Original Article

Pulmonary blood flow distribution in acute viral bronchiolitis

Paulo R. Antonacci Carvalho, Renato D. Cunha, Sérgio Saldanha Menna Barreto

Abstract

Objective: to assess lung perfusion patterns in inpatients with acute viral bronchiolitis using quantitative 99mTc-MAA scintigraphy so as to establish an association with clinical and radiological findings.

Methods: a comparative, prospective case series study with a focus on diagnosis was carried out in a population of patients with acute viral bronchiolitis admitted to Hospital de Clínicas de Porto Alegre. Inclusion criteria were age between 01 and 24 months and first sudden-onset wheezing episode, suggesting bronchiolitis. The patients in the study were submitted to clinical, radiological and 99mTc-MAA lung perfusion evaluation during the first 24 hours of admission. Statistical analysis employed t test, taking into consideration a significance level of 0.05.

Results: the regional distribution of lung blood flow in the 38 patients studied was more pronounced in the upper section of the left lung in relation to the right lung (P<0.001). The distribution gradients of blood flow between the upper and middle and upper and lower sections were higher in the left lung (P<0.001). The distribution gradients of blood flow between the middle and lower sections were higher in the right lung, but without significance. The distribution gradient of the pulmonary flow in the anteroposterior axis was >1.0 in the upper and middle sections of both lungs. In the lower section it was >1.0 only in the right lung (P<0.007). There was no association between lung blood flow distribution patterns and clinical or radiological findings.

Conclusion: there was no evidence of an association between lung blood flow distribution and ventilation-perfusion ratio in hospitalized infants with acute viral bronchiolitis; only a tendency to redirect lung blood flow towards upper lung sections was observed.


Introduction

Pulmonary circulation is a low-resistance and high-capacity circuit functionally positioned between both sides of the heart and influenced by changes in pleural and airway pressure and by the performance of both ventricles. The capillary bed or the exchange system is the functional part of pulmonary circulation.1

It is widely known that blood flow through lungs is not uniform. According to West, pulmonary circulation is divided into three functional zones, according to the influence of the pressures that interfere with pulmonary blood flow (PBF) - alveolar pressure, pulmonary artery pressure and pulmonary venous pressure. This way, PBF increases as it moves away from the apex of the lung.2
During exercise or in pathological conditions, distension and recruitment of underperfused capillaries allow the redistribution of PBF, causing an increase in cardiac output with a slight increase in pulmonary artery pressure.\textsuperscript{3,4}

Alveolar hypoxia is a powerful stimulus for pulmonary vasoconstriction. The reduction of alveolar oxygen pressure in less than 50 to 60 mmHg causes vasoconstriction of precapillary arterioles of the lung within 3 to 10 minutes, allowing the redistribution of PBF beyond hypoxic areas. At very low oxygen pressures, the local pulmonary blood flow may be virtually absent. A severe acidosis also determines pulmonary vasoconstriction and the interaction between hypoxia and acidosis seems to be remarkably important in alveolar hypoventilation, causing deviation of blood flow to better ventilated regions of the lungs. This way, an automatic mechanism of blood flow distribution is established for different pulmonary areas in relation to their ventilation level.\textsuperscript{3}

Even under normal conditions, neither alveolar ventilation nor capillary blood flow are distributed in a perfectly uniform fashion in the lung. In obstructive respiratory diseases, such as acute viral bronchiolitis (AVB), the most common functional involvement is called ventilation/perfusion ratio (V/Q). Increased lung volume or increase in functional residual capacity, increase of inspiratory and expiratory resistance and alveolar hypoventilation with hypoxemia result from the partial obstruction of small airways. Differently from alterations in the ventilatory component of the V/Q ratio in AVB, the pulmonary perfusion component has not been studied in more detail.

Quantitative lung perfusion scintigraphy with technetium-99m macroaggregated albumin ($^{99m}$Tc-MAA) can precisely and safely measure the percentage of pulmonary blood flow through the lung and pulmonary region, and can only be compared to differential bronchospirometry, which is a risky, uncomfortable method that has not been assessed in infants.\textsuperscript{4}

The present study aimed at assessing the distribution pattern of PBF in inpatients with AVB by quantitative lung perfusion scintigraphy with $^{99m}$Tc-MAA.

Patients and methods

A serial, prospective, and comparative case study of the clinical and radiological evaluation was carried out by lung perfusion scintigraphy of inpatients with AVB in the acute phase. The study population consisted of a sample (selected by convenience) of patients clinically diagnosed with AVB, admitted to pediatric units (observation ward at the emergency department, hospitalization area, and intensive care unit) of Hospital de Clínicas de Porto Alegre (the authors did not interfere with hospitalization recommendations). The study was conducted between April 1998 and September 2000, using the following exclusively clinical inclusion criteria:\textsuperscript{6,7} sudden onset of expiratory wheezing, as first episode, in patients 1 to 12 months old with signs of viral respiratory disease, such coryza, irritating cough, hyperthermia and signs of respiratory disorder (tachypnea, retraction, activity of the ala nasi, breathing effort, and cyanosis).

Patients with perinatal history of supplemental oxygen requirement and/or mechanical ventilation requirement or with congenital cardiopathy or with recognized chronic pneumopathies or with disease that may favor chronic pulmonary aspiration, besides previous history of hospital admission due to wheezing. Those patients who could not be removed from the ICU for scintigraphic examination due to their severe clinical status were not included in the study.

All patients were submitted to quantitative lung perfusion scintigraphy with $^{99m}$Tc-MAA, for assessment of PBF distribution pattern in the acute phase of AVB, that is, during the first 24 hours after hospital admission.

Technetium-99m macroaggregated albumin ($^{99m}$Tc-MAA) (DRN 4378 Technel TechneScan\textsuperscript{®} LyoMAA, Mallinckrodt Medical B.V., Holland), was previously prepared. The patient was placed in the supine position during examination for the peripheral venous administration of 50 microcurie/kg of technetium 99m. After that, an Anger camera was used for mapping and imaging (Gamma camera GE Starcam, model 4000i, USA), equipped with a low-energy, high-resolution, parallel-hole collimator. The images were made at the anterior, posterior, and right and left obliquely posterior projections, with a 2.0 zoom and a $128 \times 128$ matrix. A total of 300,000 counts were defined for each image at each projection. The images were then visually interpreted and transferred to a data processing system (Hewlett-Packard computer, Kayak XU, USA) coupled to the gamma camera. The quantification of counts were made in three areas of interest per lung, in the anterior and posterior projections, totaling 12 areas of interest per patient through a specific protocol, which did not include the correction of counts for pulmonary volume or for topography of the thorax (Figure 1). The count in absolute number per areas of pulmonary interest was later transformed into distribution percentages per area of interest, based on the total count of both lungs, translating the PBF per pulmonary region. The assessment of scintigraphic exams included the comparison between both lungs with homonymous regions, gradients between regions, and gradients of regions in the anteroposterior axis.\textsuperscript{8}

The following data about the history and physical examination of each patient were recorded: age, gender, length of disease, initial therapeutic measures, length of hospital stay, weight, heart rate, respiratory frequency, axillary temperature, oxygen saturation (by pulse oximetry), presence of wheezing, use of accessory respiratory muscles, presence of cyanosis, presence of respiratory sounds on lung auscultation and sensory disorders. The severity of respiratory disorder was measured according to the clinical...
score for the diagnosis of respiratory insufficiency, adapted for the study (Table 1). All objective measurements were made by only one observer.

To establish an association between the clinical evaluation in ABV crisis and the pulmonary perfusion pattern, the continuous variables respiratory frequency (RF) and (SaO₂) were classified into two categories each. Therefore, the categories of “61 movements per minute or higher (mpm)” (group 1) and “60 mpm or less” (group 2) were considered for RF, and “95% or less” (group 1) and “96% or higher” (group 2) were considered for SaO₂.

The patients were submitted to chest x-ray (anteroposterior and lateral projections) on admission. Several exams were led astray at the moment of interpretation or lost by the parents. The exams were jointly interpreted by two radiologists, considering the most common findings observed in patients with AVB, with no knowledge about the condition of patients. The radiological findings were later classified into two categories: normal exams or exams with only nonspecific abnormalities of AVB (bilateral hyperexpansion of lungs and diffuse interstitial infiltrate) and exams with nonspecific alterations associated with other alterations such as atelectasis and consolidation, deviation of the mediastinum, and oligemia.

This study was approved by the Scientific, Ethics and Radioprotection Committees of Hospital de Clínicas de Porto Alegre (HCPA). A written consent was obtained from the parents or guardians of all patients.

The database was organized on an Excel spreadsheet (Microsoft, Excel 97, USA). The SPSS (Statistical Package for Social Sciences), version 6.0, and Epi Info 6.04 (Centers of Disease Control) programs were used for the statistical analysis. Student t test was used to compare the means (paired samples) and to assess the association between the categorical variables and percentage means or gradients (independent samples). A P value of 0.05 was considered to be significant.

### Table 1 - Clinical score for diagnosis of respiratory insufficiency

<table>
<thead>
<tr>
<th>Variable / Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheezing</td>
<td>none</td>
<td>mild</td>
<td>acute</td>
</tr>
<tr>
<td>Use of accessory respiratory muscles</td>
<td>none</td>
<td>mild</td>
<td>maximum</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>none</td>
<td>w/ FiO₂ 0.21</td>
<td>w/ FiO₂ 0.4</td>
</tr>
<tr>
<td>Respiratory sounds</td>
<td>normal</td>
<td>non-uniforme</td>
<td>diminished or absent</td>
</tr>
<tr>
<td>Brain function</td>
<td>normal</td>
<td>depressed or agitated</td>
<td>coma</td>
</tr>
</tbody>
</table>

Interpretation: scores 2 to 5 - moderate severity (initial respiratory insufficiency); score > 5 - high severity (acute respiratory insufficiency). Adapted from Wood DW, Downes JJ, Lecks HI. A clinical scoring system for the diagnosis of respiratory failure. Am J Dis Child 1972;123:227-32.

### Results

Thirty-eight patients with AVB (22 males and 16 females) were studied. Their general characteristics and vital signs are shown in Table 2. The mean age of the patients was 2.8 months, ranging from 1 to 8 months. Two thirds consisted of infants aged up to three months.

The interval between the onset of symptoms and hospital admission ranged between 0 and 7 days (mean 3.1±2.1 days). On admission, 63.5% of the patients presented moderate expiratory wheezing, 89.5% revealed moderate use of accessory respiratory muscle, 84% did not have cyanosis, 71% had abnormal respiratory sound, and 7.5% presented involvement of brain function.

**Figure 1** - Lung perfusion scintigraphy with use of protocol that divides each lung in three areas of interest (upper, mid and lower), in the anterior and posterior projection, totaling 12 areas of interest for the quantification of counts. R - right; L - left
Table 2 - General characteristics and vital signs of patients on admission

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±SD</th>
<th>Amplitude</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>2.8±2.0</td>
<td>1.0 to 8.0</td>
<td>38</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>5.4±1.7</td>
<td>3.0 to 9.8</td>
<td>31</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>156.2±20.5</td>
<td>112 to 200</td>
<td>38</td>
</tr>
<tr>
<td>RF (mpm)</td>
<td>56.5±13.2</td>
<td>40 to 92</td>
<td>37</td>
</tr>
<tr>
<td>Axil. temp. (ºC)</td>
<td>37±0.7</td>
<td>36 to 39</td>
<td>37</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>93.5±3.7</td>
<td>83 to 98</td>
<td>25</td>
</tr>
<tr>
<td>Severity</td>
<td>3.0±1.0</td>
<td>1 to 6</td>
<td>37</td>
</tr>
</tbody>
</table>

SD: standard deviation; n: number of patients; HR: heart rate; bpm: beats per minute; RF: respiratory frequency; mpm: movements per minute; Axil. temp.: axillary temperature; ºC: Celsius; Sat.O₂: oxygen saturation.

The most commonly respiratory signs and symptoms, which integrate the clinical severity score adopted in this study, have great variability and are relatively subjective as to their assessment or interpretation. On top of that, they are interdependent variables that prevent any signs and symptoms from being used separately in comparisons or associations with other variables. The composition of signs and symptoms, which resulted in the severity score for each patient on admission, ranged from 1 to 6 (mean = 3), where the scores between 2 and 5 represented patients with moderate severity.

Discussion

The case series, in which the age of two thirds of hospitalized patients was three months or less, is in agreement with other published case reports. Apart from the patients with some kind of susceptibility, the most severe cases of AVB are more frequent among infants aged less than one year and, especially, among those between one and three months of life. Low age is one of the risk factors for hospitalization or for the development of more severe cases.
Among our patients, the RF measured on hospital admission presented a range between 40 and 92 mpm (mean 56 mpm); only 11 patients had an RF greater than 60 mpm which, in a certain way, confirms the clinical assessment of severity.

On the other hand, SaO₂ is currently considered an essential vital sign in patients with acute respiratory disorder, for its immediate availability and for its noninvasive nature. According to Welliver and Welliver, the best individual predictive value of the need for hospital admission in the cases of AVB is SaO₂ < 95%. Among our patients, mean SaO₂ was 93.5% on admission, without supplementary oxygen supply, oscillating between 83 and 98%. Out of 25 patients with SaO₂ measurement on hospital admission, 16 had SaO₂ less than or equal to 95%, and among these, only one patient had clinical score of severity close to extreme severity (score 5).

The statistical evaluation for the presence of association between clinical variables, RF and SaO₂, and lung perfusion scintigraphy did not show a significant association for any of the variables. The analysis was based on the distribution of pulmonary perfusion per region and per gradients between regions and the RF and SaO₂ variables, classified according to severity. No association was detected in SaO₂ < 95%, which could indicate low alveolar oxygen pressure, and cause hypoxic pulmonary vasoconstriction.

The radiological findings obtained from 21 patients (55% of the sample), and the clinical manifestations as well showed great variability. Over 50% of the patients had slight alterations and 47.5% presented two or more alterations, some of which were nonspecific, such as segmental or subsegmental atelectasis, consolidations, deviation of the mediastinum or regional oligemia. For Darville & Yamauchi, increased lung volume is a typical characteristic of AVB, and is present in 50% of hospitalized patients. It is indeed the only radiological finding in 15% of the patients. Consolidations are present in 25% of the children, especially, young infants. In these patients, consolidations are usually located in the medial or upper lobe, indicating a more severe disease. For Fischer, the presence of atelectasis and consolidations was observed in more than 40% of the patients with more severe disease.

In the statistical evaluation for the presence of association between radiological examination and lung perfusion scintigraphy there was no significant association for any of the variables, even in the findings that supposedly indicated increased severity.

The lack of etiological confirmation of AVB and/or the lack of radiological examination in the whole sample may have limited the selection of patients to a certain extent. This was not the aim of this study.

The assessment of PBF distribution, when both lungs were compared, according to the analyzed regions, in the anterior and posterior projections, showed significant alterations only in the upper thirds of both projections, with perfusion in the left lung (L) higher than that of the right lung (R) (Figure 1).

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**Table 3** - Comparison of the gradients means among the same regions in both lungs with integrated anterior and posterior projections\(\text{§}\) (n=38)

<table>
<thead>
<tr>
<th>Gradient</th>
<th>Mean± SD</th>
<th>Diff.</th>
<th>CI 95%</th>
<th>P-value(\text{†})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper/ Mid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>0.49±0.11</td>
<td>-0.16</td>
<td>-0.19 to -0.12</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Left</td>
<td>0.65±0.09</td>
<td>-0.12</td>
<td>-0.19 to -0.12</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Upper/ Lower</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>0.59±0.19</td>
<td>-0.14</td>
<td>-0.20 to -0.08</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Left</td>
<td>0.73±0.17</td>
<td>-0.08</td>
<td>-0.15 to -0.05</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mid/ Lower</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>1.19±0.23</td>
<td>0.06</td>
<td>0.02 to 0.15</td>
<td>0.124</td>
</tr>
<tr>
<td>Left</td>
<td>1.13±0.21</td>
<td>0.15</td>
<td>0.08 to 0.20</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

\(\text{§}\) we considered as integrated projections the total counts obtained in the anterior and posterior projections; SD: standard deviation; Diff.: difference among means; CI 95%: confidence interval of 95%; \(\text{†}\) Student t test for paired samples; *statistically significant comparison for alpha = 0.05
When the integrated anterior and posterior projections were considered, the gradients of pulmonary perfusion between homonymous regions of both lungs were significantly higher in the left lung, especially in comparisons that involved the upper region (Table 3; p < 0.001).

The different PBF distribution through both lungs in AVB could not be compared using the literature referred in our study. Menna-Barreto determined the distribution of lung perfusion with 99mTc-MAA in 15 healthy young adults, and observed significant difference in blood flow between both lungs; the perfusion in the right lung was higher than in the left lung in nine patients, equal in three, and lower in three. Other studies cited by Menna-Barreto stated that the right lung has a relatively higher blood flow than the left lung.

The detection of higher blood perfusion in upper regions in AVB may be partially explained by findings already observed in adult patients. According to West, in upper lung regions, adults have vessels that are susceptible to recruitment and distension under circumstances that require more exchanges, especially if the model of lung perfusion zones is considered. In this model, the upper regions of the lungs have lower blood perfusion in normal conditions in individuals in an upright position. This might also occur in children, but with less intensity, as they do not stand in an upright position, possibly suffering from obstruction of the airways in dependent regions, in addition to deviating from the dominant gravitational pattern, even in the anteroposterior axis of the supine position. In AVB, this gradient may be reversed due to an increase in the functional residual capacity (FRC), even under good physiological conditions of breathing (normal FRC). The studies on the comparison of supine and prone position to improve the oxygenation of patients with severe acute lung injury show that there is always an anteroposterior gradient < 1.0 in adults in any of these positions, even under normal breathing. Given infants’ posture, the findings could also indicate the adjustment of the concept of the hilar-to-peripheral gradient of blood flow distribution for this age group. This observation was made by Walther et al.,...when they studied unanesthetized lambs in prone position; they found out that the distribution of pulmonary blood flow in these animals follows a hilar-to-peripheral gradient rather than a vertical gradient.

The sample of the present study consisted of very young patients, with ongoing postnatal lung development and, possibly, a very peculiar pulmonary vascular structure. Several characteristics, including those of the airways and pulmonary vessels, are still in transition between the fetal period and their early postnatal configuration.

The distribution of pulmonary blood flow did not show characteristics that expressed the ventilation/perfusion ratio pattern in hospitalized infants with acute viral bronchiolitis. There was only a tendency towards redirecting the distribution of blood flow to upper lung regions, possibly due to the recruitment of collapsed capillaries in these regions.

Likewise, considering the presence of response to hypoxic stimuli by diffuse V/Q unbalance of AVB, it is easier to understand the redirection of blood flow towards regions with better ventilation (upper regions). In addition to the increase of a probable hypoxic pulmonary vasoconstrictor response in the vessels at the base of the lung, compared to top lung vessels, the responsiveness to acute alveolar hypoxia is likely less intense in children than in adults, as observed by Rendas et al., who suggest higher responsiveness as the development of lungs advances. The lungs in infants are more responsive to chronic hypoxia than in adults because of the pulmonary arterial vessel configuration.

The comparison of lung perfusion distribution gradients in the anteroposterior axis of all regions in both lungs showed that blood perfusion was lower than 1.0 only in the lower left lung (Figure 2). This eliminates the presence of higher PBF density in more dependent areas, that is, in the posterior region rather than in the anterior region of the lung, as described by West in adults.

Children, especially infants, who have not adopted an upright posture, possibly suffer from obstruction of the airways in dependent regions, in addition to deviating from the dominant gravitational pattern, even in the anteroposterior axis of the supine position. In AVB, this gradient may be reversed due to an increase in the functional residual capacity (FRC), even under good physiological conditions of breathing (normal FRC). The studies on the comparison of supine and prone position to improve the oxygenation of patients with severe acute lung injury show that there is always an anteroposterior gradient < 1.0 in adults in any of these positions, even under normal breathing. Given infants’ posture, the findings could also indicate the adjustment of the concept of the hilar-to-peripheral gradient of blood flow distribution for this age group. This observation was made by Walther et al., when they studied unanesthetized lambs in prone position; they found out that the distribution of pulmonary blood flow in these animals follows a hilar-to-peripheral gradient rather than a vertical gradient.

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References


Correspondence:
Dr. Paulo R.A. Carvalho
Av. Encantado, 249
CEP 90470-420 – Porto Alegre, RS, Brazil
Phone/fax: + 55 51 3330.6334
E-mail: carvalho@conex.com.br