

IMPROVED EFFICACY OF AEROSOL DELIVERY TO DISTAL AIRWAYS IN PEDIATRIC SUBJECTS USING A NEW SPACER MOUTH-MASK

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SUMMARY: Aerosol nebulization is one of the safest and most effective ways of treating airway diseases especially in children. Failure of inhaled asthma treatment is mainly due to inadequate deposition of drugs in the peripheral area of the lungs. The aim of this study was to compare the efficacy of a traditional mask and that of a new spacer mouth-mask (Nebula, Markos Mefar, Italy) when used with a jet nebulizer, by measuring aerosol deposition in the lungs, oropharynx, upper airways, and gastrointestinal tract.

Twelve children without respiratory disease aged between 8 and 13 years were included in the study. Aerosol inhalation was performed using a jet nebulizer with 2 mL of saline solution containing 20 Mci of Tc99m-DTPA. The first group initially performed aerosol inhalation using a traditional facemask and then, one week later, using the new spacer mouth-mask. The second group performed aerosol inhalation using the new spacer mouth-mask first and then, one week later, using a traditional mask. Scintigraphic ventilation images were then obtained, and aerosol deposition in the trachea, oropharynx, lungs and stomach was measured.

In the first group, the radioaerosol deposition in the peripheral lung area using the new spacer mouth-mask was greater 97.8 ± 7.0 vs 68.5 ± 7.9 ($p=0.04$). On the other hand, the oropharyngeal radioaerosol deposition was greater using the traditional mask: 50.2 ± 5.2 vs 20.3 ± 11.8 ($p=0.028$). Similarly, in the second group the peripheral lung deposition was greater and the oropharyngeal deposition was less using the new spacer mouth-mask: 97.3 ± 9.4 vs 70.2 ± 11.2 and 20.7 ± 8.9 vs 46.3 ± 16.8 ($p=0.028$ and 0.046 respectively).

In conclusion, the new design of the spacer mouth-mask allows greater aerosol deposition in the peripheral lung area and less in other parts such as the oropharyngeal area, the central airways and the stomach.

Key-words: Spacer-mask - Inhalation - Radioaerosol images.

INTRODUCTION

The delivery of aerosolized drugs to the lungs by inhalation is recognized as the safest and most effective way to treat airway diseases such as wheezy-child, asthma, etc. (1).

However, this method of administration may be challenging in early childhood and therefore many factors must be considered when selecting a suitable administration method for young children (2, 3). These factors include a lack of cooperation from the young child, the need for administration during tidal breathing and the need for a method that is suitable for both nasal and oral breathing (3). Nebulization is one of the most efficient and commonly used ways of administering drugs, especially to asthmatic children in early and late childhood (2). Failure of inhaled asthma treatment is mainly due to inadequate deposition

of drugs in the peripheral area of the lungs, i.e. the smaller airways where action is required (2). This is a major concern, especially in children, where it is due in most cases to lack of cooperation. Using the nebulization of a liquid preparation of inhaled drugs such as bronchodilators, corticosteroids, etc., they can be effectively delivered to the peripheral airways where major pathogenetic events occur. However, improvements in nebulization techniques and equipment are essential if successful treatment is to be achieved (4). The clinician who plans the treatment for asthma needs to know the characteristics of the inhalation devices in order to be able to select the most suitable device for the patient. This includes knowledge of nebulizers and spacers as well as the characteristics of the mask. Determination of the advantages and disadvantages of a particular mask will aid in designing a better treatment plan and providing more successful inhaled treatment education.

The aim of this study was to compare the efficacy of a traditional mask and a new spacer mouth-mask (Nebula, Markos Mefar, Italy) when used with a jet nebulizer, by measuring aerosol deposition in the lungs, oropharynx, upper airways, and gastrointestinal tract.

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MATERIAL AND METHODS

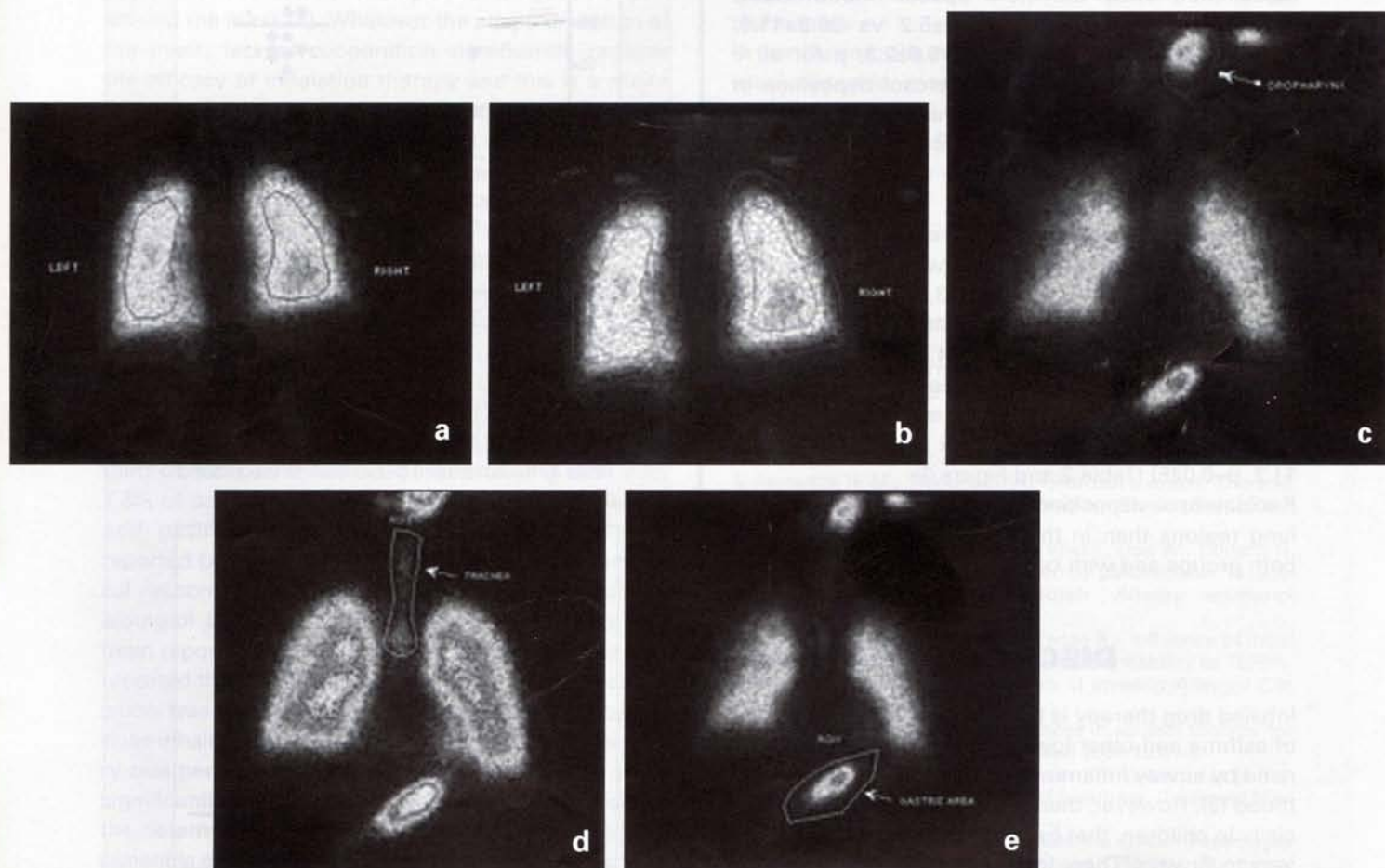
■ **Subjects:** Twelve children between 8 and 13 years of age, who had no evidence of respiratory disease, were included in the study, which was carried out in February and March 2006. These children had been referred to the Nuclear Medicine department for gastroesophageal reflux scintigraphy (GER) and ventilation images were obtained just before GER scintigraphy was taken.

■ **Study Design:** The subjects were divided into two groups. The first group initially performed aerosol inhalation using a traditional facemask and then, one week later, using the new spacer mouth-mask. The second group performed aerosol inhalation using the new spacer mouth-mask first and then, one week later, using a traditional mask. Both groups performed aerosol inhalation using a jet nebulizer for one minute with the respiratory pattern at tidal volume. Ventilation images were then obtained (Dual-Headed Gamma Camera, Siemens AG) and quantification studies were performed to measure the aerosol deposi-

tion in the trachea, oropharynx, lungs and stomach.

■ **Radionuclide Images and Quantification Analysis:** Aerosol inhalation was performed by the patients using a jet nebulizer (PharmaNeb, Marcos Mefar, Italy) with 2 mL of saline solution containing 20 Mci of Tc99m-diethylenetriaminepentaacetic acid (DTPA kit, Amersham). Tc99m-DTPA in suspension in an isotonic saline solution is not absorbed from the lungs into the bloodstream after deposition, thus helping to provide a static distribution of aerosol within the lungs during the image acquisition. The half-life of the administered Tc99m activity was not calculated since the study took a total of only 10 minutes.

A single posterior view planary ventilation image was taken. Quantification analysis was performed separately using data from the central and peripheral zones of the right and left lungs and other regions. Regions of interest (ROIs) were drawn over the interested areas which comprised the peripheral and central zones of the lungs, the oropharyngeal region, the tracheal region and the stomach, according to the previously reported modified method (Influence of inha-



Figures 1: Regions of Interest (ROIs) drawing over the interested areas to estimate the counts from central lung fields (a), peripheral zones of the lungs (b), oropharyngeal region (c), tracheal region (d) and the stomach (e).

led steroids on pulmonary epithelial permeability to Tc99m-DTPA in atopic asthmatic children (5) (Figure 1). The total lung count was estimated as the sum of the peripheral and central counts.

■ **Statistical Analysis:** Statistical analyses were performed using the SPSS 13.0 (Chicago IL) computer program. The deposition in the peripheral and central lung areas, the oropharynx, the trachea and the stomach, using the traditional and the spacer mouth-mask were compared using Wilcoxon's signed rank test with p values <0.05 considered statistically significant.

RESULTS

The age range of the children in group 1 was 8 to 11 years (mean±standard deviation (SD) 9.7±1.2). The children in group 2 were aged between 9 and 13 years (mean±SD 10.8±1.5).

In the first group, who received aerosol treatment initially with the traditional mask, the deposition of radioaerosol in the central lung area, oropharynx, trachea and stomach was higher with the traditional mask than with the new spacer mouth-mask. (110.0±20.9 vs 85.3±15.2, 50.2±5.2 vs 20.3±11.8, 17.0±1.3 vs 8.2±2.6, 13.0±3.4 vs 9.8±2.3; p for all < 0.05). On the other hand, radioaerosol deposition in the peripheral lung area was greater with the new spacer mouth-mask (97.8±7.0 vs 68.5±7.9, p=0.04) (Table 1 and Figure 2).

Similarly, in the second group, the deposition of radioaerosol in the central lung area, oropharynx, trachea and stomach was higher with the traditional mask (105.0±32.9 vs 92.3±25.3, 46.3 ± 16.8 vs 20.7±8.9, 30.7±26.1 vs 23.3±25.1, 18.3±6.6 vs 11.5±6.2 respectively, p values were 0.34, 0.046, 0.027 and 0.027 respectively). However, radioaerosol deposition in the peripheral lung area was significantly higher with the new spacer mouth-mask (97.3±9.4 vs 70.2 ± 11.2, p=0.028) (Table 2 and Figure 3).

Radioaerosol deposition was greater in the central lung regions than in the peripheral lung regions in both groups and with both masks.

DISCUSSION

Inhaled drug therapy is the mainstay of the treatment of asthma and other lower airway diseases characterised by airway inflammation from childhood to adulthood (3). However, there are important factors, especially in children, that have an influence on drug delivery to airways. These include cooperation, use of the proper mask, lower tidal volumes and inspiratory flows, determination of appropriate doses and minimisation of side effects (6). Efficient aerosol delivery

depends above all on the deposition in the lungs while minimising deposition in the gastrointestinal tract and upper airways. The aim of our study was to assess the efficacy of a new mask by measuring radioaerosol deposition in the peripheral and central lung areas, as well as in the oropharynx, the trachea and the stomach.

	Old mask	New mask	P
Peripheral lung	68.5±7.9	97.8±7.0	0.027
Central lung	110.0±20.9	85.3±15.2	0.044
Oropharynx	50.2±5.2	20.3±11.8	0.028
Trachea	17.0±1.3	8.2±2.6	0.027
Stomach	13.0±3.4	9.8±2.3	0.026

Table 1: Radioaerosol deposition in the first group with the old and the new masks.

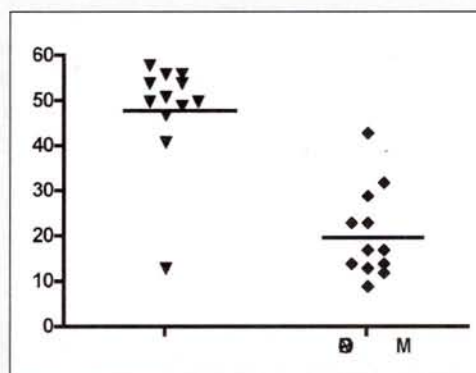


Figure 2: Radioaerosol deposition in the peripheral lung area was greater with the new spacer mouth-mask.

	Old mask	New mask	P
Peripheral lung	70.2±11.2	97.3±9.4	0.028
Central lung	105.0±32.9	92.3±25.3	0.344
Oropharynx	46.3±16.8	20.7±8.9	0.046
Trachea	30.7±26.1	23.3±25.1	0.027
Stomach	18.3±6.6	11.5±6.2	0.027

Table 2: Radioaerosol deposition in the second group with the old and new masks.

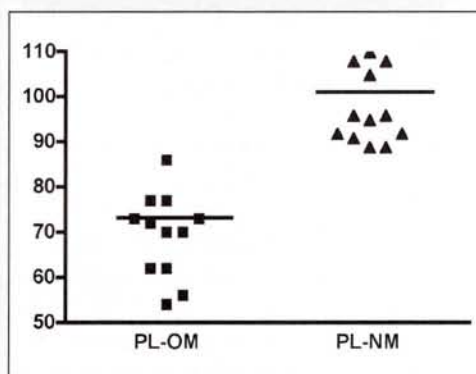


Figure 3: Radioaerosol deposition in the peripheral lung area was significantly higher with the new spacer mouth-mask.

Inhaled therapy is influenced by the interaction between the patient and the inhalation device (7). Facemasks are often used for inhalation therapy in young children (8). The factors that influence mask efficiency include mask-face seal, mask dead space, cooperation, resistance and the diluting effect of air entering the mask through the exhalation ports (9). The efficiency of drug delivery using this system depends on the fit of the mask and the patient's cooperation (10). Most of these factors are involved in masks used with spacers.

The facemask functions as an aerosol reservoir for jet nebulizers (7). Therefore, the facemasks used with the jet nebulizers should be soft enough to form a complete seal with the face (7). Other studies have also emphasised the importance of facemask design in the efficiency of drug delivery (7). If there is inadequate seal, air entry will dilute the aerosol and decrease delivery (7). However, there is an advantage of jet nebulizers in that the flow of gas from the compressor keeps the mask full of aerosol particles, thus facilitating inhalation (8). During nebulized aerosol therapy, the volume of gas containing particles may exceed the minute ventilation causing the extra gas to be lost around the mask (8). Whatever the shape or design of the mask, lack of cooperation significantly reduces the efficacy of inhalation therapy and this is a major factor in children (4). In a previous study, it was reported that round facemasks provided an increased efficacy of inhalation therapy, however these results were obtained by measuring drug accumulation in a filter positioned between the spacer and the mask and therefore did not show lung deposition (4).

The nebulizer output is similar in child and adult breathing patterns, but children inhale less of the aerosol (11). The lung deposition of albuterol delivered by jet nebulizer has been shown to be around 5.4-11.1% in children (12). Another study has reported that 1.5% of the nebulized drug reaches the right lung and that one third of that penetrates the peripheral lung area with 7.8% of deposition occurring in the upper respiratory and gastrointestinal systems. No correlation was reported between the deposition indices and the clinical response (13). The administration of radiolabeled albuterol to wheezy infants via nebulizer mask has been reported to be 2.4% (14). In another study it was reported that the percentage of pulmonary drug deposition was the same using a nebulizer or a metered-dose inhaler with holding chamber, but that the delivery rate per minute and the total dose deposited were significantly higher with the nebulizer (11). Therefore, the determination of the most suitable device for the patient is essential for successful therapy. In this study, it was detected that the peripheral lung deposition was significantly higher with the use of the spacer mouth-mask. This is a major indicator of therapy efficacy.

Scintigraphy allows the measurement of uptake and clearance of a radioactive substance labeled to a molecule with the desired biological or physiological properties (15). Planar imaging is the method of choice for assessing lung deposition of inhaled medications, and pulmonary drug delivery, i.e. total deposition of aerosols, can be assessed with scintigraphy (15). In this study, scintigraphic images were used to measure central and peripheral lung deposition and it was shown that the central lung deposition was greater with the traditional mask whereas the peripheral lung deposition was greater with the spacer mouth-mask. This finding is important since the peripheral lung area is the target of aerosol therapy.

Moreover, scintigraphy can be used to measure the distribution of the aerosol in the oropharynx and the gastrointestinal tract (1,15). In our study, the radioaerosol deposition in the oropharynx, trachea and stomach was lower with the spacer mouth-mask. This favours the prevention of side effects associated with the accumulation of aerosol particles in tissues other than the lungs. In terms of radiation, the effective dose of radiation can be kept below 1mSv with scintigraphy and this is low compared to many radiologic techniques.

In conclusion, the new design of the spacer mouth-mask allows for more efficient aerosol treatment with greater peripheral lung deposition and is expected to decrease the side effects attributed to aerosol deposition in other parts of the lungs, upper airways and stomach.

References

1. Anderson P.-J. - History of aerosol therapy: liquid nebulization to MDIs to DPIs. *Respir Care* 2005;50:1139-50.
2. Franca E.-E., Dornelas de Andrade A.-F., Cabral G., Almeida Filho P., Silva K.-C., Galindo Filho V.-C., Marinho P.-E., Lemos A., Parreira V.-F. - Nebulization associated with bi-level noninvasive ventilation: analysis of pulmonary radioaerosol deposition. *Respir Med* 2006;100:721-8.
3. Janssens H.-M., Tiddens H.-A. - Aerosol therapy: The special needs of young children. *Paediatr Respir Rev* 2006;7 Suppl 1:S83-5.
4. Esposito-Festen J., Ates B., van Vliet F., Hop W., Tiddens H. - Aerosol delivery to young children by pMDI-spacer: is facemask design important? *Pediatr Allergy Immunol* 2005;16:348-53.
5. Yuksel H., Yuksel D., Demir E., Tanac R. - Influence of inhaled steroids on pulmonary epithelial permeability to Tc99m-dTPA in atopic asthmatic children. *J Investig Allergol Clin Immunol* 2001;11:188-92.
6. Devadason S.-G. - Recent advances in aerosol therapy for children with asthma. *J Aerosol Med* 2006;19:61-6.
7. Smaildone G.-C., Berg E., Nikander K. - Variation in pediatric aerosol delivery: importance of facemask. *J Aerosol Med* 2005;18:354-63.
8. Sangwan S., Gurses B.-K., Smaildone G.-C. - Facemasks and facial deposition of aerosols. *Pediatr Pulmonol* 2004;37:447-52.
9. Amirav I., Newhouse M.-T. - Aerosol therapy with valved holding chambers in young children: importance of the facemask seal. *Pediatrics* 2001;108:389-94.

10. Louca E., Leung K., Coates A.-L., Mitchell J.-P., Nagel M.-W. - Comparison of three valved holding chambers for the delivery of fluticasone propionate-HFA to an infant face model. *J Aerosol Med* 2006;19:160-7.
11. Fink J.-B. - Aerosol delivery to ventilated infant and pediatric patients. *Respir Care* 2004;49:653-65.
12. Wildhaber J.-H., Dore N.-D., Wilson J.-M., Devadason S.-G., LeSouef P.-N. - Inhalation therapy in asthma: nebulizer or pressurized metered-dose inhaler with holding chamber? In vivo comparison of lung deposition in children. *J Pediatr* 1999;135:28-33.

13. Amirav I., Balanov I., Gorenberg M., Luder A.-S., Newhouse M.-T., Groshar D. - Beta-agonist aerosol distribution in respiratory syncytial virus bronchiolitis in infants. *J Nucl Med* 2002;43:487-91.
14. Amirav I., Balanov I., Gorenberg M., Groshar D., Luder A.-S. - Nebulizer hood compared to mask in wheezy infants: aerosol therapy without tears! *Arch Dis Child* 2003;88:719-23.
15. Eberl S., Chan H.-K., Daviskas E. - SPECT Imaging for Radioaerosol Deposition and Clearance Studies. *J Aerosol Med* 2006;19:8-20.



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