J. Pharm. Pharmacol. 1988, 40: 429–430
Communicated September 10, 1987

COMMUNICATIONS

High speed photographic analysis of aerosols produced by metered dose inhalers

R. DHAND, S. K. MALIK*, M. BALAKRISHNAN†, S. R. VERMA† *Departments of Internal Medicine and *Chest Diseases, Postgraduate Institute of Medical Education and Research, Chandigarh, and †Terminal Ballistic Research Laboratory, Chandigarh, India—160 012*

Abstract—The design of pressurized metered dose inhalers (MDI) used to assess asthma is variable. We have examined the aerosol spray flumes generated by four commercially available MDI products using high speed video photography. For this purpose a moulded jacket was designed which could hold the inhaler in an immovable position during actuation. Fresh inhalers were fitted in the jacket after thorough shaking and three successive actuations 30 s apart were filmed with a high speed video camera (200 frames s^{-1}). The aerosol, ejected at high velocity into calm room air, was seen to have a 'jet' phase followed by a 'cloud' phase as a result of particle dispersion. Filming was continued till the flume could no longer be visualized on the TV monitor. High speed photography was used to record flumes seen on the video monitor, to enable characterization of flume appearance, dimensions and mean velocity.

The use of inhaled drugs is a well-established method for treatment (Lieffer & Wittig 1975) and prophylaxis of asthma (Woolcock 1977). Pressurized metered dose inhalers (MDI) are used extensively to administer drugs directly to the respiratory tract. Variations in the formulation, type of propellant, vapour pressure, and the design of metering valves and actuators all determine the type of output from an inhaler (Sackner & Kim 1985). Photographic methods have also been used to evaluate the performance of the aerosol valve and actuator using both timed and non-timed exposures (Miszuk et al 1980; Benjamin et al 1983). However, serial changes occurring in the flume after actuation were not described. We have used a simple method employing high speed video photography to study serially the changes undergone by the flume after ejection. In this way the reliability and uniformity of aerosol flume generation by MDIs could also be assessed.

Materials and methods

To photograph inhaler flumes it was necessary to fix the inhaler rigidly in a reproducible vertical position. For this purpose a suitable jig was constructed consisting of a Plaster of Paris mould of the inhaler inside a wooden jacket. The jacket could be fixed on to metal plates at the base and back by screws.

High speed video photography. High speed video photography (200 frames s^{-1}) was with a VHS system (High Wycombe, UK) and colour TV camera (200 nac Tokyo, Japan).

Four fresh inhalers representing different inhaler products (coded A–D) were taken for testing. After being vigorously shaken for about 2 min, each was put in the mould and tested in a draught-free room with the camera positioned at the level of the inhaler and to one side so that a sideways image of the flume was obtained. A black background and scale marked at 5 cm intervals served as the backdrop against which the flumes were filmed. High intensity illumination by two flood lights (800 W each) was provided by placing the lights vertically below the flume to be filmed.

Three successive actuations of each inhaler about 30 s apart were filmed and frames taken every 5 ms from the actuation of aerosols. Each actuation was identified by a number and time recorded. These were then photographed on conventional film from the image on the TV monitor. Various parameters were calculated from a study of these photographs. The duration of each flume was taken as the time from first visualization at the actuator tip to the time of its disappearance from the video monitor. The length of each MDI from actuator orifice to the end of the actuator mouthpiece was 2·5 cm. This was added to the length of the jet visualized in the first photograph to obtain the total distance traversed in the first 5 ms, and mean velocity calculated. The distance from the identifiable edge in the photograph at 5 ms to the identifiable edge in the photograph at 10 ms was used for calculating mean velocity in the next 5 ms. To calculate the angle of delivery a horizontal line was drawn on the photograph at the level of the actuator orifice and a point was marked on this line 2·5 cm from the top of the actuator so as to identify the position of the actuator orifice. The angle between this horizontal line and another line drawn through the middle of the flume to join the position of the actuator orifice was the angle of delivery.

Results

The sequence of events following actuation of inhalers is shown in Fig. 1. Shaking of the aerosol once was adequate for three successive actuations. The first actuation of inhaler B did not produce a satisfactory flume (not shown). However, the remaining actuations of inhalers A–D gave comparable results and were seen to undergo changes which were similar and are outlined below. The various parameters analysed are recorded in Table 1.

The aerosol was ejected at a mean velocity varying from 13 to 15 m s^{-1}. In the next frame (after 5 ms) the velocity had decreased considerably to 7–8 m s^{-1} and had dropped further (3–7 m s^{-1}) in the next frame. The flume was seen to have two distinct phases: a 'jet' phase followed by a 'cloud' phase after 10–15 ms. As the flume was ejected it appeared in a dense compact stream with a definite leading edge (jet phase) and this was seen

Correspondence to: R. Dhand, Department of Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India—160 012.

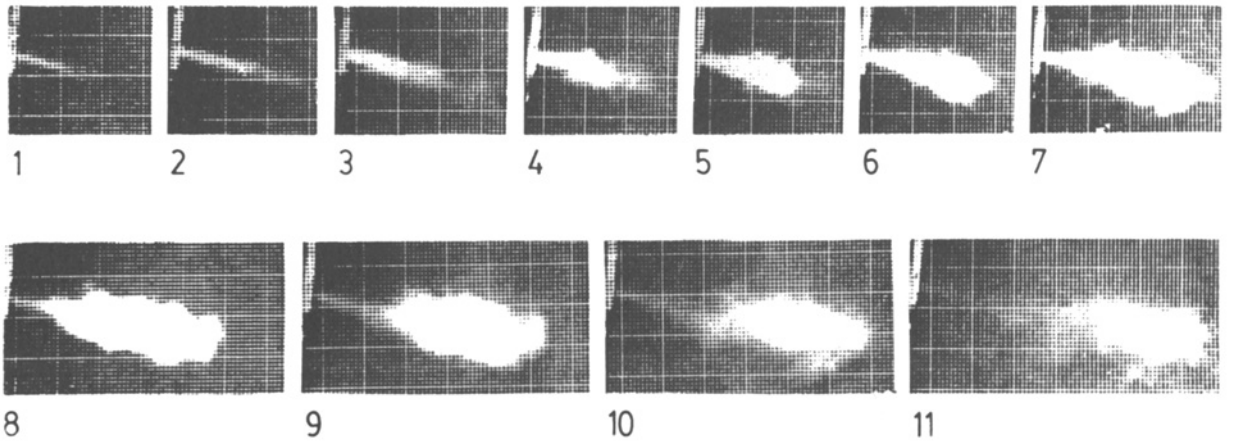

FIG. 1. A photograph showing sequential frames taken after first actuation of aerosol A. Frames 1–11 represent pictures taken 10, 15, 20, 25, 30, 40, 50, 60, 70, 80 and 90 ms after actuation. Actuations of inhalers B, C and D gave similar photographic sequences.

Table 1. Flume characteristics of metered dose inhalers.

Inhaler	Time for cloud formation (ms)	Total duration (ms)	Mean Jet velocity (metres m s^{-1}) 0–5 ms	5–10 ms	10–15 ms	Jet angle of delivery
A	10	70–80	15	7	3	75°
B	15	65–70*	15	8	7	66°
C	15	85–95	13	7	5	71°
D	15	75–80	15	7	7	73°

*One actuation of inhaler B had a duration of 30 ms.

to traverse a distance of 5–8 cm. Later the jet started dispersing into a cloud with noticeable turbulence in the centre. After a brief duration of 65–95 ms the density of the cloud diminished greatly because of dissipation, hence it could no longer be photographed. At a time when the leading edge could no longer be defined the aerosol had travelled a distance of approximately 15 cm.

Discussion

Various factors, including differences in the formulation of MDIs can theoretically influence the efficacy of inhalers (Sackner & Kim 1985). As the aerosol is ejected from the actuator orifice at a high velocity and has a brief duration ($< 0{\cdot}1$ s) the changes which it undergoes after ejection are not visible to the eye. Miszuk et al (1980) studied individual video images of flume patterns using two orthogonal images of the flume in two perpendicular planes. A close similarity was found in flume patterns of two corticosteroid inhalers and the photographic evaluation showed good correlation with the efficiency of drug delivery determined by liquid chromatography. Another study visualized aerosol flumes by using flash photography and non-timed exposures (Benjamin et al 1983). Variations in the size of actuator orifice were found to produce flumes which were not ideal and this observation was confirmed by analysing the spots produced by the aerosol jets on a silica gel thin layer chromatography plate placed at a fixed distance from the actuator. An improved technique using timed delay flash was also reported recently (Hallworth & Kedgley 1986). In that study a microphone which detected the sound of inhaler discharge was used to trigger a flash unit through a preset time delay switch and photographs of the flumes were obtained at preset time intervals. Using high speed video photography we found that we could photograph sequential changes in the jet expelled after actuation of an MDI. In this way it was possible to analyse certain characteristics of the aerosol flume and to compare these in different inhalers. As in previous studies, we also found that flumes produced by various inhalers were similar to one another.

The sequential changes undergone by aerosols produced by four different MDI were consistent. Our findings suggest that high speed video photography can be reliably used to test various inhalers. Unlike various optical particle counters (Hiller et al 1978) or the cascade impactors (Kim et al 1985), this method does not give any information about the particle size of the metered delivery. Even though the photographic method is less sophisticated, its advantage lies in the ease with which the MDI delivery can be visualized and compared. We also observed on the video monitor a significant amount of turbulence within the aerosol jet. Assessment of flume patterns may serve as a corollary to other complex measurements of droplet characteristics used for studying the efficacy of MDIs.

References

Benjamin, E. J., Kroeten, J. J., Shek, E. (1983) Characterization of spray patterns of inhalation aerosols using thin layer chromatography. J. Pharm. Sci. 72: 380–385.

Hallworth, G. W., Kedgley, D. (1986) Recording metered dose inhaler flumes by timed sequence flash photography. J. Pharm. Pharmacol. 38: 27 P

Hiller, F. C., Mazumder, M., Wilson, D., Bone, R. (1978) Aerodynamic size distribution of metered dose bronchodilator aerosols. Am. Rev. Resp. Dis. 118: 311–317

Kim, C. S., Trujillo, D., Sackner, M. A. (1985) Size aspects of metered dose inhaler aerosols. Ibid. 132: 137–142

Lieffer, K. N., Wittig, H. J. (1975) The beta-2-sympathomimetic aerosols in the treatment of asthma. Ann. Allergy 35: 69–80

Miszuk, S., Gupta, B. M., Chen, F. C., Clawans, C., Knapp, J. Z. (1980) Video characterization of flume patterns of inhalation aerosols. J. Pharm. Sci. 69: 713–717

Sackner, M. A., Kim, C. S. (1985) Auxiliary MDI aerosol delivery systems. Chest 88 Suppl: 161–170

Woolcock, A. J. (1977) Inhaled drugs in the prevention of asthma. Am. Rev. Resp. Dis. 115: 191–194