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Comparison between Siriraj Mite Allergen Vaccine and Standardized Commercial Mite Vaccine by Skin Prick Testing in Normal Thai Adults

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SUMMARY House dust mite is a major cause of allergic asthma and rhinitis in Thai population. Skin prick test (SPT) is a useful tool for the diagnosis of the IgE-mediated reactions. The imported commercial mite vaccine for SPT is available but it is relatively expensive. Aim of this study is to compare Siriraj Mite Allergen Vaccine (SMAV) with standardized commercial mite allergen vaccine by skin prick testing in normal Thai adults. A double blind, self-controlled study between the SMAV and standardized commercial mite allergen vaccine was performed by SPT in 17 normal Thai adult males and non-pregnant or non-lactating females aged 18-60 years. The study showed that 35.29 % of non atopic adults had positive SPT reaction to Dp and Df of both SMAV and standardized commercial mite allergen vaccine. Mean wheal and flare diameters from SPT of Dp and Df of SMAV showed strong correlation with standardized commercial mite allergen vaccine (r = 0.768 and 0.897 in Dp and Df respectively, p <0.001). The intraclass correlation was also excellent (0.893 and 0.775 in Dp and Df respectively). There was no significant difference in wheal and flare diameter between SMAV and standardized commercial mite allergen vaccine. No systemic or large local reaction was found in any of the study cases.

Prevalence of allergic diseases, particularly asthma, allergic rhinitis and atopic dermatitis, has increased tremendously worldwide.[1] The study among Thai adult subjects showed asthma prevalence of 10%[2] and allergic rhinitis of 26%.[2,3] IgE-mediated hypersensitivity is the major immunopathogenetic basis for allergic diseases. Our former studies showed that up to 70% of asthmatic children[4] and 50% of asthmatic adults[5] in Thailand were sensitized to house dust mite (HDM), *Dermatophagoides pteronyssinus* (Dp) and *Dermatophagoides farinae* (Df). Skin prick testing (SPT) has been used since the turn of the 20th century to determine hypersensitivity reaction to allergens. The sizes of skin testing reactions (both wheal and flare) have been shown to correlate well with level of specific IgE to the same allergen.[6] SPT is inexpensive, reliable, rapid to accomplish and safe with relatively low systemic reactions.[7] However, SPT to standardized commercial mite vaccine was shown to be positive in 30 % of normal Thai children.[8]

The imported commercial mite (Dp and Df) allergen extracts for SPT are available but rather ex-

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pensive. Siriraj Mite Allergen Vaccine (SMAV) Development Project has been initiated under the subsidization from the Faculty of Medicine Siriraj Hospital to produce internationally accepted and standardized mite allergen vaccines for both diagnostic and therapeutic purposes. Before in-vivo study of SMAV skin testing in allergic patients, the study of SMAV safety and false positive reaction should be conducted in normal adult volunteers. The aim of this study is to compare SMAV with standardized commercial mite allergen vaccine by using skin prick testing in normal Thai adults.

MATERIALS AND METHODS

This is a double-blind, self-controlled study of the SPT reactivities from SMAV and standardized commercial mite allergen vaccine by skin prick testing in normal Thai adults. The study was conducted in Thai adult males and non-pregnant or non-lactating females aged 18-60 years. The subjects had no personal history or family history of atopic diseases, mite allergy or other systemic diseases. The number of subjects to be included was at least 15 based on the estimation of 30% false positive SPT in normal population, with allowable error of 20% and the one-sided 95% confidence interval.

The study was approved by Ethics Committee of Faculty of Medicine Siriraj Hospital, Mahidol University. After written informed consent was signed, medical history was reviewed and physical examinations (which included urine pregnancy tests in female volunteers) were performed. Oral antihistamine was not used at least 10 days before SPT.

SPT was done on the back with lancets by a well trained allergy technician with full medications and standby equipment for resuscitation. Each skin test was spaced 5 cm. apart. Wheal and flare responses were measured after 15 minutes by another well trained technician. Only one technician performed the test and another measured the result throughout the study. The study extracts were labelled in code to make them blinded to the subjects, tester and evaluator. The mean wheal and flare diameters were calculated (using the sum of the longest diameter and the diameter perpendicular to it divided by 2). A mean wheal diameter of at least 3 mm greater than the negative control was considered positive.[7] Each subject received 6 points of skin prick test ; positive control, negative control, SMAV Dp, SMAV Df, commercial Dp and commercial Df. The positive control was histamine hydrochloride (10 mg/ml) and negative control was 0.03% human serum albumin diluent. The SMAV and standardized commercial vaccines (ALK Laboratories, Port Washington, New York) which were available in Thailand contained 10,000 AU of Dp antigen and 10,000 AU of Df antigen. The patients were observed for possible side effects for 30 minutes after the tests and were assessed again 2 days after the test by telephone.

Statistical analysis

SPSS version 13.0 for Windows (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The wheal and flare of SMAV (both Dp and Df) were compared with standardized commercial mite vaccines by a paired t-test with 95% confidence interval. Pearson correlation was used to calculate the correlation between wheal and flare of SMAV and commercial vaccines. A p-value of less than 0.05 is considered statistically significant.

RESULTS

Seventeen normal adult volunteers without personal history or family history of atopy were included in this study. They were 2 males and 15 females. The mean age ± SD of the volunteers was 35.7 ± 12.33 years (24 - 58 years). There were no wheal nor flare in all negative control test with serum albumin. The positive control tests with histamine were all positive. The positive SPTs to Dp and Df of SMAV and commercial vaccine were found in 6 out of 17 adult volunteers (35.29%). All of the cases with positive SPT had positive SPT to Dp and Df of both SMAV and commercial vaccines. The mean wheal and flare diameter of Dp and Df of SMAV and standardized commercial mite allergen vaccine in asymptomatic sensitized subjects was shown in Table 1. Mean (SD) wheal diameter of Dp and Df of SMAV were 1.206 (-0.188 - 2.599) and 1.235 (-0.308 - 2.778) mm larger than those of commercial vaccine but no statistical significance was found, $p = 0.085$ and 0.109, respectively. Mean (SD) flare diameter of Dp and Df of SMAV were 1.941

Table 1 Mean wheal and flare diameter of *Dermatophagoides pteronyssinus* (Dp) and *D. farinae* (Df) of SMAV and standardized commercial mite vaccine in asymptomatic sensitized subjects (n = 6)

	Mean (mm)	**SD** (mm)	**Minimum-maximum** (mm)
Wheal			
Dp			
- SMAV	8.750	4.402	4.150 – 13.050
- Commercial	5.333	2.443	3.200 – 7.850
Df			
- SMAV	8.667	3.342	5.150 – 12.150
- Commercial	5.167	3.724	3.050 – 9.100
Flare			
Dp			
- SMAV	32.750	15.013	16.950 – 48.500
- Commercial	27.250	7.306	19.600 – 34.900
Df			
- SMAV	29.917	8.760	20.750 – 39.150
- Commercial	21.250	13.830	6.750 – 35.750

Dp = *Dermatophagoides pteronyssinus*
Df = *Dermatophagoides farinae*
SD = Standard deviation

(-2.357 - 6.239) and 3.059 (-2.072 - 8.190) mm larger than those of commercial vaccine but no statistically significance was found, $p = 0.353$ and 0.224, respectively.

The correlation between wheal diameter of Dp of SMAV and standardized commercial vaccines was 0.886 ($p < 0.001$) as shown in Fig. 1 and that of Df was 0.768 ($p < 0.001$) as shown in Fig. 2. The correlation between flare diameter of Dp of SMAV and standardized commercial vaccines was 0.897 ($p < 0.001$) and that of Df was 0.769 ($p < 0.001$). Intraclass correlation of mean wheal diameter of Dp was 0.893, 95 % CI interval 0.730 - 0.958 and mean wheal diameter of Df was 0.775, 95 % CI interval 0.431 - 0.911.

There were no systemic side effect and large local reaction in any of the volunteers in both acute and late phase reaction.

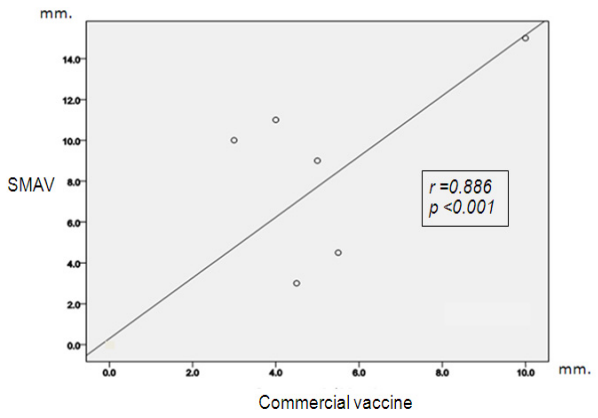

Fig. 1 Correlation between wheal diameter of *Dermatophagoides pteronyssinus* of SMAV and commercial mite vaccine in asymptomatic sensitized subjects.

DISCUSSION

Positive SPT to Dp and Df in normal adults from this study was 35.29 % which was comparable to 30 % in Thai children from previous study.[8] The previous study in adults showed that there were 12.5–67.5% of false-positive results using the house-dust mite or grass pollen allergen extracts.[9] The author stated that these might be due to contamination of the needle by another allergen vaccine and improper skin test method.[9] This result suggested that if the person had positive skin prick test to mite al-

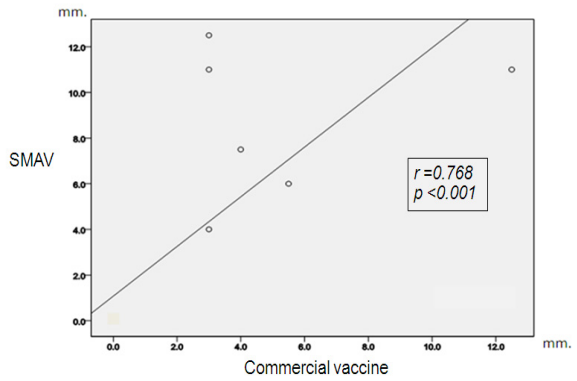

Fig. 2 Correlation between wheal diameter of *Dermatophagoides farinae* of SMAV and commercial mite vaccine in asymptomatic sensitized subjects.

lergen we should confirm the diagnosis of allergy by positive history and physical examination. On the other hand, we should follow the person that had no history of atopy but had a positive skin prick test because he might develop allergic symptoms in the future as shown by the previous studies in children and college students.[10-11]

The study showed strong correlation between wheal and flare diameters of Dp and Df of SMAV and standardized commercial mite vaccines. All of the cases that had positive SPT had positive SPT to both Dp and Df of both SMAV and the commercial vaccine.

Our study showed that there was no systemic side effect nor large local reaction in both acute and late phase reaction in all of the cases which was the same as the result of the previous studies.[12-15] A National Health and Nutritional Examination Survey in the United States in the period of 1976-1980 (NHANES II) demonstrated clearly that allergy skin testing in large number of population, did not cause any systemic reactions.[12] The rates for adverse reaction from allergy skin testing was 0.04% (95% CI, 0.01 - 0.08%). Recently, a large survey of skin testing and immunotherapy from the US demonstrated that fatality from allergy skin prick testing was reported in only one patient in a 12-year period.[13] The case was reported in 1987.[14] She was a young woman with allergic rhinitis, moderate persistent asthma, and food allergy and had a fatal anaphylactic reaction after the application of scratch tests to 90 food antigens. After that, no fatality from SPT was reported. To reduce risk of severe adverse reaction after skin test, the authors suggested that skin prick testing should be avoided in patients with uncontrolled asthma and the number of test antigens should be minimized in severe asthmatics.[13] The study in Thailand clearly demonstrated that among 5,879 patients who underwent 82,306 SPTs, no systemic reaction was observed.[15]

The results of this study suggested that SMAV could be used for SPT instead of using the more expensive imported commercial vaccine.

Conclusion

The study showed that 35.29 % of non atopic adults had positive SPT reaction to Dp and Df vaccines. No systemic or large local reaction was found in any of the study cases. There was no significant difference in wheal and flare diameter between SMAV and standardized commercial mite allergen vaccine.

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