Optimum use of a spacer device

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Abstract
Nedocromil sodium given by the Fisonair spacer should be inhaled immediately. Multiple actuations into the spacer should be avoided. Delay of 20 seconds before sampling reduced the amount of drug available for inhalation in the respirable range by 81%. Placing two actuations into the spacer reduced the amount of drug available by 47%.
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In the delivery of drugs to the respiratory tract, spacer devices are used to reduce the need to coordinate inhalation and metered dose inhaler (MDI) actuation. Optimum spacer use could improve the effectiveness of asthma management and reduce the waste of drugs which result from poor inhaler and spacer technique.¹

This study determined the effect of multiple actuations of nedocromil sodium MDI (2 mg per actuation) into the Fisonair (Fisons) spacer and delay before inhalation, on the amount of drug present in particles within the respirable range.

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Methods

The multistage liquid impinger (MSLI) was used to determine the MDI output under different conditions. This operates by drawing an aerosol through a series of stages, each containing a glass impaction plate. Aerosol velocity increases in the device and progressively smaller particles collect at each stage. A filter after the final stage collects the smallest particles. Each stage was washed first with trichlorofluoromethane to remove surfactant, then quantitatively with water. The amount of drug collected in each stage was assayed by ultraviolet spectrophotometry at a wavelength of 253 nm.

In the first experiment a standard MDI of nedocromil sodium (2 mg per actuation) was connected to the impinger by a small plastic sock and the MDI discharged into the MSLI. With the Fisonair spacer device the MDI was actuated into the device and the device immediately attached to the MSLI.

To assess the effect of residency time, the Fisonair was held adjacent to the MSLI for five, 10, or 20 seconds after MDI actuation and then attached to the MSLI. The Fisonair was positioned so that aerosol would not be drawn into the MSLI before attachment.

To assess the effect of multiple actuations into the spacer, the procedure was repeated with the MDI actuated two or three times into the Fisonair before attaching it to the MSLI.

For all of the above experiments, the aerosol was discharged through the impinger up to 12 times to facilitate the drug assay, with one minute between each actuation. Before each actuation the MDI was shaken for 10 seconds or more. Each experiment was repeated four times, and the temperature, relative humidity, and barometric pressure were recorded. The flow through the MSLI was 60±2 litres per minute.

The size distribution of the aerosol cloud was determined from the amount of drug recovered from each stage, the MSLI having been previously calibrated with an aerosol of known particle size distribution. Particles smaller than five microns (the respirable range) are thought to enter the respiratory tract. We report on the amount of drug contained in particles smaller than five and three microns, the mass median aerodynamic diameter, and the geometric standard deviation² for each experiment.

Results

Use of the Fisonair spacer increased the amount of nedocromil sodium available for inhalation by 19% and 43% in particles less than five and three microns respectively.

Drug recovery decreased with increasing residence time. After five seconds the amount of nedocromil sodium in particles less than five and three microns fell by 43%, after 10 seconds by 50% and 47% respectively, and after 20 seconds by 81% and 79% respectively.

Multiple actuations decreased drug recovery in particles less than five microns by 47% (two actuations) and 57% (three actuations). For particles less than three microns, the reduction was 48% (two actuations) and 57% (three actuations).

The amount of drug recovered (mean and SD), the mass median aerodynamic diameter, and the geometric standard deviation for the different experiments are given in the table.

Effect of different methods of use of the Fisonair on the delivery of nedocromil sodium; values are mean (SD)

Method of delivery	Amount of nedocromil sodium recovered (mg) per 2 mg actuation		Mass median aerodynamic diameter	Geometric standard deviation
	In particles <5 µ	In particles <3 µ		
Direct from MDI	0.417 (0.05)	0.206 (0.03)	–	–
By Fisonair				
Effect of residence time (delay in seconds)				
No delay	0.498 (0.08)	0.294 (0.06)	3.925 (0.53)	1.998 (0.10)
5	0.284 (0.01)	0.167 (0.01)	3.950 (0.06)	2.013 (0.05)
10	0.251 (0.08)	0.155 (0.05)	3.600 (0.32)	2.115 (0.10)
20	0.095 (0.03)	0.062 (0.02)	3.500 (0.28)	2.486 (0.53)
Effect of multiple actuations (No of actuations)				
1	0.498 (0.08)	0.294 (0.06)	3.925 (0.53)	1.998 (0.10)
2	0.264 (0.05)	0.154 (0.02)	4.425 (0.44)	1.987 (0.44)
3	0.216 (0.03)	0.126 (0.01)	4.250 (0.10)	2.082 (0.06)

Mean temperature was 22.9°C (range 21–23.5), mean barometric pressure was 996.7 mm Hg (range 985–1007.2), and the mean relative humidity was 50.5% (range 49–61).

Discussion

Nedocromil sodium is an effective anti-inflammatory agent used in the treatment of asthma.³ Those unable to coordinate inhalation and inhaler actuation due to age or disability will need to use a spacer such as the Fisonair.

We have shown that a short delay between actuation of the MDI and inhalation reduces the amount of drug in small particles considerably. The reduction in available drug with time will be more important for those who take small breaths, taking a longer time to clear the spacer. Those administering the drug to another should take care to actuate the MDI when the patient is ready.

Multiple actuations of the MDI also decrease the amount of drug recovered in respirable particles. Later actuations may cause turbulent deposition of particles onto the spacer walls. The higher concentration of particles with multiple actuations may make collisions and agglomerations more likely, increasing particle size.

Knowledge of the actual dose available for inhalation allows meaningful comparison with other drug delivery methods.

This study confirms the work of others into multiple dosing with sodium cromoglycate^{2 4 5} and radioactive tracer.⁶ However, different drug formulations and spacer devices have different physical and electrostatic properties, so that findings of one study may not be applicable to other drugs and devices.

For the administration of nedocromil sodium, use of the Fisonair spacer device increases the amount of drug available for inhalation in respirable particles provided it is inhaled immediately after actuation of the MDI, and multiple actuations into the Fisonair are avoided.

- 1 Keeley D. Large volume plastic spacers in asthma [Editorial]. *BMJ* 1992; **305**: 598–9.
- 2 O'Callaghan C, Lynch J, Cant M, Robertson C. Improvement in drug delivery from spacer devices by use of an antistatic lining. *Thorax* 1993; **48**: 603–6.
- 3 Armenio L, Baldini G, Bardare M, *et al.* Double blind, placebo controlled study of nedocromil sodium in asthma. *Arch Dis Child* 1993; **68**: 193–7.
- 4 Clark AR, Rachelefsky G, Mason PL, Goldenhersh MJ, Hollingworth A. The use of reservoir devices for the simultaneous delivery of two metered dose aerosols. *J Allergy Clin Immunol* 1990; **85**: 75–9.
- 5 Everard ML, Clark AR, Milner AD. Drug delivery from holding chambers with attached facemask. *Arch Dis Child* 1992; **67**: 580–5.
- 6 Newman SP, Millar AB, Lennard-Jones TR, Moren F, Clarke SW. Improvement of pressurised aerosol deposition with Nebuhaler spacer device. *Thorax* 1984; **39**: 935–41.