

Letter to the Editor



Sublingual Immunotherapy for Japanese Cedar Pollinosis Attenuates Asthma Exacerbation

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To the editor,

There are various factors for acute asthma exacerbation.¹ A recent article by Cho² proposed that various therapeutic options should be employed in practice for different causes of asthma exacerbation. Here, we report that sublingual immunotherapy (SLIT) for Japanese cedar pollinosis (JCP) is effective in reducing seasonal asthma worsening. In perennial asthmatics with concomitant JCP, asthma worsening is observed during the pollen season.³ SLIT for rhinoconjunctivitis due to JCP⁴ was approved in Japan in 2013. However, it remains unclear whether SLIT is effective for asthma observed with JCP.

Forty-seven asthmatics with mild-to-moderate persistent disease who had complicated JCP were enrolled. Fourteen subjects were treated with the SLIT for ≥ 1 year prior to season of cedar pollen of 2018, while 33 were not. This was a retrospective study. Most patients had visited our hospital every 2 months. In this case, medical records of patients who visited in April and May after the pollen scattering season of 2018 were extracted from the medical record. Patients with severe asthma and nonallergic asthma were excluded. Treatments of rhinitis and asthma were performed according to the Japanese guidelines. The SLIT group received a standardized JCP extract (CEDARTOLEN®; Torii Pharmaceutical Co., Ltd., Tokyo, Japan) using the protocol of SLIT for JCP.⁵ Asthma exacerbation was evaluated as defined in the American Thoracic Society/European Respiratory Society statement,⁶ and only apparent worsening, such as moderate or severe asthma exacerbation, was extracted. Statistical analyses were performed using GraphPad Prism ver. 5.04 (GraphPad Software, San Diego, CA, USA). Two-group comparisons were performed using Pearson's χ^2 tests, and Student *t*-tests or Mann-Whitney *U* tests were used to determine the significance of differences. A *P* value of < 0.05 was considered statistically significant.

Table 1. Clinical assessment of asthmatics with concomitant JCP and clinical outcomes in asthma exacerbation during cedar pollen scattering season

Variables	All patients	Non-SLIT	SLIT	P value
Patients	47	33	14	-
Prevalence of JCP	100	100	100	-
Age (yr)	52.4 ± 17.2	53.8 ± 18.1	48.9 ± 14.4	0.385
Sex				0.245
Male	12 (25.5)	7 (21.2)	5 (35.7)	
Female	35 (74.5)	26 (78.8)	9 (64.3)	
Total IgE (IU/mL)	241.2 ± 294.3	246.6 ± 226.8	228.2 ± 414.1	0.176
Specific IgE to JCP (UA/mL)	23.1 ± 26.2	25.2 ± 25.9	17.9 ± 26.1	0.356
FEV1 (L)	2.5 ± 0.8	2.4 ± 0.8	2.7 ± 0.4	0.880
Asthma treatment				0.210
ICS/LABA + LTRA	22 (46.8)	17 (51.5)	5 (35.7)	
ICS/LABA	15 (31.9)	11 (33.3)	4 (28.6)	
ICS + LTRA	5 (10.6)	3 (9.1)	2 (14.3)	
ICS	2 (4.3)	1 (3.0)	1 (7.1)	
Patients without controller	3 (6.4)	1 (3.0)	2 (14.3)	
Allergens other than JCP				
Molds	7 (14.9)	6 (18.2)	1 (7.1)	0.314
Pollens	29 (61.7)	21 (63.6)	8 (57.1)	0.749
Pets	15 (31.9)	13 (39.4)	2 (14.3)	0.086
Mites	24 (51.1)	19 (57.6)	5 (35.7)	0.212
Insects	9 (19.1)	5 (15.2)	4 (28.6)	0.248
Seasonal asthma exacerbation*				0.004
Exacerbated	13 (27.7)	13 (39.4)	0 (0)	
Not exacerbated	-	20 (60.6)	14 (100)	

Data are shown as mean ± standard deviation or number (%).

JCP, Japanese cedar pollinosis; SLIT, sublingual immunotherapy; IgE, immunoglobulin E; FEV1, forced expiratory volume in one second; ICS, inhaled corticosteroids; LABA, long-acting β_2 agonist; LTRA, leukotriene receptor antagonist.

*Exacerbation was evaluated based on the American Thoracic Society /European Respiratory Society statement,⁶ and moderate to severe exacerbation was detected: a deterioration in symptoms and/or lung function with increased rescue bronchodilator use lasting for ≥ 2 days was categorized as moderate, and a need for hospitalization or 2 or more courses of oral corticosteroids was as severe.

Table 1 shows the characteristics of patients and clinical outcomes. No difference was observed in either age, sex, sensitized allergens, forced expiratory volume in one second, or asthma therapy between the 2 groups. Thirteen out of the 33 non-SLIT group patients experienced apparent asthma exacerbation during cedar pollen season. In contrast, none of the SLIT-treated group patients showed seasonal asthma exacerbation. The rate of asthma exacerbation was significantly different ($P < 0.01$) between the 2 groups. As expected, rhinoconjunctivitis symptoms were fewer in the SLIT group (data not shown).

SLIT is effective in some allergic asthma. Marogna *et al.*⁷ compared the effects of SLIT and inhaled corticosteroids in patients with mild asthma and concomitant rhinitis due to grass pollen allergy, and showed that asthma symptoms decreased significantly in both groups; however, improvements were greater in the SLIT group. We observed that asthma exacerbation during cedar pollen season in Japanese asthmatics with JCP could be sufficiently prevented by SLIT for JCP. Although the presence of limitations, such as the small sample size and the absence of a placebo setting, this study is the first observation indicating that SLIT for JCP certainly attenuates the risk of asthma exacerbation during pollen season. Our results suggest that SLIT for JCP should be more positively considered for patients who suffer from asthmatic worsening during the scattering season of JCP.

This study was approved by the Institutional Review Board (IRB) of Saitama Medical University Hospital (IRB No.18015).

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