

Effects of Salbutamol Delivery From a Metered Dose Inhaler Versus Jet Nebulizer on Dynamic Lung Mechanics in Very Preterm Infants With Chronic Lung Disease

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Summary. Treatment of chronic lung disease of prematurity requires effective aerosol delivery of different therapeutic agents. Aerosols can be generated by a metered dose inhaler (MDI) or a jet nebulizer. An MDI combined with a spacer device is easier to use and avoids undesirable effects noted in conjunction with jet nebulization. We compared the clinical effectiveness of 200 µg (2 puffs) salbutamol delivered from an MDI in conjunction with a valved spacer device (Aerochamber®), and 600 µg given via jet nebulizer (PariBaby®) on 2 consecutive days, the order being randomized. Thirteen spontaneously breathing very preterm infants [mean (SD) gestational age 27.2 (1.8) weeks; birth weight 0.90 (0.34) kg] were studied at a corrected age of 37 (2.3) weeks. Mean (SD) study weight was 1.83 (0.38) kg. Dynamic lung compliance and resistance were determined from measurements of flows, volumes, and transpulmonary pressures, using a pneumotachometer and a small esophageal microtransducer catheter before and 20 min after salbutamol application.

Baseline values before salbutamol administration were similar on both occasions: the mean (SD) compliance was 7.7 (3.0) mL · kPa⁻¹ · kg⁻¹ pre-MDI plus-spacer and 8.4 (3.1) pre-jet nebulizer; the resistance was 10.4 (4.0) kPa · L⁻¹ · s pre-MDI plus-spacer and 9.7 (3.4) pre-jet nebulizer. Following salbutamol, compliance did not change significantly with either MDI plus spacer or jet nebulizer. Resistance fell significantly with MDI plus spacer (mean -2.2; 99.9% CI -0.35, -4.35) and jet nebulizer (-2.4; 99% CI -0.39, -4.42). We conclude that even in small preterm infants 200 µg salbutamol via MDI plus spacer improves dynamic resistance as effectively as 600 µg via jet nebulizer and may therefore be a preferable mode of aerosol administration.

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Key words: Inhalation technique; very premature infant; bronchodilator; bronchopulmonary dysplasia; dynamic lung mechanics; albuterol.

INTRODUCTION

Despite major advances in neonatology over the last few years, chronic lung disease of prematurity remains one of the main problems in the care of very premature infants. Although the long-term benefits have not been proved, early inhalation of bronchodilators and anti-inflammatory agents such as steroids has become increasingly important in the treatment of pulmonary disease in this group of patients.^{1–8} Aerosol treatments can be delivered from metered dose inhalers (MDI) with a spacer or as a solution aerosolized by a jet nebulizer. Although there are some in vitro studies comparing the efficacy of these two methods, it remains unclear whether aerosol treatment via MDI plus spacer or nebulization should be chosen for routine clinical use.^{9–11} Only one recently published study using radiolabeled aerosol has compared deposition from an MDI and a jet nebulizer in infants with bronchopulmonary dysplasia, showing low deposition by either method and marked inter- and intra-

subject variability in both.¹² We have used conventional jet nebulization for inhaled medications except for steroids. However, not only have in vitro studies favored the use of an MDI plus spacer, but there are also advantages in terms of handling and timing when using an MDI compared with a nebulizer. Since it is widely accepted that bronchodilators can improve lung function even in preterm infants with evidence of chronic lung disease, we compared the clinical efficacy of MDI and jet nebuliza-

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TABLE 1—Anthropometric Characteristics of Study Population

Patient no.	Gestational age (weeks)	Birth weight (kg)	Ventilated (days)	Postconceptional age (weeks)	Study weight (kg)	Study length (cm)
1 ¹	28	1,120	8	40	2,660	44
2 ¹	27	730	6	40	1,980	42
3 ¹	25	490	6	39	2,095	41
4 ¹	28	640	10	40	1,820	39
5	29	1,215	1	37	2,220	44
6 ¹	28	900	7	37	1,685	40
7	28	1,280	5	32	1,520	38
8 ¹	27	985	3	36	1,600	40
9	28	1,050	12	36	1,630	41
10 ¹	28	660	0	37	1,400	37
11 ¹	24	450	10	36	1,235	34
12 ¹	24	640	15	36	1,960	42
13	30	1,580	6	36	1,970	43
Mean	27.2	903	6.9	37.1	1,830	40.4
(SD)	(1.8)	(339)	(4.2)	(2.3)	(379)	(2.9)

¹Chronic lung disease of prematurity; for definition see text.

tion by measuring the effect of salbutamol on dynamic lung mechanics in a randomized cross-over study.

MATERIALS AND METHODS

Subjects

Thirteen spontaneously breathing preterm infants with a mean (SD) gestational age (GA) of 27.2 (1.8) weeks were studied at a mean (SD) corrected age of 37.1 (2.2) weeks. Patients were eligible for the study when they had already received aerosol treatment for clinical evidence of chronic lung disease ($n = 9$) or when they had shown a positive bronchodilator response in their routine lung function test ($n = 4$). Chronic lung disease was defined as oxygen dependency at 36 weeks postconceptional age plus an abnormal chest x-ray. Lung function measurements were made routinely before discharge in all preterm infants who had required mechanical ventilation for more than 24 h and/or had respiratory symptoms including wheeze or recurrent apnea beyond 36 weeks postconceptional age. The measurements included dynamic lung mechanics as described below, lung volume measurements by nitrogen washout if possible, and rapid thoracic compression for measurements of flow volume relationships in larger infants (i.e., >2.5 kg). During these

initial measurements, response to nebulized salbutamol (600 μ g via jet nebulizer) was assessed provided the infant remained asleep long enough (all measurements being performed in natural unsedated sleep). A positive bronchodilator response was defined as a change in either dynamic compliance or resistance of more than twice the individual's coefficient of variation.

The mean (SD) birth weight of the infants was 903 (339) g; the weight at the time of the study was 1.83 (0.36) kg. Details of the infants are given in Table 1. For the actual study, each infant was given aerosolized salbutamol on two separate occasions, once from an MDI attached to a spacer and once from a jet nebulizer; the measurements were performed 24 h apart in random order.

The study was approved by the local ethics committee, and written informed consent was obtained from all parents prior to the measurements.

Aerosol Administration

Following an interval of at least 8 h after the last inhalation treatment, salbutamol was administered by one of the following methods in randomized order, the other treatment being given the next day, exactly 24 h apart.

Nebulizer

Nebulization was given with a jet nebulizer (PariBaby®, Pari, Starnberg, Germany). A total of 600 μ g salbutamol (3 droplets of the salbutamol inhalation solution) was diluted in 2 mL of physiological saline (NaCl 0.9%) and nebulized completely using a gas flow of 8 L/min. This is the dose conventionally given in our neonatal intensive care unit if there is evidence of airway

Abbreviations

$C_{L,dyn}$	Dynamic lung compliance
CV	Coefficient of variation
GA	Gestational age
MDI	Metered dose inhaler
MLR	Multiple linear regression analysis
MTC	Microtransducer catheter
$R_{L,dyn}$	Dynamic lung resistance
SD	Standard deviation

obstruction. The aerosol was administered via a face mask (Laerdal Resuscitation Mask® size 0, Laerdal, Stavanger, Norway), held firmly to the infant's face and covered both mouth and nose.

MDI

Salbutamol (200 µg, 2 puffs) was given from an MDI via a 145 mL valved holding chamber device (Aero-chamber®, Trudell Medical, Canada). After the holding chamber had been loaded with a single puff from the MDI, the attached face mask was applied firmly over the infant's mouth and nose and the infant was allowed to breathe for 30 s. This procedure was repeated to deliver the second puff. Prior to each puff, the MDI canister was shaken vigorously.

Lung Function Measurements

Before and 15–30 min after salbutamol inhalation dynamic lung mechanics were measured in natural unseeded sleep using esophageal manometry.

A small flexible 3 Fr microtransducer catheter (MTC®, Dräger, Netherlands), which has recently been validated by our group for use especially in this group of infants, was inserted through the nose into the esophagus.¹³ Initially, it was passed into the stomach, as shown by positive pressure swings during inspiration and then withdrawn through the cardiac sphincter until maximal negative pressure swings with minimal cardiac artifacts were observed.

Flow and airway opening pressure were measured using a small Hans-Rudolph pneumotachograph (0–10 L/min) with two ports for flow measurement and one port for airway opening pressure. Volume was digitally integrated from flow. A size 0 face mask (Rendell-Baker) attached to the pneumotachograph was then applied over the mouth and nose with a thin ring of therapeutic silicone putty between the infant's face and the mask to obtain an airtight seal. Once the infant was breathing regularly in quiet sleep as assessed by behavioral criteria,¹⁴ an occlusion test was performed to validate the position of the MTC®.¹³ Esophageal pressure was assumed to be a true reflection of alveolar and transpulmonary pressure when the ratio of esophageal to airway opening pressure changes during occlusion was between 0.95 and 1.05. Otherwise, the catheter position was adjusted until a valid occlusion test was obtained. A period of at least 3 min of quiet and regular breathing was then recorded on a personal computer at a sampling rate of 100 Hz with data acquisition software developed in our department and stored for later analysis. Of the data recorded, a series of consecutive regular breaths just before or following a satisfactory occlusion test was used for calculation of dynamic mechanics.

Dynamic lung compliance ($C_{L,dyn}$) and lung resistance ($R_{L,dyn}$) were calculated from flow, volume, and transpulmonary pressure (esophageal pressure – pressure at the airway opening) using multiple linear regression analysis (MLR). Only results with a coefficient of determination (estimate of the goodness of fit of the calculated pressure) ≥ 0.95 are reported. The mean (SD) of the first 25 breaths matching these criteria is reported, except for three infants in whom only 12, 15, and 17 satisfactory breaths, respectively, were available for analysis.

All infants were monitored throughout the test with a pulse oximeter (Nellcor) for oxygen saturation and heart rate. Infants with chronic lung disease of prematurity who were still oxygen dependent were given intermittent inspired oxygen to maintain saturations between 93 and 95%. The additional flow was stopped before the recordings for analysis began. Therefore, no correction for differences in inspired gas composition was made to the flow signals.

Statistical Analysis

Lung function data were analyzed for differences using a paired t-test for within-group comparisons of pre- and post-salbutamol values of dynamic mechanics and an unpaired t-test for comparison between the different modes of inhalation and day to day changes. A *P* value of <0.05 was considered significant. It was estimated that the number of infants included in the study would give a power of 90% at the 5% significance level to detect a bronchodilator effect with each of the two modes of inhalation and a power of 80% to detect a difference between them. The individual response to salbutamol was considered significant with a difference before and after intervention of more than twice the individual coefficient of variation of the baseline measurement.

RESULTS

Inhalation of salbutamol was tolerated equally well using either the MDI-plus-spacer or the jet nebulizer. On average heart rate increased only by 10 bpm. No infant showed oxygen desaturations during or following salbutamol inhalation other than the desaturation that occurred intermittently and spontaneously during the pre-study period, with a rapid return to normal values.

The baseline measurements showed no significant difference between consecutive study days. Mean (SD) $C_{L,dyn}$ was 15.0 (2.1) mL · kPa⁻¹ [1.5 (0.2) mL · cmH₂O⁻¹] pre-jet nebulizer inhalation and 13.7 (1.5) mL · kPa⁻¹ [1.4 (0.2) mL · cmH₂O⁻¹] pre-MDI-plus-spacer. The mean of the individual CVs was 13.0 and 10.7%, respectively. For $R_{L,dyn}$, the mean (SD) baseline values were 9.7 (1.1) kPa · L⁻¹ · s [95.3 (10.8) cmH₂O · L⁻¹ · s] pre-nebulizer and 10.4 (1.2) kPa · mL⁻¹

TABLE 2—Effects of Salbutamol Inhalation via MDI Plus Mask Versus Nebulizer on Dynamic Lung Compliance in Very Premature Infants With Chronic Lung Disease

Patient no.	Dynamic compliance (mLkPa)													
	Aerochamber®							PariBaby®						
	Pretreatment			Post-treatment			Δ	Pretreatment			Post-treatment			Δ
	Mean	SD	CV	Mean	SD	CV		Mean	SD	CV	Mean	SD	CV	
1	9.3	0.5	5.6	9.7	0.6	5.9	-0.3	12.2	1.1	9.1	11.2	1.0	8.7	1.0
2	9.8	1.5	15.2	13.0	1.2	9.4	-3.2	8.2	0.4	4.4	18.9	4.3	23.0	-10.6
3	26.4	2.6	9.9	17.7	1.0	5.9	8.8	29.7	6.6	22.4	22.5	1.3	6.0	7.2
4	7.5	1.5	19.5	9.0	2.1	23.2	-1.4	8.2	1.6	19.5	10.1	1.7	16.9	-1.9
5	16.9	1.5	8.6	24.8	4.6	18.6	-7.9	21.4	2.9	13.5	23.0	0.6	2.5	-1.6
6	15.8	1.7	10.7	14.2	1.0	7.4	1.6	15.9	1.2	7.5	15.7	2.0	13.0	0.2
7	18.5	1.7	9.1	21.8	1.6	7.1	-3.4	13.5	1.7	12.2	15.5	2.6	16.9	-1.9
8	7.4	0.6	8.1	8.5	0.5	5.8	-1.1	9.9	1.3	12.7	10.9	0.8	7.6	-1.0
9	18.1	3.0	16.7	20.2	3.7	18.1	-2.1	18.8	3.3	17.4	14.6	1.7	11.4	4.2
10	11.3	1.0	8.9	14.1	1.4	10.1	-2.8	16.4	0.8	4.8	16.5	2.3	13.8	0.0
11	9.6	0.8	8.7	10.1	0.6	6.3	-0.5	12.0	1.0	8.5	13.4	1.1	8.5	-1.4
12	11.0	1.0	8.8	11.3	0.8	7.4	-0.3	12.7	2.9	22.7	13.7	2.0	14.7	-1.0
13	16.3	1.8	11.3	16.9	2.3	14.0	-0.6	15.7	2.4	15.0	18.3	2.3	12.3	-2.5
Group mean	13.7		10.7	14.7		10.7	-1.0	15.0		13.0	15.7		11.9	-0.7
(SD)	(5.5)		(3.9)	(5.2)		(5.9)	(3.7)	(5.9)		(6.2)	(4.1)		(5.4)	(4.1)

• s [102.1 (11.8) cmH₂O • L⁻¹ • s] pre-MDI-plus-spacer, the mean (SD) CV of variation being 12.1% (4.4 and 8.3) for either method. There was no significant difference between baseline compliance and resistance measurements on the two occasions (95% CI -5.9, 3.3 for compliance, and -2.4, 3.65 for resistance). However, individual between-measurement variability (baseline measurement pre-MDI-plus-spacer and pre-jet nebulizer, respectively) was marked in some infants, ranging from -5.1 to 5.0 mL • kPa⁻¹ for $C_{L,dyn}$ and -4.3 to 6.4 kPa • L⁻¹ • s for $R_{L,dyn}$, respectively.

Following salbutamol inhalation, $C_{L,dyn}$ did not change significantly using either mode of delivery. The mean (SD) change was -1.0 ± 3.7 mL • kPa⁻¹ for the MDI plus spacer and -0.7 (4.1) following jet nebulizer inhalation. However, there was a significant fall in $R_{L,dyn}$, the mean (SD) change following MDI plus spacer being 2.2 (1.8) kPa • L⁻¹ • s ($P < 0.001$; CI 0.04, 4.35) and 2.4 (2.4) post-salbutamol inhalation via jet nebulizer ($P < 0.01$; CI 0.39, 4.42). There was no significant difference between the two methods of delivery of salbutamol.

Individual results are given in Tables 2 and 3. The change in dynamic lung compliance is shown for each infant in Figure 1; a value below zero reflects a rise in compliance following salbutamol (i.e., $C_{L,dyn}$ post-salbutamol greater than during the baseline measurement). The change in $R_{L,dyn}$ is shown in Figure 2; a value above zero ($\Delta R_{L,dyn} = R_{L,dyn} \text{ pre} - R_{L,dyn} \text{ post}$) reflects an improvement. Only one child showed a mild increase in resistance following jet nebulization, and in two infants, no change in $R_{L,dyn}$ was detected. There was a trend for those infants with the highest resistance during the baseline measurements to show the greatest improvement; however, this correlation was statistically not sig-

nificant. When the individual CV ($CV = SD/\text{mean} \%$) is taken into account, there was a significant improvement (change of more than twice the CV) in resistance in 7 of 13 infants following MDI-plus-spacer and in 8 of 13 following jet nebulizer therapy. No infant showed a paradoxical response.

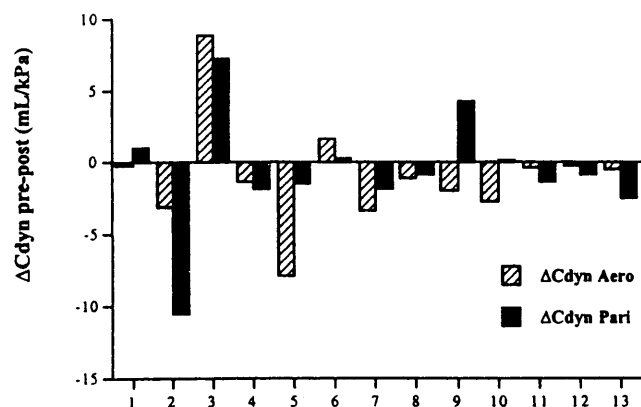
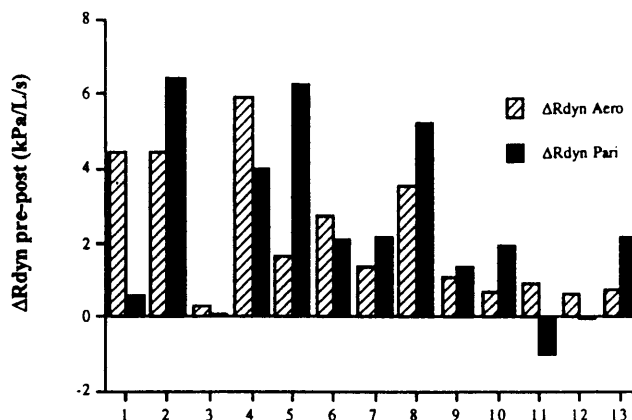
DISCUSSION

This study confirms previously published findings that inhaled salbutamol has a beneficial effect on lung mechanics in preterm infants with signs of chronic lung disease. Resistance improved in all but one patient, with no significant deterioration in any of the infants studied, neither following inhalation via MDI-plus-spacer nor via jet nebulizer. This is in contrast to earlier studies on the effect of beta-agonist inhalation in early infancy.¹⁵ However, there was no consistent change in compliance following either mode of inhalation. This may be due to volume changes following salbutamol inhalation (i.e., less gas trapping); however, lung volumes were not measured in this investigation. An alternative explanation may be that the dose administered was not sufficient.

More importantly, we could not demonstrate a difference between the effect of 600 μ g salbutamol given via jet nebulizer over 5–10 min and the effect of 200 μ g salbutamol given by MDI-plus-spacer. The doses were chosen for clinical reasons, 3 drops (600 μ g) of salbutamol diluted in normal saline being the dose conventionally used in our department. It was felt that a microgram-equivalent dose of an MDI would have been inappropriately high when compared with doses used in older subjects. Also, previous studies using 200 μ g salbutamol from an MDI-plus-spacer have demonstrated the effect

TABLE 3—Effects of Salbutamol Inhalation via MDI Plus Mask Versus Nebulizer on Dynamic Lung Resistance in Very Premature Infants With Chronic Lung Disease

Patient no.	Dynamic resistance (kPa/L/s)													
	Aerochamber®							PariBaby®						
	Pretreatment			Post-treatment			Δ	Pretreatment			Post-treatment			Δ
	Mean	SD	CV	Mean	SD	CV		Mean	SD	CV	Mean	SD	CV	
1	16.1	1.6	10.2	11.7	1.2	10.2	4.4	9.7	0.5	5.6	9.1	0.3	3.0	0.6
2	11.9	1.2	10.4	7.6	0.4	5.7	4.4	14.8	1.1	7.7	8.5	0.9	10.4	6.4
3	8.0	0.6	7.5	7.8	0.7	8.4	0.3	9.3	1.6	17.5	9.2	0.5	5.5	0.1
4	16.3	2.2	13.7	10.4	2.5	24.5	5.9	13.3	2.1	15.8	9.3	1.4	14.8	3.9
5	8.6	2.1	23.9	6.8	1.1	16.5	1.7	12.9	1.2	9.6	6.6	0.8	12.0	6.2
6	7.8	0.7	8.8	5.0	0.3	6.0	2.8	6.9	0.6	8.0	4.8	0.2	5.0	2.1
7	6.2	0.6	9.9	4.7	0.5	10.6	1.4	7.6	0.8	9.8	5.5	0.4	7.7	2.2
8	16.0	1.7	10.7	12.5	0.8	6.7	3.5	15.2	1.6	10.5	9.9	0.7	6.5	5.2
9	4.4	0.5	11.4	3.3	0.6	17.6	1.1	5.5	0.7	12.8	4.0	0.5	12.5	1.4
10	13.4	1.0	7.5	12.6	1.2	9.5	0.7	10.8	0.3	2.9	8.9	0.8	8.4	2.0
11	10.4	1.6	15.1	9.5	0.5	5.3	0.9	8.0	0.6	7.3	9.0	1.0	11.5	-1.0
12	8.1	1.0	12.7	7.4	0.9	11.5	0.7	5.1	1.9	36.3	5.1	1.0	19.2	-0.0
13	7.6	1.2	15.2	6.9	0.9	13.4	0.8	7.5	1.0	13.9	5.3	0.4	7.4	2.2
Group mean (SD)	10.4 (4.0)		12.1 (4.4)	8.2 (3.0)		11.2 (5.6)	2.2 (1.8)	9.7 (3.4)		12.1 (8.3)	7.3 (2.1)		9.5 (4.5)	2.4 (2.4)

**Fig. 1.** The change in dynamic lung compliance ($C_{L,dyn}$) is shown for each infant (13). A value below zero reflects an improvement in compliance following salbutamol (i.e., $C_{L,dyn}$ post-salbutamol greater than during baseline measurement).**Fig. 2.** The change in dynamic lung resistance ($R_{L,dyn}$) is shown for each infant (13). A value above zero ($\Delta R_{L,dyn} = R_{L,dyn}$ pre - $R_{L,dyn}$ post) reflects an improvement.

on lung mechanics in preterm infants.² For older infants, toddlers, and school-aged children it is now widely accepted that inhalation therapy is as good when given by MDI via spacer as when using a conventional jet nebulizer.^{4,16-19} However, to our knowledge, there has been no previous study comparing the clinical efficacy of MDI via spacer versus jet nebulizer aerosol delivery in spontaneously breathing preterm infants with chronic lung disease.

Whereas in vitro studies and studies in animal models have clearly favored the use of a MDI-plus-spacer for delivery of aerosolized drugs⁹⁻¹¹ with a more than tenfold dose deposited compared with jet nebulization, these findings were not confirmed in the recent study of infants with chronic lung disease of prematurity.¹² The dose deposited as measured by radiolabeled salbutamol was be-

low 1% for either mode of delivery. However, assuming that the dose of salbutamol deposited in the infants in the present study is equally low, there is still a measurable clinical effect. We chose salbutamol as a widely used bronchodilator because clinical efficacy can be assessed by measuring pulmonary mechanics. It was not the aim of the study to demonstrate bronchodilator responsiveness in this group of infants, which has been demonstrated before in numerous studies. It was our intent to assess clinical efficacy of aerosol treatment by these two methods of aerosol delivery, and the results can now be applied to other aerosolized medications. Aerosol treatment including aerosolized anti-inflammatory agents have become increasingly important in the long-term care of preterm infants, and the efficacy of these therapies cannot be measured easily. Because of the variable

response to salbutamol with regard to lung mechanics observed in this group of preterm infants, and the marked within-subject between-occasion variability in baseline measurements, the proposed model to assess clinical efficacy of different modes of aerosol administration may not be ideal. However, the direct way of demonstrating in vivo deposition using radiolabeled aerosols, as recently reported, should not be repeated unnecessarily for ethical reasons.¹² Although some of the existing literature suggests a very reproducible response to bronchodilators in spontaneously breathing preterm infants with statistically significant reduction in airway resistance, individual responses in these studies look more variable than the group results suggest.^{8,20} We are not aware of any published data on the short- and long-term variability of the bronchodilator response in preterm infants with which to compare our data. Within-subject variability in sedated preterm infants with chronic lung disease has been reported to be as high as 35% over a period of 4–8 days.²¹ Baseline variability over the 2-day period in the present study is similar, with the exception of two infants, which may potentially be attributed to the fact that all measurements were performed in unsedated sleep. The observed variability highlights the problems that may occur when using lung function parameters as outcome measures of longitudinal intervention studies in preterm infants with lung disease.

There are other potentially confounding factors in this study: dose-related responses were not assessed, and it may be that the maximum effect on mechanics would have been reached using a dose of 100 µg with either mode of delivery. Measurement of time-response curves was not attempted, although it has been demonstrated that salbutamol has a maximum effect on heart rate after 45–60 min in preterm infants with subacute respiratory distress syndrome.⁵ We may, therefore, have missed the maximum effect on mechanics. In the study by Lee and co-workers,⁵ there was a continuously increasing effect for up to 45 min following administration. Jet nebulization takes between 5 and 10 min, whereas the MDI-plus-spacer takes only about 1 min to administer. With an interval of 15–30 min from start of nebulization to end of nebulization and eventual measurement of lung mechanics, there was more time for salbutamol to have an effect when the nebulizer rather than the MDI-plus-spacer was used. The results which demonstrated a similar effect following MDI plus spacer and jet nebulizer may, therefore, be biased in favor of the nebulizer due to the longer time interval. However, the study design with all infants studied in natural unsedated sleep and an interval between feeds of only 2 h did not allow a more complicated protocol.

In the present study, the effect on pulmonary mechanics obtained with the Aerochamber® and the PariBaby® may only apply to the two devices evaluated and cannot

be generalized to other means of delivering aerosolized salbutamol or other medications to preterm infants with chronic lung disease. We chose these devices because the PariBaby® is the commonly used jet nebulizer for infants in our region. The Aerochamber® is the spacer device that has been studied most thoroughly in vitro and in animal model studies. Furthermore, it has the advantage of having a flexible connector for the MDI such that MDIs from different companies can be attached without difficulties.

Perhaps the most important difference between the two modes of delivering aerosolized medications is the timing: whereas it takes at least 5 min to nebulise 2 mL of a solution with the jet nebulizer, administration of medication with an MDI via spacer is completed within a minute. In the present study, the conditions for delivery were optimal, with the infant sleeping and the mask firmly applied over mouth and nose. Even under these circumstances, there was no advantage of the jet nebulizer with respect to effect of salbutamol on lung function. However, patient or parental compliance with administration of medications prescribed depends to a certain degree on the method used to deliver an aerosol. Compliance is less likely with a more complex procedure. Even in a neonatal unit with trained staff, we have observed some difficulty in adhering to recommendations with respect to jet nebulization. With clinical effects being at least similar for the two modes of delivering aerosolized salbutamol, the MDI-plus-spacer may, therefore, be a preferable method of drug delivery.

In summary, this study confirms the beneficial effect of inhaled salbutamol on lung mechanics in preterm infants with signs of chronic lung disease. The beneficial effect is not as consistent as has previously been suggested. We did not demonstrate a difference in effectiveness of aerosol delivery between a jet nebulizer and an MDI plus spacer. The present data may not be transferable to other devices and other drugs. The much shorter delivery time, and easier handling of an MDI-plus-spacer for staff in a neonatal unit and for parents may make an MDI-plus-spacer the preferable device for delivering inhaled medications to this group of infants.

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