Name of Sponsor/Company
University of Dundee

Title of Study
Evaluation of beta-blockers for the treatment of asthma. A randomised controlled trial of propanolol.

Investigators
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Study centre(s)
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Publication (reference)
SHORT PM, WILLIAMSON PA, ANDERSON WJ, **LIPWORTH BJ**. Randomised placebo controlled trial to evaluate chronic dosing effects of propranolol in asthma. **Am J Respir Crit Care Med** 2013;187:1308-1314

Date of first enrolment	**Phase of development**
09/04/2010	Phase II
Date of last completed	
16/03/2012	

Objectives
To establish effects of chronic dosing with 'beta-blockers' on airway tone and hyper-reactivity in mild Asthmatics.

Methodology
A double-blind randomized placebo-controlled crossover trial of propranolol in patients with mild-to-moderate asthma receiving ICS was performed. Participants underwent a 6- to 8-week dose titration of propranolol or placebo as tolerated to a maximum of 80 mg per day. Tiotropium was given for the first 4 to 6 weeks of each treatment period.

Number of patients planned
20 enrolled to complete 15

Number of patients analysed
18

Diagnosis and main criteria for inclusion
Stable, methacholine responsive (PC_{20} < 8 mg/mL), mild-to-moderate asthmatics receiving $\leq$ 1000 µg/day of ICS (BDP equivalent).

Test product dose
Arm A
Propanolol 10 mg BD (1 week)
Propanolol 20 mg BD (1 week)
Propanolol 80 mg SR OD (4 weeks)

Arm B
Placebo Propanolol 1 tab BD (1 week)
Placebo Propanolol 2 tabs BD (1 week)
Placebo Propanolol 1 tab OD (4 weeks)

Duration of treatment
12 weeks (2 treatment periods of 6 weeks)

Reference therapy
Placebo Propanolol (see Test Product Dose)

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Criteria for evaluation

Primary Endpoint
Methacholine PC_{20}

Secondary Endpoints
Histamine challenge, pulmonary function, mini-asthma quality of life questionnaire (mini-AQLQ), and asthma control questionnaire (ACQ).

Statistical methods
Data were assessed for normality with the Shapiro-Wilk test and box plots.

For all outcomes, comparisons were made by a multifactorial analysis of variance model, including sequence, visit, treatment, and patient effects, with Bonferroni corrections for pairwise comparisons.

All analysis was performed using SPSS version 18.

Summary Conclusions

Results
No significant difference was observed in methacholine or histamine challenge after exposure to propranolol versus placebo. For methacholine challenge, the doubling dilution difference was 0.04 (95% confidence interval [CI], 20.56 to 0.63), P = 0.89. Albuterol recovery at 20 minutes after histamine challenge was partially attenuated by propranolol versus placebo: FEV_1% mean difference, 5.28 (95% CI, 2.54–8.01), P = 0.001.

After chronic ß-blockade there was a small worsening in FEV_1% predicted of 2.4% (95% CI, -0.1 to 4.8), P = 0.055. No difference was found for ACQ or mini-AQLQ.

Conclusion
This is the first placebo-controlled study to assess the effects of chronic nonselective b-blockade in asthma, showing no significant effect of propranolol compared with placebo on either methacholine or histamine airway hyper-responsiveness and no change in ACQ or AQLQ.

Date of the report: 03/08/2015