

Letter to the Editor

Comparison of the aerosol velocity of Respimat[®] soft mist inhaler and seven pressurized metered dose inhalers



Dear Editor,

Inhalation therapy is the mainstream treatment for bronchial asthma and chronic obstructive pulmonary disease (COPD). At present, hand-held devices for inhalation therapy, including pressurized metered dose inhalers (pMDIs), dry powder inhalers (DPIs) and Respimat[®] soft mist inhaler (SMI) are used. In pMDIs and Respimat[®] SMI, the spray velocity is one of the most important aerosol characteristics affecting the deposition in the lung,¹ thereby providing 1 criterion for the selection of drug preparations for clinical cases. Therefore, the aerosol spray velocities of seven pMDIs containing hydrofluoroalkane (HFA) propellant and one Respimat[®] SMI were measured using particle image velocimetry² (PIV), a well-established method in fluid dynamics.

Four pMDIs contain short-acting beta-agonist (SABA), three pMDIs are for inhaled corticosteroids (ICSs), and Respimat[®] SMI is for tiotropium. SABAs include salbutamol (Salbutamol·GSK and Salbutamol·3M), fenoterol, and procaterol. ICSs include fluticasone propionate (FP), beclomethasone dipropionate (BDP), and ciclesonide (CIC).

At each measurement the pMDIs were shaken well and then the drug aerosols were sprayed approximately ten times in the air. After confirming that the aerosol spray was stable, the average of 30 spray velocities (10 sprays/device × 3 devices) per each product was used for analysis. In this study, Respimat[®] SMI was measured without shaking.

Using PIV, the velocity of the tip of the drug aerosol cloud sprayed in the atmosphere was measured at positions 80-/100-mm from the end of the nozzle of the pMDIs and SMI in view of closed-mouth and open-mouth methods. Briefly, spraying the drug aerosol from an inhaler against the laser (Pegasus-PIV, New Wave Research, CA, USA), the movement of the aerosol cloud is lighted up by a thin laser sheet light and photographed at 3000 frames per second using a CCD high-resolution camera (FASTCAM SA3, Photron, Tokyo, Japan). Using the calibration vision set out in a longitudinal direction, the tip of the aerosol cloud is read by viewing the acquired image. Figure 1 shows a series of images of aerosol clouds.

The location (mm) of the tip of the aerosol cloud is plotted on an abscissa axis and the relative time (ms) in which 0 indicates that of the first appearance of the tip in a series of images is plotted on the longitudinal axis. The velocity at each point is interpolated by polynomial regression. For example, the velocity at position 80-mm is

calculated based on data approximated by the polynomial regression shown below.

$$"1/(\text{relative time at position 80.5 mm} - \text{relative time at position 79.5})"$$

The mean aerosol velocities of all inhalation drug products tested in this study are shown in Figure 2. There are large differences in the aerosol velocity among pMDIs for SABA. The velocity of the pMDI for Salbutamol·GSK was the fastest (8.91/7.34 m/s at positions 80-/100-mm distant from the end of nozzle, respectively) and that of the pMDI for fenoterol was the slowest (2.47/1.71 m/s at positions 80-/100-mm distant from the end of nozzle, respectively) of all the pMDIs for SABA.

The aerosol velocity of the pMDI for FP (9.15/7.80 m/s at positions 80-/100-mm from the end of nozzle) was higher than those of pMDIs for BDP and CIC. Respimat[®] SMI for tiotropium generated an aerosol spray of the slowest velocity (0.84/0.72 m/s at positions 80-/100-mm distant from the end of nozzle) of all the products tested in this study.

All inhalation drug products used in this study are clinically used in Japan. Although other factors than spray velocity have not been evaluated, this study is the first report comparing the spray velocities of pMDIs for SABA and ICS and Respimat[®] SMI for tiotropium using a similar method, temporally and spatially.

As shown in Results, the aerosol velocity of pMDI for fenoterol was slower than those of the other 3 pMDIs for SABA. Usmani *et al.*³ reported that faster inspiratory flows decreased total lung deposition and increased oropharyngeal deposition for larger particles, with less bronchodilation. Therefore, in terms of spray velocity, fenoterol was the most favorable bronchodilator.

pMDIs for ICS are divisible into two groups according to the spray velocity. As shown in Results, pMDIs for BDP and CIC generate almost the same velocity, which was slower than that of pMDI for FP. As I previously reported that the particle size distribution of the aerosols generated from these pMDIs had the same bi-modal distribution,⁴ I infer that the inhalers for BDP and CIC are the same. In addition, these findings explain why inhalation from pMDIs for BDP⁵ and CIC⁶ results in higher pulmonary deposition than that from pMDI for FP,⁷ especially in the peripheral regions of the lung.

I previously reported that the aerosol velocity of pMDI for the FP/formoterol combination agent was slower than that of pMDI for the FP/salmeterol combination.⁸ Thus, I measured the spray velocity of all HFA-pMDI preparations used in Japan. Consequently, I found a large difference in the aerosol velocity of HFA-pMDIs,

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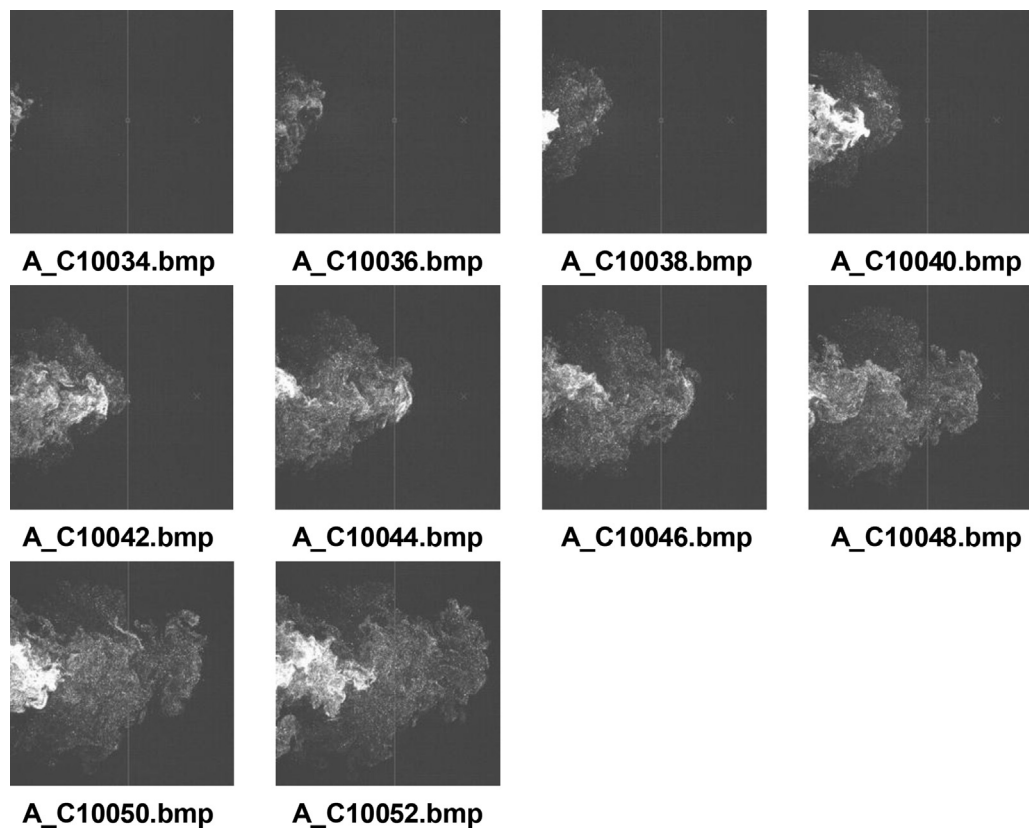


Fig. 1. A series of real images of an aerosol cloud.

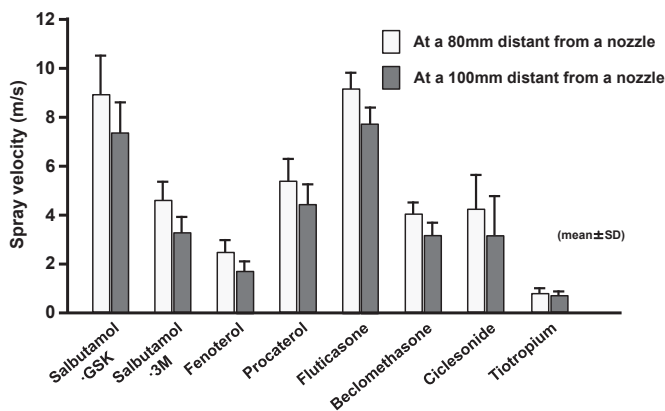


Fig. 2. Spray velocities of four pMDIs for SABA, three pMDIs for ICS and Respimat® SMI for tiotropium.

although most HFA-pMDIs have a smaller delivery orifice that may result in a more slowly delivered aerosol plume, compared with chlorofluorocarbons-driven pMDIs.

As shown in Results, Respimat® SMI for tiotropium generated the slowest spray velocity of all inhalation drug products used in this study. It has also been reported that Respimat® SMI generates a much longer spray duration than other pMDIs.⁹ Additionally, I and Ichinose have reported that the particle size distribution of aerosols generated from the SMI showed a bi-modal distribution, with peaks at around 0.5 μm and 5 μm .¹⁰ Therefore, these findings suggest that Respimat® SMI is the best portable inhaler for the treatment of central and peripheral airways.

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Conflict of interest

The author has no conflict of interest to declare, although Airway Institute in Sendai has a deal with Astellas Pharma, AstraZeneca, Kyorin Pharmaceutical, GlaxoSmithKline, and Nippon Boehringer Ingelheim.

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