

## Case Report

# Cockroach Cluster Immunotherapy with Anti-IgE (Omalizumab) versus Conventional Immunotherapy or Anti-IgE (Omalizumab) alone in Five Cases of Allergic Rhinitis with Asthma

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- Allergen Immunotherapy; Subcutaneous Immunotherapy Cluster Immunotherapy; Maximum Tolerance Dose; Maintenance Dose; Cockroach Allergy; Immunoglobulin E; Pulmonary Function Test; Anti-IgE; Omalizumab

**Abstract**

Cockroaches are the important source of proteins which causes Immunoglobulin E (IgE) mediated inflammation associated with high risk of exacerbation in Allergic Rhinitis with mild to moderate asthma.

We evaluated three cases on combined Anti-IgE (Omalizumab) along with effective dose of Cockroach allergens extract by Subcutaneous Cluster-Allergen- Immunotherapy compared to our fourth case on conventional-Subcutaneous Allergen Immunotherapy (SCIT) without Anti-IgE (Omalizumab). Our fifth case of persistent severe steroid-dependent Bronchial Asthma was given Omalizumab alone. We suggest that combination of Anti-IgE (Omalizumab) with Allergen Immunotherapy (AIT) is safe and well tolerated having synergistic effect. This approach results in better outcome to achieve rapid, maximum tolerance dose (MTD) and decrease in symptom and medication scoring with good quality of life.

**ABBREVIATION**

AIT: Allergen Immunotherapy; SCIT: Subcutaneous Immunotherapy; MTD: Maximum Tolerance Dose; MD: Maintenance Dose; PFT: Pulmonary Function Test; RCAT: Rhinitis Control Assessment Test; ACT: Asthma Control Test; PEF: Peak Expiratory Flow Rate

**INTRODUCTION**

The incidence of cockroach allergy is rising and is found in at least 30-40% of atopic patients. Bernton and Brown were the first to report positive skin tests to cockroach antigens in 44% of 755 allergy-clinic patients in 1964. In our country (India) cockroach sensitization was found in 8-26% of allergic patients in previous studies but recent report shows it to be 53% based on skin tests [1].

There are 4500 known species of cockroach commonly found in urban dwellings worldwide. Only 5 varieties, The American cockroach, German cockroach, Oriental (*Blatta orientalis*), Dusky or Smoky brown (*Periplaneta fuliginosa*) and Brown-banded (*Supella longipalpis*) are frequently found in homes and they potentially contribute to indoor allergens. The most common

domiciliary cockroach species are *Blattella Germanica* (Bla g 1, German Cockroach GC) and *Periplaneta americana* (Per a 1, American cockroach AC). GC is a small cockroach, approximately  $\frac{3}{4}$  of an inch in length (three quarters) which commonly infests houses in USA. AC is a large cockroach approximately two inches in length that infests houses, schools, hospitals and other large buildings. AC is less fertile than GC which requires higher temperatures and humidity for optimal population growth. GC is commonly found in cool and dry climates such as Europe and USA whereas the larger AC (35-53 mm vs 16 mm in length), prefers hot, humid conditions such as tropical countries eg. Thailand, Taiwan and Brazil [2].

Cockroach allergen is comprised of at least 10 groups of distinct proteins, including Bla g 1 and Per a 1 (midgut microvilli proteins) Bla g 2 and Per a 2 (Inactive aspartic proteases), Per a 3 (Arylphosphorin/ hemocyanin), Bla g 4 and Per a 4 (mole pheromone transport lipocalins, Bla g 5 and Per a 5 (glutathione-S-transferase), Bla g 6 and Per a 6 (Troponins), Bla g 7 and Per a 7 (Tropomyosin), Bla g 8 (myosin light chain), Bla g 9 and Per a 9 (arginine kinases), Per a 10 (Serine proteases). Among German cockroach, Bla g 1 and Bla g 2 are two major allergens that have been used as biomarkers of environmental exposure

in indoor environment [3]. Bla g 1 and/ or Bla g 2 allergen exposure of > 2 U/g of dust is thought to be a strong risk factor for cockroach sensitization and increased morbidity and high risk of exacerbation in Allergic Rhinitis and asthma symptoms [4,5].

Allergens are produced in the digestive tract and excreted with feces (group 1 and 2, Per a 3) or secretion from the male reproductive tract during sexual activity (Bla g 4 and Per a 4) and also from muscle proteins (group 6, 7 and Bla g 8). These Allergens become airborne in particles of 10-40 um in diameter, which may reach the lungs and induce IgE-mediated inflammation. Bla g 2 was able to induce IgE production at level of exposure 10-100 fold lower than cat and dust mite allergens. The proposed sensitizing threshold of Bla g 2 is 0.98 ug/g dust (2U/g) whereas those of mite group 1 and cat allergen are 2 ug/g dust and 8 ug/g dust respectively [6].

There is a high prevalence of co-sensitization to dust mite and cockroach allergens. Both usually share same indoor environment and some major allergens like tropomyosin involved in cross-reactivity among insects, mites, crustaceans, mollusks and parasites. Cockroach extracts used for diagnosis and treatment are still non-standardized because there is no immuno-dominant single allergen. It has been shown that the mean potency of three US German extracts was 3300 BAU/ml, whereas standardized mite, cat or grass extracts present typically 5000 to 100,000 BAU/ml. So mixture of five cockroach allergens Bla g 1 and Per a 1, Bla g 2, Bla g 4, Bla g 5 and Bla g 7 and or Per a 7 would be expected to diagnose 50% to 64% of cockroach allergic patients worldwide [7].

The diagnosis of cockroach allergy was based on using crude extracts by in-vivo skin testing (allergens by Allergo pharma, Germany) and/or in-vitro measurements of specific IgE (ThermoFisher, ImmunoCap) to cockroach and has distinct characteristics of perennial in nature, increased symptoms in winter season and may have steroid dependency [8,9].

Kang et al., completed a 5-year long trial of subcutaneous mix cockroach (German, American and oriental) extract Immunotherapy (a cumulative dose of 65,600 proteins nitrogen units over the 60-month trial), found reduction of symptom and medication scoring, an increase in cockroach specific blocking antibodies and blunted in-vitro basophil histamine release [10].

In 2011 Srivastava et al., completed a double-blind placebo-controlled trial of American cockroach immunotherapy in patients with Asthma, Rhinitis or both., they found significant reduction in symptoms and medication scoring as well as a reduction in Specific IgE and increase in cockroach specific IgG after 2 years of Immunotherapy with a lab prepared aqueous extract containing 3 mg/ml of protein from American cockroach [1].

In Cluster Immunotherapy the Allergen vaccine is injected two to three times in a day, 30 minutes apart at variable interval of 7-12 days, during build-up phase and maintenance doses can be achieved in 6 to 8 weeks. While in conventional Immunotherapy maintenance dose (MD) is achieved after 15 to 16 weeks [11]. Three of our patients took combined cluster immunotherapy along with injection Anti-IgE (Omalizumab), while fourth patient took conventional immunotherapy without

Anti-IgE (omalizumab). We found in three cases that combined Cluster Immunotherapy with Omalizumab is effective, rapid and safe treatment with effective MTD of 2.5 mg per dose than conventional Immunotherapy with dose adjustment of 1.5 mg per MTD and also concerned with risk of anaphylaxis.

Our fifth patient suffering from severe persistent steroid-dependent Asthma was given only Anti-IgE (omalizumab) along with avoidance measures has shown decreased intensity and severity along with controlled symptoms with reduction in the oral corticosteroids.

## CASE DISCUSSION

### Case number 1

23-year-old male, case of Chronic Rhinosinusitis with nasal polyps (recurrent episodes of shortness of breath, nose block and loss of smell, operated for nasal polyp in 2015) and Allergic Asthma since childhood poorly responding to symptomatic treatment. His symptoms get aggravated on exposure to dust, winter season and pollutants.

NCCT PNS (15.07.2017)- revealed near soft tissue opacification of paranasal sinuses represent? chronic sinusitis? fungal sinusitis. However, possibility of long-standing polyposis could not be ruled out.

In-vivo and In-vitro test: Skin Prick Test (SPT) - Total IgE- 2144.1 IU/ml, Absolute Eosinophil Count (AEC)-825 cells/UL, Serum cortisol-6.5 mcg/dL. Skin Prick Test (SPT) was positive for Cockroach-9 mm, D. pteronyssinus-4mm, D. farinae-4mm, Fish- 2mm.

Specific IgE were positive for Cockroach-20.40 Kua/l, D. pteronyssinus-3.60 Kua/L, D. farinae-4.21 Kua/l, Aspergillus fumigatus-1.38 Kua/l, Candid albicans-2.03 Kua/l, Fish 8.01 Kua/l.

### Recommendation

Combined Subcutaneous Cluster Allergen Immunotherapy (SCIT)- Cockroach, German 1:20 concentration (Greer Lenoir, NC US.) with effective dose along with Inj Omalizumab 150mg once a month was started by gradual up-dosing protocol of build-up phase to achieve MTD / Maintenance dose (2.5mg per month) given every 4 weeks with supportive therapy for 1 year. His nasal and respiratory symptoms were better controlled with normal Lung function and 5-10% variability by PEFr measurement. *Rhinitis Control Assessment Test* (RCAT) and *Asthma Control Test* (ACT) scoring improved from 11/12<sub>Baseline</sub> to 23/21 respectively. The patient is currently under follow-up and undergoing treatment.

### Case number 2

14-year-old male, case of persistent Bronchial Asthma (episodes of shortness of breath, cough and wheeze on and off) since childhood, very poor response to symptomatic treatment but some benefit with Oral Corticosteroids (OCS). His symptoms get aggravated on exposure to dust and in basement areas.

In-vivo and In-vitro test: Skin Prick Test (SPT)- Total IgE- 482.4 IU/ml. Absolute Eosinophil Count-426 cells/uL, Serum

cortisol-9.4 mcg/dl. Skin prick Test were positive for- cockroach-9mm, D. petronyssinus-4mm, D. farinae-4mm, Pennisetum-4mm, Prosopis juliflora-5mm, Brassica-5mm, Fish (cod)-<3mm.

Specific IgE were positive for Cockroach-2.38 Kua/l, D. petronyssinus-0.98 Kua/l, D. farinae-1.35 Kua/l, Common ragweed-0.27 Kua/l, Fish-<0.1 kua/L.

### Recommendation

He was given combined Subcutaneous Cluster Cockroach Allergen Immunotherapy (SCIT) with effective dose (2mg per month) by gradual up-dosing protocol of build-up phase to achieve MTD along with Inj Omalizumab 150mg once a month with supportive therapy for 2 years with no adverse effects. His symptoms are well controlled. His RCAT and ACT scoring improved after 6 months (Baseline=13/14) (22/21)\*

### Case number 3

24-year-old male, case of severe Allergic Rhinitis with perennial Bronchial Asthma (recurrent episodes of cough, wheezing, shortness of breath, and sneezing on and off) since 4 years. Symptoms exacerbate on exposure to dust, damp and dirty places.

In-vivo and In-vitro test: Skin Prick Test (SPT)- Total IgE-695.0 IU/ml, Absolute Eosinophil Count (AEC)-126 cells/uL, Serum Cortisol-6.2 mcg/dL. Skin Prick Test (SPT) were positive for Cockroach-6mm, D. pteronyssinus-4mm, D. farinae-4mm, Parthenium hysterophorus (Congress grass)- 5mm, Prosopis juliflora (Mesquite)-5mm, Fish (Cod)- <3mm.

Specific IgE were positive for Cockroach-7.98 Kua/L, D. pteronyssinus-0.64 Kua/l, D. farinae- 0.61 Kua/l.

### Recommendation

Combined Cockroach Subcutaneous Cluster Allergen Immunotherapy (SCIT) with effective dose 2.5mg per month along with Inj Omalizumab 150mg once a month was started by gradual up-dosing protocol of build-up phase to achieve MTD / Maintenance dose given every 4 weeks with supportive therapy for 1 year. His respiratory symptoms were stable with normal Lung function and 5% variability by PEFr measurement. RCAT and ACT scoring improved from 11/12<sup>Baseline</sup> to 23/22 respectively. PEFr increased from 300 L/mt to 600 L/mt.

### Case number 4

13 years old male, case of Allergic Rhinitis with mild to moderate Bronchial Asthma (cough, rhinitis, wheezing on and off) since childhood. Symptoms exacerbate on exposure to dust and pollutants and are more during the night. He was prescribed oral and inhaled corticosteroids with anti-histamines but had no relief.

In-vivo and In-vitro test: Skin Prick Test (SPT)- Total IgE-247 IU/ml, Absolute Eosinophil Count-502 cells/uL, Skin Prick Test were positive for Cockroach- 8mm, D. pteronyssinus- 5mm, D. farinae- 5mm, Fish- <3mm.

Specific IgE were positive for Cockroach-9.47 Kua/L and negative for D. pteronyssinus- <0.1 Kua/l, D. farinae- <0.1 Kua/l, Fish- <0.1 Kua/L.

### Recommendation

Subcutaneous Cockroach conventional Allergen Immunotherapy (SCIT) with effective dose (1.5mg per 0.3ml of 1:200/ month) was started by gradual up-dosing protocol of build-up phase to achieve MTD given every 4 weeks with supportive therapy for 2 years. Duration of Cockroach extract conc. (5mg ml<sup>-1</sup>) for conventional AIT (2 years) as per schedule (1:20000 X 6 weeks, 1:2000 X 6 weeks, 1:200 X 3 weeks) with increasing concentration) but developed adverse effect during build-up phase (grade II/ III anaphylaxis with 2mg of dose) so 1.5 mg per Maximum tolerance Dose (MTD) was continued for 2 years

His nasal and respiratory symptoms were better controlled with normal Lung function and 5-10% variability by PEFr measurement.

### Case number 5

48 years old female, case of Allergic Rhinitis with severe steroid dependent Asthma (recurrent complaints of cough, wheeze, sneezing, Rhinitis, shortness of breath on and off) since 4 years. She had taken multiple courses of oral and inhaled corticosteroids, anti-histamines, oral antibiotics with no relief. Symptoms get worsened on reducing methylprednisolone (8mg/day) and aggravated on exposure to dust and at the site of cockroach infestation.

In-vivo and In-vitro test: Skin Prick Test (SPT)- Total IgE-407 IU/ml, Absolute Eosinophil Count-120 cells/uL, Serum Cortisol-14.49 mcg/dl (16mg of methylprednisolone ) Skin Prick Test were positive for Cockroach- 8mm and negative for D. pteronyssinus-<3mm, D. farinae-<3mm, Fish- <3mm.

Specific IgE were positive for Cockroach-5.46 Kua/L, D. pteronyssinus- 0.51 Kua/l, D. farinae-0.34 Kua/l.

### Recommendation

Injection Omalizumab (Anti-IgE) 150 mg started every 4 weeks along with avoidance measures. AIT was relatively contraindicated because of poor lung function. The patient is currently under follow-up with low dose of oral corticosteroids (4mg and 8 mg of methyl prednisolone alternate day).

### DISCUSSION

Insect inhalant allergens are found indoors, outdoors, in homes and at work places. Cockroach allergen induce inflammation not only due to cockroach allergen themselves but also due to enzymatic protease activity & ligands for pattern recognition receptors. Skin testing using crude whole-body extracts of three common species: American, German and Oriental cockroach is the gold standard to diagnose cockroach allergy. In our five cases, diagnosis of cockroach allergy was based on SPT of 1:10 concentration (Greer Lab Inc) along with specific IgE (ThermoFisher, ImmunoCap). Allergen Immunotherapy practice parameter third update (AIPP) provides new dosing recommendation for non-standardized extracts distinguishing between pollen (0.5 ml of 1:100 or 1:200 vol/vol) and cockroach (highest tolerated dose) extracts [11]. So, effective dose of cockroach allergen extract is not known and it is not clear how

effective the treatment is for respiratory allergic diseases such as in Rhinitis or Asthma (evidence category C and evidence quality optional). Immunotherapy is clinically significant when a patient's symptom scoring is reduced by >30% [12].






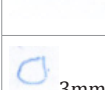

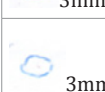

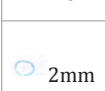
In our case number 4 we started conventional AIT with cockroach allergen extract (Greer Lab Inc) without Omalizumab for 2 years but patient got 2 episodes of grade II/ III anaphylaxis as per grading system recommended by European Academy of Allergy and Clinical Immunology (EAACI) at a dose of 2 mg during build-up phase [13]. Patient could tolerate Maximum Tolerance Dose (MTD) 1.5 mg per dose only. Though the patient responded to the conventional Immunotherapy with dose adjustment but concerned with risk of anaphylaxis, the subsequent doses were given under supportive therapy. Though the WHO recommends Allergen Immunotherapy should last for at least 3 years. In our case on conventional immunotherapy even though the efficacy was satisfying and clinically meaningful we could observe our patient for only 2 years because of the fear of adverse effects.

In view of concern regarding severe systemic reactions/ anaphylaxis during build-up phase in conventional AIT we started combination of Omalizumab (Anti-IgE) along with non-standardized cockroach extract in our three cases (case number

1, 2 and 3). We found administration of Omalizumab (Anti-IgE) is safe and effective we could achieve the effective tolerance dose of 2.5 mg as maintenance dose and reduce the risk of systemic reaction. We suggest that Omalizumab (Anti-IgE) is an added treatment option in those who failed to achieve the intended maintenance dose in conventional AIT because of severe systemic adverse effects. In our patients, combination treatment of Omalizumab and AIT resulted in prolonged inhibition of allergen-IgE binding compared with either treatment alone. Anti IgE (Omalizumab) is a humanized monoclonal anti-IgE antibody which suppresses the IgE mediated release of inflammatory mediators which that binds to circulating IgE molecules, thus interrupting the allergic cascade downstream the IgE production of B cells thus amplifying the therapeutic effect of AIT. Moreover, there is a long-term efficacy of combining Anti-IgE (Omalizumab) and Allergen Immunotherapy, as it might offer synergistic effects [14-16] (Table 1-5).

Our case number 5 of ACO (Asthma- COPD Overlap) has had history of frequent exacerbation and poor lung function (FEV1 <50% of predicted) in which AIT is relatively contraindicated. She was highly sensitized to cockroach, her symptoms get worse in winter season and were perennial in nature, was steroid




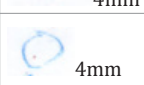


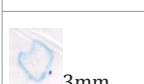
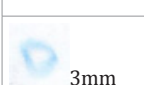
**Table 1 (a):** Clinical characteristics of case number 1.

	Case number 1						
	Aug 2016	Oct 2017					
<b>RCAT/ACT scoring</b>	11/12 <sub>Baseline</sub>	23/21					
<b>Total IgE</b>	2144 IU/ML	2612 IU/ml					
<b>Eosinophil % / AEC</b>	13.1 % / 825cells/ul	5.7% / 571 cells/ul					
<b>Serum cortisol</b>	6.5 mcg/ml on 5mg prednisolone	5.3 mcg/ml without prednisolone					
<b>PFER variability/ FEV1</b>	350/450 L/mt / 65% of predicted	500/550 L/mt / 78% of predicted					
	<b>SPT wheal size      Specific IgE</b>	<b>SPT wheal size      Specific IgE</b>					
	 6mm      N/A	 5mm      N/A					
	 9mm      20.40 kua/l	 5mm      12.6 kua/l					
	 4mm      3.60 kua/l	 3mm      <0.1 kua/l					
	 4mm      4.21 kua/l	 3mm      <0.1 kua/l					
	 3mm      8.01 kua/l	 2mm      <0.1 kua/l					
<table border="1"> <tr><td>Histamine</td></tr> <tr><td><b>Cockroach</b></td></tr> <tr><td>D. pteronyssinus</td></tr> <tr><td>D. farinae</td></tr> <tr><td>Fish (cod)</td></tr> </table>	Histamine	<b>Cockroach</b>	D. pteronyssinus	D. farinae	Fish (cod)		
Histamine							
<b>Cockroach</b>							
D. pteronyssinus							
D. farinae							
Fish (cod)							

**Table 1 (b):** AIT schedule of case number 1.

Doses (5mg ml <sup>-1</sup> )	0.05/0.1ml	0.1/0.2 ml	0.2/0.2 ml	0.2/0.3 ml	0.5 ml (2.5mg)	0.5 ml as MD
Cluster Dose frequency	First day	10-12 days	10-12 days	15-20 days	20-30 days	4-6 weeks
Combined Cockroach extract conc. (5mg ml <sup>-1</sup> , 1:200 conc.) for Cluster AIT (2 years) as per schedule along with Inj Omalizumab (150mg) X 15 days before AIT followed by once in a month for 17 months.						
MD-maintenance dose (2.5mg), conc.-concentration, AIT-Allergen Immunotherapy						

**Table 2 (a):** Clinical characteristics of case number 2.





		Case number 2	
		July 2014	June 2016
<b>RCAT/ACT scoring</b>		13/14 <sub>Baseline</sub>	22/21
<b>Total IgE</b>		482.4 IU/ML	441 IU/ml
<b>Eosinophil % / AEC</b>		3.2 % / 426 cells/ul	1.1% / 150 cells/ul
<b>PEFR variability/ FEV1</b>		200-250 L/mt/ 61% of predicted	300-350 L/mt / 75% of predicted
		<b>SPT wheal size</b>	<b>Specific IgE</b>
<b>Histamine</b>		5mm	N/A
<b>Cockroach</b>		9mm	2.38 kua/l
<b>D. pteronyssinus</b>		4mm	0.98 kua/l
<b>D. farinae</b>		4mm	1.35 kua/l
		<b>SPT wheal size</b>	<b>Specific IgE</b>
		5mm	N/A
		5mm	1.91 kua/l
		3mm	0.80 kua/l
		3mm	0.83 kua/l

**Table 2 (b):** AIT schedule of case number 2.

Doses (5mg ml <sup>-1</sup> )	0.05/0.1ml	0.1/0.2 ml	0.2/0.2 ml	0.2/0.2 ml	0.4 ml (2 mg)	0.4 ml as MD
Cluster Dose frequency	First day	10-12 days	10-12 days	15-20 days	20-30 days	4-6 weeks

Combined Cockroach extract conc. (5mg ml<sup>-1</sup>, 1:200 conc) for Cluster AIT (2 years) as per schedule along with Inj Omalizumab (150mg) X 15 days before AIT followed by once in a month for 10 months.  
maintenance dose (2 mg), conc.-concentration, AIT-Allergen Immunotherapy

**Table 3 (a):** Clinical characteristics of case numbe 3.

		Case number 3	
		April 2019	
<b>RCAT/ACT scoring</b>		11/12 <sub>Baseline</sub>	
<b>Total IgE</b>		695.0 IU/ML	
<b>Eosinophil % / AEC</b>		2.3 % / 126 cells/ul	
<b>PEFR variability/ FEV1</b>		450 /500 L/mts / 76% of predicted	
		<b>SPT wheal size</b>	<b>Specific IgE</b>
<b>Histamine</b>		5mm	N/A
<b>Cockroach</b>		6mm	7.98 kua/l
<b>D. pteronyssinus</b>		4mm	0.64 kua/l
<b>D. farinae</b>		4mm	0.61 kua/l

dependent (8mg of methylprednisolone) with high dose of Inhaled corticosteroids along with long acting B2 agonist or an alternate controller (leukotriene receptor antagonist or theophylline). Patient was started on Omalizumab every four weeks along with avoidance measures. She responded clinically with supportive

therapy after 16 weeks and low dose oral corticosteroids and is currently under follow-up. Lai et al in systemic review reported long term efficacy and safety of Omalizumab in patients with persistent uncontrolled allergic asthma [17,18].

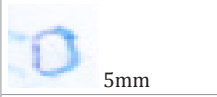
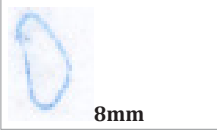


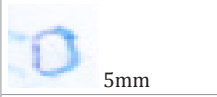
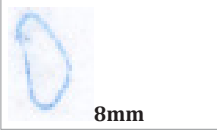










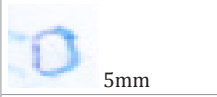
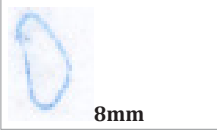








**Table 3 (b):** AIT schedule of case number 3.

Doses (5mg ml <sup>-1</sup> )	0.05/0.1ml	0.1/0.2 ml	0.2/0.2 ml	0.2/0.3 ml	0.5 ml (2.5 mg)	0.5 ml
Cluster Dose frequency	First day	10-12 days	10-12 days	15-20 days	20-30 days	4-6 weeks

Combined Cockroach extract conc. (5mg ml<sup>-1</sup>, 1:200 conc.) for Cluster AIT (1 year) as per schedule along with Inj Omalizumab (150mg) X 15 days before AIT followed by once in a month for 4 months.  
 maintenance dose (2.5 mg), conc.-concentration, AIT-Allergen Immunotherapy

**Table 4 (a):** Clinical characteristics of case number 4.




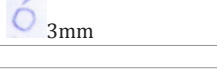



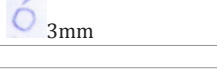



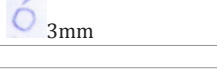
	Case number 4																					
	Jan 2006	May 2008																				
<b>RCAT/ACT scoring</b>	12 <sub>Baseline</sub> /11 <sub>Baseline</sub>	22/23																				
<b>Total IgE</b>	247.0 IU/ML	140 IU/ml																				
<b>Eosinophil % / AEC</b>	7 % / 502 cells/ul	3.5% / 150 cells/ul																				
<b>PEFR variability/ FEV1</b>	200-250 L/mt / 65% of predicted	400-450 L/mt / 78 % of predicted																				
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**Table 4 (b):** AIT schedule of case number 4.

Doses (5mg ml <sup>-1</sup> ) 1:200 conc.	0.1ml	0.2 ml	0.3 ml	0.3 ml	0.4 ml	0.3 ml (2mg) as MTD
Conventional Dose frequency	First day	7 days	7 days	7 days	Adverse reaction	Continued for 2 years

Conventional Allergen Immunotherapy with Cockroach extract conc. (5mg ml<sup>-1</sup>, 1:200 conc.) X 2 years as per schedule, got adverse reaction-anaphylaxis at 0.4 ml (Inj Adreanaline, anti-histamine and steroid given).  
 MTD-maximum tolerance dose (2.5 mg), conc.-concentration, AIT-Allergen Immunotherapy

**Table 5:** Clinical characteristics of case number 5.

	Case number 5											
<b>RCAT/ ACT scoring</b>	12/10 <sub>Baseline</sub>											
<b>Total IgE</b>	407 IU/ML											
<b>Eosinophil % / AEC</b>	2.5% / 120 cells/ul											
<b>PEFR variability/ FEV1</b>	250 L/mt , 350 L/mt after bronchodilator/ <50% of predicted											
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To summarize, our three cases (case number 1,2 and 3), indicate that the addition of Omalizumab as an adjunct to Cluster AIT, can have a greater reduction in symptom and medication scoring, is safe & effective than conventional AIT alone as in case number 4. In case number 5 of unstable steroid dependent severe Bronchial Asthma, Omalizumab (anti-IgE) decreases the severity and intensity of the disease as well as has steroid sparing effect.

## CONCLUSION

Combined Subcutaneous allergen immunotherapy (SCIT) with omalizumab is a paradigm shift in management of Allergic Rhinitis and mild to moderate asthma. In our three patients, combined cluster immunotherapy with Anti-IgE (Omalizumab) has shown marked reduction in symptoms, medication scoring and adverse effects during build-up phase compared to conventional immunotherapy. Moreover, omalizumab (Anti-IgE) alone represents the pivotal management for severe persistent steroid-dependent Asthma. However further studies and case-reports are needed to confirm these promising results.

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