Clinical and transcutaneous oxygen saturation characteristics in hospitalized infants with acute viral bronchiolitis

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Abstract

Objective: To describe the clinical characteristics of infants with acute viral bronchiolitis (AVB) and to assess the influence of oxygen desaturation time (DT) as a prognostic test to estimate the evolution of such patients.

Methods: We performed a cohort study with 111 hospitalized patients diagnosed with AVB receiving oxygen therapy through nasal prong. The outcomes were: length of admission, length of oxygen therapy and time elapsed to read 95% saturation in room air. A severity score was obtained twice a day based on clinical signs during the time when the patient required oxygen supplementation. After the supply of oxygen was interrupted, the time required for transcutaneous oxygen saturation decreased to 90% and 85%. The $\chi^2$ test or Fisher’s exact test were used to compare categorical variables. The t test or Mann-Whitney’s test were used for numerical variables. Spearman’s correlation was used to evaluate associations in continuous variables with asymmetric distribution.

Results: Most patients (61.3%) were younger than 4 months. Patients with wheezing history (45%) were analyzed separately and had similar results to those of the group with AVB ($p \leq 0.05$). Twenty-six patients (23%) had moderate or severe malnutrition. All patients were using bronchodilators; 20% were using systemic corticosteroids; and 47%, antibiotics. The median time of oxygen therapy required for a reading of 95% oxygen saturation in room air was 83 hours (IQI 55-128). The median of length of admission was 7 days (IQI 5-10.5). Little clinical variability was observed in the period studied. No significant correlations were found between the clinical scores, DT and the outcomes.

Conclusions: DT was not useful as an aid to assess AVB patients on oxygen therapy in this study. It is possible that this tool could have been more useful in patients with more clinical variability.


Introduction

Acute viral bronchiolitis (AVB) is one of the most common causes of lower respiratory tract infections among children less than a year old and is responsible for a significant number of hospitalizations.1

Diagnosis of AVB is primarily clinical. The disease is defined as the first episode of a lower respiratory complaint among children less than 12 months old preceded by a prodrome period of three to five days with signs of upper respiratory tract infection, with coryza, coughing and fever, which develops over the following days with tachypnea, coughing, wheezing and signs of breathing difficulties.2,3 It is generally a benign, auto-limiting condition which, nevertheless, causes significant
morbidity in small infants and patients carrying chronic diseases and often causes long-term respiratory symptoms.

An understanding of the conditions which control the evolution of AVB can help to predict the resources which should be made available for treatment to be adequate. Oxygen therapy is a therapeutic resource which has gained wide acceptance for this disease and pulse oximetry is the most practical evaluation for adjusting it to the needs of each patient. Accepting transcutaneous hemoglobin oxygen saturation (HbSat) to be a trustworthy measurement of oxygenation, the time taken for this measurement to fall after oxygen is withdrawn (DT - desaturation time) can indicate a need for more treatment. Potentially, DT could also provide additional information of a prognostic nature on AVB patients. Thus, an attempt was made to describe the clinical characteristics of hospitalized infants diagnosed with AVB during the first days of hospital stay and, additionally, to investigate whether DT has a prognostic component in relation to patients hospitalized for AVB. Severity was ascertained by means of the length of hospital stay, the length of time oxygen therapy was used for, and the time taken to reach 95% saturation on room air.

**Patients and Methods**

During the period between May and October 2001, a cohort study was performed of 111 patients between 1 and 12 months of age, interned at the Hospital da Criança Santo Antônio, in Porto Alegre, diagnosed with AVB by the treating doctor upon admission, HbSat lower than 95% and on oxygen therapy via extranasal catheter for less than 24 hours. Those among the 111 who did not meet AVB diagnosis criteria, after a detailed assessment, having presented previous wheezing history, were then analyzed separately.

Children with cardiocirculatory diseases (such as, for example cyanotic congenital cardiac disease), neuromuscular diseases (such as cerebral palsy and Werdnig-Hoffmann disease) or others which affect respiratory function (such as congenital metabolic diseases) were excluded. Around 70% (n = 194) of the exclusions were due to the infant presenting HbSat greater or equal to 95% in room air.

Clinical assessments were performed twice a day (morning and afternoon), during the period in which the patient required supplementary oxygen (until HbSat 95% was achieved in room air), up to a maximum of ten times. Those patients who were included had their oxygen withdrawn and their HbSat monitored. The time taken for HbSat to fall to 90% (DT90) and then to 85% (DT85) was measured - for a maximum of 5 minutes.

Saturation was measured using pulse oximeters by Omehda, model 3800, and Instramed - MiniScope II. Respiratory viruses (pl) were tested for by indirect immunofluorescence (manufacturer Chenicon - Respiratory Panel I Viral Screening The Identification Kit) using a sample of nasopharyngeal secretion, by aspiration with a suction catheter number 6 or 8, according to normal hospital routine.

Based on the recorded clinical data, a severity score was built, adapted from that used by Fischer. The scale included respiratory rate, (> 60 breaths per minute = 1 point), nasal flaring (present = 1 point), subcostal retraction (present = 1 point), intercostal retraction (present = 1 point), suprasternal retraction (present = 1 point), cyanosis of the extremities (present = 1 point) and compression of the nail bed with slow capillary refill (present = 1 point). In the absence of a symptom no point was added. The maximum score was 7 and the minimum zero.

Sample size was calculated based upon a pilot study performed with 20 patients. For correlations between DTs and scores and outcome, it was found that to obtain an alpha of 0.5 and 95% power, twenty patients with all data complete would be necessary in order to achieve a correlation coefficient (r) of 0.7.

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences), version 6.0, and EpiInfo 6, version 6.04d.

Initially, characteristics were described in general then grouped by previous episodes of wheezing: frequency tables were created for the categorical variables and mean averages calculated (and standard deviations) or medians (and interquartile intervals 25-75) for continuous variables, for which box diagrams were also drawn.

Either the chi-square or Fisher’s exact test were used to compare categorical variables between groups and the t or Mann-Whitney test for numerical variables. The Spearman correlation was used to evaluate associations between asymmetrically distributed continuous variables (severity score, length of hospital stay, total oxygen therapy time until saturation reached 95% in room air). A critical alpha level of 5% was adopted for all comparisons except for multiple comparison correlations where the Bonferroni correction was used (30 correlations: p ≤ 0.002; 10 correlations: p ≤ 0.005).

Data on weight and stature for age were input and analyzed on the dedicated Epi-Info module which uses the NCHS tables (EpiNut). The project was submitted to the Ethics Committee at the Complexo Hospitalar Santa Casa in Porto Alegre and to the Research and Post-Graduate Group at the Hospital de Clínicas in Porto Alegre, and was approved by both bodies. Authorization was requested from those responsible for the patients and given on an informed consent form. The research team did not interfere with the patients’ prescriptions.
Results

One hundred and eleven patients were included. There was a slight predominance of the male sex (54%) and an elevated frequency of patients less than four months old (n = 68; 61.3%). The most prevalent months were June and July (n = 52; 47%).

Morbid antecedents were characterized according the variables in Table 1. Previous diagnoses revealed that 21% of the patients had a history of AVB, 14% of pneumonia, 4% of asthma and 3% of bronchitis.

The majority of respiratory manifestations previous to hospitalization as reported by family members occurred three days before admission: “lack of air” in 64% (n = 101), “chest noises” in 55% (n = 104), “fever” in 72% (n = 74) and arrested breathing in 94% (n = 16).

When the characteristics of patients with previous histories of wheezing were compared with those of patients who had not had this antecedent, no significant differences were observed in terms of sex, prematurity, previous mechanical ventilation, birth weight, current weight and stature or period of hospital stay (p < 0.05).

With respect of nutritional status, when premature patients had been excluded, 26 patients (23%) presented moderate or severe malnutrition.

In terms of diagnosed infectious complications, it was observed that 23 patients (20.7%) presented pneumonia, six (5.4%) acute otitis media and two (1.8%) septicemia. It was observed that 29 patients (26.1%) had one or more associated diagnosis of bacterial infection.

Despite the initial diagnosis for all patients being acute viral bronchiolitis, other diagnostic labels were defined during the period of hospitalization, such as: bronchospasm (n = 29; 26.1%), bronchopulmonary dysplasia (n = 1; 0.9%), asthma (n = 4; 3.6%), wheezing child (n = 2; 1.8%) and post-viral bronchiolitis (n = 1; 0.9%).

All of the patients were prescribed nebulization with a bronchodilator (fenoterol) and only one child received intravenous bronchodilator (Salbutamol). Systemic corticosteroids were used with around half of the population (n = 59; 53.2%), the majority with previous history of wheezing (n = 39; 78%). Intravenous systemic antibiotic use, observed in 52 children (46.8%), was uniformly distributed in relation to previous wheezing (n = 26 in each group): 52% of patients with previous wheezing and 42.6% of those suffering their first episode (p = 0.427).

Viral etiology returned 77 negative results (69.4%) and 17 children had positive test results (15.3%), 14 with respiratory syncytial virus and the remainder (three cases) with influenza virus. The tests were not performed for 17 patients (15.3%).

With respect of sequential measurements, it can be observed that average clinical scores were between 4 and 5, with no variation between the groups with and without previous wheezing. Analyzing correlations between clinical scores and length of hospital stay and period of oxygen therapy, the correlation coefficients varied from -0.007 to 0.44 with no significant correlations being observed (p < 0.002), either in the general group or in the group with no previous wheezing history.

Taking period of oxygen therapy as an example (Figure 1), a reduction in the number of patients was observed at each measurement made.

Five children (4.5%) evolved to the point of requiring mechanical ventilation, the majority of them (n = 4) having a history of wheezing.

Those patients who were having their first wheezing episode had a median for total supplementary oxygen use of 107 hours. The median of oxygen use until the infant reached a saturation of 95% in room air was 83 hours and the length of hospital stay was 7 days for the same group.

<table>
<thead>
<tr>
<th>Antecedents</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>26</td>
<td>23.4</td>
</tr>
<tr>
<td>Birthweight &lt; 2,500 g</td>
<td>15</td>
<td>13.6</td>
</tr>
<tr>
<td>Previous wheezing</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>Previous hospital admission due to wheezing</td>
<td>31</td>
<td>27.9</td>
</tr>
<tr>
<td>Previous oxygen therapy for longer than 7 days</td>
<td>19</td>
<td>17.1</td>
</tr>
<tr>
<td>Use of O₂ for at least 30 days</td>
<td>19</td>
<td>17.1</td>
</tr>
<tr>
<td>Previous use of mechanic ventilation</td>
<td>9</td>
<td>8.1</td>
</tr>
</tbody>
</table>

n = number of children.
The children with histories of wheezing had similar averages except for length of hospital stay, as can be seen in Table 2. There were eight discharges before the patients reached a 95% saturation level in room air, for which reason only 103 patients have measurements for period of oxygen therapy with this outcome. In terms of length of hospital stay, it was observed that 47.7% were hospitalized for 7 days or less.

Desaturation times at 90% presented few variations in terms of the medians at different measurement points, as can be seen in Figure 2. The DTs for 85% also did not reveal a declining pattern.

There was no statistical difference for the groups with and without previous wheezing in respect of DT90. It was not possible to make this comparison for DT85, due to the reduced number of patients in both categories.

There were no significant correlations between desaturation times (90% and 85%) and the proposed outcomes - period of supplementary oxygen use during hospital stay, oxygen therapy time before reaching 95% saturation or more and the length of hospital stay - taking p ≤ 0.002. The correlation coefficients between DT90 and outcomes varied from -0.0047 to 0.83.

**Discussion**

Empirically, the measurement of DT has been performed at the Pneumology Ward at the Hospital da Criança Santo Antônio, in Porto Alegre, especially in patients on prolonged oxygen therapy. No study had yet evaluated the relationship between O₂ desaturation times after the suspension of... - Rubin FM et alii

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**Figure 1** - Number of patients under oxygen therapy during the first days of hospital stay

**Table 2** - Oxygen therapy and length of hospital stay

<table>
<thead>
<tr>
<th>Results</th>
<th>No previous wheezing</th>
<th>Previous wheezing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Median (IQI)</td>
</tr>
<tr>
<td>Total O₂ (h)</td>
<td>61</td>
<td>107 (70-160)</td>
</tr>
<tr>
<td>O₂ for 95% sat (h)</td>
<td>56</td>
<td>83 (55-128)</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>61</td>
<td>7 (5-10)</td>
</tr>
</tbody>
</table>

n = number of children, h = days, IQI = interquartile interval, total O₂ = total time of oxygen therapy during hospital stay, O₂ for 95% sat = length of oxygen therapy up to the first transcutaneous saturation of oxygen of 95% hemoglobin in room air, hospital stay = period of time the patient stayed in hospital.
supplementary oxygen and the evolution of infants hospitalized for AVB.

One hundred and twenty-two children were eligible for the study and, of these, 96% were studied, thus achieving a representative patient sample meeting the proposed criteria. Taking the natural history of AVB into account, in which the most intense alterations generally occur during the first days of the disease, the period of monitoring appears to have been sufficiently prolonged to allow for the detection of the event’s severity.

In terms of season of admission, sex and age, the results of this study were similar to those of the study by Fischer, carried out at the same hospital. Other authors also produced similar findings.

Elevated prevalence was identified of both prematurity (23%) and low birth weight (14%). The association between AVB and low birth weight has been highlighted by an earlier study and deserves greater attention. According to the author, the identification of the role of this condition in AVB prognosis and risk could contribute to a better understanding of its morbidity.

The majority of the clinical manifestations which resulted in hospitalization occurred during the preceding three days, which is typical of the acute nature of the disease.

The diagnosis of AVB included criteria which have been used by other authors, reiterating the importance of clinical factors to the definition of the disease. Some authors have questioned the fact that AVB diagnosis criteria excludes patients with recurrent wheezing episodes.

The difficulty in diagnosing infants presenting wheezing was also observed in this study, as shown by the large number of different diagnostic labels employed during hospital stay: bronchospasm, bronchopulmonary dysplasia, asthma, wheezing child and post-viral bronchiolitis.

As oxygen desaturation time after withdrawal of supplementary oxygen possibly involves pathophysiological mechanisms that are similar both for infants with AVB and those with recurrent wheezing (reduction of the airways, edema, inflammatory reaction), it was decided not to exclude the latter group. Furthermore, the statistical analysis for this group was performed separately and revealed no differences from the population as a whole. Additionally, this study evaluated the variable “desaturation” in infants with acute episodes of lower respiratory tract diseases with the objective of establishing clinically useful parameters. It does not, therefore, appear to be a significant limitation that the patients may or may not have a definitive diagnosis of AVB.

As described above, the two groups of patients, those with AVB and those with a history of wheezing, were homogenous in terms of the majority of factors under investigation.

The viral etiological investigation was one of the limitations faced in this study, since the population could have been better defined if a higher level of positivity had been returned. A number of different technical impediments could possibly have influenced the results since the tests were performed within the normal hospital routine. As has already been mentioned, this limitation did not prejudice the analysis as the patients studied had acute respiratory disease.
An elevated frequency of malnutrition was encountered. This condition in children with AVB merits further investigation since few studies have evaluated it specifically.23,24 It is known that the immunoresponsiveness of malnourished patients can be affected and, potentially, contribute to unfavorable evolution. Fischer15 observed that severe malnutrition increases the risk of patients evolving to worse prognosis (relative risk 2.0).

The treatment of AVB has changed little over the years and, in many cases, the therapeutic strategy employed lacks supporting evidence.25 A meta-analysis involving eight randomized clinical trials concluded that bronchodilators produce a modest improvement in clinical scores and for a short period of time (the inclusion of patients with previous wheezing could have resulted in bias in favor of the use of bronchodilators). They do not, however, reduce the length of hospitalization, do not improve oxygenation measurements or reduce the need for admission.26 Martinón-Torres et al.25 found that, despite the lack of favorable evidence for the use of beta 2 agonist for AVB and the fact that the recommendation which has gained greatest acceptance is not to use it routinely, this type of medication is still widely used (around 80% of patients). All of the patients in the current study were given inhaled bronchodilators, generally by nebulization with fenoterol.

A high frequency of systemic corticosteroid use was recorded with AVB patients (20%), which is a practice that is not recommended. Its use was much more common among the children with a previous history of wheezing (78%), which could reflect a tendency to interpret such patients as being asthmatics. Some studies have found positive effects from the use of corticoids with AVB. A meta-analysis including six randomized clinical trials and a total of 347 patients stands out. It was carried out in order to determine whether systemic corticosteroids are effective in the treatment of bronchiolitis in hospitalized infants. Those children who received corticosteroids had a significant improvement to duration of symptoms and a discrete reduction in length of hospital stay when compared with a group which received a placebo. However this analysis had limitations - such as heterogeneous clinical trials, two studies which did not exclude patients with previous wheezing, the adoption of different clinical scoring systems and publication bias itself - make these results questionable.27

There was also an elevated frequency of systemic antibiotic therapy use (47%). Henderson and Rubin,28 assessing children interned for AVB, observed that around half of the patients received antimicrobials, a third with no documented evidence of a bacterial infectious focus. Furthermore, with almost 80% of the patients who received antibiotics, their use was a result of an erroneous diagnosis of bacterial pneumonia. This situation reflects the reluctance of pediatricians to attribute abnormal radiographic findings to viral pathogens in AVB, despite the evidence in medical literature that antibiotics are of no benefit in this context.

The median for oxygen use with AVB patients and the period of oxygen therapy until 95% saturation was achieved in room air were similar to the results found by Fischer.15

Despite the results reported by much research into AVB, in clinical practice differences are still observed between different centers in terms of length of hospitalization.29,30 In the greater part of Europe, infants admitted to hospital are discharged only when fully recovered. The average stay is between eight and nine days.31 In North America, Australia, the United Kingdom and Finland, the average length of hospital stay is four days.8 Taking the segment of the population that is predominantly cared for at the hospital where the research took place into account, it is possible that socio-economic level may have influenced the length of certain patients’ stays.

With respect of the clinical scoring system applied, little change was observed during the period under study, which suggests little clinical variation of the patients being assessed. Fischer15 found more marked differences. One factor which could be implicated in the fact that results were homogeneous is the selection criteria adopted. The patients presented moderately severe clinical status. The low frequency of patients requiring mechanical ventilation is evidence of the exclusion of more severe cases. The exclusion of patients who did not require oxygen therapy and of those who required higher concentrations of oxygen may have contributed to the similarities within the population studied. Taking the period of oxygen therapy as an example, the same tendency for which Fischer15 found evidence was observed with a reduced number of patients due to improved clinical status on each day of the assessment as they no longer needed oxygen. This issue may also have contributed to the low level of clinical variation among the clinical scores since only patients on oxygen therapy were assessed. The correlations between clinical scores and outcomes (period of oxygen therapy and length of hospital stay) were not significant for the AVB patients, also probably as a result of selection criteria.

As occurred with the clinical scores, the DTs observed presented few variations. It is probable that this low level of data variation is related with the issue, already broached, of the population studied being homogeneous. The DTs did not reveal significant correlations with outcomes (period of oxygen therapy, time taken to reach 95% saturation in room air and length of hospital stay). An analysis of data which included more serious cases would possibly reveal more expressive results.

One further point which could have interfered with the results was the use of two oximeters with different characteristics during the study. The equipment could...
present differences in terms of response to desaturation, with one piece of apparatus being faster than the other. However, in addition to there having been no marked difference in DT results, it also appears that such variation is more accentuated during severe hypoxemia. Trivedi et al.\textsuperscript{32} compared the efficiency and response times for desaturation and resaturation of seven pulse oximeters during induced hypoxemia with eight volunteers (FiO\textsubscript{2} 10\%). The majority of the models tested performed well, but were inefficient when oxygen saturation reached approximately 75\% or less. The greatest difference in response time to desaturation, between the fastest and the slowest oximeter, was 13 to 29 seconds. There were no statistical differences between the oximeter during the resaturation phase.

It can be perceived, from the data presented, that the idea of using DTs for oxygen as an auxiliary element in the assessment of patients on oxygen therapy can neither be refuted nor upheld. It is possible that, evaluating patients who differ clinically to a greater degree, these measurements (DTs) may prove important. Further studies are necessary to better assess the usefulness of DT with infants suffering from acute obstructive pulmonary disease. It is also important to point out that transcutaneous oxygen saturation remains a valuable functional parameter in the clinical monitoring of AVB, especially with hospitalized patients.

References