

Brief Communication



A Prospective Study to Compare Clinical Outcomes of Allergic Rhinitis Between Older and Younger Adults: A Potential Effect of Depression in Older Patients

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ABSTRACT

Although younger patients with allergic rhinitis (AR) have been successfully treated with pharmacotherapy, there are no definitive data on treatment outcomes in older patients with AR. We performed a prospective study of 51 older adults with AR (aged over 65 years) and 101 younger AR patients (aged from 19 to 40 years) to compare clinical outcomes between the 2 groups and to evaluate the impact of depressed mood on treatment outcomes in older AR patients. Changes in total symptom scores (TSS), rhinitis-specific quality of life questionnaire (RQLQ) results, rhinitis control assessment test (RCAT) results and visual analog scale (VAS) scores were evaluated after 4-week treatment according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guideline, and the severity of depressed mood was assessed by using the geriatric depression scale. After 4-week treatment, younger AR patients had greater improvements in clinical scores compared with older adults; differences in least squares mean changes from baseline in older patients vs. younger patients were 1.71 ($P = 0.004$) for TSS, 10.84 ($P < 0.001$) for RQLQ, 0.80 ($P = 0.275$) for RCAT, and 8.60 for VAS score ($P = 0.061$). Multiple logistic regression analysis showed that the severity of depressed mood was independently associated with severe chronic upper airway disease (adjusted odds ratio, 1.385; $P = 0.004$). Our results suggest that older AR patients are less responsive to standard treatment compared with younger AR patients and that depressed mood is strongly associated with the increased risk of uncontrolled AR in older AR patients.

Keywords: Allergic rhinitis; aged; treatment; mood; depression; quality of life; visual analog scale; classification

INTRODUCTION

Although allergic rhinitis (AR) is common in older adults, it is often ignored, underdiagnosed and undertreated.¹ Although AR is not a life-threatening condition, it can affect quality of life and is a risk factor for poor asthma control.^{2,3} The prevalence of AR in older adults ranges from 10% to 25% and the increasing number of older patients with AR raises concern about proper diagnosis and treatment of older AR patients.^{4,7}

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Disclosure

There are no financial or other issues that might lead to conflict of interest.

The characteristics and clinical outcomes of older patients with AR may differ from those of younger patients with AR. Age-related factors, such as structural changes and immunosenescence, may contribute to the pathogenesis of rhinitis in older adults.⁸ The decline in physical performance and cognitive impairment leading to misunderstanding of their disease status pose a significant challenge to the management of older AR patients. Poor adherence and depressed mood of older adults may affect treatment outcomes.⁹ Nevertheless, there have been few studies on the outcomes of treatment in older AR patients compared with younger AR patients.

In a 4-week prospective observational study, we investigated the clinical features of older and younger AR patients, and compared the treatment outcomes between them. In addition, we identified factors associated with uncontrolled AR status even after pharmacotherapy according to the guidelines in older AR patients.

MATERIALS AND METHODS

Study subjects

We conducted a prospective observational study of 152 patients with moderate/severe or intermittent/persistent rhinitis according to the Allergic Rhinitis and its Impact on Asthma (ARIA) classification from March 2015 to September 2018 at a tertiary care university hospital in Korea. All patients had a history of allergic sensitivity as evidenced by a positive skin prick test (allergen/histamine ratio of wheal size ≥ 1) and/or elevated serum specific immunoglobulin E (IgE) level (≥ 0.35 kU/L) to at least 1 common aeroallergen (pollens, house dust mites, animal dander and mold). The patients with any paranasal sinus disease or clinical signs of infection were excluded. The subjects were classified as the older AR group (aged over 65 years, $n = 51$) and the younger AR group (aged from 19 to 40 years, $n = 101$). They had been treated with oral second-generation antihistamines, leukotriene-receptor antagonists and intranasal steroids according to the ARIA guideline during a 4-week study period. All subjects agreed to participate voluntarily in the study and provided written consent before participating in this study. This study obtained Ajou University Institutional Review Board approval (AJIRB-MED-MDB-14-349).

Variables

Demographic and clinical characteristics, including age, disease duration, medical history, concomitant diseases, complete blood cell count with differentials, serum levels of specific IgE and skin prick test results were collected at baseline. AR severity was evaluated using clinical scores, including 6-item total symptom score (TSS-6), rhinitis-specific quality of life questionnaire (RQLQ), rhinitis control assessment test (RCAT) and visual analog scale (VAS) score at baseline and after 4 weeks of treatment.^{10,12} Medication adherence and patient satisfaction with medications were assessed after 4 weeks of treatment.¹³ In the older group, the severity of depressed mood was measured using the 15-item geriatric depression scale (GDS-15) during a 4-week study period.¹⁴ The GDS-15, which has been validated as a screening tool for depression in older adults, consists of 15 items with yes/no questions and a cutoff score of ≥ 6 is considered as indicative of depression.¹⁵ Despite proper pharmacological treatment based on the guidelines, many patients with AR were in poorly controlled status, which was defined as severe chronic upper airway disease (SCUAD).¹⁶ A previous definition of SCUAD was used in the present study: a VAS level of patients' global discomfort of AR symptoms ≥ 50 mm (0- to 100-mm scale) and/or severe ocular symptoms (E-RQLQ ≥ 2.5 , and the cutoff level at the 75th percentile of E-RQLQ).¹⁷

Statistical analysis

All statistical analyses were performed using IBM SPSS 25.0 (IBM Corp., Chicago, IL, USA). The χ^2 test or Fisher's exact test was used to examine differences in categorical variables between the older and younger patients, and the *t* test or the Mann-Whitney *U* test was applied to determine differences in continuous variables between the 2 groups. Differences in least squares (LS) means changes from baseline for clinical scores were used to compare the older vs. younger patients. Factors associated with SCUAD were assessed by using multivariate logistic regression analyses with age, sex and disease duration as covariates.

RESULTS

Differences in clinical characteristics between the older and younger AR patients

A total of 152 AR patients were recruited and completed the study during a 4-week study period. The demographic and clinical characteristics were compared between the older (*n* = 51) and younger (*n* = 101) groups (**Table 1**). The proportion of patients who did not take medications regularly at enrollment was significantly higher in the older group than in the younger group (27.5% vs. 6.9%, *P* < 0.001). The older group more frequently had comorbid asthma than the younger group (58.8% vs. 38.6%, *P* = 0.018), but less frequently comorbid atopic dermatitis (15.7% vs. 34.7%, *P* = 0.014). The proportion of patients monosensitized to common aeroallergens was higher in the older group than in the younger group (49.0% vs. 12.9%, *P* < 0.001), whereas the rate of polysensitized patients was significantly higher in the younger group than in the older group (*P* < 0.001). The serum levels of specific IgE to D1 (*Dermatophagoides pteriygium*) and D2 (*D. farina*) were lower in the older group than in the younger group (5.85/ μ L vs. 15.38/ μ L, *P* = 0.017; 8.44/ μ L vs. 19.45/ μ L, *P* = 0.009 for each).

Comparison of changes in clinical scores from baseline between the older and younger groups

There were no significant differences in the type of medications between the older and younger groups during the study period. After the 4-week treatment, all clinical scores, including TSS-6, RQLQ, RCAT, and VAS score, were significantly improved from baseline in the younger group (all *P* < 0.001), whereas only 2 clinical scores, including TSS-6 and RCAT, were significantly improved in the older group (*P* = 0.016 and *P* = 0.004, respectively) (**Supplementary Table S1**). Compared with the older group, the younger group showed significantly improved scores from baseline in TSS-6 (LS mean difference 1.71, *P* = 0.004) and RQLQ (LS mean difference 10.84, *P* < 0.001) (**Figure**). The improvement in RCAT (LS mean difference 0.80, *P* = 0.275) and VAS score (LS mean difference 8.60, *P* = 0.061) tended to be greater in the younger group than in the older group, albeit without any statistical significances. We also found significant correlations among changes in TSS-6, RQLQ, RCAT, and VAS score in both groups (all *P* < 0.001) (**Supplementary Table S2**). Medication-related adverse events were not observed in the 2 groups during 4 weeks of treatment.

Factors associated with SCUAD in the older group

In the older group, 11 (21.5%) patients presented poorly controlled rhinitis with SCUAD after the treatment (VAS level \geq 50 mm and/or severe ocular symptoms with E-RQLQ \geq 2.5). Multivariate logistic regression analyses showed significant associations between SCUAD and GDS-15 scores (odds ratio [OR], 1.385; *P* = 0.004), treatment adherence (OR, 0.965; *P* = 0.029), and patient satisfaction with medications (OR, 0.395; *P* = 0.029) after adjustment for

Table 1. Comparison of clinical characteristics between the older and younger AR adults

Characteristics	Older AR group (n = 51)	Younger AR group (n = 101)	P value
Age (yr)	70.8 ± 5.4	28.9 ± 5.9	< 0.001
Female (%)	24 (47.1)	46 (45.5)	0.860
Disease duration (yr)	12.2 ± 16.5	10.9 ± 7.7	0.592
Smoking status (%)			< 0.001
Current	1 (2.0)	15 (14.9)	
Former	20 (39.2)	12 (11.9)	
Never	30 (58.8)	74 (73.3)	
Classification of AR (%)			0.278
Seasonal AR	4 (7.8)	14 (13.9)	
Perennial AR	47 (92.2)	87 (86.1)	
Medication use before study entry (%)			
Oral antihistamine	35 (68.6)	79 (78.2)	0.197
LTRA	22 (43.1)	12 (11.9)	< 0.001
Intranasal steroid	21 (41.2)	62 (61.4)	0.018
No medication	14 (27.5)	7 (6.9)	< 0.001
Comorbid condition (%)			
Hypertension	28 (54.9)	1 (1.0)	< 0.001
Diabetes	10 (19.6)	0	NA
Vascular disease	6 (11.8)	0	NA
Thyroid disease	9 (17.6)	3 (3.0)	0.002
Asthma	30 (58.8)	39 (38.6)	0.018
Atopic dermatitis	8 (15.7)	35 (34.7)	0.014
CBC with differentials (/ μ L)			
Blood neutrophil count	4,002.9 ± 1,627.6	3,934.2 ± 1,669.0	0.810
Blood eosinophil count	226.1 ± 199.5	261.3 ± 247.2	0.379
Skin prick test (positive result)			< 0.001
0–1	25 (49.0)	13 (12.9)	
2–3	10 (21.7)	10 (10.0)	
4–5	7 (15.2)	15 (15.0)	
≥ 6	4 (8.7)	62 (62.0)	
Serum levels of specific IgE (/ μ L)			
Der p-specific IgE	5.85 ± 17.92	15.38 ± 22.04	0.017
Der f-specific IgE	8.44 ± 19.65	19.45 ± 24.31	0.009
Birch-specific IgE	1.10 ± 1.70	9.68 ± 15.45	0.050
Mugwort-specific IgE	1.17 ± 1.62	3.07 ± 8.08	0.190

Values are presented as mean ± standard deviation or number (%). The χ^2 test was used for categorical variables, and the t-test was used for continuous variables.

AR, allergic rhinitis; LTRA, leukotriene-receptor antagonist; CBC, complete blood cell; *Der p*, *Dermatophagoides pteronyssinus*; *Der f*, *Dermatophagoides farinae*.

age, sex, and disease duration (**Table 2**). When older patients were divided into the 2 groups according to GDS-15 scores, the prevalence of SCUAD was higher in patients with than without depression (47.4% vs. 6.3%, $P < 0.001$).

DISCUSSION

To the best of our knowledge, this is the first prospective trial to investigate treatment outcomes in older AR patients compared with younger AR patients. The present study demonstrated that older AR patients were less responsive to pharmacological treatment based on the ARIA guideline compared with younger AR patients. Although the majority of older AR patients achieved symptom-controlled status after treatment, one-fifth of them remained in a poorly controlled state of SCUAD, which may have been attributed to treatment adherence, patient satisfaction with medications and the severity of depressed mood.

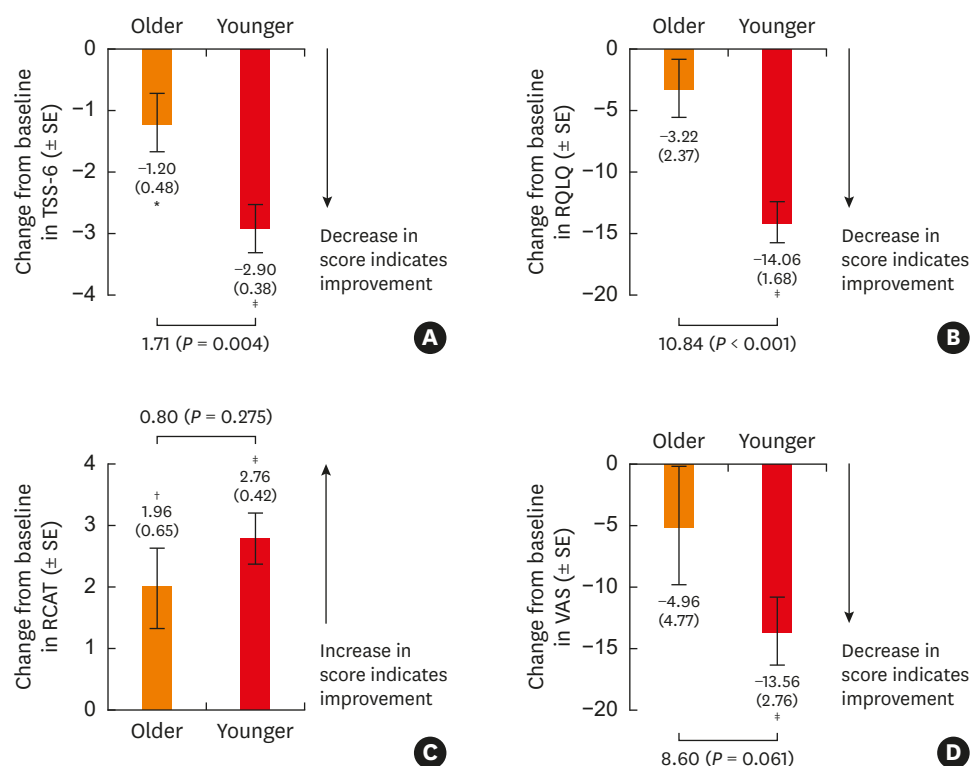


Figure. LS mean changes from baseline in TSS-6, RQLQ, RACT, and VAS in the older and younger patients after 4-week treatment. *P* value represents change from baseline in each clinical score. (A) TSS-6, range of 0 to 18; higher scores indicate worse rhinitis symptoms. (B) RQLQ, range of 0 to 140; higher scores indicate worse rhinitis symptoms. (C) RACT, range of 0 to 30; higher scores indicate better rhinitis symptoms. (D) VAS, range of 0 to 100; higher scores indicate worse rhinitis symptoms.

LS, least squares; TSS-6, 6-item total symptom score; RQLQ, rhinitis-specific quality of life questionnaire; RACT, rhinitis control assessment test; VAS, visual analog scale; SE, standard error.

**P* < 0.05; †*P* < 0.01; ‡*P* < 0.001.

Table 2. Multivariate logistic regression analyses for factors associated with SCUAD

Variables	Adjusted OR (95% CI)	<i>P</i> value
Blood neutrophil, absolute count (/ μ L)	1.000 (1.000–1.001)	0.172
Blood eosinophil, absolute count (/ μ L)	1.002 (0.997–1.006)	0.513
Atopy		
Monosensitization	Reference	
Polysensitization	1.129 (0.129–9.917)	0.913
Treatment adherence (%)	0.965 (0.937–0.993)	0.015
Satisfaction with medication, per increase of 1 level	0.396 (0.172–0.911)	0.029
GDS-15, per increase of 1 scale	1.385 (1.112–1.724)	0.004

The analyses included 51 older patients after adjustment for age, sex, and disease duration. SCUAD represented uncontrolled rhinitis despite proper pharmacologic treatment based on guidelines. Atopy was evaluated by a positive skin prick test (allergen/histamine ratio of wheal size ≥ 1) or elevated serum specific IgE level (≥ 0.35 kU/L) to common aeroallergens (pollens, house dust mite, animal dander, and mold). Satisfaction was measured in 4 ordinal levels: extremely dissatisfied (level 1), dissatisfied (level 2), satisfied (level 3), and extremely satisfied (level 4). Depression was measured using the GDS-15, a higher score indicates more severe depressive symptoms. SCUAD, severe chronic upper airway disease; OR, odd ratio; CI, confidence interval; GDS-15, 15-item geriatric depression scale; IgE, immunoglobulin E.

Although there are many clinical practice guidelines for the treatment of AR, they provide limited guidance on its diagnosis and management in older adults. In the present study, the clinical features of the older AR group (particularly atopic status and medication use) were different from those of the younger AR group, and the older group were less responsive to guideline-directed pharmacotherapy compared with the younger AR group. The diminished

responsiveness to treatment in older AR patients might be explained by the following considerations. First, AR in older AR patients can be comorbid with non-allergic rhinitis (NAR).¹ Oral second-generation antihistamines are not effective in the treatment of NAR, although oral first-generation antihistamines may be beneficial for its anticholinergic properties.¹⁸ Recognition of these comorbid conditions will help clinicians provide the appropriate treatment. Secondly, changes in immune cell function, including diminished T-cell proliferative responses and decreased B-cell activity, may be associated with increased risk of infections in older AR patients, which contribute to poorly controlled symptoms of rhinitis.⁸ Thirdly, comorbidity in older AR patients leads to the use of other drugs, such as antihypertensive agents, alpha-adrenergic antagonists, and antipsychotics, which can cause a drug-induced rhinitis. Finally, with aging, structural changes leading to decrease in nasal airflow and increase in the viscoelastic properties of nasal mucus may reduce responsiveness to topical medications. In such older AR patients, nasal irrigation is helpful in removing secretions and washing out allergens and irritants, which can improve the responsiveness to topical medications.¹⁹

Several studies have suggested the association between AR and depression^{8,9,20}; however, it is not clear whether the severity of depressed mood is independently associated with SCUAD. Multivariate logistic regression analysis in the present study demonstrated that depression could be a dominant determinant of SCUAD in older AR patients. A plausible explanation for this may be that inflammatory pathways in AR and depression are mediated by similar cytokines, such as interleukin-6 and tumor necrosis factor α .²⁰ Physicians treating AR patients should be aware of comorbid depression and consult with psychiatric specialists about its management.

This study has some limitations. First, because subjective symptom-rating scales may not be entirely accurate particularly in older AR patients, a potential bias cannot be completely avoided. For this reason, we assessed rhinitis symptoms using 4 valid tools and found significant correlations among the 4 clinical variables. Secondly, a 4-week treatment period might be insufficient to evaluate clinical outcomes in either group. However, the treatment guideline of ARIA recommended that the therapeutic effects of a treatment option for AR be assessed after 2–4 weeks of treatment.²¹ Thirdly, NAR and atrophic rhinitis may be more prevalent in older AR patients than in younger AR patients, which may have affected the treatment outcomes in the present study. Although it is difficult to distinguish between AR and NAR due to their heterogeneous clinical features, future studies are needed to assess whether they coexist or not. Finally, comorbidities in older AR patients lead to the use of concomitant medications, which can have affected the treatment outcomes. Further studies after controlling for potential confounders are warranted.

Despite these limitations, this is the first prospective trial to investigate clinical characteristics and treatment outcomes in older AR patients compared with younger AR patients. The results of this study have clinical implications in the treatment of older AR patients. Further studies are needed to establish more effective therapeutic strategies tailored to older AR patients.

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SUPPLEMENTARY MATERIALS

Supplementary Table S1

Clinical scores including TSS-6, RQLQ, RCAT, and VAS at baseline and in week 4 in the older and younger AR patients

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Supplementary Table S2

Correlations among changes in TSS-6, RQLQ, RCAT, and VAS scores

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