



# Daytime Sleepiness and Sleep in allergic rhinitis'

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## ABSTRACT

### Objective

Today, in Japan, over 20 million peoples are suffered from Hay fever caused by cedar pollen, and every year, they are disturbed with severe symptoms during season just 2-3mth. In clinically, there is a big problem about QOL including daytime sleepiness and sleep problems.

### Methods

Purpose of this study is To clarify the influence of hay fever on sleep and day time sleepiness subjectively. 22 patients with hey fever caused by cedar Pollen were enrolled. We evaluated sleep architecture and objective sleepiness between before the season & on season using PSG and MSLT.

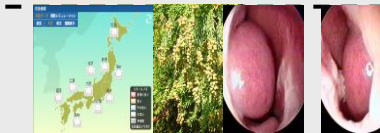
### Results

WASO (wake time after on set) showed significantly increase during on season rather than before season: from 16.4 to 29.7min. AHI does not change for the worse during on season. In 11 patients with nasal obstruction ,total nasal resistance > 0.3pa/cm/sec, out of 22, Rate of rem -sleep decreased (from 24.2 to 20.8%) and mean MSLT decreased (from 12.4 to 8.5min) significantly. Especially 4 out of 11 showed severe sleepiness that was recognized as disease (MSLT< 5min) on season.

### Conclusion

There are strong associations between nasal symptom especially nasal obstruction, sleep quality and daytime sleepiness.

## INTRODUCTION



**Background:** In ARIA 2001 (Allergic Rhinitis and its Impact on Asthma), a disease severity classification for allergic rhinitis is listed in the beginning. For moderate-Severe grade allergic rhinitis there are four clinical manifestations, one of which is some form of sleep disorder. (1) In other words the influence on sleep of allergic rhinitis was recognized to be a factor determined to be important in diagnosing the severity of allergic rhinitis. Recent epidemiological studies in the United States show that for both adult and pediatric allergic rhinitis patients, sleep was one of main QOL problems. (2,3). Furthermore a recent review article (4,5) showed that allergic rhinitis influences sleep more than expected, and a sleep disorder due to allergic rhinitis may influence symptoms in the daytime including sleepiness. However, details of the association between allergic rhinitis and sleep disorders are still unclear. And also, In an international classification of sleep disorder 2nd, sleep disorder related allergic rhinitis is not defined.

## OBJECTIVE

To evaluate daytime sleepiness and sleep architecture in patients with hay fever caused by cedar pollen objectively

## METHODS AND MATERIALS

**Subjects:** 24 untreated males (Mean age : 31.95±10.13, Mean BMI: 21.19±2.41) with hay fever caused by cedar pollen. The diagnosis of hay fever caused by cedar pollen was based on conventional clinical criteria: positive skin reaction to antigens, immunoglobulin E concentration, and medical history.

**Setting:** Crossover study, In Sleep Laboratory

**Methods:** To evaluate nasal obstruction using a Rhinomanometer, daytime sleepiness using the multiple sleep latency test, and sleep quality using PSG.

**Data Analysis:** To compare following parameter between on season and off season

Daytime Sleepiness: Mean Sleep Latency Time(MSLT min)

Sleep Architecture :Sleep Efficiency (SE), WASO (Wake After Sleep Onset), Sleep Latency (SL), REM Sleep Latency (RL), Arousal Index (Ari), %stage1, %stage3+4, % stageREM, Apnea Hypopnea Index(AHI), %CT90

Nasal Obstruction: Total Nasal Resistance:supine position: 100pa (pa/cm3/sec)

Statistical Analysis : Man-U, Multivariate Logistic regression analysis. Relative risks were calculated at 95% confidence intervals. All P values are two-tailed. (SPSS ver17.0)

## RESULTS

As a result of the screening study, one out of 24 was diagnosed as narcoleptic and another one was diagnosed with moderate OSAS. 22 were analyzed in the end, because two had been excluded.

- 1.WASO showed significant increase on season rather than off season.(Fig1)
- 2.There are no difference in most of sleep parameter between on and off season. (Fig2,3)
- 3.AHI did not change for the worse during on season.(Fig4)
- 4.A significant difference was not admitted in a nasal resistance .(Fig5)
- 5.There are no significant difference in MSLT between on and off season.(Fig6)
6. MSLT has decreased during the season by 14 patients in 22.
7. As a result of the Multivariate Logistic Regression analysis, the strongest predictor of the patient who had accompanied an increase in daytime sleepiness on season was nasal resistance > 0.33pa/cm3/sec (Fig7)
8. For some allergic patients, daytime sleepiness becomes worse overall during the on-season. The predictive factor of the sleepiness aggravation is nasal obstruction. Furthermore, in the high nasal resistance group, a significant decrease in REM sleep is showed during the on-season. In the allergic patients, nasal obstruction or pathologic aggravation affects the sleep, and daytime sleepiness results.(Figs8,9)

## DISCUSSION

The first report using an objective evaluation on the sleep and breathing of allergic rhinitis patients was carried out by Lavie and others (6). Increase of nasal resistance due to allergic rhinitis increased micro-arousal on EEG, and they reported that the nasal resistance also influenced sleep. Furthermore, Young (7) and others pointed out that nasal obstruction was a factor in obstructive sleep apnea (OSA) during sleep, as shown by an epidemiological investigation. There is also a report that nasal obstruction influences sleep on its own. Udaka, Hiraki and others (8,9) showed that nasal obstruction without snoring influences sleepiness. Furthermore, nasal obstruction without allergic rhinitis influences sleepiness. In other words, these studies suggest that sleepiness may be directly caused by nasal obstruction, and not just because of sleep apnea as previously believed.

The study of allergic rhinitis has been conducted from the viewpoint of chronobiology as well. Reinberg (10) reported the rhythm of nose symptoms (sneezing, mucus, nasal obstruction, itch of the flower) in allergic rhinitis and compared symptoms during daytime with nighttime. He found that symptoms worsened during sleep, from sleep onset to morning. There are a few possible reasons why nose symptoms are aggravated during sleep: 1) More time asleep increases physiological nasal cavity resistance. 2) Night retention of nasal mucus, including antigen material. 3) Decline of sleeping cortisol level during the circadian rhythm. It is thought that 3 is related to the following reports. Aoyagi (11) and coworkers reported that histamine levels in the nasal mucus of allergic rhinitis patients early in the morning when getting up are significantly higher compared to the daytime. Furthermore, Bellia and others reported that urinary LT4 significantly increased in patients with nocturnal asthma during the night.

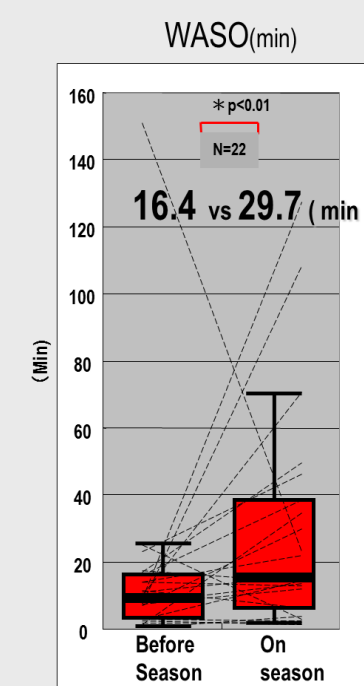
In other words an association between the condition of a patient and circadian rhythm of the allergic disease is pointed out. Furthermore, various mediators isolated in allergic rhinitis may influence the sleep/wake center. Krouse (13) and others report that Plasma IL1β, IL4, IL10 rise in the allergic rhinitis patients, and that REM sleep decreases. Interestingly, histamine, PGD2, etc. are known physiological substances that regulate sleep/wake rhythm, and resemble known mediators of allergic disease. Furthermore, it is reported that IL6 influences circadian rhythm and has some relationship with sleep(14). It is reported that some inflammatory mediators including TNF-α, IL-6, etc affect the sleep/wake center and are implicated as a disease sleep substance(15). Therefore, I think that a mediator with allergic disease specificity may influence sleep/wake regulation. However, there is no report yet, and details are unclear. As for the reason why allergic rhinitis influences sleep, these three following hypotheses are presented:

- 1) Nasal obstruction due to allergic rhinitis causes Obstructive Sleep Apnea, and as a result, a sleep disorder causes sleepiness.
- 2) Directly, nasal obstruction is related to sleepiness by obstructing the quality of the sleep (regardless of OSA).
- 3) Allergic disease by itself influences the sleep/wake center (through an inflammatory mediator) and causes a sleep disorder and sleepiness

All these hypotheses may further be affected by changes in brain chemistr due to circadian rhythm. Clearly, the relationship between nasal obstruction, allergic disease, sleep disorders, OSAS, inflammatory mediators and the sleep/wake center are not yet clear.

(Figure1)

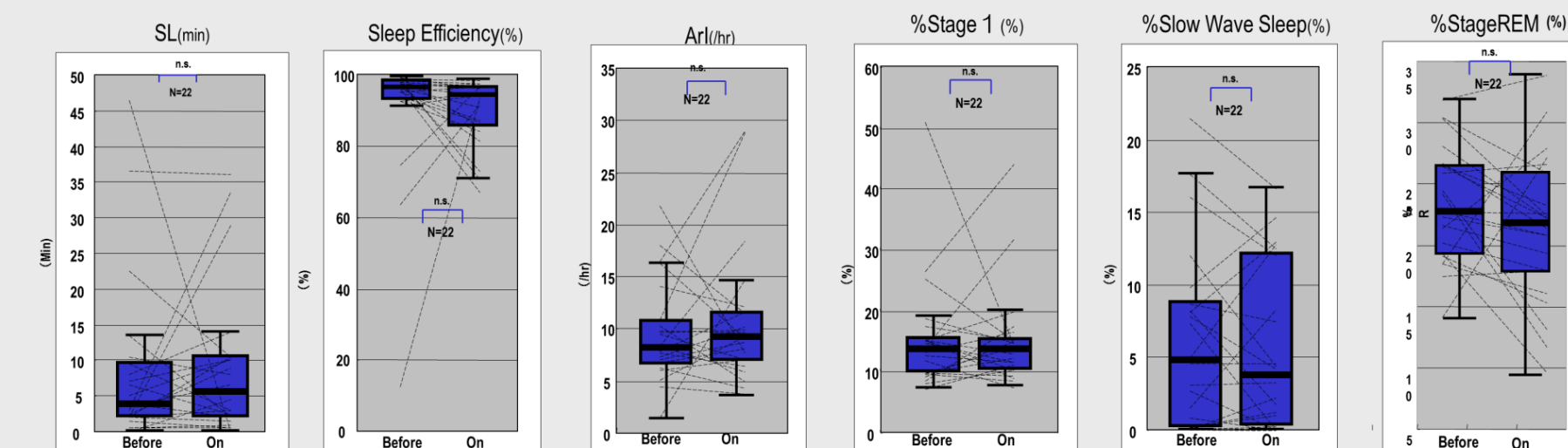
Sleep Architecture Between On & Off Season



WASO showed significant increase on season rather than off season.

(Figure2,3)

Sleep Architecture Between On & Off Season



There are no difference in most of sleep architecture between on and off season.

(Figure7)

Independent predictor of an increase in daytime sleepiness (Multivariate Logistic Regression analysis)

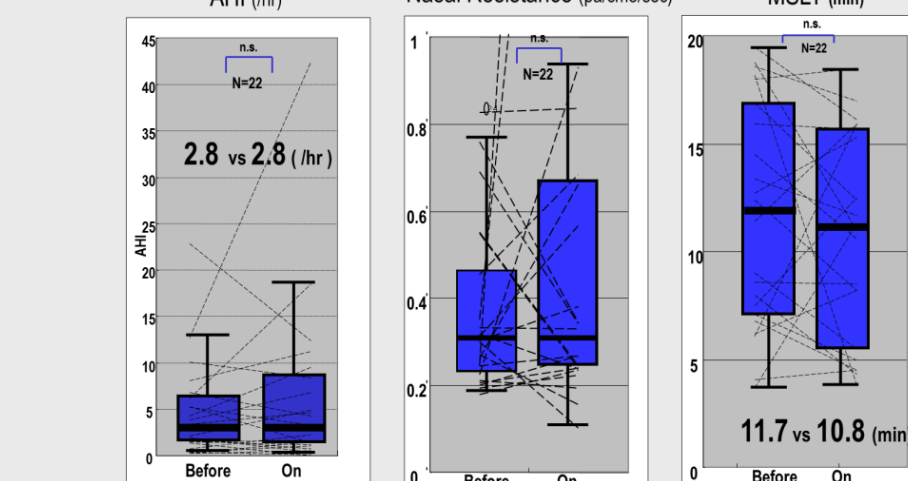
Dependent variables  
Whether Mean Sleep Latency Time increases at the on season or not?  
Independent variables (factor)  
Age, Sex, BMI, Sleep (PSG parameters), Nasal resistance:100pa(cm3/sec)

Variable	Sig	95% CI for Exp(B)	Predicted
Constant	536	.714	0 1 Correct
Nasal Resistance > 0.33 (Palcm3sec)	.036	12.6 (1.19-133.89)	00 7 1 87.5% (Sensitivity)
Constant	.536	.714	00 1 5 9 64.3% (Specificity)
Overall 72.7% (Accuracy)			

The strongest predictor of daytime sleepiness is Nasal Resistance  
The highest accuracy rate is 72.7% using this statistical model.  
(Sensitivity 87.5%, Specificity 64.3%)

(Figure4,5,6)

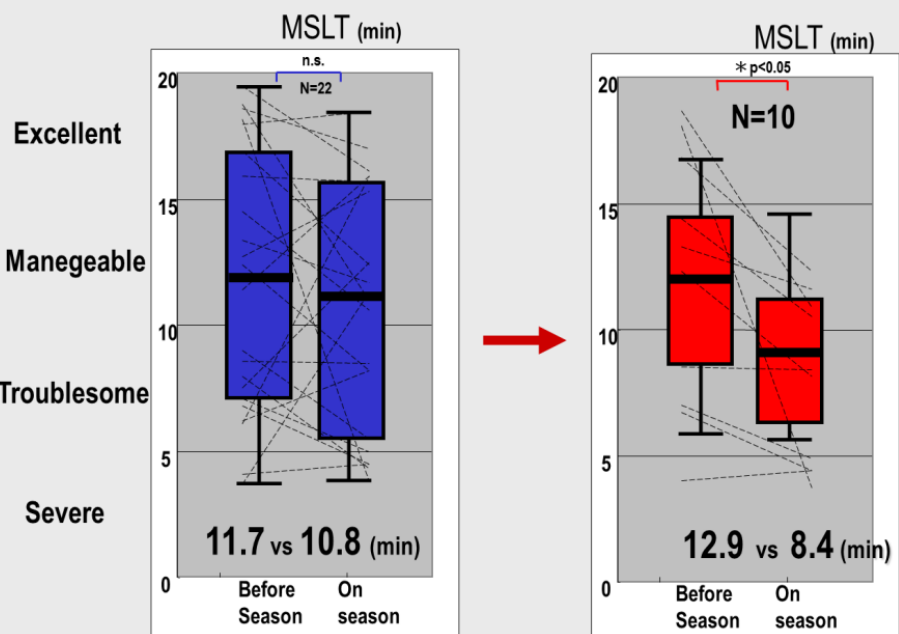
AHI, Nasal Resistance, MSLT Between Between On & Off Season



3 out of 22 without OSAS (AHI<10) in the screening test showed 10 or more AHI in the baseline examination. AHI did not change for the worse during on season except 2 case. In just 2 case, AHI increased (>15) on season. The mean sleep latency has decreased by 14 patients of 22.

(Figure8)

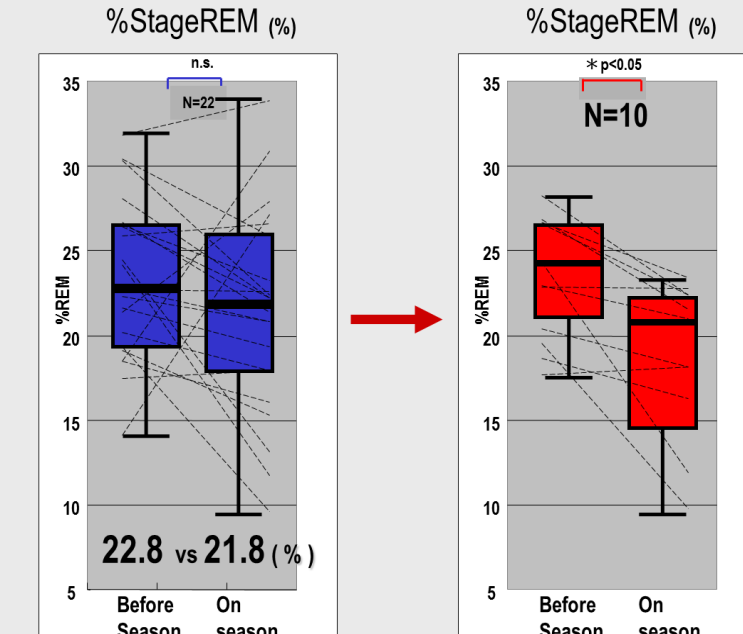
MSLT between Between On & Off Season



In patients with high nasal resistance, daytime sleepiness increased significantly.

(Figure9)

%REM Sleep Between On & Off Season



In patients with high nasal resistance, REM sleep decreased significantly, too.

## CONCLUSIONS

For some allergic patients, daytime sleepiness becomes worse overall during the on-season. The predictive factor of the sleepiness aggravation is nasal obstruction. Furthermore, in the high nasal resistance group, a significant decrease in REM sleep is showed during the on-season. Clearly, the relationship between nasal obstruction, allergic disease, sleep disorders, inflammatory mediators and the sleep/ wake center are not yet clear. Further study is needed.

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