



Relative lung and systemic bioavailability and oropharyngeal deposition of salbutamol inhaled through pMDI alone and with an improved Able spacer

Wesam G Ammari¹, Rabab Tayyem², Mohammed Abu Fara² and Mark Sanders³

¹Faculty of Pharmacy and Medical Sciences, Al-Ahliyya Amman University, Jordan, ²ACDIMA Centre for Bioequivalence and Pharmaceutical Studies, Jordan, ³Clement Clarke International, United Kingdom

Introduction

- Many patients using pressurized metered dose inhalers (pMDIs) have difficulties coordinating the beginning of slow inhalation with device actuation which adversely affects lung deposition [1, 2].
- Valved holding chambers (known as spacers) are attached to pMDIs to overcome this problem [3, 4].
- A recently improved version of Able spacer (AS) (Clement Clarke International, UK) is made of a special transparent polymer that incorporates silver ion anti-microbial technology to protect from contamination and microbial growth (Figure 1).
- The AS valve has been improved to operate at low flows typical of tidal flow rates of younger patients.
- Our study aimed to evaluate the relative lung and systemic bioavailability and oropharyngeal deposition of salbutamol following inhalation through Ventolin pMDI alone and with AS.

Methods

- Study design: Investigational, two-period, two-sequence, randomized, crossover bioavailability/pharmacokinetic study (Figure 2).
- In each period, subjects were trained rigorously to inhale 2 doses, separated by 30-60 seconds, of 100 µg salbutamol per dose from the pMDI either alone or attached to AS.
- Immediately after each dose inhalation, the subject was given 20 mL water to mouthwash and gargle, which was then pooled for salbutamol assay.
- Each volunteer gave urine samples 0.5 hr (pre-) and 0.5 hr post-inhalation. Then, they pooled their urine over 24 hrs post-inhalation.
- Salbutamol outcome measures:
 - 1) Relative lung bioavailability: By 0.5-hr urinary salbutamol excretion pharmacokinetic method (USAL0.5).
 - 2) Relative systemic bioavailability: By 0.5 - 24 hour urinary excretion of salbutamol and its metabolite (USALMET24).
 - 3) Oropharyngeal deposition.
- Salbutamol was quantified using developed solid phase extraction and LC-MS/MS methods.



Figure 1: The Able spacer.

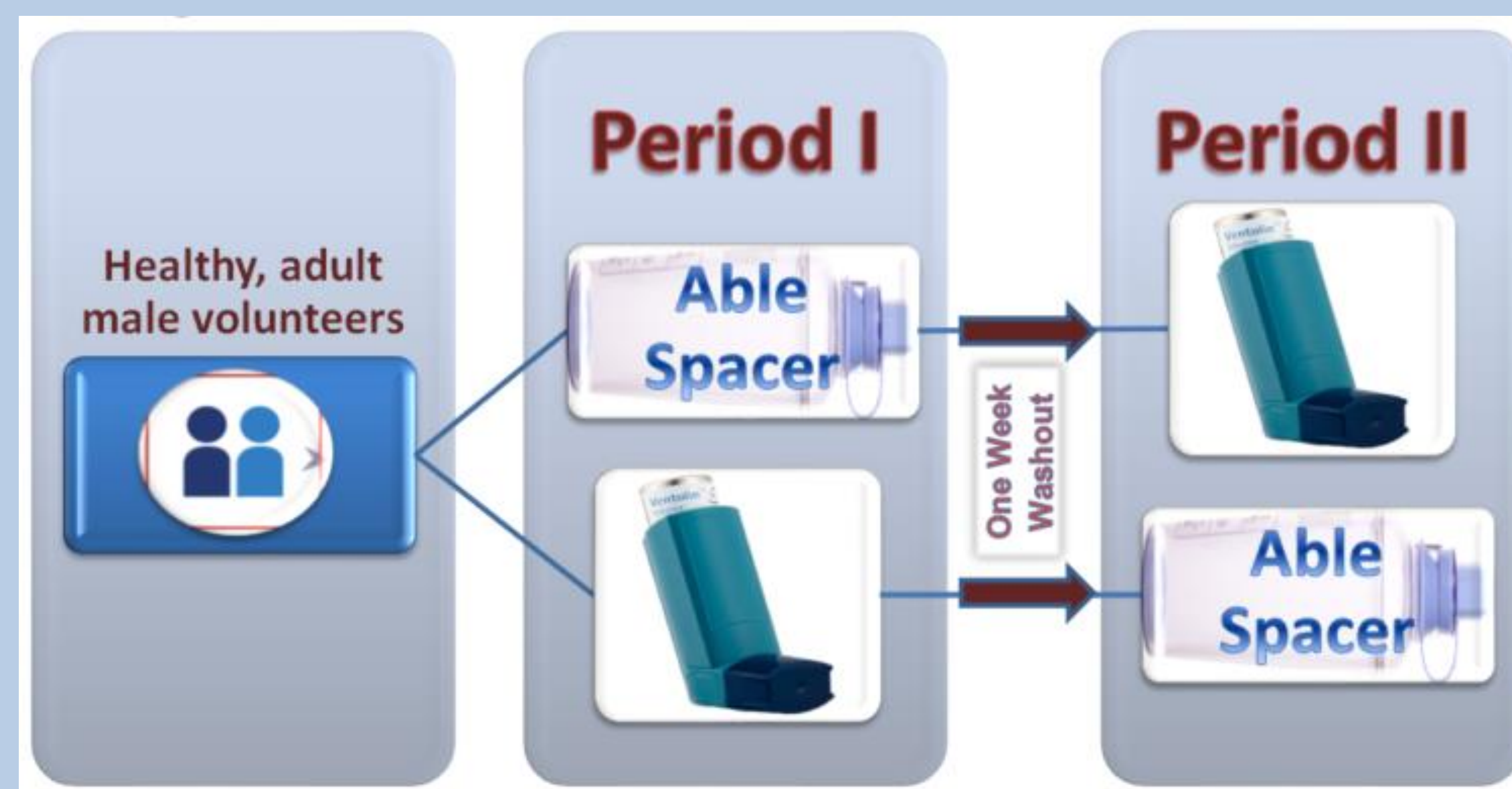


Figure 2: Study schematic.

Table 1: Mean (SD) fate of inhaled salbutamol (2 x 100µg)

n = 10 subjects	pMDI alone	pMDI + AS
USAL 0.5 hr (µg)	6.17 (3.83)	15.66 (12.95)
Relative lung bioavailability*	3.09 (1.92)	7.83 (6.47)
USALMET 24 hrs (µg)	49.12 (30.74)	51.99 (21.67)
Relative systemic bioavailability*	24.56 (15.37)	25.99 (10.83)
Oropharyngeal deposition (µg)	11.11 (2.85)	0.36 (0.38)

*expressed as % of nominal dose (SD).

Results

- Ten male subjects (Mean (SD) age: 30.7 (9.9) years) participated.
- The study results are presented in Table 1.
- Statistically, the AS increased significantly ($p < 0.05$) the salbutamol delivery to the lungs and reduced ($p < 0.001$) its oropharyngeal impaction, compared with the pMDI alone.
- Both inhalation methods gave comparable systemic salbutamol exposure ($p > 0.05$).

Conclusions

- The Able spacer improves the inhaled salbutamol dose to the lungs and minimizes its precipitation in the oral cavity.
- In real-life, the oropharyngeal deposited salbutamol is subsequently swallowed and absorbed. This adds to its systemic bioavailability. Accordingly, the AS is also expected to result in lower systemic salbutamol exposure.
- The AS can thus give an added therapeutic benefit particularly in subjects with pMDI technique issues.



References

- (1) Ammari WG and Chrystyn H. J Asthma 2013; 50(5):505-513.
- (2) Ammari *et al.* Pulm. Pharmacol. Therap. 2017; 43:46-54.
- (3) Price *et al.* Respiratory Medicine 2013; 107(1): 37-46.
- (4) Reznik *et al.* Clinical Pediatrics 2014; 53(3): 270-276.

Conflict of interest

- WGA received an unconditional funding from Clement Clarke International (CCI) to conduct this academically initiated study.
- RT and MAF have no conflict of interest.
- MS is the Chief Technology Officer at CCI.

Corresponding Author

Dr. Wesam G Ammari
w_ammari@hotmail.com
wammari@ammanu.edu.jo