Budesonide/Formoterol Easyhaler®: Performance Under Simulated Real-Life Conditions

Haikarainen J, et al. Pulm Ther. 2017.

This slide deck represents the opinions of the authors. Sponsorship for this study was funded by Orion Corporation Orion Pharma. For a full list of acknowledgments and disclosures for all authors of this article, please see the full text online.

Abbreviations

COPD	= Chronic Obstructive Pulmonary Disease
DD	= Delivered Dose
DPI	= Dry Powder Inhalers
FPD	= Fine Particle Dose
GSD	= Geometric Standard Deviation
ICS	= Inhaled Corticosteroid
LABA	= Long-Acting β_2-Agonist
MMAD	= Mass Median Aerodynamic Diameter

Introduction

- Inhaler devices containing ICS and LABA are widely used for the treatment of specified patient groups with asthma and COPD.
- The first ICS/LABA inhaler device on the market was the Symbicort® Turbuhaler® (AstraZeneca, UK).
- Secondary entry products containing ICS and LABA have been developed including the budesonide/formoterol Easyhaler® (Bufomix Easyhaler®, Orion Corporation Orion Pharma, Finland).
- Inhaler devices should perform consistently, delivering a predictable and reproducible drug dose during repeated use.
- This study tested in vitro drug delivery characteristics of the Easyhaler and the Turbuhaler at different air flow rates.
- The Easyhaler was also tested under stressed conditions - exposure to moisture, dropping, vibration and freezing/thawing.

Methods

- A total of 36 inhalers from two batches of both the Easyhaler and Turbuhaler (160/4.5 µg strength) were used to assess the effect of flow rate; six inhalers for each of the three flow rates for uniformity of DD, FPD, MMAD and GSD.
- Consistency of DD, FPD, MMAD and GSD were determined for each inhaler at three different flow rates: 10th, 50th and 90th percentile air flows.
- Dosing properties as a function of inhaler life were tested.
- The effects of moisture, dropping, vibration and freezing/thawing on DD and FPD were tested with two to four inhalers per test using all three strengths of Easyhaler: 80/4.5, 160/4.5 and 320/9 µg.

Results

- The Easyhaler, 160/4.5 µg, showed statistically significantly better dose consistency at all three inhalation flows compared with the Turbuhaler, 160/4.5 µg, ($p < 0.001$ for three flow rates).
- Exposure to moisture, dropping, vibration and freezing/thawing did not affect DD or FDP.
- These results were similar for all three tested Easyhaler strengths.

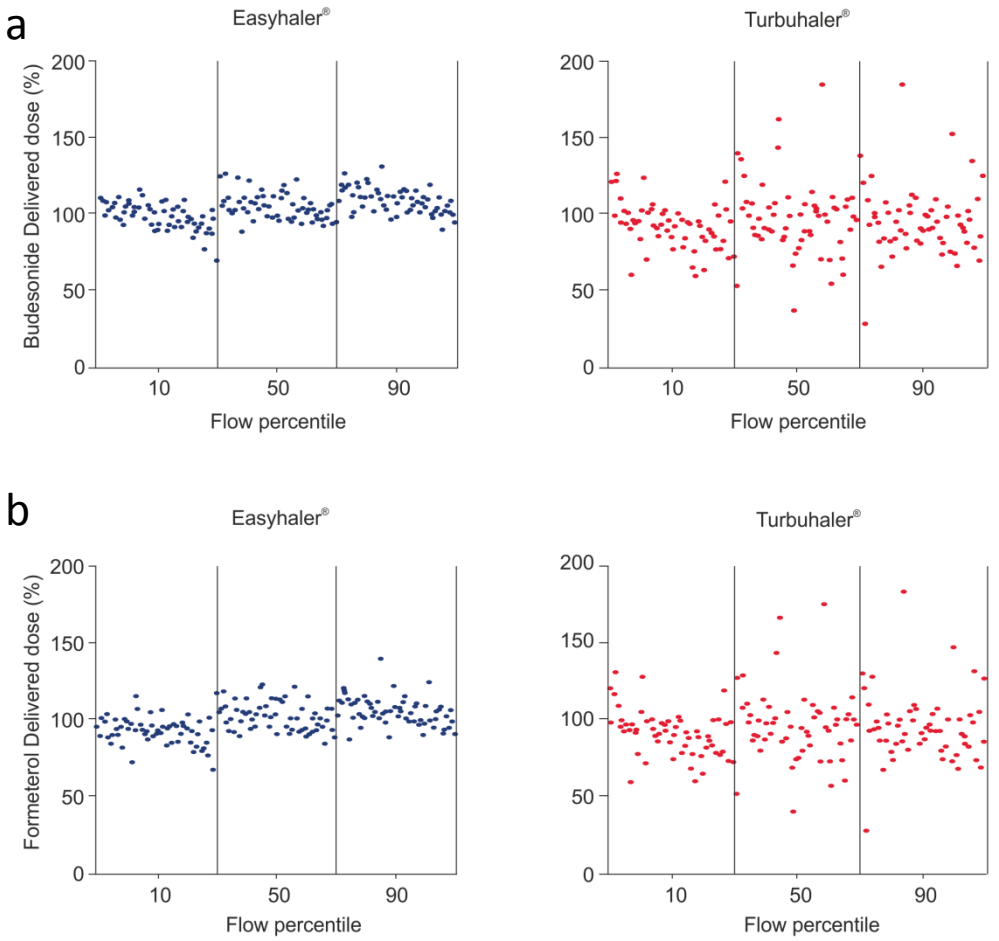

Fig. 1 a, b Dose delivery of budesonide (Fig. 1a) and formoterol (Fig. 1b) from two budesonide/formoterol multi-dose DPIs, the Bufomix Easyhaler® and the Symbicort®Turbuhaler® (160/4.5 µg) at three different flow rates. The delivered dose is expressed as a percent of the nominal labelled dose. Each data print represents a single dose actuation.

Discussion

- Dal Negro stated that DPIs should be effective, reproducible, precise, stable, comfortable, versatile and environmentally compatible [1]; however, for practical reasons, commercially available DPIs do not fulfil all of these criteria perfectly.
- Previous reviews of the Easyhaler have concluded that the device came closer to Dal Negro's "ideal inhaler" than many other inhalers [2,3].
- This study showed a statistically significantly better dose consistency for the Easyhaler compared with the Turbuhaler at all three levels of tested flow rates.
- A limitation of the study is that it is based on current standard methods; however, progress has since been made in developing more advanced in vitro methods.

[1] Dal Negro RW. Dry powder inhalers and the right things to remember: a concept review. Multidiscip Respir Med. 2015;10:13.
[2] Chrystyn H. Closer to an 'ideal inhaler' with the Easyhaler: an innovative dry powder inhaler. Clin Drug Investig. 2006;26:175–83.
[3] Chrystyn H, Haahtela T. Real-life inhalation therapy—inhaler performance and patient education matter. Eur Respir Dis. 2012;8:11–8.

Conclusion

- The results of studies reported here indicate that the budesonide/formoterol Easyhaler delivers consistently accurate doses throughout inhaler life.
- Dose consistency was superior compared with the budesonide/formoterol Turbuhaler at all tested flow rates.
- Consistency of overall dosing was maintained under exposure to stressed conditions and variations in temperature and humidity as well as after dropping, vibration and freeze/thaw tests.

Acknowledgments

- The studies and publication charges were funded by Orion Corporation Orion Pharma, Espoo, Finland.
- All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis.
- Disclosures: Jussi Haikarainen is an employee of Orion Corporation. Tero Löytänä is an employee of Orion Corporation. Anita Happonen is an employee of Orion Corporation. Paula Rytilä is an employee of Orion Corporation. Olof Selroos and Sirpa Metsärinne have nothing to disclose.
- Compliance with ethics guidelines: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was not applicable as there is no clinical data.

Copyright