The effect of oral corticosteroids on circulating type-2 cytokine producing cells in patients with severe eosinophilic asthma

Gareth Hynes[1], Simei Go[1], Jian Luo[1,2], Rahul Shrimanker[1], Catherine Borg[1], Clare Connolly[1], Luzheng Xue[1] and Ian Pavord[1]

Respiratory Medicine Unit

University of Oxford

Nuffield Department of Medicine

Introduction

Oral corticosteroids are an important treatment for severe eosinophilic asthma and feature prominently in international guidelines for the management of asthma.[1]

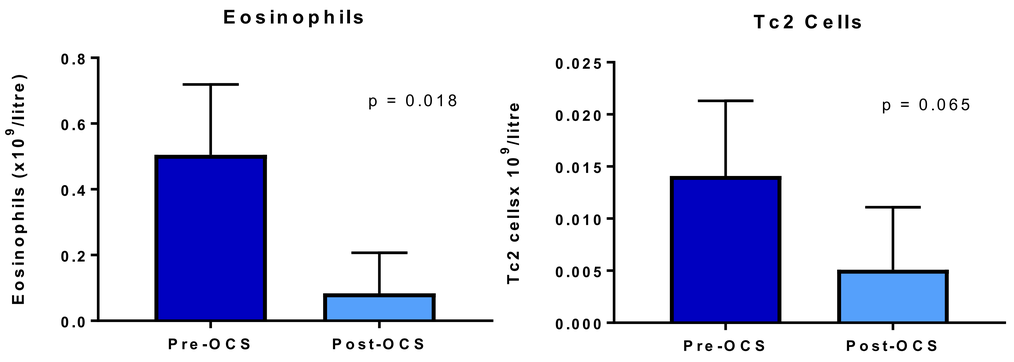
It has been hypothesised that type-2 cytokine producing cells including helper T cells (Th2), cytotoxic T cells (Tc2) and innate lymphoid cells (ILC2) are key drivers of severe eosinophilic asthma.[2] However the effect of oral corticosteroids (OCS) on the circulating levels of these type-2 cytokine producing cells is unknown.

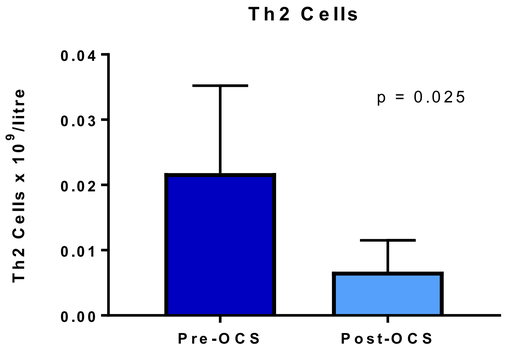
Methods

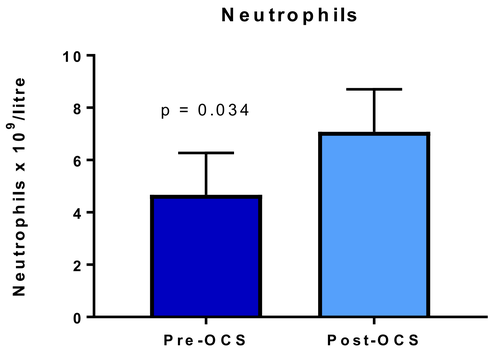
Oral corticosteroid-naïve patients with eosinophilic inflammation were identified in our severe asthma clinic in Oxford, UK. These patients were invited to attend for assessment before commencing and followed up directly after a course of oral prednisolone at a dose of 30mg daily.

Clinical measurements including spirometry, sputum cell differential count, fractional exhaled nitric oxide (FeNO) and asthma symptom scores were collected, and whole blood was assessed by flow cytometry.

Results







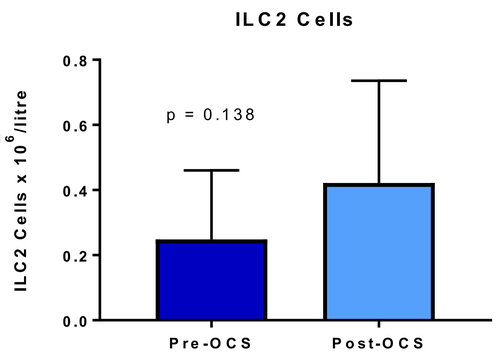


Figure Legend

Graphs show mean number of circulating immune cells as identified by flow cytometry. Error bars represent standard deviations around the mean.

Th2 – type 2 helper T cells;
Tc2 – type 2 cytotoxic T cells;
ILC2 – innate lymphoid cell type 2.

Six patients (4 female) were assessed. The mean age was 57.5 years. The median inhaled beclomethasone dipropionate equivalent dose was 1600 micrograms per day and median duration of prednisolone was 11 days.

Patients clinically improved after treatment with a mean forced expiratory volume in one second (FEV1) improvement of 0.2 litres, a mean FEV1 % predicted improvement of 11%, a mean 5-point asthma control questionnaire (ACQ-5) improvement of 0.9 points and a mean FeNO improvement of 20 parts per billion.

Measured by flow cytometry peripheral blood eosinophil counts fell from 0.51 to 0.1 x 10^9/litre (p=0.018), neutrophils increased from 4.67 to 7.08 x 10^9/litre (p=0.034), Th2 cells fell from 0.0218 to 0.0067 x 10^9/litre (p=0.025), Tc2 cells fell from 0.0141 to 0.0051 x 10^9/litre (p=0.065) and ILC2 cells increased from 0.248 to 0.429 x 10^6/litre (p=0.138).

Flow cytometry analysis was performed on FlowJo v10 (Oregon, US), and statistical analysis on Graphpad Prism v7 (La Jolla, US).

Conclusion

In our patients with severe eosinophilic asthma a course of oral corticosteroids resulted in clinical improvement and a decrease in circulating eosinophils, Th2 cells and Tc2 cells. ILC2s however remained unchanged.

This suggests that ILC2s are resistant to oral corticosteroids and given the clinical improvement seen after corticosteroid treatment this cell type may not be a significant driver of eosinophilic inflammation in our cohort of patients with severe eosinophilic airways disease.

References

1. Global Initiative for Asthma: Global strategy for asthma management and prevention. Global Initiative for Asthma (2018).

2. Brusselle, G. et al. Eosinophils in the spotlight: eosinophilic airway inflammation in nonallergic asthma. Nat. Med. 19, 977–979 (2013).

Affiliations

1. Respiratory Medicine Unit, Nuffield Department of Medicine, and Oxford Respiratory NIHR BRC, University of Oxford.

2. Department of Respiratory and Critical Care Medicine, West China School of Medicine and West China Hospital, Sichuan University, China.

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