Name of Sponsor/Company
University of Dundee

Title of Study
Reversibility of Acute β-Blocker Induced Bronchoconstriction

Investigators
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Study centre(s)
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Publication (reference)
SHORT PM, WILLIAMSON PA, LIPWORTH BJ. Sensitivity of impulse oscillometry in beta-blockers induced bronchoconstriction and beta-agonist bronchodilation in asthma. Ann Allergy Asthma Immunol 2012;109:412-415

Date of first enrolment	**Phase of development**
13/04/2010 **Date of last completed** 16/09/2010	Phase IV

Objectives
To compare the sensitivities of IOS and spirometry in assessing bronchoconstriction to propranolol and bronchodilation with salbutamol.

Methodology
Patients with mild-to-moderate persistent stable asthma taking 1,000 µg/day or less beclomethasone dipropionate equivalent received 10 or 20 mg of oral propranolol followed by histamine challenge, with recovery to nebulized salbutamol (5 mg). Spirometry and IOS were measured before and 2 hours after beta-blocker, post histamine, and 20 minutes post-salbutamol.

Number of patients planned
Sufficient to complete 14 per protocol

Number of patients analysed
13

Diagnosis and main criteria for inclusion
Mild-to-moderate, persistent, stable asthma taking ≤ 1,000 µg/day BDP equivalent of inhaled corticosteroids. FEV_1 > 80% predicted. Aged 18 to 65 years. Airway hyper-responsiveness to histamine challenge. Non-smoker.

Test product dose

10 mg oral Propranolol
20 mg oral Propranolol

Duration of treatment
2 – 3 weeks (single dose of 10mg or 20 mg of oral Propanolol administered at 2 separate study visits)

Reference therapy
N/A

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Criteria for evaluation

Primary Endpoint
Change in FEV_1 (ml) post-salbutamol post-histamine challenge

Secondary Endpoints
Full Spirometry and IOS pre and post challenge, Staged recovery with bronchodilator therapy post histamine challenge, Serum K+, brain derived neurotrophic factor (BDNF), eosinophil derived neurotoxin (EDN), and cyclic adenosine monophosphate (cAMP), β2 genotyping, blood pressure and heart Rate.

Statistical methods
Data were analyzed for normality with Shapiro-Wilk tests and Boxplots. Pre vs post percentage change (95% CI) values were calculated and compared with paired Student *t*-tests for spirometry and IOS indices after bronchoconstriction to propranolol and bronchodilatation to salbutamol. Standardized response means (SRM) were also calculated. All statistical analyses were performed using SPSS version 17.

Summary Conclusions

Results
Thirteen participants (mean age, 34 years) completed the protocol. Eleven participants received 20 mg of propranolol: 2 received 10 mg, because this dose caused more than 10% decrease in forced expiratory volume in 1 second (FEV_1) on the test-dose algorithm. All IOS indices (R5, R5-R20, AX, RF) showed significant worsening of airways resistance or reactance to propranolol. FEV_1 but not FEF25-75 showed significant deterioration after beta-blocker (mean percent change, 4.6% and 6.2%). The magnitude of change was consistently higher for parameters of IOS, with the largest change being observed with R5 and RF (mean percent change, 30.8% and 39.4%). The SRMs for IOS outcomes were better than for spirometry. All measures of lung function showed significant bronchodilator response, with the best SRMs seen in R5 and RF.

Conclusion
IOS is a more sensitive response outcome than spirometry with respect to bronchoconstriction to oral propranolol and bronchodilatation after salbutamol in patients with mild to moderate asthma.

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