Name of Sponsor/Company
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Title of Study
Comparative Study Of The Systemic Bioactivity Of HFA-Fluticasone Propionate via Anti-Static Spacer Devices

Investigators
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Study centre(s)
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Publication (reference)
NAIR A, MENZIES D, HOPKINSON P, McFARLANE L, LIPWORTH BJ. In vivo comparison of the relative systemic bioavailability of fluticasone propionate from three anti-static spacers and a metered dose inhaler. Br J Clin Pharmacol 2009;67:191-198

End of Trial
29.05.2007

Objectives
The aim of the study was to determine the relative bioavailability of hydrofluoroalkane (HFA) Fluticasone Propionate (FP) to the lungs via anti-static plastic (Zerostat-V and Aerochamber Max), metal (Nebuchamber) anti-static spacers and metered dose inhaler [Flixotide Evohaler (pMDI)].

Methodology
A randomized, double-blind, double-dummy, four-way crossover design was used. Eighteen mild to moderate asthmatics received single doses of placebo/HFA-FP 2mg via the 280-ml Zerostat-V (ZS); 250-ml Nebuchamber (NC); 197-ml Aerochamber Max (AC); and pMDI (EH).Measurements of OUCC and EMUCC were made at baseline and 10 h after each dose.

Number of patients planned
20

Number of patients analysed
18

Diagnosis and main criteria for inclusion
Stable, mild-to-moderate persistent asthma, aged 18–65 years, maintenance dose of ICS of up to 1000 µg of HFA BDP or equivalent, FEV_1 >60% predicted, and a positive methacholine challenge.

Test product dose

Arm A
8 puffs of Placebo via Aerochamber Max
8 puffs of Placebo via Zerostat
8 puffs of Placebo via Nebuchamber
8 puffs of FP 250 µg HFA via pMDI Evohaler Actuator

Arm B
8 puffs of Placebo via Aerochamber Max
8 puffs of Placebo via Zerostat
8 puffs of FP 250 µg HFA via Nebuchamber
8 puffs of Placebo via pMDI Evohaler Actuator

Arm C
8 puffs of Placebo via Aerochamber Max
8 puffs of FP 250 µg HFA via Zerostat
8 puffs of Placebo via Nebuchanber
8 puffs of Placebo via pMDI Evohaler Actuator

Arm D
8 puffs of FP 250 µg HFA via Aerochamber Max
8 puffs of Placebo via Zerostat
8 puffs of Placebo via Nebuchamber
8 puffs of Placebo via pMDI Evohaler Actuator

Duration of treatment
Treatment arms administered one per visit, with a 5-day washout period between visits.

Reference therapy
None

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Criteria for evaluation

Primary Endpoint
Overnight urinary cortisol–creatinine ratio.

Secondary Endpoints
Early morning urinary cortisol to creatinine ratio.

Statistical methods
A sample size of 16 completed patients per protocol was chosen to power the study at 80% to detect a 20% difference in overnight urinary cortisol–creatinine ratio, using data from a previous study that detected a 50% difference between spacer and pMDI with a sample size of 14 completed patients. Datasets were analysed for patients who completed the crossover study per protocol. The OUCC and EMUCC data were log transformed, and all data was tested for normality prior to analysis. Comparisons were made using repeated measures general linear model analysis of variance with Bonferroni correction for multiple comparisons, set with 95% confidence intervals (CIs) for differences. All effects are reported as being significant <0.05 (two-tailed) and violation of sphericity of within-subject effects was tested with the Mauchly's test. The analysis was carried out using SPSS Version 13 (SPSS Inc., Chicago, IL, USA).

Summary Conclusions

Results
Significant suppression of OUCC and EMUCC occurred from baseline with all three spacers, but not Evohaler (geometric mean fold suppression, 95% confidence interval): ZS, 2.74 (1.75, 4.30), $P < 0.001$; NC, 3.31 (1.81, 6.06), $P < 0.001$; AC, 4.98 (3.39, 7.31), $P < 0.001$; and for EH this was 1.42 (0.92, 2.21), $P = 0.169$ (equating to a 64, 70, 80 and 30% fall in OUCC via the ZS, NC, AC and EH devices, respectively). There were significant differences between all three spacers *vs.* EH. When compared with the Evohaler, the Zerostat V resulted in 48% greater suppression ($P = 0.009$); the Nebuchamber 57% greater suppression ($P = 0.001$); and the Aerochamber Max 71% greater suppression of OUCC ($P < 0.001$).

Conclusion
All three antistatic spacers significantly increased the relative systemic bioavailability of HFA-FP compared with the standard pMDI.

Date of the report: 08.06.2016