



ORIGINAL ARTICLE

The use of helium-oxygen mixture in the ventilation study of children with chronic obstructive lung disease

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Abstract

Objective: to study the distribution of Tc-99m DTPA radioaerosol when heliox or oxygen are used in the nebulization of children and adolescents with chronic obstructive pulmonary disease during pulmonary ventilation scintigraphy.

Material and methods: clinical randomized and controlled trial. Patients with chronic obstructive pulmonary disease (5 to 18 years old) who required pulmonary scintigraphy between March 1996 and September 1998 were included. Obstruction of the lower airway was measured by spirometry. Patients were randomized into two groups according to the gas used for nebulization during scintigraphy: heliox (80% helium and 20% oxygen) or oxygen. Scintigraphy studies were expressed as slope of the cumulative pulmonary radioactivity uptake curve and as the maximal cumulative radioactivity in the lung. The mean diameter of the Tc-99m DTPA particles generated by heliox and oxygen was measured by laser diffraction.

Results: ten patients were allocated in each group. There were no statistical differences ($P>0.05$) in terms of gender, main diagnosis, signs of malnutrition, mean values of weight, height, body area, or spirometry results. The mean slope in the heliox group (5.039 ± 1.652) was significantly different ($P=0.018$) from the mean slope of the oxygen group (3.410 ± 1.100). The mean slope of patients with severe airflow obstruction in the heliox group was statically different ($P=0.017$) from the mean slope of patients with airflow obstruction in the oxygen group. In both groups, patients without evidence of airflow obstruction were similar in terms of mean slopes ($P=0.507$) and mean cumulative radiation in the lung ($P=0.507$). The mean diameter of heliox-generated Tc-99m DTPA particles was 2.13 μ m (± 0.62). This was statistically different ($P=0.004$) from the mean diameter of oxygen-generated particles (0.88 ± 0.99 μ m).

Conclusions: nebulization with heliox was more efficacious than nebulization with oxygen for distribution and dispersion of Tc-99m DTPA radioaerosol in the lungs of children and adolescents with chronic obstructive pulmonary disease submitted to ventilation scintigraphy. The benefits of heliox over oxygen are more evident in the presence of lower airway obstruction. Without airway obstruction, we did not observe any difference in the distribution and dispersion of radioaerosol in the lungs. Although the mean diameter of the Tc-99m DTPA particles generated by heliox and oxygen was significantly different, the particles generated by both gases were still within the recommended range (between 1 and 5 μ m). Therefore, this difference does not account for the effects of heliox observed in this study.

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Introduction

Air moves from the environment into the pulmonary parenchyma through ducts called airways. The pharynx, the larynx, and the extrathoracic portion of the trachea constitute the upper airway. The lower airway is constituted by the

intrathoracic portion of the trachea, the bronchi, and the bronchioles.¹ Obstructive airway disease results from a significant decrease in the lumen of any of these segments, compromising airflow.¹⁻⁵

Although the alveolar surface is reduced in newborns, the lower airway ramification is already defined; this configuration will not change as the child grows to become an adult.^{2,5} There are several differences between the airways in adults and children; the main distinction concerns the diameter and length of the airways.^{2,6} The reduced caliber of lower airways allows for an elevated resistance to airflow, favoring obstruction.^{2,3,5,7} This anatomic feature is one of the reasons for the high prevalence of chronic obstructive diseases in the lower airways, which have been reported to affect up to 20% of the children in different populations.⁸⁻¹⁰

Resistance to gas flow in the airway depends mainly on the following three factors: (a) flow type (laminar or turbulent); (b) gas viscosity and density; (c) airway diameter.

In the past, pulmonary resistance until 5 years of age was thought to result from difficulties in the flow of air inside airways with a diameter of less than 2 mm. After this age, the resistance offered by the large airways would predominate, while peripheral airways would contribute with only 10% of the total airflow resistance in the lungs.^{2,5,11} Currently however, turbulent airflow is seen as responsible for most of the pulmonary resistance in the large airways, both in children and adults.¹²

From a clinical point of view, a more intense obstruction results in reduced delivery of inhaled drugs and in increased resistance to treatment. In these situations, the small volume associated with a turbulent flow makes the distribution of drugs inside the bronchi more difficult.^{7,13-16} According to some studies, less than 3% of the inhaled drug volume reach the lower airways.¹⁷

In order to counterbalance the low efficacy of nebulized beta-adrenergic agents in children with bronchospasm, the mode of drug administration is often changed by increasing the dose, reducing nebulization intervals, or changing the method of delivery.^{7,13,14} This raises the question of whether it would be legitimate to consider the use of a gas with a lower density (rather than air or oxygen) for nebulization, so as to overcome airway turbulence and ensure the delivery of larger amounts of beta-adrenergic agents to the bronchi of patients with intense obstruction.

Helium was isolated from the atmospheric air by Ramsay, in 1895. Four decades later, Barach published the first scientific articles proposing its use to treat respiratory obstruction of the larynx, trachea or bronchi.^{18,19}

Helium is an inert gas of unknown toxicity. Since its relative gaseous density is much smaller than that of air or oxygen, it presents a much less turbulent, and more laminar flow than those gases.^{20,21} The density of helium is estimated to be one-seventh that of the nitrogen-oxygen mixture. The advantage of this low density is that it favors a more laminar

flow through the obstructed airways, decreasing the probability of a turbulent flow, and neutralizing the effect of increased resistance.^{22,23} Based on these properties, a helium-oxygen mixture (heliox) was initially used in the treatment of patients with upper airway obstruction.²²⁻²⁶

Several studies show that the decrease in turbulence and resistance is directly associated with the concentration of heliox. A maximal effect is obtained with a ratio of 80% helium:20% oxygen.²²

Although a reasonable number of works confirm the safety and efficacy of heliox in the treatment of patients with respiratory obstruction, more detailed studies are still required before the use of heliox can be routinely indicated. If heliox does indeed promote a less turbulent flow, easing ventilation and oxygenation in partially obstructed areas, it is possible to assume that the distribution and discharge of bronchodilators in the lower airways of children with bronchospasm crises would improve with the use of heliox instead of oxygen or compressed air for nebulization.

Therefore, the objective of the present study was to document and compare the efficacy of nebulization with heliox (80%) and oxygen in terms of the distribution and deposition of technetium-99m diethylene triamine pentaacetate (Tc-99m DTPA) particles in children with obstructive pulmonary disease submitted to ventilation scintigraphy.

Materials and methods

We performed a crossover, controlled and randomized clinical trial at the Nuclear Medicine and Pulmonary Services, Hospital de Clínicas de Porto Alegre, between March 1996 and September 1998. The research protocol was approved by the research ethics committee at the Hospital. An informed consent form was signed by the parents or legal guardians of all the children included in the study.

Patients between 5 and 18 years of age with a diagnosis of chronic obstructive pulmonary disease (COPD) were consecutively included in the study, regardless of etiology. All of these patients were followed by the pediatric pulmonary team at Hospital de Clínicas de Porto Alegre, and had been referred for scintigraphic evaluation of pulmonary ventilation between March 1996 and September 1998.

Patients who were not able to complete or adequately perform the evaluations (spirometry and/or scintigraphy) were excluded. Other exclusion criteria included neuropsychomotor involvement preventing understanding and/or collaboration to perform the tests; severe dyspnea with indication for hospitalization or immediate therapeutic intervention; pregnancy; test results that did not fulfill the minimum quality standards established by the Nuclear Medicine (scintigraphy) and Pulmonary (spirometry) Services; and refusal to participate in the study or to sign an

informed consent form.

Concomitantly to the scintigraphic study, patients were submitted to pulmonary function tests (spirometry), in order to confirm and quantify the degree of lower airway obstruction. Assessment parameters were forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), forced expiratory flow rates at 75% of FVC (FEF 75%), and forced expiratory coefficient in 1 second (FEC1). Results were interpreted and expressed in percentages of normality, based on the values considered normal for the specific age, sex and height.^{2,27-29}

In the present study, airflow obstruction was defined as FEC1 below 0.75 and FEF75% below 0.25 on spirometry. Currently, these two parameters are considered as the most sensitive to determine the presence of lower airway obstruction.²⁸⁻³¹

Patients were distributed into two groups, according to the gas used for ventilation scintigraphy: heliox (80% helium and 20% oxygen), or oxygen. Patients were randomly distributed into each group, picked by lot. The two groups had the same number of participants. All patients, regardless of the gas used, were submitted to pulmonary scintigraphy with Tc-99m DTPA radioaerosol.

Tc-99m DTPA radioaerosol was administered using a portable equipment specifically designed for pulmonary inhalation of radioactive aerosols (Aerogama, Medical, Porto Alegre, RS, Brazil). This equipment employs oxygen with flows of 10 l/min and Tc-99m DTPA aerosol particles with a mean diameter of 0.88 μ (standard deviation = 0.96 μ).³²

The test was carried out with patients in the sitting position. The procedure lasted about 10 minutes. The facial mask was completely insulated, and patients were asked to perform inspiratory and expiratory movements without effort. The tests were supervised always by the same physician, who corrected possible errors in the procedure.

Before being tested, all children and adolescents included in this study were trained by the same instructor. In addition to receiving technical instructions, during the training patients had time to get familiar with the mask. After the training, nebulization was carried out.

The sequential measurement of thoracic radioactivity was performed immediately after the end of nebulization using a scintillation gamma camera (Anger, model MB 9200 - Gamma Müvek, Budapest, Hungary), equipped with a low-energy collimator. The measurement of thoracic radioactivity was performed in 10-second intervals for 15 minutes (total of 90 expositions). The reading of the radioactivity absorbed by each lung area is cumulative. At the end of the test (after 15 minutes), it is possible to express, in counts, the maximum amount of radioactivity accumulated by the right lung (RmaxR), by the left lung (LmaxR), and the mean for both lungs (MmaxR). These data can be presented numerically (measurement by time

elapsed), or as a radioaerosol acquisition curve for each lung, with variable degrees of inclination (30° to 60°), according to the speed of radioactivity uptake in each lung. The speed of radioactivity uptake is related to the resistance in lower airways. At the end of a variable period (8 to 15 minutes), this curve hits a peak of maximum cumulative concentration, followed by a plateau in which no increase in radioaerosol concentration can be observed with time.

The slope of the radioactivity uptake curve in the heliox and in oxygen groups was compared. Faster uptake in either lung is reflected by a more inclined line, closer to the vertical axis. On the other hand, difficult absorption and distribution of radioaerosol in the lungs is reflected by a less inclined (smaller slope), more horizontal line (closer to the X-axis) that reaches the peak and the plateau much later. In the present study, the slopes for both lungs (R-slope and L-slope) and the mean inclination for each patient (M-slope) were considered.

The mean diameter of aerosol particles generated by the Aerogama nebulizer when oxygen or helium were delivered was determined by laser ray diffraction (measured by conventional Fourier optics using a Droplet and Particulate Analyzer - Malvern series 2600). This determination was performed at the Polytechnic School (Universidade de São Paulo). The instrumental conditions employed were air-dispersed droplet spray, with a 63-mm lens.

For both groups (heliox and oxygen), continuous variables were expressed as mean and standard deviation (\pm SD), while categorical variables were expressed as percentage (%) or descriptively. Student's t-test was used for comparison of continuous variables, whereas the chi-square test with Yates' correction or Fischer's exact test when necessary was used to analyze categorical variables. Significance was established at $P < 0.05$.

In order to estimate the sample size required to compare the two groups in terms of radioactivity uptake slope, we established the following criteria: (i) minimum difference to be tested: 20%; (ii) significance level (a): 0.05; (iii) statistical power (1-b): 0.80. Based on these three criteria, and considering the findings of our previous pilot study with healthy adults, as well as the results of other previously published studies, the minimum sample size was estimated at 10 individuals per group. To ensure the validity of our results and to attenuate the effect of possible losses, we added 10% to this sample estimation, which resulted in a sample size of 22 patients to be included in the study.

Results

From March 1996 to September 1998, 22 consecutive children and adolescents between the ages of 5 and 18 years who were diagnosed with COPD were referred to scintigraphic evaluation of pulmonary ventilation. All fulfilled the inclusion criteria.

From the 22 patients initially included in the study, two (one in the heliox and the other in the oxygen group) were excluded due to technical problems in the performance of the scintigraphic study: in one patient, the facial mask was not adequately insulated during the exam; in the second patient, the measurement of irradiation started too late, so that positive counts were observed even at the “zero” moment. Therefore, 20 patients finished the study.

Following randomization as previously described, 10 individuals were included in each group. Eleven patients were male (55%), with a mean age of 9.25 (± 3.06) years (6 to 16 years), and a median of 8 years of age. There was no difference between the groups concerning mean age ($P=0.83$), weight ($P=0.76$), height ($P=0.89$), and body surface area ($P=0.86$). Both groups were also similar in terms of distribution of main diagnosis and gender.

As shown in Table 2, no statistical difference was found between the two groups (heliox versus oxygen) in terms of FVC ($P=0.21$), FEV1 ($P=0.61$), FEC1 ($P=0.70$), or FEF75% ($P=0.94$). Table 3 shows radioactivity uptake slope results. The group receiving Tc-99m DTPA radioaerosol using heliox (heliox group) presented significantly higher slope values than the oxygen group for the mean slope of right lungs ($P=0.023$), left lungs ($P=0.049$), and both lungs ($P=0.018$).

In order to evaluate the influence of pulmonary obstruction to airflow on the uptake of radioaerosol by the lungs with oxygen or heliox, we stratified the groups into two subgroups, according to the findings of the pulmonary function study. Airflow obstruction was considered in individuals presenting an FEC1 <0.75 on spirometry, associated with an FEF 75% <0.25 . Six individuals in the heliox group (heliox with airflow obstruction) and other four in the oxygen group (oxygen with airflow obstruction) fulfilled this definition. In Table 4, we describe and compare the means of spirometry and scintigraphy results taking into

consideration the two subgroups of patients that used heliox for the nebulization of Tc-99m DTPA radioaerosol. When comparing patients with airflow obstruction (heliox) with those without airflow obstruction (heliox), we observed a statistically significant difference in the mean values for FEC1 ($P=0.0007$) and FEF 75% ($P=0.0022$). We also observed that the maximal mean cumulative radiation in both lungs in patients in the heliox with airflow obstruction subgroup ($2,755,891\pm 801,859$) was significantly higher ($P=0.045$) than in the heliox without airway obstruction subgroup ($1,598,075\pm 675,310$). However, the mean slope in the two subgroups was not significantly different ($P=0.1283$).

Mean spirometry and scintigraphy results for the two subgroups of patients using oxygen for the nebulization of Tc-99m DTPA radioaerosol are described and compared in Table 5. When comparing the patients defined as presenting airflow obstruction (oxygen) with those defined as not presenting airflow obstruction (oxygen), we observed statistically significant differences in the mean values for FEC1 ($P=0.008$) and FEF 75% ($P=0.029$). However, the mean maximal cumulative irradiation in both subgroups was not statistically different ($P=0.960$); similar results were observed from mean Mslope results ($P=0.903$).

In Table 6, we describe and compare mean spirometry and scintigraphy results in the two subgroups of patients defined as presenting airflow obstruction (heliox and oxygen). The obstructive component in these patients, measured by FEC1 and FEF 75%, was not statistically different ($P=0.639$ and 0.386 , respectively). Concerning assessment of the effect of the gas used (heliox versus oxygen) in the administration of Tc-99m DTPA radioaerosol in patients with the same degree of obstruction, we observed that the heliox with airflow obstruction subgroup presented a $5,697 (\pm 1,365)$ MSlope, which was significantly higher ($P=0.017$) than the $3,467 (\pm 651)$ MSlope presented by the oxygen with airflow obstruction subgroup.

Table 1 - Characteristics of the groups using heliox or oxygen for delivery of Tc-99m DTPA radioaerosol on ventilation scintigraphy

Groups	Weight (kg)	Height (cm)	Body surface (m ²)	Age (years)	Gender (M:F)	Diagnosis
Heliox						
Means	33.33	136.89	1.104	9.40	5:5	Asthma (5)
(SD)	(16.31)	(14.23)	(0.29)	(2.63)		CF (5)
Oxygen						
Means	30.70	135.30	1.081	9.10	6:4	Asthma (2)
(SD)	(12.09)	(20.44)	(0.30)	(3.57)		CF (8)
*P	0.764	0.889	0.860	0.833	NS	NS

* Student's t-test

M:F= male to female ratio; CF = cystic fibrosis

Table 2 - Mean spirometry values for the groups using heliox or oxygen for delivery of Tc-99m DTPA radioaerosol on ventilation scintigraphy

	FVC (% of expected)	FEV₁ (% of expected)	FEC₁	FEF 75% / FVC
Heliox				
Means	94.20	83.90	76.50	38.30
(SD)	(21.19)	(24.78)	(14.65)	(30.84)
Oxygen				
Means	82.60	78.10	79.20	39.30
(SD)	(19.39)	(25.62)	(16.66)	(30.53)
*P	0.218	0.613	0.705	0.943

* Student's t-test.

FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 second; FEC₁: forced expiratory coefficient in 1 second; FEF 75%/FVC: forced expiratory flow rates at 75% of forced vital capacity.

Table 3 - Slope of the Tc-99m DTPA uptake curve in the groups using heliox or oxygen for delivery of radioaerosol on ventilation scintigraphy

Group	R-slope	L-slope	M-slope
Heliox			
Means	4.920	5.157	5.039
(SD)	(1.379)	(2.272)	(1.652)
Oxygen			
Means	3.363	3.458	3.410
(SD)	(1.412)	(1.135)	(1.100)
*P	0.023	0.049	0.018

* Student's t-test

Slope: inclination of the radioaerosol uptake curves in the right (R) and left (L) lungs. M-slope: mean inclination in right and left lungs.

Table 4 - Influence of lower airway obstruction in pulmonary scintigraphy of patients using heliox to deliver Tc-99m DTPA radioaerosol

	FEC₁ Mean (SD)	FEF 75%/FVC Mean (SD)	MmaxR Mean (SD)	M-slope Mean (SD)
Heliox with airflow obstruction (n=6)	66.5 (7.01)	18.17 (4.36)	2755.891 (801.859)	5.697 (1.365)
Heliox without airflow obstruction (n=4)	91.5 (7.85)	68.5 (28.21)	1598.075 (675.310)	4.052 (1.707)
*P	0.0007	0.0022	0.045	0.1283

* Student's t-test

FVC: forced vital capacity; FEC₁: forced expiratory coefficient in 1 second; FEF 75% FVC: forced expiratory flow rates at 75% of forced vital capacity; MmaxR: maximal cumulative irradiation; M-slope: mean inclination in right and left lungs; Heliox with airflow obstruction: patients of the heliox group with alterations in FEC₁ and FEF 75% FVC; Heliox without airflow obstruction: patients in the heliox group without alterations in FEC₁ and FEF 75% FVC.

Table 7 describes and compares mean spirometry and scintigraphy results for the two subgroups of patients defined as not presenting airflow obstruction (heliox and oxygen). We observed that the mean FEC₁ and FEF 75% values in these patients were within a normal range, without statistical difference (P=0.721 and 0.506, respectively). There was no difference between the heliox without airflow obstruction and the oxygen with airflow obstruction subgroups in terms of mean maximal cumulative irradiation (P=0.795) and MSlope (P=507).

In Table 8, we present the mean diameter of Tc-99m DTPA radioaerosol particles generated by the Aerogama nebulizer, using heliox or oxygen at a 10 l/min flow. The mean diameter of the Tc-99m DTPA radioaerosol particles generated when heliox was used was 2.13 m (±0.62), which was significantly higher (P=0.004) than the diameter of particles generated when oxygen was used for nebulization (0.88 ±0.99m).

Discussion

The present study shows that nebulization with heliox was more efficacious than nebulization with oxygen for distribution and dispersion of particles in the lower airways of children and adolescents with chronic obstructive pulmonary. This was probably due to the physicochemical properties (low density and high viscosity) of heliox. The benefic effects of heliox in comparison to oxygen become more evident as the degree of airflow obstruction increases. In the absence of significant airflow obstruction, the performance of both gases is very similar, so that there is no advantage in replacing oxygen with heliox in these situations. These conclusions are based on the following:

(a) The group submitted to ventilation scintigraphy with heliox presented a significantly higher mean slope (P=0.018) than the group that used oxygen for nebulization.

(b) In the heliox group, patients with reduced FEC1 and FEF 75% presented a cumulative radiation concentration in the lungs that was significantly higher ($P<0.05$) than that observed in patients of the same group who did not present evidence of airflow obstruction on spirometry.

(c) Again in the heliox group, patients with reduced FEC1 and FEF 75% presented a mean slope significantly higher ($P=0.017$) than the mean slope of patients in the oxygen group with evidence of airflow obstruction on spirometry.

(d) In the oxygen group, patients with and without evidence of airflow obstruction on spirometry presented no statistically significant differences in terms of either mean slopes ($P=0.903$) or cumulative concentration of pulmonary irradiation ($P=0.960$).

(e) Patients in the heliox and oxygen groups without evidence of airflow obstruction on spirometry presented no statistically significant differences in terms of either mean slopes ($P=0.507$) or cumulative concentration of pulmonary irradiation ($P=0.795$).

(f) The mean diameter of particles produced when oxygen and heliox were used for nebulization was within the recommended limits (between 1 and 5 μ m).

Considering the sample size, the methodology employed, and possible operational limitations, we had previously defined that best method to assess the outcome of scintigraphy in this study would be by measuring the slope of radioactivity uptake curves in the lungs. The use of slopes to evaluate and compare the effects of heliox in experimental situations has already been tested by Houck *et al.*,²² who examined several concentrations of heliox administered by artificial systems, which generated different patterns of resistance.

The slope expresses the relation between the amount of pulmonary radioactivity and the time spent. Thus, a higher slope value is explained by at least one of the following possibilities: (i) increased availability of radioaerosol in the area under assessment (i.e. facility in the transportation or diffusion of radioaerosol particles); (ii) a greater deposition of radioactivity in certain lung areas (caused by an alteration in the physicochemical properties of radioaerosol particles); (iii) less time required for the uptake of this radioactivity (i.e. a more laminar flow favoring distribution in less time).

Based on this evaluation parameter, we were able to demonstrate that the group that used heliox to deliver Tc-99m DTPA radioaerosol presented better results in terms of radioactivity acquisition slopes than the group that used oxygen. This result supports the hypothesis of this work and the conclusion that heliox, due to its physical properties,^{22,23,25,33} promotes a better dispersion and distribution of radioaerosol particles than oxygen.

The characteristics of the flow of each gas as it passes through the cylindrical tube are described by Reynolds's equation (rVd/m), where r is the gas density, V is the velocity, d is the diameter of the tube, and m is the gas viscosity.^{20-22,34} Thus, if this equation is applied to a gas that has low density and high viscosity, such as heliox, the result will be a small number. According to Reynolds, results close to or above 2,000 units are associated with a high probability increased flow turbulence.^{21,22}

With high flows of oxygen or air inside the trachea and main bronchi, Reynolds's equation exceeds 2,000 to 2,500 units,^{21,22,34} thus reflecting a more turbulent flow. Under these circumstances, dispersed particles, even if presenting an adequate diameter to reach the lower airways, will end up retained in the large upper airways, due to the impact against internal walls, which results from the turbulent flow.^{21,35-37}

Table 5 - Influence of lower airway obstruction in pulmonary scintigraphy of patients using oxygen to deliver Tc-99m DTPA radioaerosol

	FEC1 Mean (SD)	FEF 75%/FVC Mean (SD)	MmaxR Mean (SD)	M-slope Mean (SD)
Oxygen with airflow obstruction (n=4)	63.25 (14.11)	15.00 (6.73)	1784.600 (1067.550)	3.467 (651)
Oxygen without airflow obstruction (n=6)	89.83 (6.42)	55.52 (29.41)	1750.758 (983.646)	3.373 (1.385)
*P	0.008	0.029	0.960	0.903

* Student's t-test

FVC: forced vital capacity; FEC1: forced expiratory coefficient in 1 second; FEF 75% FVC: forced expiratory flow rates at 75% of forced vital capacity; MmaxR: maximal cumulative irradiation; M-slope: Mean inclination in right and left lungs; Oxygen with airflow obstruction: patients of the oxygen group with alterations in FEC1 and FEF 75% FVC; Oxygen without airflow obstruction: patients in the oxygen group without alterations in FEC1 and FEF 75% FVC.

Table 6 - Patients with lower airway obstruction using oxygen or heliox to deliver Tc-99m DTPA radioaerosol on ventilation scintigraphy

	FEC1 Mean (SD)	FEF 75%/FVC Mean (SD)	MmaxR Mean (SD)	M-slope Mean (SD)
Heliox with airflow obstruction (n=6)	66.5 (7.01)	18.17 (4.36)	2755.891 (801.859)	5.697 (1.365)
Oxygen with airflow obstruction (n=4)	63.25 (14.11)	15.00 (6.73)	1784.600 (1067.550)	3.467 (651)
*P	0.639	0.386	0.137	0.017

* Student's t-test

FEC1: forced expiratory coefficient in 1 second; FEF 75% FVC: forced expiratory flow rates at 75% of forced vital capacity; MmaxR: maximal cumulative irradiation; M-slope: Mean inclination in right and left lungs; Heliox with airflow obstruction: patients of the heliox group with alterations in FEC1 and FEF 75% FVC; Oxygen with airflow obstruction: patients in the oxygen group with alterations in FEC1 and FEF 75% FVC.

In our study, patients in the heliox and oxygen groups presented the same anthropometric characteristics and similar spirometric results. Based on these findings, it is fair to suppose that the dynamic characteristics of the airways in these patients should also be similar. Therefore, two variables of Reynolds's equation - airway diameter (d) and velocity (V) of gas flow in the airway - were probably constant in the two groups.

Keeping the analysis of results under the focus of Reynolds's equation, the only difference between the two gases in the present study must be attributed to differences

in viscosity and density. Since heliox presents lower density and higher viscosity than oxygen, we believe that its flow, more laminar in the large airways, was responsible for the significantly higher slope presented by this group when compared to the group using oxygen for nebulization of Tc-99m DTPA radioaerosol. In the small airways, due to their large cross-sectional area, the airflow is slower and more laminar even with heavier gases.³⁵ However, in the central airways, where the flow is faster and thus more turbulent, a less dense gas will maintain its laminar flow, so that more radioactive particles can reach peripheral airways. This effect shown in our study by the slope values observed.

Table 7 - Patients without lower airway obstruction using oxygen or heliox to deliver Tc-99m DTPA radioaerosol in pulmonary ventilatory scintigraphy

	FEC1 Mean (SD)	FEF 75%/FVC Mean (SD)	MmaxR Mean (SD)	M-slope Mean (SD)
Heliox without airflow obstruction (n=4)	91.5 (7.85)	68.5 (28.21)	1598.075 (675.310)	4.052 (1.707)
Oxygen without airflow obstruction (n=6)	89.8 (6.42)	55.5 (29.41)	1750.758 (983.646)	3.373 (1.385)
*P	0.721	0.506	0.795	0.507

* Student's t-test

FVC: forced vital capacity; FEC1: forced expiratory coefficient in 1 second; FEF 75% FVC: forced expiratory flow rates at 75% of forced vital capacity; MmaxR: maximal cumulative irradiation; M-slope: Mean inclination in right and left lungs; Heliox without airflow obstruction: patients of the heliox group without alterations in FEC1 and FEF 75% FVC; Oxygen without airflow obstruction: patients in the oxygen group without alterations in FEC1 and FEF 75% FVC.

Table 8 - Mean diameter of Tc-99m DTPA radioaerosol particles generated when heliox or oxygen were used for nebulization

	Heliox (10 l/min)	Oxygen (10 l/min)	P*
Mean diameter of particles (±SD)	2.13 (0.62)	0.88 (0.99)	0.004
Diameter at which 95% of particles are filtered	2.40 mm	2.25 mm	NS

* Student's t-test

Due to the characteristics attributed to heliox,^{21,35-37} it is possible that the radioaerosol particles transported by this gaseous mixture have been carried through a more laminar flow than that provided by oxygen. This laminar status of the flow avoided loss of radioaerosol by impaction and sedimentation in the larger airways, allowing a greater parcel of radioaerosol to reach the lower in less time.

In a similar study, Anderson et al.³⁸ assessed the deposition and retention (in 24 hours) of 111 I-labeled Teflon particles with a 3,6 m diameter following nebulization with heliox (80:20) or compressed air. Those authors employed used 0.5 and 1.2 l/min flows (smaller than in present study). The study showed: (i) less deposition of radioaerosol in extrapulmonary sites (mouth and pharynx) when heliox was used; (ii) a significantly higher radioaerosol retention rate (after 24 hours) in the lung areas of patients who used heliox, in comparison to those who used compressed air; (iii) the higher the degree of airway obstruction, the greater the efficacy of heliox. Those findings are in agreement with the results of our study.

Obviously, our results must be evaluated taking into consideration the limits imposed by the small number of individuals in each group, especially in the cases without statistical significance (items c and d). Nevertheless, when the comparison of results involving two populations with a small number of subjects attains statistical significance (items a and b), it is reasonable to believe that the phenomenon observed is important and meaningful. Considering these findings, it is possible to assume that the effects of the heliox mixture on the penetration and distribution of Tc-99m DTPA radioaerosol in lung areas will probably become more evident as the degree of obstruction presented by the patient increases.

In the analysis of the subgroups, heliox produced statistically significant differences when it was used to deliver radioaerosol in individuals defined as presenting

airflow obstruction. These individuals, when using heliox, obtained significantly better results than patients with airflow obstruction that used oxygen, as well as better results than the patients in the heliox group without airflow obstruction.

These findings, which are in agreement with the results reported by other investigators,^{22,38} emphasize that the benefits of the laminar flow provided by heliox are restricted to cases of turbulent flow associated with airway obstruction. In the absence of these conditions, heliox does not seem to present any advantage in relation to oxygen or air.

It is questionable whether these benefits should be attributed only to the properties of heliox (lower density and higher viscosity), or if other factors have also influenced these results.

Among possible confusion factors, the size of the radioaerosol particles generated by heliox is worthy of mention. This factor may have influenced the results obtained with heliox in our study. In this sense, it is crucial that the mean diameters of the particles generated by both gases be measured and compared: as we know, particles presenting a very reduced diameter have an increased power of penetration in lung areas, while large particles are retained in the large airways.^{36,37} Therefore, depending on the mean diameter of these particles, we would be able to partially or totally explain the results obtained.

As shown in Table 8, the Tc-99m DTPA particles generated when heliox was used for nebulization presented a mean diameter of 2.13 m (±0.62), which was significantly higher (P=0.004) than the mean diameter presented by oxygen-generated particles, 0.88 m (±0.99). This result, analyzed strictly from a statistical point of view, may provide further evidence to the qualities presented by heliox, since all the benefic effects observed in this study occurred despite the fact that this gas has generated radioaerosol particles with a much larger mean diameter than the particles generated by oxygen.

Even if true from a mathematical perspective, this difference in the mean diameter of the particles generated by the two gases does not have any clinical relevance, since, by definition, in order to attain the smaller airways, inhaled particles must have mean diameters between 1 and 5 μm ,^{2,6,14-16,35-37} and both gases produced radioaerosol particles with mean diameters within this recommended range (and which were adequate for this type of exam). Therefore, the observed difference in mean diameter probably does not account for the results obtained in the present study using heliox for nebulization in pediatric patients with chronic obstructive disease of the lower airways.

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