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TECHNICAL NOTE

Electrostatic charge on a plastic spacer device influences the delivery of salbutamol

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ABSTRACT: The aim of this study was to determine whether electrostatic charge on a plastic spacer decreases the delivery of salbutamol from a pressurized metered-dose inhaler (pMDI) and, if so, to find an optimal and practical treatment to remove the charge.

Ten single actuations from a salbutamol pMDI were drawn through different Volumatic® spacers at a constant flow of 60 L·min^{-1}. The efficacies of different methods of removing charge were tested, including detergent coating of the spacers. A multistage liquid impinger was used to determine the particle size distribution of the output of the pMDI through the Volumatic® spacers. The electrostatic charge on the inner surface of the spacers was measured both quantitatively with an electrometer, and qualitatively by the attraction of a thin strip of cellulose membrane to the wall of the spacer. Each experiment was repeated four times.

Ionic detergent coating of the spacers removed the charge for at least 24 h. This resulted in an increase of 55–70% in small particle (<6.8 μm) delivery compared to delivery from new spacers with high charge.

We have demonstrated that electrostatic charge plays a major role in the delivery of salbutamol through plastic spacers. Adequate treatment with ionic detergent removes the charge and improves drug delivery.

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Pressurized metered-dose inhalers (pMDIs) have been used to deliver aerosols to the lower respiratory tract of patients for many years. Their widespread popularity is largely attributable to their convenience. However, the use of pMDIs is associated with a number of problems, which have limited their effectiveness. The most important problems are co-ordination difficulties, and high oropharyngeal deposition resulting from pMDI actuation directly into the mouth [1]. These problems have been greatly reduced by the development of spacer devices [2, 3]. The main concept of a spacer device is that of a chamber reservoir, where the actuated aerosol cloud can be held prior to inhalation by the patient.

The delivery of an aerosol through a spacer device depends on many different parameters [4]. One of these is the electrostatic charge on the plastic spacer device. Recent work has suggested that the charge generated by a pMDI by itself is low [5]. However, due to the characteristics of polycarbonate chambers, considerable electrostatic charge can be induced under certain conditions. Electrostatic charge on an object may be either positive or negative, caused by frictional contact with a material of different dielectric constant [6]. The actuated aerosol may be attracted to the wall of the spacer by the electrostatic charge and, thus, retained within the chamber. Therefore, the electrostatic charge on the spacer device may influence the delivery of aerosol [7].

The aim of this study was to determine by laboratory testing, whether electrostatic charge on a plastic spacer influences the availability of the actuated aerosol for inhalation, and, if so, to find the optimal treatment of a spacer in order to minimize its electrostatic charge, to decrease the amount of drug retained within the chamber, and hence to increase the delivery of the drug.

Materials and methods

Study design

Measurement of electrostatic charge (both quantitative and qualitative) and drug delivery was carried out on the following Volumatic® spacers (Allen and Hanbury's, Australia): 1) new spacers which had been stored in their original plastic bag; 2) patients' old spacers; and 3) spacers, which were rubbed with a thin piece of clear plastic to generate electrostatic charge.

In addition, an attempt was made to remove the electrostatic charge from plastic-rubbed spacers in the following manner: 4) water-rinsed and cotton towel-dried; 5) water-rinsed and drip-dried for 2 h; 6) covered internally with aluminium foil (to provide a conducting layer on the inner surface of the spacer); 7) treated with antistatic spray (Armor All protectant; Armor All products, USA); 8) coated with cationic detergent (Cetrimide 40%; Princess Margaret Hospital Pharmacy, Australia); 9)

coated with anionic detergent (Liquid pyroneg; Diversey, Australia); or 10) coated with nonionic detergent (Premium; Able Westchem, Australia).

Finally, the routine methods used by patients to clean and store their spacers were assessed by asking 29 asthmatic children and their parents in our out-patient clinic to complete a questionnaire with the following questions: How long have you had your spacer? How often do you clean your spacer? How do you clean it? Do you towel dry your spacer or allow it to drip dry? and How do you store your spacer?

Methods

The detergent coating was carried out in the following manner: 1) The spacer was immersed in diluted cationic (1:125), anionic (1:250) or nonionic (1:1000) detergent for 1 h and drip-dried for 2, 4, 12, or 24 h. Detergents were diluted as recommended by the manufacturers. 2) The spacer was immersed in diluted cationic (1:125) or anionic (1:250) detergent for 1 h, drip-dried for 1 h and stored either wrapped in a plastic bag or unwrapped for 1 week. 3) The spacer was washed in diluted cationic (1:125), anionic (1:250) or nonionic (1:1000) detergent and cotton towel-dried.

Electrostatic charge was assessed both quantitatively and qualitatively. Quanitative measurement of electrostatic charge on each spacer was performed using an electrometer (Model 37C; Electronic Instruments Ltd, Jacoby Mitchell, Sydney, Australia). The 35cc ionization chamber, normally used with this electrometer, was replaced by a metal electrode of area 20×19 mm. This had its surface insulated by a 0.8 mm thick piece of Teflon, so that touching a charged surface would not discharge it. The electrometer gave a reading in roentgen which could be converted into coulombs (C) using the relationship for a 35cc ionization chamber that 1 roentgen is equivalent to 11.7 nC. The surface charge density was calculated by dividing the measured charge by the electrode area of 3.8×10^{-4} m^2. For ease of comparison, surface charge density was classified into the following three categories: none (negligible charge 0–1.2 µC·m^{-2}); low charge (1.2–3.3 µC·m^{-2}); and high charge (3.3–6.7 µC·m^{-2}). Measurements on a charged sheet of perspex indicated that the readings were reliable provided the surface charge was low enough to avoid spontaneous discharge due to air ionization. This only appeared at charge densities above those observed in practice. The readings had no dependence on the proximity of the electrode to the charged surface provided that this was within millimetres. In addition, qualitative assessment was carried out using a thin strip of cellulose membrane (1×5 cm). The attraction of the cellulose depended on the charge on the surface of the spacers. Using this method, the charge on the spacer surface was again classified as none, low or high.

Drug delivery through the spacers was measured by the following method. The salbutamol pMDI (Ventolin; Allen and Hanbury's, Australia) was shaken for 30 s and two actuations were wasted prior to testing. The pMDI was then actuated into the Volumatic® spacer, which was attached to a high performance multistage liquid impinger (MSLI) (Copley, Nottingham, UK). Air was drawn through this system at a continuous flow of 60 L·min^{-1}. Ten single actuations were then introduced into the spacer, with 5 s intervals between each actuation. The pMDI was shaken vigorously in the intervals between actuations.

After actuating the pMDI, the aerosol was drawn through the device with the entraining airflow. Droplets were deposited on the actuator, the throat or one of four stages, and the site of deposition was determined by the particle size of the droplets. The MSLI had been calibrated by the manufacturer so that particles >13, 6.8–13, 3.1–6.8 and <3.1 µm were deposited on stages 1, 2, 3 and 4, respectively. Calibration was performed using both monodisperse dioctylphthalate (DOP) droplets produced by a vibrating orifice aerosol generator and polydisperse DOP and an aerodynamic particle sizer.

The actuator, spacer, throat and each of the stages of the MSLI were separately washed with 40 mL of methanol. Five millilitres of 0.1 M NaOH was added to each wash and the volume was then made up to 50 mL with methanol. The absorbance (λ=246 nm) of each sample was measured in duplicate on a spectrophotometer (Hitachi U-2000; Japan). The concentration of salbutamol in each sample was obtained by using the absorbance of a standard solution containing a known concentration of salbutamol. The standard curve for salbutamol was linear (r^2=1.00) for concentrations between 0 and 21 µg·mL^{-1}. Each experiment from actuation of the pMDI to the measurements of the drug concentration was repeated four times. All measurements were undertaken under the following atmospheric conditions: mean temperature was 22.9°C (range 22–25°C), and mean barometric pressure was 763 mmHg (range 756–770 mmHg).

Analysis

Statistical analysis was carried out using analysis of variance (ANOVA) (StatView 512+; Albacus Concepts Inc., CA, USA) with a significance level of 95% ($p<0.05$).

Results

Quantitative and qualitative measurements of electrostatic charge gave concordant results for all spacers. We present the amount of drug delivered in particles <6.8 µm for the various spacers in tables 1 and 2.

New and patients' old spacers

New spacers had a high electrostatic charge on their inner surface, and delivery of particles <6.8 µm was low. Patients' old spacers still had detectable charge in either the low or high range. However, the amount of drug delivered in particles <6.8 µm was higher ($p<0.001$) than from new spacers. There was no significant difference in electrostatic charge or delivery of particles <6.8 µm between new and plastic-rubbed spacers.

Water rinsed

When plastic rubbed spacers were water-rinsed and either towel- or drip-dried, their electrostatic charge was

Table 1. – Electrostatic charge and drug delivery of particles <6.8 µm as a percentage of the total amount in different Volumatic® spacers (n=4)

Spacers	Charge	Drug delivery# %
New	High	30±3 (26–32)
Old	Low-high	37±4 (33–41)
Plastic-rubbed	High	32±3 (29–36)
Water-rinsed, towel-dried	Low-high	33±1 (32–34)
Water-rinsed, 2 h drip-dried	Low-high	33±1 (32–35)
Inside aluminium foil covered	None	48±2 (45–50)
Antistatic spray treated	None	43±1 (42–44)

#: mean±SD, and range in parenthesis.

still detectable. As the charge decreased only slightly after these treatments, there was no significant improvement in drug delivery of particles <6.8 µm.

Aluminium foil

When plastic-rubbed spacers were covered internally with aluminium foil there was no detectable charge. Drug delivery of particles <6.8 µm was higher ($p<0.001$) in spacers covered with aluminium foil when compared to new, patients' old, plastic-rubbed and water-rinsed spacers. There was no significant difference in electrostatic charge or delivery of particles <6.8 µm between spacers covered with aluminium foil when compared to ionic detergent coated spacers, drip-dried for up to 24 h (fig. 1).

Cationic and anionic detergent

Ionic detergent coating removed the electrostatic charge from plastic-rubbed spacers for at least 24 h. However, when spacers coated with ionic detergent were stored for 1 week a low charge was detected, whether or not they were wrapped in a plastic bag. Drug delivery of particles <6.8 µm was higher ($p<0.001$) in spacers coated with ionic detergent, even when they were towel-dried when compared to plastic-rubbed spacers. However, storage for 1 week reduced the positive effect on drug delivery (fig. 2).

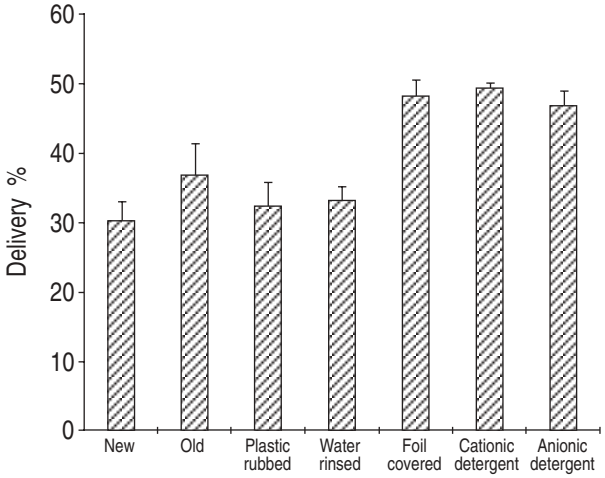

Fig. 1. – Drug delivery of particles <6.8 µm as a percentage of the total amount in spacers (n=4): new; patients' old; plastic-rubbed; water-rinsed and 2 h drip-dried; aluminium foil covered; cationic detergent coated and 24 h drip-dried; and anionic detergent coated and 24 h drip-dried. Values are presented as mean and SD.

Nonionic detergent

Spacers coated with nonionic detergent still had a low electrostatic charge. They showed a higher ($p<0.001$) delivery of particles <6.8 µm when drip-dried for up to 12 h when compared to plastic-rubbed spacers. However, when drip-dried for longer than 12 h this effect was eliminated (fig. 2).

Questionnaire

Analysis of the questionnaire showed that spacers are used for up to 5 yrs. Our patients washed their

Table 2. – Electrostatic charge and drug delivery of particles <6.8 µm as a percentage of the total amount in detergent coated Volumatic® spacers (n=4)

Treatment	Cationic detergent coated spacers		Anionic detergent coated spacers		Nonionic detergent coated spacers	
	Charge	Delivery %	Charge	Delivery %	Charge	Delivery %
Detergent coated, 2 h drip-dried	None	51±4 (48–55)	None	49±2 (46–50)	Low	44±1 (44–45)
Detergent coated, 4 h drip-dried	None	50±1 (49–52)	None	47±1 (46–47)	Low	43±1 (41–44)
Detergent coated, 12 h drip-dried	None	47±2 (45–49)	None	48±1 (47–49)	Low	44±1 (43–45)
Detergent coated, 24 h drip-dried	None	49±1 (49–50)	None	47±2 (44–48)	High	37±2 (35–39)
Detergent coated, 1 week drip-dried	None-low	43±1 (42–44)	None-low	44±2 (42–46)	-	-
Detergent coated, 1 week stored in plastic bag	Low	43±1 (42–45)	Low	44±1 (42–45)	-	-
Detergent washed, towel-dried	None	48±1 (47–50)	None	46±1 (44–47)	Low	42±2 (40–44)

Values are presented as mean±SD, and range in parenthesis.

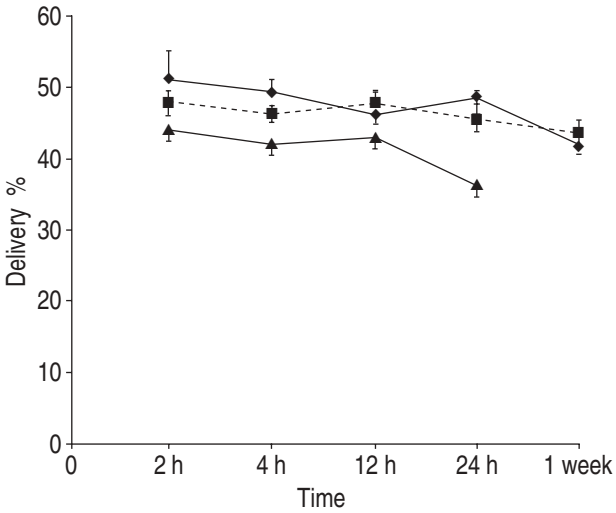

Fig. 2. – Drug delivery of particles <6.8 µm as a percentage of the total amount in detergent coated spacers allowed to drip dry for 2, 4, 12, 24 h and 1 week (n=4). —◆—: cationic; - - -■- - -: anionic; —▲—: nonionic. Values are presented as mean±SD.

spacers at least monthly and some washed them after each use. Spacers were water-rinsed by 62% of the patients, whilst they were immersed in detergent and then allowed to drip dry by 38%. Spacers were towel-dried after washing by 24% of the patients. Most patients (72%) stored their spacers unwrapped and 28% patients wrapped their spacers in plastic bags.

Discussion

We have shown that electrostatic charge on the inner surface of a plastic spacer device greatly influences the delivery of salbutamol generated by pMDIs. This is in accordance with previous studies delivering sodium cromoglycate and budesonide through a spacer [7, 8]. Electrostatic charge attracts the particles to the spacer wall and, thus, decreases drug delivery. This effect plays a major role in new spacers, which have a high electrostatic charge. This problem remains in patients' old spacers albeit to a lesser extent.

Conducting materials hold no electrostatic charge. A spacer of steel should, therefore, solve the problem of reduced drug delivery due to electrostatic charge [9]. We showed in our laboratory study that the level of electrostatic charge on a plastic spacer depends on the treatment of the spacer. In previous studies, antistatic lining was used to remove the charge [7, 8]. This may not be a useful treatment in practice. Rinsing the spacers with water, as it is generally recommended by drug companies, does not significantly reduce the charge or improve drug delivery. Adequate treatment with detergent, however, reduced or even eliminated the electrostatic charge and improved drug delivery.

When spacers with a high electrostatic charge were coated with ionic detergent, charge was eliminated for at least 24 h. If these spacers were stored for 1 week, whether or not wrapped in a plastic bag, the charge increased but was still lower than in new, patient's old or water-rinsed spacers. Nonionic detergent was less efficient and low charge was detectable after 2 h of drip drying, which built up to a high level after 24 h.

In summary, ionic detergent coating of spacers significantly improved drug delivery of particles <6.8 µm. This treatment made them equivalent to spacers internally covered with conducting material. Coating a plastic spacer by an easy and cheap method using ionic detergent may avoid the need to have millions of plastic spacers worth millions of dollars replaced by new spacers of conducting material. Coating the surface with ionic detergent may build a conducting layer, which removes the charge and is, therefore, superior to coating with nonionic detergent. Household detergents usually contain a mixture of cationic, anionic and nonionic detergents [10].

Instructions by the company for cleaning the Volumatic® specify that the spacer should be rinsed in water; however, this treatment does not remove charge. Despite the instructions, patients clean and store their spacers in a variety of ways. It is important to have uniform recommendations. We recommend, that under ideal conditions spacers should be freshly coated with ionic detergent every 24 h. However, practically speaking, once a week may be sufficient. In addition, the spacers should be stored unwrapped.

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