Name of Sponsor/Company
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Title of Study
A Proof of Concept Study to Investigate the Potential Role of Acetylsalicylic Acid (Aspirin) as an Anti-Inflammatory Agent for the Treatment of Asthma

Investigators
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Study centre(s)
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Publication (reference)
MENZIES D, NAIR A, MELDRUM KT, HOPKINSON P, LIPWORTH BJ. Effect of aspirin on airway inflammation and pulmonary function in patients with persistent asthma. J Allergy Clin Immunol 2008;121:1184-1189

Objectives
To establish the effect of aspirin on pulmonary inflammation and function in patients with persistent asthma

Methodology
After withdrawal of their usual anti-inflammatory medication, patients with mild-to-moderate persistent asthma undertook double-blind, randomized, crossover treatment with 75 mg/day aspirin and placebo for 3 weeks each. Treatment evaluation included histamine challenge, spirometry, impulse oscillometry, total and alveolar exhaled nitric oxide measurement, and serum thromboxane B2 and 15-epilipoxin A4 levels.

Number of patients planned
A total of 20 subjects to be randomized to ensure that 14 complete the protocol

Number of patients analysed
15

Diagnosis and main criteria for inclusion
Adult (>18 years), patients with mild-to-moderate persistent asthma, FEV_1 > 60% predicted, on daily ICS dose of $\leq$ 1000 mcg/day BDP. Patients with reported NSAID or aspirin hypersensitivity, past or present GI hemorrhage and ulcers, or unstable asthma requiring oral corticosteroids in the 3 months before trial commencement were excluded from participation. Before entering the trial, each participant underwent a modified oral aspirin challenge to ensure they exhibited no features suggestive of aspirin intolerance.

Test product dose

Aspirin 75 mg + Ranitidine 300 mg daily (3 weeks)

Placebo 1 tab + Ranitidine 300 mg daily (3 weeks)

Duration of treatment
6 weeks (2 treatment periods of 3 weeks)

Reference therapy
Placebo (see Test Product Dose)

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Primary Endpoint
Change in the concentration of Histamine causing a 20% fall in FEV_1 (Histamine challenge test)

Secondary Endpoints
Exhaled Nitric Oxide; Alveolar Nitric Oxide; Bronchial Nitric Oxide flux; Airway resistance, impedance, reactance and resonant frequency using impulse oscilometry; FEV_1, FVC and FEF_{25-75} ; Peripheral eosinophil count; Peripheral Eosinophilic Cationic Protein; Serum 15-epi-lipoxin A_4 levels; Serum Thromboxane levels; Morning Peak Expiratory Flow rate; Daily and Overnight Symptom scores

Statistical methods
SPSS version 12 (SPSS, Inc, Chicago, Ill) and Prism version 4 for Macintosh (GraphPad Software, Inc, San Diego, Calif) were used to perform the statistical analysis. A sample size of 13 patients was estimated to give 80% power to detect a 1 doubling-dilution shift in histamine PC20 values (the primary outcome), assuming a 0.8 within-patient SD in doubling-dilution shift. As such, it was intended to recruit a total of 20 patients to allow for a potential 30% dropout rate. All data were assessed for normality by using distribution plots, and if appropriate, non-Gaussian data were log transformed before analysis. Treatment effect was evaluated by means of ANOVA of values at baseline and after each randomized therapy, followed by pairwise multiple range testing with the Bonferroni correction (the overall α error was set at .05) to obviate the effect of sequential comparisons

Summary Conclusions

Results
Compared with placebo, there were no differences in histamine PC_{20} values (0.17 doubling-dilution shift; 95% CI, -0.38 to 0.73; P = 1), exhaled nitric oxide levels (0.95-fold change; 95% CI, 0.45-2.00; P = 1), or any other inflammatory, spirometric, or oscillometry measurements. Aspirin led to a significant decrease in thromboxane B2 levels (17.53-fold difference; 95% CI, 5.46-56.49; P <.001). Baseline 15-epilipoxin A4 levels were increased at 4.88 ng/mL, and there was no increase with aspirin versus placebo (0.99-fold difference; 95% CI, 0.79-1.24; P = 1).

Conclusion
In this preliminary study of 15 patients, low-dose aspirin did not lead to increased 15-epilipoxin A4 synthesis or alter inflammatory markers in patients with mild-to-moderate persistent asthma.

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