

Comparison of skin reaction by skin prick testing and skin endpoint titration testing in the patients allergic to dust mites or cockroaches

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Objective : *To compare the results of skin reaction by skin prick testing and skin endpoint titration (SET) testing in the patients who were allergic to dust mites or cockroaches.*

Setting : *Rhinology-Allergy Clinic, Department of Otolaryngology, Faculty of Medicine, Chulalongkorn University.*

Subjects : *Thirty-four patients with symptoms of allergic rhinitis and allergy to dust mites (Der p or Der f) or cockroaches (Per a or Bla g).*

Research design : *Cross-sectional prospective study.*

Patients : *Thirty-four patients with symptoms of allergic rhinitis and allergy to dust mites (Der p or Der f) or cockroaches (Per a or Bla g) by skin prick test with the mean age of the fourteen men and twenty women was 33.18 years (ranged 17 - 53) were recruited into the study. The patients underwent skin tests, SET technique, for allergens they were allergic to.*

Method : *Results of skin prick reaction grading and endpoints of SET were measured, and their correlation were studied.*

Results : There were correlations between the grades of skin prick reaction and the endpoints of SET in the patients who were allergic to Der p and those who were allergic to Der f (the correlation coefficient = 0.762 : $p < 0.01$ and 0.748 : $p < 0.01$, respectively). The median endpoints of SET in the patients with 4+, 3+, 2+, and 1+ skin prick reactions to Der p were: 7, 5.5, 4, and 4, respectively; and to Der f : 7, 5, 4, and 3, respectively. Between the two groups of patients who were allergic to Per a and those who were allergic to Bla g, there were no correlations between the grades of skin prick reaction and the endpoints of SET (the correlation coefficient = .0396, and 0.36, respectively). The median endpoints of SET in the patients who were allergic to Per a or Bla g tended to be less than those who were allergic to Der p or Der f who had the same skin prick reaction grading.

Conclusion : According to SET, the beginning dose of immunotherapy with 0.05 ml of a 1:10,000 to 1:100,000 wt/vol concentration of Der p or Der f in the patients who have high skin prick reactions is too high and unsafe, and it is not potent enough in the patients who have low skin prick reactions. The grading of skin prick reaction cannot predict the endpoint of SET in the patients who are allergic to Per a and those who are allergic to Bla g.

Key words : Skin prick test, Skin endpoint titration, Allergic rhinitis.

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- วิธีการศึกษา-วัดผล** : ทำการวัดและรวบรวมผลของการตอบสนองทางผิวหนังด้วยวิธีสะกิดผิวหนังเป็นเกรดต่าง ๆ และผลของวิธี skin endpoint titration เป็น endpoint เบอร์ต่าง ๆ และศึกษาความสัมพันธ์ระหว่างเกรดของวิธีสะกิดผิวหนังและ endpoint ของวิธี skin endpoint titration โดยใช้สถิติ Spearman's rank correlation
- ผลการศึกษา** : ในผู้ป่วยที่แพ้ไรฝุ่นชนิด Der p และผู้ป่วยที่แพ้ไรฝุ่นชนิด Der f พบว่ามีความสัมพันธ์ระหว่างเกรดของวิธีสะกิดผิวหนังและ endpoint ของวิธี skin endpoint titration (correlation coefficient = 0.762 : $p < 0.01$ และ 0.748 : $p < 0.01$ ตามลำดับ) โดยค่ามัธยฐานของ endpoint ในผู้ป่วยที่มีผลการทดสอบทางผิวหนังด้วยวิธีสะกิดให้ผลบวกต่อ Der p เกรด 4, 3, 2 และ 1 เท่ากับ 7, 5.5, 4, และ 4 ตามลำดับ และในผู้ป่วยที่ให้ผลบวกต่อ Der f เท่ากับ 7, 5, 4 และ 3 ตามลำดับ ส่วนในผู้ป่วยที่แพ้แมลงสาบชนิด Per a และผู้ป่วยที่แพ้แมลงสาบชนิด Bla g พบว่าไม่มีความสัมพันธ์กันระหว่างเกรดของวิธีสะกิดผิวหนังและ endpoint ของวิธี skin endpoint titration (correlation coefficient = 0.396 และ 0.36 ตามลำดับ) อย่างไรก็ตามค่ามัธยฐานของ endpoint ในผู้ป่วยที่แพ้แมลงสาบมีแนวโน้มที่จะน้อยกว่าผู้ป่วยที่แพ้ไรฝุ่นเมื่อเทียบในเกรดเดียวกันของวิธีสะกิดผิวหนัง

สรุป

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เมื่อเปรียบเทียบกับวิธี *skin endpoint titration* ปริมาณยาที่เริ่มต้นฉีด สำหรับการทำภูมิคุ้มกันบำบัดด้วยขนาด 0.05 มล. ของ 1:10,000 ถึง 1:100,000 wt/vol ในผู้ป่วยที่แพ้ Der p หรือ Der f ที่มีเกรดของวิธีสะกิดผิวหนังสูง ๆ มีปริมาณมากเกินไป และไม่ปลอดภัย ส่วนในผู้ป่วยที่มีเกรดของวิธีสะกิดผิวหนังต่ำ ๆ ปริมาณยานี้อาจต่ำเกินไป ทำให้เสียเวลาในการฉีดโดยเปล่าประโยชน์ ส่วนในผู้ป่วยที่แพ้ Per a หรือ Bla g ไม่พบว่ามีความสัมพันธ์ของเกรดของวิธีสะกิดผิวหนัง และ endpoint ของวิธี *skin endpoint titration*

The traditionally accepted test for inhalant allergy is skin test, which may be conventionally done (skin prick with or without 1-2 dilution intradermal injection) or skin endpoint titration techniques. The skin prick testing is typically a first step in screening because it is a rather safe, rapid and easy technique. However, it is less sensitive and less reproducible but more specific than single-dilution intradermal test.⁽¹⁾ It is also considered that prick-puncture results better correlate with the patient's symptoms.⁽²⁾ Skin endpoint titration (SET) involves serial testing with several dilutions of the treatment allergen or mixture of allergens to identify the lowest dilution that produces a positive skin reaction. SET is a valid method for obtaining semiquantitative information about a person's sensitivity and for determining a safe beginning dose for immunotherapy. However, SET has some disadvantage, i.e., being time consuming and more difficult than the conventional technique.⁽³⁾ Immunotherapy can also be done, based on skin prick testing or SET. In the skin prick testing based immunotherapy, the positive and selected allergens are weekly injected, beginning with 0.05 ml of a 1:10,000 to 1:100,000 wt/vol concentration of allergen with the goal of achieving a maintenance dose of 0.50 ml of a 1:100 concentration.⁽⁴⁾ In SET based immunotherapy, the allergens are started with 0.05 ml of the endpoint and gradually increased to a maintenance dose similar to the conventional technique.⁽⁵⁾ SET allows the initiation of immunotherapy with a safe but relatively potent dose, and allows the beginning dosage for each positive responding allergen to vary, depending on its specific "endpoint".⁽³⁾

Due to the advantages and disadvantages of these two skin testing techniques for immuno-

therapy, we designed the study to compare the results of skin reaction by skin prick testing and skin end point titration techniques in the patients who were allergic to dust mites (*Dermatophagoides pteronyssinus* (*Der p*) or *Dermatophagoides farinae* (*Der f*) or cockroaches (*Periplaneta Americana* (*Per a*) or *Blattella germanica* (*Bla g*)) whether there are correlations between these two techniques.

Materials and Methods

Thirty-four patients with symptoms of allergic rhinitis and allergy to dust mites (*Der p* or *Der f*) or cockroaches (*Per a* or *Bla g*) by skin prick test, underwent skin testing for the allergens to which they were allergic by skin end point titration technique. The skin prick skin test was performed according to the method described by Demoly *et al.*⁽¹⁾ using disposable needle (25 gauge) whereas SET was performed according to the method of Dixon.⁽⁶⁾ The allergen extracts were manufactured by Greer Laboratories, Inc. The Spearman's rank correlation was used to determine the correlation between the skin spick reacting grading and the endpoint of SET.

Results

Thirty-four patients with symptoms of allergic rhinitis and allergy to dust mites (*Der p* or *Der f*) or cockroaches (*Per a* or *Bla g*) were recruited into this study. The mean age of the fourteen men and twenty women was 33.18 years (ranged 17 - 53). Twenty-nine patients were allergic to *Der p*; twenty-six were allergic to *Der f*; twenty were allergic to *Per a*; and twenty-two were allergic to *Bla g*.

In the group of twenty-nine patients who were allergic to *Der p*, five patients had skin prick reaction grade 1; nine grade 2; eight grade 3; and seven grade 4. In the group of twenty-six patients who were allergic to *Der f*, six patients had skin prick reaction grade 1; five grade 2; ten grade 3; and five grade 4. In the group of twenty patients who were allergic to *Per a*, four patients had skin prick reaction grade 1; five grade 2; ten grade 3; and one grade 4. In the group of twenty-two patients who were allergic to *Bla g*, five patients had skin prick reaction grade 1; six grade 2; ten patients 3; and one grade 4.

The results of endpoint from SET technique in each patient were shown in figure 1. The median endpoints of *Der p* in each skin prick reaction grading were as follows: grade 1 = 4 (ranged 3 - 5); grade 2 = 4 (ranged 2 - 5); grade 3 = 5.5 (ranged 4 - 6); grade 4 = 7 (ranged 6 - 7). The median endpoints of *Der f* in each skin prick reaction grading were as follows: grade 1 = 3 (ranged 2 - 5); grade 2 = 4 (ranged 2 - 5); grade 3 = 5 (ranged 4 - 6); and grade 4 = 7 (ranged 6 - 7). The median endpoints of *Per a* in each skin prick reaction grading were as follows: grade 1 = 2 (ranged 1 - 3); grade 2 = 3 (ranged 1 - 5); grade 3 = 3.5 (ranged 2 - 5); and graded 4 = 3. The median endpoints of *Bla g* in each skin prick reaction grading were as follows: grade 1 = 1 (ranged 0 - 2); grade 2 = 2.5 (ranged 1 - 5); grade 3 = 2.5 (ranged 1 - 4); and grade 4 = 2 (Table 1 and Figure 1).

The Spearman's rank correlation was used to determine the correlation between the grades of skin prick reactions and the endpoints of SET. The correlation coefficient of *Der p* is 0.762 ($p < 0.01$); *Der f*, 0.748 ($p < 0.01$); *Per a*, 0.396; and *Bla g*, 0.36.

Table 1. Median endpoint of skin and titration.

SPT grading	Allergen			
	<i>Der p</i>	<i>Der f</i>	<i>Per a</i>	<i>Bla g</i>
1	4	3	1	2
2	4	4	2.5	3
3	5.5	5	2.5	3.5
4	7	7	2	3

Discussion

In the patients who were allergic to *Der p* and those who were allergic to *Der f*, there were correlations between the grades of skin prick reaction and the endpoints of SET (the correlation coefficient = 0.762 and 0.748, respectively). This meant that the higher the grade of skin prick reaction, the higher was the predicted number of the endpoint of SET, shown in table 1. However, due to the median endpoints of SET in the patients with 4+ skin prick reactions to *Der p* and *Der f* were: 7 and 7, respectively (the dilution of allergens of endpoint #7 is 1:1,562,500 wt/vol and #6 is 1:312,500 wt/vol), the beginning dose of immunotherapy with 0.05 ml of a 1:10,000 to 1:100,000 wt/vol concentration of allergen in these patients was too high and unsafe. In the lower grades of skin prick reaction, the numbers of the endpoints were usually less than #5 (the dilution of allergens of endpoint #5, #4, #3, #2, and #1 were: 1:62,500, 1:12,500, 1:2,500, 1:500, and 1:100 wt/vol, respectively). Therefore, the beginning dose of immunotherapy with 0.05 ml of a 1:100,000 wt/vol concentration of allergen in these patients was not potent enough.

In the patients who were allergic to *Per a* and those who were allergic to *Bla g*, there was no correlation between the grades of skin prick reaction

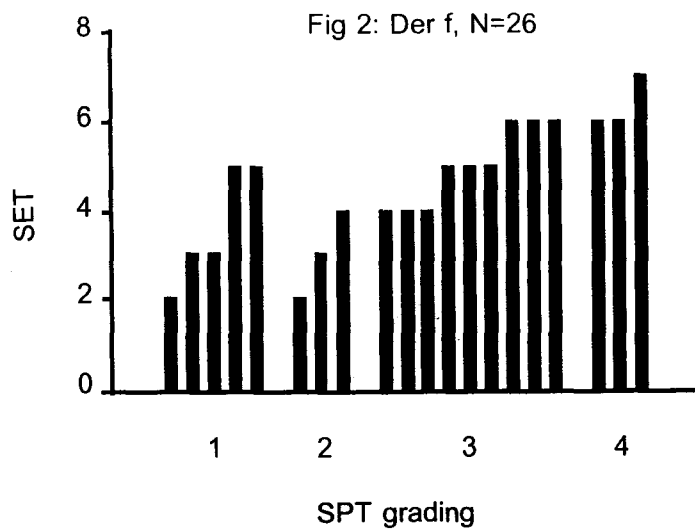
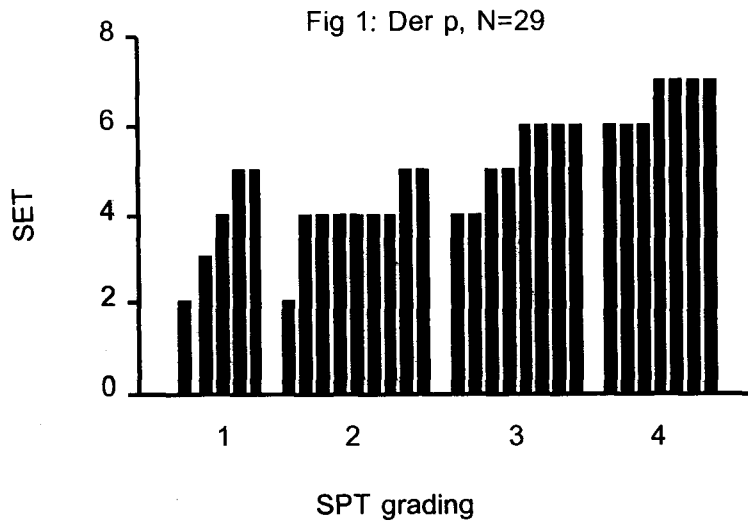


Figure 1. The results of endpoint from SET technique in each patient .

SET = Skin endpoint titration, SPT = Skin prick test, Der p = Dermatophagoides pteronyssinus, Der f = Dermatophagoides farinae, Per a = Periplaneta americana, Bla g = Blattella germanica

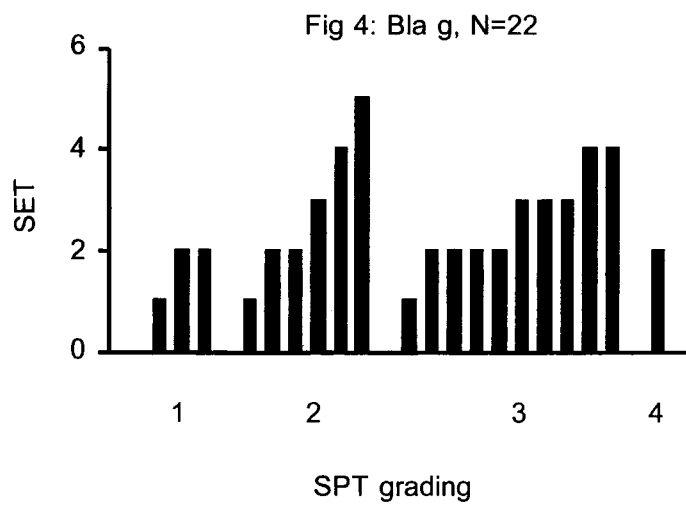
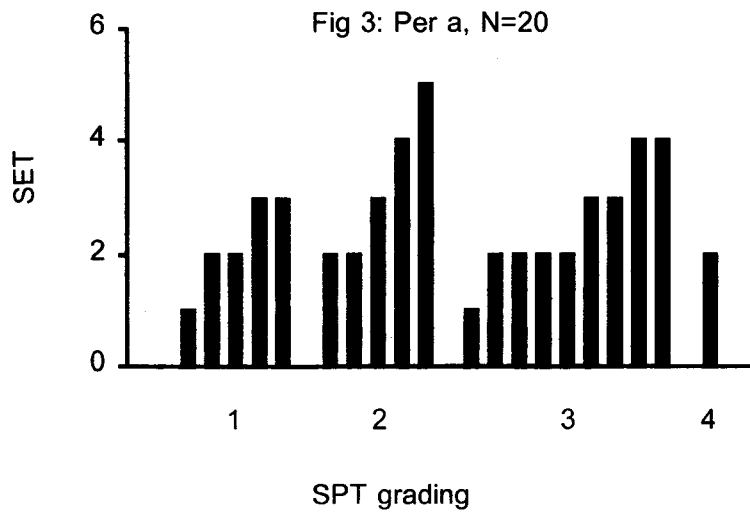


Figure 1. The results of endpoint from SET technique in each patient .

SET = Skin endpoint titration, SPT = Skin prick test, Der p = Dermatophagoides pteronyssinus, Der f = Dermatophagoides farinae, Per a = Periplaneta americana, Bla g = Blattella germanica

and the endpoints of SET (the correlation coefficient = 0.396, and 0.36, respectively). The grades of skin prick reaction could not predict the number of the endpoints of SET. The medians of endpoints of SET in the patients who were allergic to *Per a* or *Bla g* tended to be less than that of the patients who were allergic to *Der p* or *Der f* who had the same skin prick reaction grading (Table 1).

Due to the advantages and disadvantages of skin prick testing and skin endpoint titration testing for inhalant allergens that we mentioned above and the data from this study, we recommend the following:

1. Skin testing for inhalant allergens should start with skin prick testing as a screening skin test and as a guide to select allergens for immunotherapy.
2. SET should be performed in all selected allergens to determine the beginning dose for immunotherapy.

Conclusion

According to SET, the beginning dose of immunotherapy with 0.05 ml of a 1:10,000 to 1:100,000 wt/vol concentration of *Der p* or *Der f* in the patients who have high skin prick reactions is too high and unsafe, and it is not potent enough in the patients who have low skin prick reactions. The grades of skin prick reaction cannot predict the endpoint of SET in the patients who are allergic to *Per a* and to *Bla g*. However, the medians endpoint of SET tended to be less than that of the patients who were allergic to *Der p* or *Der f* who had the same skin prick reaction grading. Due to some advantage and disadvantage of the skin prick test and skin endpoint titration test for inhalant allergens and the data collected from this study, skin prick test should be used as a screening

skin test and as a guide for the selection of allergens for immunotherapy; and SET should be performed in all selected allergens to determine the beginning dose for immunotherapy.

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