Abstract

Objectives: To describe the clinical and laboratory characteristics of patients on long-term home oxygen therapy followed up by the home care program of Hospital das Clínicas, School of Medicine, Universidade de São Paulo, during a period of 8 years; to compare groups with and without secondary pulmonary hypertension; and to estimate the cost of the program using oxygen concentrators vs. oxygen cylinders provided by the hospital.

Methods: A descriptive, retrospective cohort study of patients on long-term home oxygen therapy followed up from 2002 to 2009 at the Unit of Pulmonology, Children's Institute, Hospital das Clínicas, School of Medicine, Universidade de São Paulo.

Results: We studied 165 patients, of whom 53% were male, with the following medians: age at the beginning of oxygen therapy – 3.6 years; duration of oxygen therapy – 7 years; and survival time after beginning of oxygen therapy – 3.4 years. The main diagnoses were: cystic fibrosis (22%), bronchopulmonary dysplasia (19%), and bronchiolitis obliterans (15%). Of the 33 patients who underwent spirometry, 70% had severe obstructive lung disease. Echocardiogram was performed in 134 patients; 51% of them had secondary pulmonary hypertension. There was a statistically significant association between pulmonary hypertension and need of higher oxygen flows (chi-square, p = 0.011), and between pulmonary hypertension and longer duration of oxygen therapy (Logrank, p = 0.0001). There was no statistically significant difference between survival time after the beginning of oxygen therapy and pulmonary hypertension. The average monthly costs of the program were US$ 7,392.93 for concentrators and US$ 16,630.92 for cylinders.

Conclusions: Long-term home oxygen therapy was used to treat different chronic diseases, predominantly in infants and preschool children. There was a high frequency of pulmonary hypertension associated with longer periods of oxygen use and greater oxygen flow, without association with survival rate. The use of concentrators instead of cylinders may reduce costs significantly.


Introduction

The number of patients requiring long-term home oxygen therapy (LTOT) has been increasing every year. This therapeutic method has been used more often to treat several chronic lung diseases in pediatric patients with the purpose of reducing morbidity and improving the patients’ quality of life. This practice makes it possible to optimize bed occupancy rates, reduce the duration and number of hospitalizations and thus decrease hospital costs.

LTOT is recommended for children and adolescents mainly because of its importance in providing and maintaining...
patients’ appropriate cognitive development and height and weight growth, preventing sudden death in infants and minimizing the effects of pulmonary hypertension (PH).

There are few studies in Brazil analyzing the characteristics of the pediatric population using LTOT as a therapeutic resource and describing the major diseases and specific conditions that require this intervention. On the other hand, updated national pediatric guidelines have not been established regarding the clinical and laboratory parameters that guide its main recommendations and provide guidance regarding the advantages and disadvantages of the main methods of administration, estimates of duration, and quantification of costs.

Based on this context, we conducted a study whose objectives were: to describe and characterize the population of children and adolescents followed up at the Unit of Pediatric Pulmonology of the Children’s Institute, Hospital das Clínicas, School of Medicine, Universidade de São Paulo (HC-FMUSP), who had used or were using LTOT in terms of their clinical and laboratory characteristics; to compare groups of patients with and without secondary PH (SPH) with respect to time and intensity of LTOT; and to compare the costs of the program using oxygen concentrators vs. oxygen cylinders.

Patients and methods

This is a retrospective descriptive cohort study of 165 patients followed up at the Unit of Pediatric Pulmonology of the Children’s Institute, HC-FMUSP from 2002 to 2009, who underwent home oxygen therapy.

All children and adolescents on LTOT were strictly evaluated by the medical staff of the Unit of Pulmonology regarding the initial recommendation of oxygen treatment ($O_2$). The patients were evaluated again after 3 months and, after that, approximately every 6 months in order to decide for the maintenance, discontinuation or change in the amount of $O_2$ administration.

During each evaluation, we measured $O_2$ saturation of oxyhemoglobin ($SaO_2$) using a NONIN pulse oximeter, model 8000AA, for 20 minutes at rest and on room air, with subsequent reassessment of the amount of $O_2$ required to maintain appropriate levels of $O_2$ saturation.

Oxygen therapy was prescribed for children and infants with $SaO_2$ levels below 93%, for adolescents with $O_2$ blood pressure below 55 mmHg or $O_2$ saturation lower than 89%, and for cystic fibrosis patients with $O_2$ saturation below 90%. The discontinuation of oxygen therapy was recommended when the patient had $O_2$ saturation on room air equal to or lower than 92% and higher than or equal to 95% in cases with associated PH.

Diagnostic criteria for PH were: systolic pulmonary artery pressure above 35 mmHg or mean pulmonary artery pressure higher than 25 mmHg, measured using the two-dimensional transthoracic Doppler echocardiogram.

Data on clinical and laboratory characteristics were collected from medical records and a questionnaire administered to patients and/or guardians after they signed an informed consent form. The research project was approved by the Research Ethics Committee of HC-FMUSP (CAPesq).

Statistical analysis

The age at the beginning of $O_2$ use (a continuous variable) was described as median (maximum and minimum values). The nominal variables (city of residence, sex, diagnosis of underlying disease, presence of PH, intensity of $O_2$ flow, $O_2$ administration device, $O_2$ providing system, diagnosis related to pulmonary function test) were described as frequencies. The analysis of duration of $O_2$ use and survival after the beginning of LTOT were performed using Kaplan-Meier curves. In the analysis of the subgroups with and without PH, frequencies (duration of $O_2$ use and intensity of flow) were compared using the chi-square test; and Kaplan-Meier curves were compared using the Logrank test. We used the statistical software SPSS 13.0 for the analyses and the significance level was set at 5%.

Cost analysis

We decided to calculate the average monthly cost of the LTOT program based on the monthly averages of patients according to type of system used (cylinder or concentrator), during the period between July 2007 and June 2008. As the cost for the use of the cylinder varies according to the amount of $O_2$ consumed, it was necessary to calculate the average monthly consumption of $O_2$ in this period, in cubic meters, multiplying the average monthly consumption of $O_2$ per patient by the monthly average of patients using the cylinder.

The average monthly cost of the program regarding the use of the concentrator was calculated by multiplying the average monthly consumption of $O_2$ by the value in U.S. dollars per cubic meter of $O_2$ in this period. The average monthly cost of the program regarding the use of the concentrator was calculated by multiplying the monthly average of patients using the concentrator by the monthly rental value of the device in dollars. To perform the calculations related to the concentrator we did not include the energy expenses resulting from its use because these costs are not paid by the hospital.

Results

Most patients (68%) lived in São Paulo; 53% were male; the age at the beginning of LTOT ranged from 0.1 to 21.5
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years (median: 3.6 years); and about 1/3 of the sample initiated the use of O₂ in the first year of life.

The main diagnoses of chronic underlying disease were: cystic fibrosis, bronchopulmonary dysplasia, and bronchiolitis obliterans (Table 1).

Table 1 - Distribution of 165 patients on LTOT according to the underlying diseases

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic fibrosis</td>
<td>36 (22)</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia</td>
<td>31 (19)</td>
</tr>
<tr>
<td>Bronchiolitis obliterans</td>
<td>25 (15)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>16 (10)</td>
</tr>
<tr>
<td>Chronic aspiration lung disease</td>
<td>14 (8)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Pulmonary malformations</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Chest wall disorders</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Neurovascular disease</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Primary pulmonary hypertension</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Other diagnoses*</td>
<td>13 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>165 (100)</td>
</tr>
</tbody>
</table>

LTOT = long-term home oxygen therapy.

Regarding the main underlying diseases, the median duration of O₂ use was 7 years and the median of survival time was 13.4 years.

With respect to the costs related to the type of O₂ providing system used, the average monthly cost of the program using concentrators was US$ 7,392.93 and the program using cylinders cost US$ 16,630.92, that is, the use of a concentrator instead a cylinder could lead to a 54% reduction in costs.

Discussion

In the present study, there was a slight prevalence (53%), age at the beginning of LTOT ranged from 0.1 to 21.5 years (median: 3.6 years), and most patients (28%) initiated O₂ use in the first year of life. Such result was also found by Mocelin et al.,15 who conducted a retrospective study of 40 children on LTOT.

Bronchopulmonary dysplasia was the most prevalent diagnosis among the underlying diseases of those patients who initiated LTOT in the first year of life. Although bronchopulmonary dysplasia is considered the main reason...
for LTOT recommendation in children, in our study, this was the second most frequent underlying disease (19%), being preceded only by cystic fibrosis (22%), which can be explained by the fact that the Children’s Institute of HC-FMUSP is an excellence center for this disease.9,16 Similarly to other studies, in the present study, most patients with bronchopulmonary dysplasia received O₂ for a period shorter than 1 year (median 11 months), but slightly longer than the period found by other authors (median 3-8 months).10,15-17

In our study, bronchiolitis obliterans was the third most frequent underlying disease (15%) with a median duration of O₂ use of 2.3 years. Similarly, Norzila et al.16 found a frequency of 17% and the median duration of O₂ use was also 2.3 years in their study (n = 12). Another prospective Chilean study followed up 18 children diagnosed with bronchiolitis obliterans during 5 years; of these, 27.8% needed LTOT, and after 1 year LTOT was discontinued in 100% of the cases.18

Patients with cystic fibrosis showed a much higher percentage of deaths (22%) than patients with bronchopulmonary dysplasia (3%) and those with bronchiolitis obliterans (4%). Such findings were expected because, for cases of cystic fibrosis and neuromuscular disease, LTOT is usually recommended in more advanced stages with poor prognosis, unlike other child and infant diseases, for which, in most cases, LTOT is recommended with the prospect of discontinuation after a certain period of time.10

In December 2008, the database of the British Thoracic Society, which includes records of England and Wales, presented a sample of 828 children on LTOT.10 The main diagnoses of this sample were: bronchopulmonary dysplasia (60%), neuropathy (7%), neuromuscular disease (7%), heart disease (5%), and interstitial lung disease (2%).10 Considering this database, only the diagnosis of heart disease showed the same frequency as that found in our study (5%).

According to these findings, each study had different frequencies for the diagnoses related to the underlying diseases. This may be related to the particular characteristics of each center, such as, for example, to be an excellence center for a specific type of disease and/or to use different criteria to recommend LTOT use and its discontinuation.

Among all patients who were on night LTOT (35%), a large percentage of them (56%) had started the process of discontinuation. However, there was continuous daily O₂ use in most cases (65%), with prevalence of flows lower than 2 L/min using nasal cannula (87%), which is equivalent to one inspired fraction of oxygen (FiO₂) of 28%. In a study involving children with post-infectious bronchiolitis on LTOT, the authors also demonstrated that low concentrations of O₂ (FiO₂: 25 to 40%) were sufficient to achieve optimal levels of oxygen saturation in most patients.19 As a result of the low flows used, the nasal cannula, similarly to what happens in most services, is the oxygen administration device most widely used in adults, children and adolescents because it is more comfortable than the mask and ensures constant oxygenation.10,20
Two studies have reported that most patients remained on LTOT for long periods; even so, these periods were shorter than the one found in our study (median = 7 years). In one of these studies, the sample included only patients with bronchiolitis obliterans (median = 3.2 years); in the other study, (median = 1 year), 75% of patients had this diagnosis. In both studies, the authors have report that at the end of the study, most patients had good clinical outcome.\textsuperscript{15,19}

One of the great differences between our study and the other studies published in Brazil and abroad is related to the approach of survival in children and adolescents on LTOT, since we could not find scientific publications on this topic. In our study, we demonstrated that the median survival of 165 patients after they started using LTOT was 13.4 years, and 67% of patients survived until the end of the study.

With regard to pulmonary function tests, most of the 33 patients who underwent spirometry had severe obstructive lung disease (70%). This can only be explained by the fact that most patients had cystic fibrosis or bronchiolitis obliterans, and their median age was 16 years. In this context, the disease is in advanced stage, especially in patients with cystic fibrosis, which explains the result obtained on the spirometry.

The high percentage of patients diagnosed with SPH (51.49%) on the echocardiogram draws attention to the fact that there is high incidence of SPH in adolescents and children who need LTOT. Unfortunately, the diagnosis of SPH is usually delayed, and this disease is often underdiagnosed, which worsens the prognosis because of late treatment.\textsuperscript{13}

Most patients with and without SPH used \(O_2\) continuously, and there was no statistically significant difference between the two groups regarding the time of daily \(O_2\) use, but there was a higher percentage of patients with SPH who required oxygen flows higher than 2 L/min, and such difference was statistically significant. The group of patients with SPH also had longer time of \(O_2\) use; a statistically significant difference when compared with those without SPH, which was expected because SPH is one of the aggravating factors of the underlying disease. Based on these findings, we concluded that patients with SPH need higher \(O_2\) flows for longer periods, which is probably related to the fact that they are more severe patients. The survival time was shorter in the group with SPH compared with the group without SPH, but this difference was not statistically significant.

Because this was a retrospective and long-term study, one of its limitations is related to data collection regarding the tests (echocardiogram and spirometry). First, not all patients underwent the tests, and when these were performed, they were conducted at different times, which prevents us from correlating such data with the patients’ clinical conditions and LTOT phase.

It is important to highlight that although LTOT is an expensive therapy, hospitalization has higher costs compared with other clinical and surgical treatments used to improve the quality of life and increase survival of adults with chronic obstructive pulmonary disease.\textsuperscript{21,22} In addition, studies in adults with chronic obstructive pulmonary disease have shown a decrease in the use of emergency services by these patients after they start using home oxygen therapy.\textsuperscript{1,13,24}

A study published in 2004, comparing two medical care services for a period of 2 years with regard to the frequency of LTOT recommendation for oxygen-dependent patients admitted to the neonatal unit, showed that the costs related to post-discharge care were similar for both services. However, the total cost was significantly higher in the service where LTOT recommendation was less frequent because of the costs with longer hospital stays.

The literature on LTOT comparing the frequency of use of different types of oxygen providing equipment and costs in several countries is scarce. The few studies published do not identify a country as a model of cost-effectiveness in relation to the type of oxygen providing system and show that the choice of the type of system varies according to local tradition and economic interests of the domestic market.\textsuperscript{23}

In Brazil, just like in the United States and other developed countries, the concentrator is the less expensive system.\textsuperscript{19,15} The use of concentrators is more economically viable because in addition to being approximately twice less expensive, as shown in the results above, it is safer than the cylinder regarding the possibility of accidents. Similarly to what happens in our service, in other national excellence centers for pediatric respiratory care, the use of concentrators is more prevalent.\textsuperscript{15}

As there are few studies on LTOT in children and adolescents, there is also lack of consensus about several aspects of the therapeutic method used in this population. Therefore, many of the recommendations suggested by the guidelines\textsuperscript{10} on LTOT in children, recently published (2009) by the British Thoracic Society, are based on the authors’ clinical practice. Hence, broader studies about LTOT, such as multicenter trials, are needed in this age group.\textsuperscript{3}

It would be also interesting to conduct studies evaluating these patients’ adherence to treatment, an issue that has been extensively focused on adults, because of its importance in terms of the clinical outcome of patients after LTOT initiation, as well as with respect to the burden it poses on the health system. There is a shortage of Brazilian studies describing the prevalence and cost of LTOT in several states and municipalities.

We conclude that in the present sample of the Children’s Institute of HC-FMUSP, which provides tertiary care for highly complex diseases, LTOT was used in different chronic
diseases for correction of hypoxemia and SPH most often in infants and preschool-aged patients, and cystic fibrosis, bronchopulmonary dysplasia, and bronchiolitis obliterans were the most prevalent diseases. LTOT duration for patients with these pathologies was quite long. Based on our results, we reached the conclusion that SPH was also frequent in patients on LTOT and that its presence is associated with the need of longer treatment and increased oxygen flows with no association with survival time.

In terms of costs, it can be inferred by the estimates obtained in our study that the use of concentrators instead of oxygen cylinders in LTOT programs for children and adolescents may significantly reduce the economic burden of this therapeutic resource.

References

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