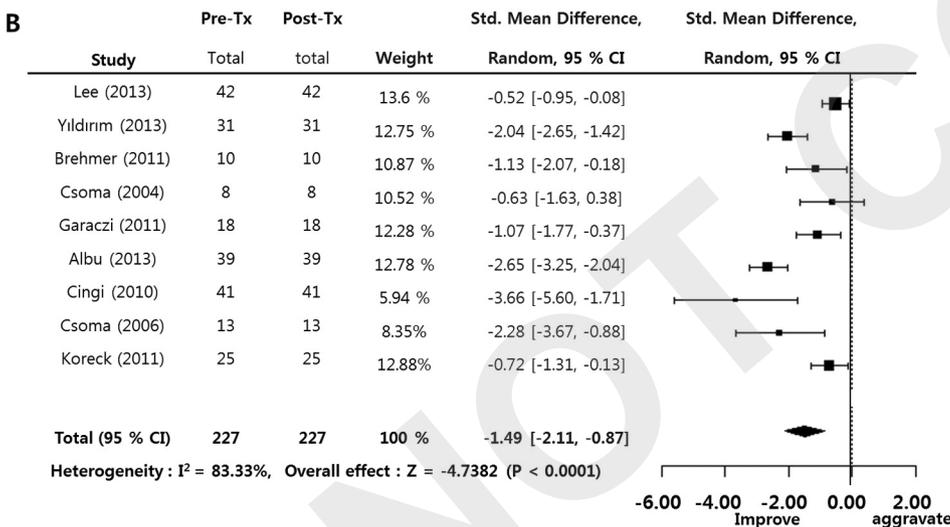
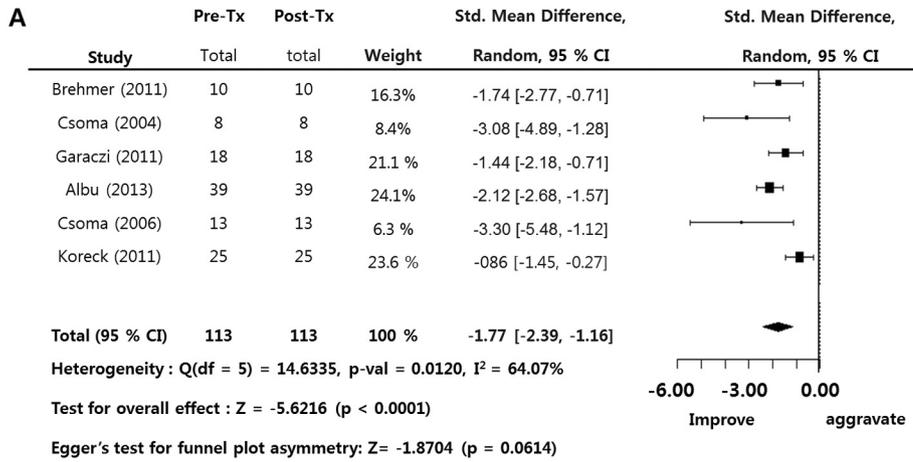
### Data Extraction and Risk of Bias Assessment

Data from included studies were extracted by using standardized forms and were independently checked by two reviewers (H.K.C., S.H.H.). The outcomes analyzed were nasal symptom AR scores,<sup>5,7,8,11-16</sup> disease-specific QOL questionnaire assessments,<sup>3,5,11,14,17</sup> and endoscopy findings<sup>9,16</sup> (nasal discharge or turbi-

nate hypertrophy). The outcomes analyzed were derived from comparisons between pre- and postprocedural values or between postprocedural and control (sham or antihistamine) during a follow-up period (within 1 month after starting the endonasal phototherapy). The data abstracted included patient number, grading scale, and *p* values from comparisons between pre- and postprocedural values or between postprocedural and control values. The risk of bias for each study was evaluated by using the Cochrane Risk of bias tool to assess the quality of the enrolled studies (Table 1).

### Statistical Analysis

A meta-analysis of the selected studies with a continuous measure was performed by using 'R' statistical software (R Foundation for Statistical Computing, Vienna, Austria). The standardized mean difference (SMD) was chosen to calculate the effect sizes used to assess



**Figure 2.** Posttreatment (phototherapy) versus pretreatment. (A) SMD of total nasal symptom scores, (B) itching scores, (C) nasal obstruction scores, (D) rhinorrhea scores, and (E) sneezing hours in the total nasal symptom score. Total = no. participants per group.

nasal symptoms scores and QOL. For the endoscopy findings (nasal discharge or turbinate hypertrophy), an outcome incidence analysis was performed by using the odds ratio calculated by using the Mantel-Haenszel method. Heterogeneity was calculated by using the

$I^2$  test. Simultaneously, an Egger's test was used to detect publication bias, and Duval and Tweedie's trim and fill was applied to adjust for missing studies and to correct the overall effect size regarding publication bias.

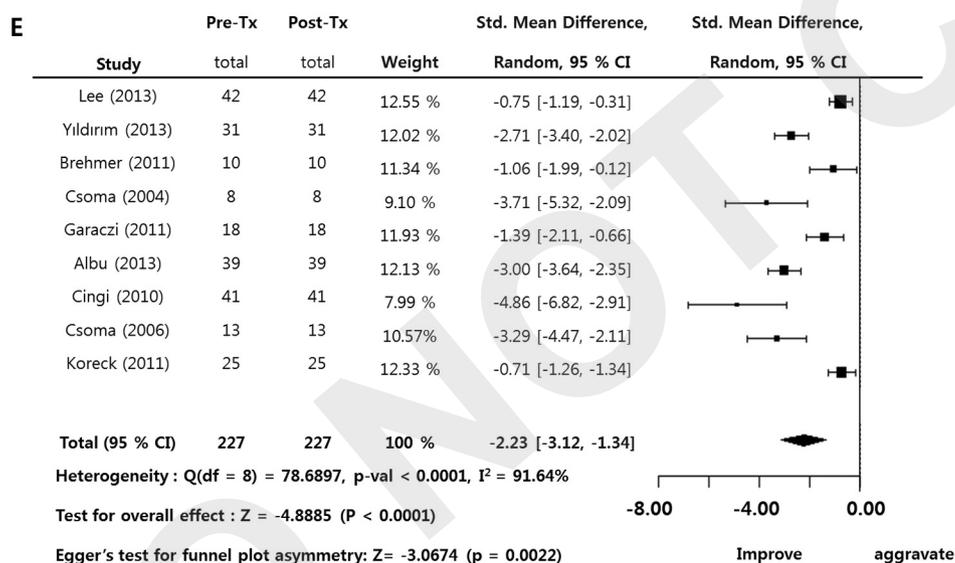
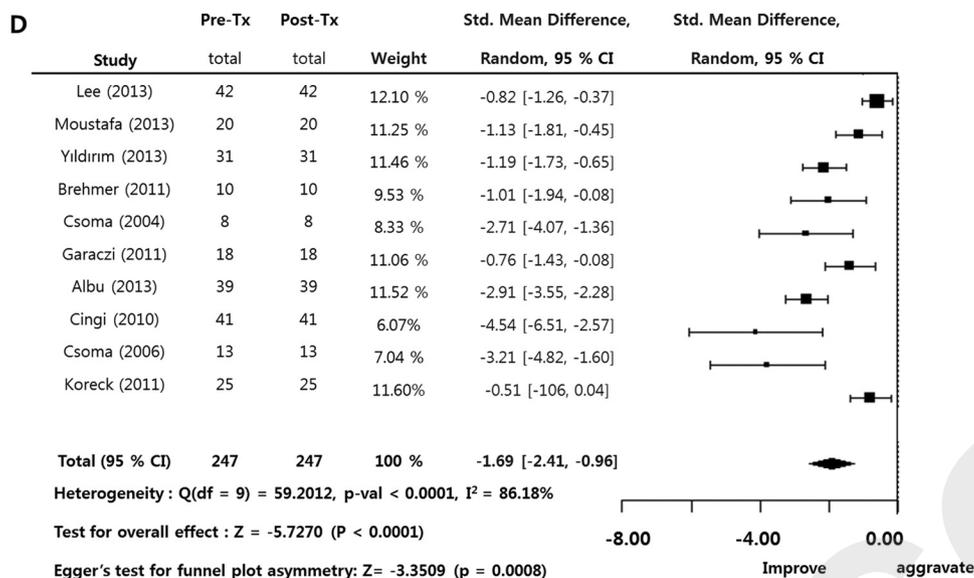


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## RESULTS

Thirteen studies with 679 participants were reviewed and included in the meta-analysis. The results of the bias assessment and the study characteristics are described in Table 1.

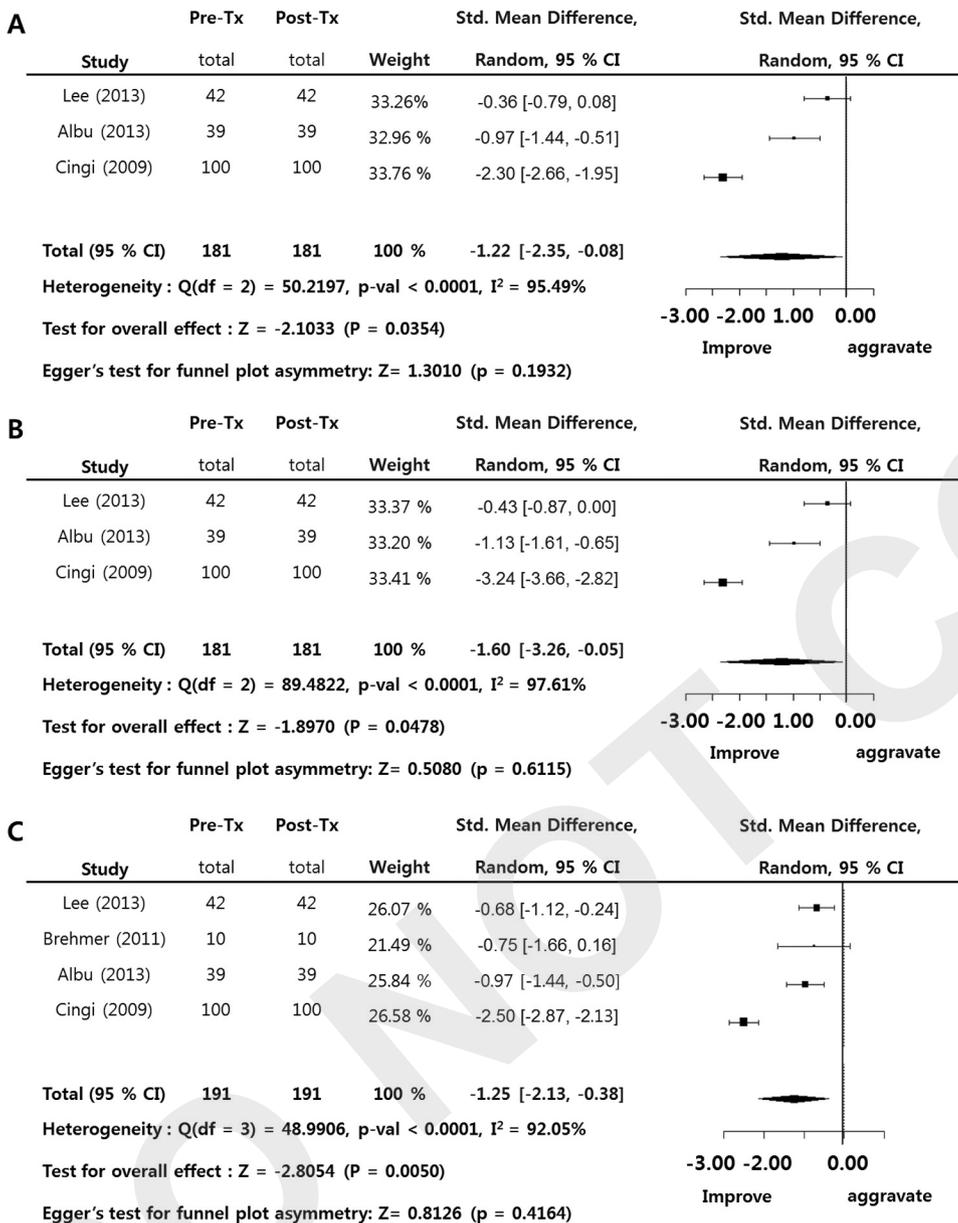
### Change in Nasal Symptoms Scores and QOL After Phototherapy

Ten studies assessed the efficacy of phototherapy on the reduction of nasal symptom scores. Phototherapy significantly reduced the total symptom score ( $SMD = -1.7740$ ;  $p < 0.0001$ ) and the scores for nasal itching ( $SMD = -1.4893$ ;  $p < 0.0001$ ), nasal obstruction ( $SMD = -1.6861$ ;  $p < 0.0001$ ), rhinorrhea ( $SMD = -1.9288$ ;  $p < 0.0001$ ), and sneezing ( $SMD = -2.2305$ ;  $p < 0.0001$ ) compared with pretreatment values. Significant interstudy heterogeneity was detected in all the scores ( $I^2 > 50\%$ ). The results of the Egger's test ( $p < 0.05$ ) of nasal obstruction, rhinorrhea, and sneezing indicated a source of bias in the included studies. However, the classic fail-safe N at all scores was  $>200$ . Moreover, Duval and Tweedie's trim and fill of all nasal symptom scores revealed no difference between observed and adjusted values. Consequently,

the results demonstrated that the selected studies were not biased (Fig. 2).

Four studies assessed the efficacy of phototherapy on improvement of QOL. Phototherapy significantly improved sleep ( $SMD = -1.2176$ ;  $p = 0.0354$ ), practical issues ( $SMD = -1.6019$ ;  $p = 0.0478$ ), non-hay fever symptoms ( $SMD = -1.2547$ ;  $p = 0.0050$ ), nasal symptoms ( $SMD = -2.0268$ ;  $p = 0.0303$ ), limited activity ( $SMD = -2.1751$ ;  $p = 0.0409$ ), eye symptoms ( $SMD = -1.1745$ ;  $p = 0.0121$ ), and emotional problems ( $SMD = -1.2384$ ;  $p = 0.0081$ ) compared with pretreatment values. Significant interstudy heterogeneity was found in all the scores ( $I^2 > 50\%$ ). The Egger's test results ( $p < 0.05$ ) only revealed a source of bias of eye symptoms in the selected studies. However, the classic fail-safe N of all the scores was  $>100$ . Moreover, Duval and Tweedie's trim and fill of all QOL values indicated that no difference existed between the observed and adjusted values, which demonstrated that the selected studies were not biased (Fig. 3).

To standardize the patients according to the type of AR, we performed subgroup analysis (perennial or seasonal AR). These analyses revealed that phototherapy had a significantly greater effect in improving the symptom and QOL in patients with sea-



**Figure 3.** Posttreatment (phototherapy) versus pretreatment. (A) SMD of sleep, (B) practical issues, (C) non-hay fever symptoms, (D) nasal symptoms, (E) limited activity, (F) eye symptoms, and (G) emotional problems in the Rhinitis Quality of Life Questionnaire. Total = no. participants per group.

sonal AR than in patients with perennial AR. Phototherapy produced no statistically significant effect on nasal itching and sneezing in patients with perennial AR, despite the large effect size ( $SMD > -1.00$ ;  $p > 0.05$ ). These results indicated that the type of AR influenced the overall analyzed outcomes (Tables 2 and 3)

### Change in Endoscopic Findings After Phototherapy

Two studies assessed the efficacy of phototherapy on improvement of endoscopic findings. Phototherapy significantly improved nasal discharge (log odds ratio =  $-4.2731$ ;  $p < 0.0001$ ) and turbinate hypertrophy (log odds ratio =  $-1.4493$ ;  $p = 0.0083$ ) compared with pretreatment values. There was no significant interstudy heterogeneity ( $I^2 < 50\%$ ), and the classic fail-safe N of all the scores was  $>10$ , which indicated that the selected studies were not biased (Fig. 4).

### Phototherapy Versus Control (sham or antihistamine group) (change of nasal symptoms scores)

Six studies involved a comparison of the reduction in nasal symptom scores between phototherapy treatment and a control.

Control groups were divided in two groups such as sham or antihistamine group. In two of the six studies, phototherapy significantly reduced the nasal itching score ( $SMD = -0.42$ ;  $p = 0.0317$ ), nasal obstruction ( $SMD = -0.51$ ;  $p = 0.0093$ ), and rhinorrhea ( $SMD = -0.39$ ;  $p = 0.0434$ ) compared with the antihistamine group. However, no differences were detected in sneezing ( $SMD = 0.09$ ;  $p = 0.8191$ ) or total symptom score ( $SMD = -0.28$ ;  $p = 0.1661$ ). Further, no significant interstudy heterogeneity ( $I^2 < 50\%$ ) was detected for any of the outcomes except sneezing. Phototherapy exhibited a weak significant reduction in symptoms compared with the antihistamine values, and the classic fail-safe N was  $<3$ . These results indicated that the selected studies were biased and that the results of these studies might fail to demonstrate a benefit associated with phototherapy when compared with antihistamines.

Conversely, in four of the six studies, phototherapy significantly reduced all symptom scores compared with the sham group, and the effect size of all scores was  $<0.5$ . There was significant interstudy heterogeneity ( $I^2 > 50\%$ ) for nasal itching and obstruction score. The results of the Egger's test ( $p < 0.05$ ) for nasal itching and obstruction scores indicated

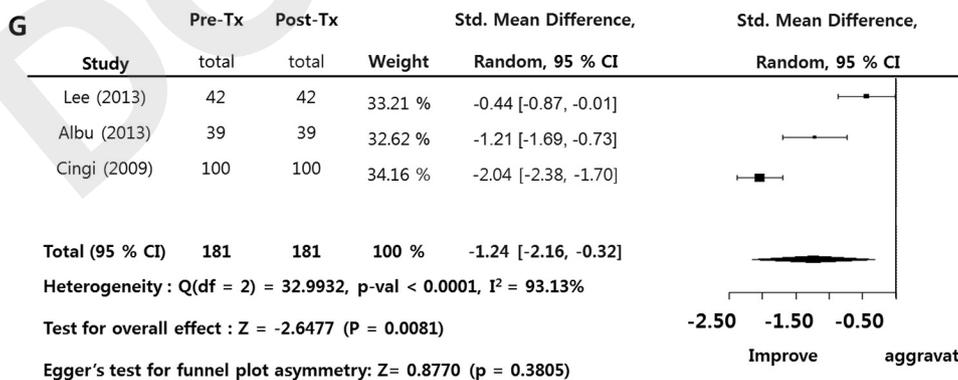
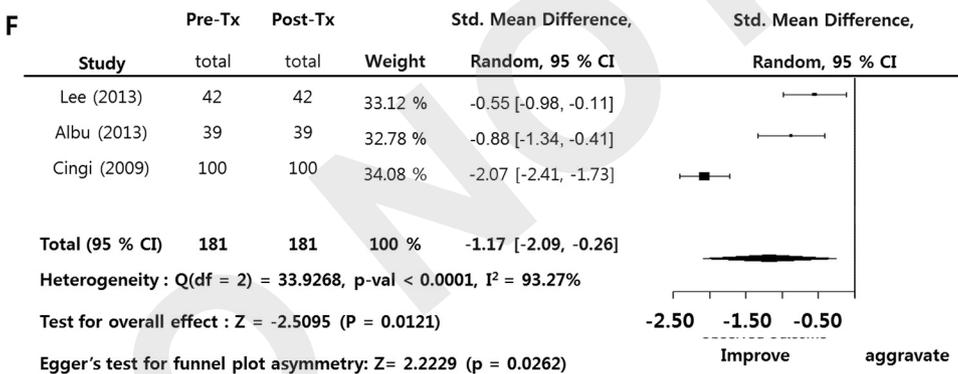
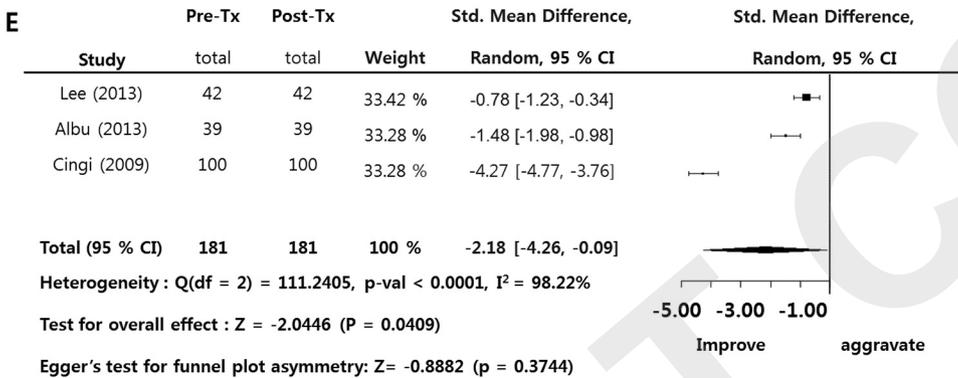
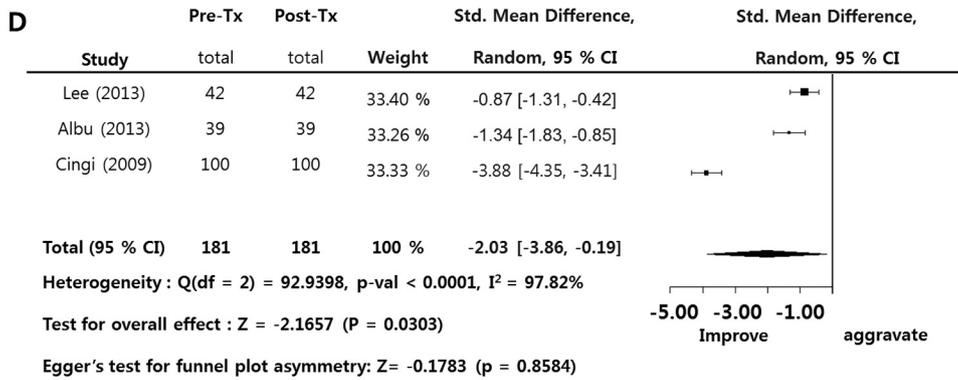


Figure 3. Continued.

a source of bias in the selected studies. However, the classic fail-safe N of all scores was  $< 20$ . Moreover, Duval and Tweedie's trim and fill of all the nasal symptom scores revealed no difference between the observed and the adjusted values, which indicated that the selected studies were not biased (Table 4).

## DISCUSSION

Outcome measurements used to assess of the severity and control of AR include subjective evaluation of symptoms by self-reported scales (or questionnaires) or objective measurements of nasal flow by

Table 2 Subgroup analysis of the effects of endonasal phototherapy on the allergic nasal symptoms according to type of AR

	Allergic Nasal Symptoms				
	Nasal Itching	Nasal Obstruction	Rhinorrhea	Sneezing	Total Score
Overall results (perennial AR)					
Effect size	-1.26	-1.00	-1.26	-1.71	
	[-2.75, 0.22]	[-1.30, -0.69]	[-2.17, -0.36]	[-3.63, 0.21]	
I <sup>2</sup> , %	93.62	0.00	86.55	95.45	
p	0.0963	<0.0001	0.0060	0.0809	
Overall results (seasonal AR)					
Effect size	-1.58	-2.07	-2.28	-2.41	-1.77
	[-2.32, -0.83]	[-3.13, -1.00]	[-3.13, -1.44]	[-3.50, -1.32]	[-2.39, -1.15]
I <sup>2</sup> , %	79.94	87.77	82.00	90.21	64.07
p	<0.0001	0.0001	<0.0001	<0.0001	<0.0001

Table 3 Subgroup analysis of the effects of endonasal phototherapy on the Rhinitis Quality of Life Questionnaire according to type of allergic rhinitis

	Quality of Life Related Rhinitis						
	Sleep	Practical Issues	Non-Hay Symptoms	Nasal Symptoms	Limited Activity	Eye Symptoms	Emotional Problems
Overall results (perennial AR)							
Effect size	-0.35	-0.43	-0.68	-0.86	-0.78	-0.54	-0.43
	[-0.78, 0.07]	[-0.86, 0.00]	[-1.12, -0.24]	[-1.31, -0.41]	[-1.22, -0.33]	[-0.98, -0.11]	[-0.87, -0.01]
I <sup>2</sup> , %	0.00	0.00	0.00	0.00	0.00	0.00	0.00
p	0.10660	0.0500	0.0024	0.0001	0.0005	0.0136	0.0470
Overall results (seasonal AR)							
Effect size	-1.64	-2.18	-1.44	-2.60	-2.87	-1.48	-1.64
	[-2.95, -0.34]	[-4.25, -0.12]	[-2.55, -0.34]	[-5.09, -0.11]	[-5.60, -0.14]	[-2.65, -0.31]	[-2.45, -0.83]
I <sup>2</sup> , %	94.87	97.62	92.32	98.13	98.31	93.92	86.75
p	0.0131	0.0377	0.0102	0.0400	0.0391	0.0131	<0.0001

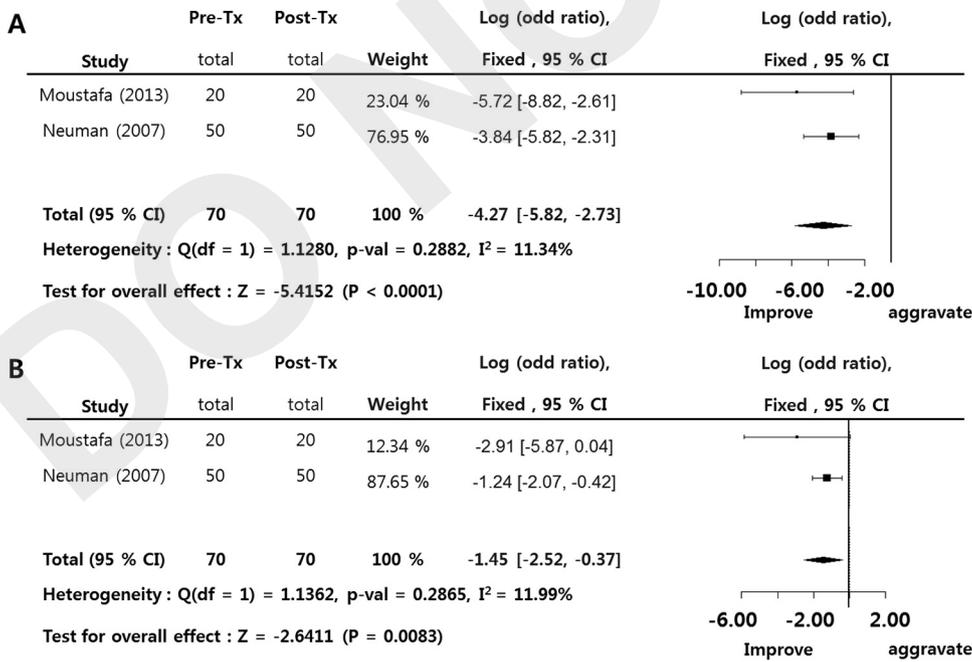


Figure 4. Posttreatment (phototherapy) versus pretreatment. Odds ratio of the incidence of nasal discharge (A) and turbinate hypertrophy (B) in the endoscopic findings. Total = no. participants per group.

rhinomanometry, assessment of nasal secretions by weighing tissue paper, and the monitoring of airway inflammation.<sup>18</sup> Self-reported scales, such as the visual analog scale or total nasal symptom score, have been used extensively to assess the severity of rhinitis as well as the efficacy of therapeutic interventions proposed by the Joint Task Force on Practice Parameters for the assessment of AR symptom

severity. The Rhinitis Quality of Life Questionnaire has also been used worldwide in adult and adolescent patients with AR to assess the effect of pharmacologic therapies, allergen avoidance, and homeopathy because the effect of these scores are parallel to the effects of conventional medical outcome measurements.<sup>19,20</sup> Therefore, this study attempted to assess the extent of rhinitis control by using the

Table 4 Subgroup analysis of the effects of endonasal phototherapy on the allergic nasal symptoms in randomized-controlled studies

	Allergic Nasal Symptoms				
	Nasal Itching	Nasal Obstruction	Rhinorrhea	Sneezing	Total Score
Overall results (antihistamine)					
Effect size	-0.42	-0.51	-0.39	0.09	-0.28
	[-0.80, -0.04]	[-0.90, -0.13]	[-0.78, -0.01]	[-0.69, 0.88]	[-0.67, 0.11]
I <sup>2</sup> , %	0.00	0.00	0.00	71.11	3.42
p	0.0317	0.0093	0.0434	0.8191	0.1661
Overall results (sham)					
Effect size	-0.53	-1.01	-0.91	-0.78	-0.53
	[-0.86, -0.21]	[-1.63, -0.40]	[-1.15, -0.66]	[-1.19, -0.37]	[-0.80, -0.26]
I <sup>2</sup> , %	163.12	78.86	0.00	45.88	0.0
p	0.0014	0.0012	<0.0001	0.0002	0.001

self-reported scales as well as the QOL questionnaire. In addition, endoscopic examinations performed by clinicians that generated valuable information on the appearance of the mucosa and assessed rhinitis symptoms were included to obtain objective assessments.<sup>3,9</sup>

In a previous study,<sup>21</sup> it was reported that a meta-analysis was not possible due to differences in methodologies, including more than one light source and different application periods of endonasal phototherapy. Consequently, the conclusion was reached that further research by using standardized reporting methods was needed. However, several meta-analyses that assessed procedures were performed, including studies of similar procedures performed by more than one operator, similar methods applied by using different materials, and different application times and agent dosages.<sup>22-24</sup> Phototherapy was carried out by using different light sources and different wavelength ranges with various schedules. Further, the potential existed that each phototherapy procedure was influenced by patient anatomy and surgeon skill, which might have prevented the rigorous and standardized review of the enrolled studies. Although the various wavelength ranges, such as UV and visible light, narrow-band red light, low-level energy laser, and far infrared ray, have different mechanisms, most studies demonstrated symptomatic improvement and better QOL scores without significant differences in overall symptom grading scores or questionnaire results, regardless of the type of light source.<sup>21</sup> Therefore, this study included analyses with broad standardization criteria (different ranges of wavelengths and schedules of phototherapy) that assessed the reduction in nasal symptom scores and the improvement in QOL before and after treatments. We also assessed the improvement in nasal symptom scores compared with outcomes of other therapies (sham or antihistamine).

Our results indicated that the nasal symptom score (total symptom score, nasal itching score, nasal obstruction, rhinorrhea, and sneezing) and QOL (sleep, practical issues, non-hay fever symptoms, nasal symptoms, limited activity, eye symptoms, and emotional problems) after phototherapy were significantly lower compared with the respective pretreatment values. In the endoscopic findings, phototherapy significantly improved nasal discharge and turbinate hypertrophy compared with pretreatment values. Moreover, the common representation of the SMD was effect size (Cohen's d), which indicated that larger sizes were more effective in clinically meaningful terms. The SMD of the symptom score and QOL measurements typically exceeded 0.8, which signified that these effect sizes were clinically significant during posttreatment periods.<sup>25</sup> The nasal symptom score and QOL questionnaire were used as reliable measurements to assess the severity of rhinitis and the efficacy of therapeutic interventions. In addition, the endoscopic findings reported by clinicians served as objective criteria for the assessment of the appearance of the mucosa and associated nasal inflammation. Consequently, endonasal phototherapy could considerably improve nasal symptoms and might reduce disease-specific discomfort.

In this study, we compared the efficacy of phototherapy in improving nasal symptom scores with the efficacy of antihistamines or a sham treatment. Phototherapy significantly reduced the nasal itching score, nasal obstruction, and rhinorrhea compared with the antihistamine group, in which the SMD was approximately <0.5. However, no significant differences were detected between phototherapy and antihistamine treatment for sneezing and total symptom score. Conversely, when compared with a sham treatment, phototherapy improved all nasal symptom measurements. In addition, the outcomes exhibited higher effect sizes than the comparative antihistamine group values, in which the SMD was >0.5. These results might be explained by the fact that both endonasal phototherapy and antihistamines are effective in reducing clinical symptoms in patients with AR in the selected studies despite the somewhat larger effect of phototherapy compared with antihistamines. In particular, among the symptoms considered, the improvement in nasal obstruction was relatively higher with phototherapy as opposed to antihistamines. This finding can be explained by the fundamental mechanisms of action of the two different treatments. In contrast to antihistamines, which predominantly influence histamine-mediated features of the allergic process, phototherapy has a different, more-complex mechanism of action. A previous study demonstrated that apoptosis of T lymphocytes in skin disease reduces the number and function of dendritic cells and increases immunomodulatory cytokines.<sup>3</sup> Similar results concerning immunomodulatory cytokines and T lymphocytes have been observed after other well-established AR therapies, such as topical glucocorticoids or immunotherapy.<sup>14</sup>

However, a notable outcome was that the SMD of phototherapy compared with sham treatment was smaller than the SMD of phototherapy compared with preprocedure measurements. A possible explanation for this difference was that all selected studies that compared the phototherapy SMD with sham treatments were placebo controlled. However, most of the relevant studies that compared the phototherapy SMD with preprocedure measurements were case-controlled studies. Consequently, to ensure an accurate evaluation of the efficacy of the procedure in the case-controlled studies, a placebo effect should be considered. Patient-reported scores, such as the visual analog scale or total nasal symptom score, are subjective scores, which could be influenced by a placebo effect.<sup>22</sup> Patients typically tend to exaggerate the procedural effect, which might have caused the larger effect size in the case-controlled studies. However, despite the difference in the degree of SMD, the resulting SMD for the two measurements were in the similar direction and were statistically significant. In particular, all effect sizes in the placebo-controlled studies were >0.5, which might mean that these procedures had a clinical effect. The results might also indicate that, irrespective of a potential placebo effect, phototherapy demonstrated a decrease in the severity of the patient symptoms.

Nevertheless, there were some limitations to this study. The first limitation pertains to the lack of multicenter, double-blinded, and randomized trials, and the short follow-up period. The average follow-up duration of most studies was only 1 month, whereas two studies had 3-month follow-up periods, and one study had a 12-month duration of follow-up. The structural changes and biochemical activity initially induced by the procedure would reduce inflammation in the surrounding tissue but return to the original condition later, which might be one of the reasons why the AR symptoms often recur after medication and immunotherapy. However, data are lacking, and multicenter and double-blinded trials and long-term follow-up studies are needed. The second limitation was that we could not evaluate the objective measurements such as nasal airflow or inflammatory markers. Although the pathophysiology of sinonasal symptoms is complex and involves overlapping psychological, physiologic, and anatomic variables, the clinical benefits of phototherapy, regardless of wavelength, appear to be related exclusively to symptomatic improvement.<sup>21</sup> To verify the phototherapy mechanism of action in AR, it is essential to evaluate the objective airflow parameters and the local and systemic biomarkers of inflammation, but these measurements were frequently omitted due to the high cost and inconvenience. The third limitation was that we could not evaluate the long-term adverse effects of endonasal treatment. Because clinical use of endonasal phototherapy appears to be safe and well tolerated,<sup>21</sup> we did not evaluate the adverse effect of phototherapy during application. However, it was unclear if UV irradiation or thermal exposure of nasal mucosa could result in DNA damage or irreversible changes in long-term follow-up. Further, we could not evaluate the long-term adverse effects of regular endonasal treatment because most of the studies were concluded after one treatment course.<sup>21</sup> Thus, had larger studies been conducted, it might have been possible to reach more definite conclusions. Future research should focus on the quality of the study methodology and ensuring adequate statistical power. However, given our results, it seems reasonable to conclude that this method might be an attractive alternative to conventional treatment for patients with AR.

## CONCLUSION

This meta-analysis demonstrated that phototherapy for treatment of AR could decrease symptomatic complications and improve QOL regarding rhinoconjunctivitis, although the mechanism of action is not clear. In the future, if more basic science and clinical trials regarding this novel approach are conducted, then phototherapy might be regarded as a mainstream treatment for AR.

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