



Differential Effects of Obesity on Eosinophilic vs. Non-Eosinophilic Asthma Subtypes

Seema Mukadam, Jamie Zacharias, Maria Paula Henao, Jennifer Kraschnewski & Dr Faoud Terrence Ishmael

To cite this article: Seema Mukadam, Jamie Zacharias, Maria Paula Henao, Jennifer Kraschnewski & Dr Faoud Terrence Ishmael (2017): Differential Effects of Obesity on Eosinophilic vs. Non-Eosinophilic Asthma Subtypes, Journal of Asthma, DOI: [10.1080/02770903.2017.1365886](https://doi.org/10.1080/02770903.2017.1365886)

To link to this article: <http://dx.doi.org/10.1080/02770903.2017.1365886>



Accepted author version posted online: 28 Aug 2017.



Submit your article to this journal [↗](#)



Article views: 22



View related articles [↗](#)



View Crossmark data [↗](#)

Seema Mukadam^a, Jamie Zacharias^b, Maria Paula Henao^c, Jennifer Kraschnewski^d, Dr Faoud Terrence Ishmael MD, PhD^e

Pennsylvania State University College of Medicine, Medicine, 500 University Dr, H171, Hershey, 17033 United States

^aCorresponding Author Email: smukadam1@hmc.psu.edu

^bCorresponding Author Email: jzacharias@hmc.psu.edu

^cCorresponding Author Email: mhenao@hmc.psu.edu

^dCorresponding Author Email: jkraschnewski@hmc.psu.edu

^eCorresponding Author Email: fishmael@hmc.psu.edu

Abstract

OBJECTIVE: Asthma is a heterogeneous disease composed of multiple disease subtypes. Obesity may worsen asthma, although the mechanism is poorly understood and its effects on different subtypes are not well characterized. We sought to determine whether obesity affects eosinophilic asthma differently from non-eosinophilic asthma. **METHODS:** Charts of 196 persistent asthmatics were reviewed. Subjects were categorized by BMI (obese ≥ 30 kg/m²) and blood eosinophilia based on two different cutoffs (≥ 200 or ≥ 400 cells/ μ l): eosinophilic, non-obese (E-NO), eosinophilic, obese (E-O), non-eosinophilic, non-obese (NE-NO), and non-eosinophilic, obese (NE-O). We analyzed clinical parameters across these groups to determine associations with obesity and/or eosinophilia. **RESULTS:** Obesity was highly prevalent in our population (50.5%, 99/196). The majority of asthmatics were female (75.5%), though the ratio was lower in the E-NO group (56%). The NE-NO group was associated with lowest asthma severity, lower atopy, and less medication use. Regardless of eosinophilia, obesity was associated higher ICS doses and lower FVC%-predicted than their non-obese counterparts. Obesity was associated with reduced FEV1% only in the non-eosinophilic group. Eosinophilia was also associated with reduced FEV1% in the non-obese subjects, but FEV1% was not further reduced in the E-O group compared to the E-NO and NE-O groups. Similar findings were observed regardless of whether the blood eosinophil cutoff was 200 or 400 cells/ μ l. **CONCLUSION:** Multiple clinical features of asthma are adversely affected by obesity, which may affect eosinophilic and non-eosinophilic subtypes differently.

Introduction

The relationship between asthma and obesity is emerging as a central issue, given the increasing prevalence of both diseases and their co-existence. Numerous studies have shown that the obesity rate in asthma is as high as 50%¹. Obesity in asthma has been associated with worse asthma control and increased need for higher doses of medications. The interrelationship between asthma and obesity is multifactorial. For example, use of systemic corticosteroids and inability to exercise because of asthma symptoms may both result in weight gain, while obesity can be associated with physiological changes in lung function (such as restriction), co-morbid diseases, and deconditioning². Furthermore, there is emerging data that obesity can affect the nature of asthmatic inflammation, which can alter disease control, severity, and response to treatment³. Multiple studies have shown that asthma control is often worse in obese patients, and that obesity tends to be associated with lower atopy^{4,5}. Veen et al. found that obesity in asthma was related to lower sputum eosinophil and FeNO levels⁶.

The interpretation of these studies is made increasingly difficult by the emergence of numerous distinct asthma phenotypes, which may reflect different pathophysiologies, clinical presentations, natural histories, and response to medications. Cluster analyses of clinical features of asthma have identified asthma phenotypes that vary with atopy, severity, eosinophilia, and medication use^{7,8}. Elevated blood eosinophil levels have been found to be correlated with worse asthma control and severe asthma exacerbations^{9,10}. Other studies have differentiated asthma subtypes using gene expression signatures and eosinophil levels to define “Th2-high” and “Th2-low” asthmatics¹¹. Th2-high asthma is characterized by atopy, high eosinophils, and response to corticosteroids. Th2-low asthma is associated with low atopy, low eosinophils, and a poor response to corticosteroids^{12,13}.

The presence of these asthma phenotypes raises the questions of whether obesity and sex affect these phenotypes differently. In a study by Leynaert, et al., females were shown to have a higher prevalence of asthma than males in the setting of non-allergic asthma, regardless of obesity¹⁴. It has been shown, however, that obesity is associated with non-allergic asthma, which may help to contribute to this underlying association with sex¹⁴. There is a crucial need to understand how all of these factors are related in asthma.

In this study, we sought to determine whether obesity differentially modified atopy, lung function, medication use, and asthma severity in eosinophilic vs. non-eosinophilic asthma subtypes. To better understand these relationships, we analyzed persistent asthmatics that presented to our asthma clinic and them into four groups: 1. eosinophilic, non-obese (E-NO), 2. eosinophilic, obese (E-O), 3. non-eosinophilic, non-obese (NE-NO), and 4. non-eosinophilic, obese (NE-O). The effects of obesity and eosinophilia on multiple markers of atopy, lung function, and medication use were studied. The findings and their implications are discussed herein.

Methods

Following University IRB approval, a retrospective electronic health record review was performed on all persistent asthmatics that presented to the specialty asthma clinic between July 2015 and

June 2016 (n = 196). The clinic is run by the Section of Allergy and Immunology in an academic setting at a tertiary care center, and sees patients from primarily rural and suburban settings. Patients were diagnosed with asthma based on clinical symptoms consistent with asthma, and evidence of airway hyper-reactivity in the past 5 years (increase in FEV1 of $\geq 12\%$ and 200 ml after bronchodilator or 4 weeks of anti-inflammatory treatment). Additionally, patients were determined to be mild, moderate, or severe asthmatics based on the NHLBI guidelines for classification of asthma severity¹⁵. Patients were classified as obese or non-obese based on a BMI cutoff of 30 kg/m², and eosinophilic using two different blood eosinophil levels, either ≥ 200 cells/ μ l or ≥ 400 cells/ μ l¹⁶⁻¹⁸. Clinical features collected included spirometry data (FEV1% predicted, FEV1, FVC, FVC% predicted, FEV1/FVC ratio), total inhaled corticosteroid (ICS) dose per day, total number of asthma controller medications, total number of allergens positive on a panel of either skin prick testing or ImmunoCAP testing to 17 relevant indoor and outdoor allergens in the Northeast U.S. (trees: maple, birch, oak, elm, ash, hickory; grass: timothy; weeds: ragweed, English plantain; cockroach; dust mites: dematophagoides farinae and pteronyssinus; animals: cat, dog, mouse; molds: alternaria, aspergillus, penicillium), blood eosinophils, and total IgE levels. Two tailed T-test was used to assess differences in two groups for continuous variables or Fisher Exact Test for categorical variables (significance cutoff of $p \leq 0.05$). For analysis across more than two groups, ANOVA with Tukey post-test for multiple comparisons was performed (significance cutoff of $p \leq 0.05$). Graphpad Prism v. 6.0 was used for all statistical analysis.

Results

Demographics

Of the 196 persistent asthmatics, 148 (75.7%) were female, and 50.5% were obese (Table 1). We categorized subjects as eosinophilic or non-eosinophilic using two different cutoff values, 200 cells/ μ l and 400 cells/ μ l. The higher cutoff of 400 cells/ μ l was based on recent studies that used this value¹⁹; whereas the eosinophil value of 200 cells/ μ l represents the median eosinophil value in our patient population. Age did not differ statistically across groups when using 200 cells/ μ l as a cutoff value, but the NE-O group was older than the NE-NO group when 400 cell/ μ l was used as the cutoff. We did not have data on age of asthma onset in our cohort. The race in our population was predominantly Caucasian, and stable across groups, as shown in Table 1.

There was a significant female predominance ($p = 0.009$) in all groups with the exception of the E-NO group, which was comprised of 56% males and statistically different from the other three groups (Table 1). These sex differences were similar in the NE-NO, NE-O and E-O groups.

We also compared asthma severity between the groups. Non-eosinophilic, non-obese subjects were the least likely to have severe asthma, and this trend held regardless of eosinophilic cutoff level.

Effect of Obesity on Lung Function

We next compared lung function across the four groups. The NE-NO subjects had the best lung function of the four groups (FVC% predicted, FEV1% predicted, FEV1/FVC ratio) (Table 1). The FVC% predicted was reduced in obese subjects in both the eosinophilic and non-eosinophilic ($p < 0.001$) groups to

a similar extent (Table 1). FEV1% was relatively preserved in the NE-NO group ($p = 0.010$), but decreased in the other 3 groups, indicating that both obesity and eosinophilia affected FEV1% (Table 1). Similarly, the FEV1/FVC ratio was lower in all groups compared to NE-NO. Interestingly, the eosinophilic obese group had a high FEV1/FVC ratio compared to the eosinophilic non-obese group. This higher FEV1/FVC ratio in the E-O subjects may be attributed to primarily to the low FVC in this group, which was lower than the other 3 groups.

We also assessed FEV1 reversibility with bronchodilator. All subjects had at least 12% reversal in FEV1 (and >200 ml increase) at least once at any point within the past 5 years to be included in the study. However, for our analysis, we used only those subjects with FEV1 reversal studies within a year of our study (138/196 subjects). Using the eosinophil cutoff of 200 cells/ μ l, we did not observe any effects of obesity in the non-eosinophilic (FEV1%change: NE-NO: 12.5 ± 12.84 vs. NE-O: 12.8 ± 10.3 , $p = 0.925$) or eosinophilic (E-NO: 19.6 ± 15.5 vs. E-O: 17.9 ± 12.4 , $p = 0.579$). There was a trend towards an increase in bronchodilator reversal with eosinophilia in the non-obese group (E-NO vs. NE-NO, $p = 0.065$). Similar trends were observed with the 400 cell/ μ l eosinophil cutoff: (FEV1%change: NE-NO: 14.6 ± 16.0 vs. NE-O: 15.5 ± 12.1 , $p = 0.768$; E-NO: 19.6 ± 10.2 vs. E-O: 17.4 ± 11.2 , $p = 0.531$).

Effect of Obesity on Controller Medication Use

A comparison of daily ICS doses among the four groups showed that the eosinophilic and non-eosinophilic obese subjects required a higher ICS doses per day than the non-obese groups (Table 1). Thus, regardless of the eosinophilic status, patients with obesity utilized higher doses of corticosteroids. However, whether or not the corticosteroids are effective in improving asthma outcomes in obese patients is unclear. Regarding the total number of required asthma controller medications, the NE-NO group had a lower requirement than the NE-O group, and this was seen for both the 200 and 400 cell/ μ l cutoffs. In the 400 cell/ μ l cutoff categorization, E-NO subjects also required less controller medication use than those in the E-O group.

Effect of Obesity on Atopy

Obesity did not affect the IgE level or number of positive aeroallergens in the eosinophil or non-eosinophilic groups, regardless of which eosinophil cutoff value was used. When using the 200 cell/ μ l cutoff, we found that the obese eosinophilic patients had a lower number of positive skin tests compared to non-obese eosinophilic patients (Table 1). However, this trend did not reach statistical significance when we used a cutoff of 400 cells/ μ l.

Discussion

Asthma is a heterogeneous disease that can be modulated by different factors. In our study, we found that non-obese, non-eosinophilic asthmatics were associated with the mildest and easiest to control asthma based on lung function, lower ICS doses/day, and less need for controller medications. Obesity was associated with worse clinical features of asthma, some of which were independent of eosinophil levels, while others differed depending on eosinophilic status. These factors may have important prognostic and

therapeutic implications that affect asthma management. The implications of these findings are associated herein.

Interestingly, the majority of our findings were similar regardless of whether we used a blood eosinophil cutoff of 200 cells/ μ l or 400 cells/ μ l. Given the observation that subjects with a blood eosinophil cutoff of 150 cells/ μ l respond to mepolizumab¹⁶, and the finding in our population that the median eosinophil value in persistent asthmatics was 200 cells/ μ l, eosinophilic asthma may be present in subjects with a lower blood eosinophil count than previously realized. However, this conclusion has to be taken with caution, as blood eosinophils may fluctuate over time and may not correlate completely with airway eosinophilia. In addition, obesity may alter trafficking of eosinophils to the lung, and this could be a confounder²⁰. Thus, while our findings suggest usefulness of blood eosinophil measurements at these cutoffs, findings will need to be validated with further studies.

Our observations regarding the increased utilization of ICS in obese asthmatics is consistent with published literature that showed an association between obesity and higher use of ICS, as well as reduced response to glucocorticoids in obese, asthmatic children²¹. Sutherland et al. found that these effects may in part be due to reduced activation of the signaling molecule MKP1, which is partially responsible for steroid responses²². It remains to be seen whether obese asthmatics need a higher dose of ICS to maintain control, or whether this class of medication is ineffective in this group of patients. It may also be necessary to consider that sub-phenotypes exist within obese asthmatics. Jeong et al. identified distinct obese asthma phenotypes when considering frequency of asthma symptoms and relationship to percent body fat²³. These studies suggest that a different treatment strategy may be needed in obese asthmatics and that we need better tools to characterize asthma in these patients.

In this study, there were a number of findings related to the relationship between lung function, obesity, and eosinophilia. The effect of obesity on reduction of FVC% may be explained by physiologic effects of obesity, where a reduction in vital capacity has been observed. As would be expected in this case, we saw an inverse relationship between FVC% and BMI in both eosinophilic and non-eosinophilic groups (Table 1). Furthermore, FEV1% was reduced by both obesity and eosinophilia, indicating that both are negative modifiers of lung obstruction. FEV1% was highest in NE-NO subjects (Mean $\pm$ SD, 81.7 $\pm$ 18.0%), and reduced by the presence of obesity in the NE-O group (76.8 $\pm$ 16.5%). The E-NO subjects had a greater reduction in FEV1% than NE-O subjects (69.6 $\pm$ 16.8% vs. 76.8 $\pm$ 16.5%), indicating that eosinophilia was a stronger negative modifier of FEV1%. Targeting eosinophilia may be a useful marker for treatment. Aziz-Ur-Rehman et al. showed that maintenance of sputum eosinophil counts less than 3% in severe, prednisone dependent asthmatics resulted in fewer exacerbations and better FEV1 preservation²⁴. This is consistent with our research that shows eosinophilia negatively affects asthma outcomes, in particular FEV1%. It will be interesting to see whether these strategies would be equally successful in managing obese eosinophil phenotypes. It is interesting that the combination of obesity and eosinophilia (using both 200 and 400 cell/ μ l cutoffs) did not have additional effects on reducing FEV1% further. It is possible that both processes affect a common pathway, such that the combination does not produce additive effects.

Both obesity and eosinophilia appeared to increase the need for multiple controller medications. In the non-eosinophilic group, approximately twice as many NE-O subjects needed >1 controller medication compared to NE-NO subjects. Eosinophilia was also a risk factor for medication utilization, as E-NO had a need for >1 controller medications compared to NE-NO. Surprisingly, the combination of obesity and eosinophilia did not increase the need for >1 controller medications further. It is possible that our sample size is too small to detect additive effects of obesity and eosinophilia for this measurement, that quantifying the number of controllers needed is not an adequate representation of difficult to control asthma, or that the combination of eosinophilia and obesity does not make asthma more difficult to control than either alone (along the lines of what we observed for FEV1%). Future studies will be needed to shed more light on this observation. Additionally, this raises the questions about how treatments should be targeted to individual patients for personalized medicine approaches. Stratifying patients by eosinophilia and allergic sensitization has been proposed as a phenotype-specific approach²⁵.

As such, we also analyzed the effect of obesity and eosinophilia on atopy to determine whether this approach would still be valid in obese asthmatics. Total IgE levels and number of subjects with aeroallergen sensitivity (at least one positive aeroallergen test) were not affected by obesity in the non-eosinophilic group. The main measure that suggested an interaction between obesity and atopy was the number of positive aeroallergen tests in patients with allergic sensitization. The E-O subjects had a lower number of positive aeroallergen tests (mean $\pm$ SD, 5.1 ± 3.5 vs. 7.2 ± 4.6) compared to the E-NO group in the 200 cell/ μ l cutoff (but not the 400 cell/ μ l cutoff). Thus, if there is an effect of obesity on atopy, it may be a small effect.

Regarding race and sex demographics, our population across all groups was predominantly Caucasian (Table 1). In regards to sex there was a significant predominance of females in our cohort (75%). This finding are consistent with recent findings by Greenblatt et al., who found that obesity was one of the strongest modifiable risk factors of asthma in women²⁶. The finding that the female predominance of asthma was decreased in the eosinophilic, non-obese group is interesting. There are indications that eosinophilia is in general more common in males¹⁸, and it is possible that obesity modifies this sex-specific effect.

Conclusion

In summary, the identification and classification of patients into different asthma phenotypes based on both objective testing as well as consideration of obesity and sex, could be an important step in individualizing asthma treatments in the future. Asthmatics that are obese or eosinophilic (and both) may require specific treatment plans, and emerging anti-eosinophil therapies may be an important consideration. However, it is important to point out there were a number of limitations in our study that could impact the interpretations of our findings. First, our sample size was relatively small, and this was a retrospective study based on a cross-sectional analysis of data from the initial presentation of asthmatics to our clinic. In addition, we did not have data on the age of asthma onset. Clearly, larger prospective studies are needed to address these concerns and to better understand the effects of obesity on asthma in the context of these phenotypes. Understanding these relations may be essential to predict asthma outcomes in certain groups and tailor phenotype-specific therapies.

Disclosure

The author reports no conflicts of interest in this work.

References

- 1 Novosad S, Khan S, Wolfe B, Khan A. Role of Obesity in Asthma Control, the Obesity-Asthma Phenotype. *J Allergy* 2013; **2013**: 1–9.
- 2 Abbas Q, Kooragayalu S, Vasudevan V, Vasudevan V, Shahzad S, Arjomand F *et al*. PFT pattern of restrictive ventilatory defect in obesity and its diagnostic value. *Chest* 2011; **140**: 684A–684A.
- 3 Leiria LOS, Martins MA, Saad MJA. Obesity and asthma: beyond TH2 inflammation. *Metabolism* 2015; **64**: 172–181.
- 4 Çelebi Sözen Z, Aydın Ö, Mungan D, Mısırlıgil Z. Obesity-asthma phenotype: Effect of weight gain on asthma control in adults. *Allergy Asthma Proc* 2016; **37**: 311–317.
- 5 Sutherland ER, Stream A, Lehman E, King T. Obesity And Disease Phenotypes In Mild-To-Moderate Persistent Asthma. American Thoracic Society, 2011, pp A2660–A2660.
- 6 van Veen IH, ten Brinke A, Sterk PJ, Rabe KF, Bel EH. Airway inflammation in obese and nonobese patients with difficult-to-treat asthma. *Allergy* 2008; **63**: 570–574.
- 7 Moore WC, Meyers DA, Wenzel SE, Teague WG, Li H, Li X *et al*. Identification of Asthma Phenotypes Using Cluster Analysis in the Severe Asthma Research Program. *Am J Respir Crit Care Med* 2010; **181**: 315–323.
- 8 Howrylak JA, Fuhlbrigge AL, Strunk RC, Zeiger RS, Weiss ST, Raby BA *et al*. Classification of childhood asthma phenotypes and long-term clinical responses to inhaled anti-inflammatory medications. *J Allergy Clin Immunol* 2014; **133**: 1289–1300, 1300.e1–12.
- 9 Zeiger RS, Schatz M, Li Q, Chen W, Khatri DB, Gossage D *et al*. High Blood Eosinophil Count Is a Risk Factor for Future Asthma Exacerbations in Adult Persistent Asthma. *J Allergy Clin Immunol Pract* 2014; **2**: 741–750.e4.
- 10 Price DB, Rigazio A, Campbell JD, Bleecker ER, Corrigan CJ, Thomas M *et al*. Blood eosinophil count and prospective annual asthma disease burden: a UK cohort study. *Lancet Respir Med* 2015; **3**: 849–858.
- 11 Woodruff PG, Modrek B, Choy DF, Jia G, Abbas AR, Ellwanger A *et al*. T-helper Type 2–driven Inflammation Defines Major Subphenotypes of Asthma. *Am J Respir Crit Care Med* 2009; **180**: 388–395.
- 12 Bhakta NR, Woodruff PG. Human asthma phenotypes: from the clinic, to cytokines, and back again: Cytokine-based asthma phenotypes. *Immunol Rev* 2011; **242**: 220–232.
- 13 Borish L. The immunology of asthma. *Ann Allergy Asthma Immunol* 2016; **117**: 108–114.

- 14 Leynaert B, Sunyer J, Garcia-Esteban R, Svanes C, Jarvis D, Cerveri I *et al.* Gender differences in prevalence, diagnosis and incidence of allergic and non-allergic asthma: a population-based cohort. *Thorax* 2012; **67**: 625–631.
- 15 Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma—Summary Report 2007. *J Allergy Clin Immunol* 2007; **120**: S94–S138.
- 16 Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A *et al.* Mepolizumab Treatment in Patients with Severe Eosinophilic Asthma. *N Engl J Med* 2014; **371**: 1198–1207.
- 17 Castro M, Zangrilli J, Wechsler ME, Bateman ED, Brusselle GG, Bardin P *et al.* Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet Respir Med* 2015; **3**: 355–366.
- 18 de Groot JC, Storm H, Amelink M, de Nijs SB, Eichhorn E, Reitsma BH *et al.* Clinical profile of patients with adult-onset eosinophilic asthma. *ERJ Open Res* 2016; **2**: 00100–2015.
- 19 de Groot JC, ten Brinke A, Bel EHD. Management of the patient with eosinophilic asthma: a new era begins. *ERJ Open Res* 2015; **1**: 00024–2015.
- 20 Desai D, Newby C, Symon FA, Haldar P, Shah S, Gupta S *et al.* Elevated Sputum Interleukin-5 and Submucosal Eosinophilia in Obese Individuals with Severe Asthma. *Am J Respir Crit Care Med* 2013; **188**: 657–663.
- 21 Forno E, Lescher R, Strunk R, Weiss S, Fuhlbrigge A, Celedón JC. Decreased response to inhaled steroids in overweight and obese asthmatic children. *J Allergy Clin Immunol* 2011; **127**: 741–749.
- 22 Sutherland ER, Goleva E, Strand M, Beuther DA, Leung DYM. Body Mass and Glucocorticoid Response in Asthma. *Am J Respir Crit Care Med* 2008; **178**: 682–687.
- 23 Jeong A, Imboden M, Hansen S, Zemp E, Bridevaux P-O, Lovison G *et al.* Heterogeneity of obesity-asthma association disentangled by latent class analysis, the SAPALDIA cohort. *Respir Med* 2017; **125**: 25–32.
- 24 Aziz-Ur-Rehman A, Dasgupta A, Kjarsgaard M, Hargreave FE, Nair P. Sputum cell counts to manage prednisone-dependent asthma: effects on FEV1 and eosinophilic exacerbations. *Allergy Asthma Clin Immunol* 2017; **13**. doi:10.1186/s13223-017-0190-0.
- 25 Terl M, Sedlák V, Cap P, Dvořáková R, Kašák V, Kočí T *et al.* Asthma management: A new phenotype-based approach using presence of eosinophilia and allergy. *Allergy* 2017. doi:10.1111/all.13165.
- 26 Greenblatt R, Mansour O, Zhao E, Ross M, Himes BE. Gender-specific determinants of asthma among U.S. adults. *Asthma Res Pract* 2017; **3**. doi:10.1186/s40733-017-0030-5.

Table 1 Demographics and clinical features of study population

	Eosinophil Cutoff of 200 cells/microliter						Eosinophil Cutoff of 400 cells/microliter					
	NE-NO (n = 52)	NE-O (n = 40)	p-value	E-NO (n = 45)	E-O (n = 59)	p-value	NE-NO (n = 72)	NE-O (n = 77)	p-value	E-NO (n = 25)	E-O (n = 22)	p-value
Age (Y), mean (SD)	43.1 (19.5)	49.6 (13.1)	0.07	45.0 (20.4)	49.8 (14.8)	0.169	44.7 (19.6)	50.6 (14.2)	0.0437	42.0 (20.6)	47.5 (14.0)	0.3013
Male/Female, (%female)	8/44 (85)	11/29 (73)	0.20	20/25 (56)	11/45 (80)	0.009	15/57 (79)	20/57 (74)	0.56	11/14 (56)	2/20 (91)	0.010
Race (White, Black, Hispanic, Other)	36,7,5,4	31,4,4,1		31,6,4,4	39,9,7,4		48,10,9,5	60,9,5,3		19,3,1,2	10,4,6,2	
BMI, mean (SD)	24.8 (3.7)	38.6 (7.4)	<0.001	25.5 (3.5)	38.4 (6.3)	<0.001	24.8 (3.8)	38.6 (6.6)	<0.001	26.1 (2.9)	38.2 (7.6)	<0.001
FVC%, mean (SD)	89.2 (14.9)	76.8 (16.5)	<0.001	84.3 (14.6)	73.1 (14.5)	<0.001	88.9 (14.3)	75.3 (15.6)	<0.001	81.4 (15.4)	67.5 (21.6)	<0.001
FEV1%, mean (SD)	81.7 (18.0)	70.7 (18.9)	0.010	69.6 (16.8)	66.9 (18.4)	0.770	80.3 (17.6)	70.1(18.5)	0.0013	64.3 (15.3)	67.5 (18.4)	0.556
FEV1/FVC, mean (SD)	0.76 (0.12)	0.72 (0.13)	0.140	0.66 (0.11)	0.73 (0.10)	0.002	0.74 (0.11)	0.73 (0.11)	0.64	0.63 (0.11)	0.71 (0.11)	0.029
ICS dose/day, mean (SD)	407 (383)	618 (328)	0.012	547 (392)	743 (334)	0.018	501 (213)	677 (350)	0.029	447 (280)	763 (315)	0.048
# needing >1 controller/total	15/52 (29%)	26/40 (65%)	0.001	23/45 (51%)	31/59 (52%)	.885	21/72 (29%)	36/77 (47%)	0.030	8/25 (32%)	15/22 (68%)	0.046
Eosinophils, mean (SD)	97 (47)	103 (50)	0.585	500 (297)	445 (280)	0.327	148 (95)	192 (108)	0.009	679 (292)	708 (312)	0.740
Total IgE, mean (SD)	341.7 (799.3)	349.9 (769.3)	0.9646	473.2 (942.7)	317.7 (422)	0.294	310 (674)	296.7 (591.0)	0.903	645.6 (1210.4)	448.0 (557.9)	0.515
Severe asthma, % (n)	6 (3)	32 (13)	0.002	29 (13)	37 (22)	0.529	8 (6)	30 (23)	<0.001	40 (10)	45 (10)	0.377
Aeroallergen Sensitivity, % (n)	54 (28)	65 (26)	0.29	70 (33)	73 (41)	1.00	57 (41)	64 (49)	0.503	80 (20)	86 (19)	0.142
For allergic subjects:												
Total # Allergens Tested Positive, mean (SD)	6.7 (5.2)	5.2 (3.3)	0.210	7.2 (4.6)	5.1 (3.5)	0.030	6.9 (5.0)	5.2 (3.5)	0.050	7.0 (4.7)	5.0 (3.3)	0.142
Pollen Sensitivity (%)	79	58		76	59		76	59		75	53	
Cockroach Sensitivity (%)	32	27		24	22		29	22		20	21	
Dust Mite Sensitivity (%)	61	77		88	66		63	69		95	65	
Animal Sensitivity (%)	61	65		76	68		66	67		70	60	
Mold Sensitivity (%)	32	27		39	27		32	29		40	27	

Downloaded by [University of Liverpool] at 11:13 14 September 2017