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BRIEF REPORT

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National survey in pediatric patients on Long-Term Home Oxygen Therapy

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ABSTRACT

This study aims to describe current prescriptive practices regarding home long-term oxygen therapy (LTOT) in Italian pediatric population. The Chronic Respiratory Insufficiency and Long-Term Ventilation Study Group produced a survey that was sent to the referents of the Italian Society of Infantile Respiratory Diseases and of the Italian Society of Neonatology. Forty-two responses were collected from different centers: 32 (76%) participants declared to be LTOT prescribers. Of these, 8 (25%) reported following more than 30 patients, 3 (9%) between 20-30 patients, 9 (28%) between 10-20, 12 (37%) less than 10 patients. Twenty (63%) use blood gas test to decide starting

LTOT, 7 (22%) use daytime and/or night-time oximetry, 5 (16%) use both. Twenty-two (69%) prescribe high-flow oxygen (HFNC), of which 8 (36%) to more than 5 patients/year and 14 (64%) to less. Patients receiving HFNC suffer from bronchopulmonary dysplasia (10/26, 38%), neurological disease (6/26, 23%), interstitial disease (6/26, 23%), oncological disease (2/26, 8%) or cystic fibrosis (2/26, 8%).

Results show that pediatric patients on LTOT are fewer than adult ones; most are infants with bronchopulmonary dysplasia or children with neurological disabilities, reflecting the increasing reality of medically complex children. Most prescribers use blood gas tests to initiate LTOT, despite the availability of less invasive methods such as oximetry. The data collected will prove to be useful to produce official recommendations to standardize LTOT indications, devices and therapeutic purposes.

Impact statement: There is a need for standardization of prescriptive practices for home long-term oxygen therapy (LTOT) in Italian pediatric population; the creation a national dataset could be useful for this aim.

Key words

LTOT; HFNC; long-term ventilation; chronic respiratory insufficiency; guidelines; survey.

BACKGROUND

Long-term oxygen therapy (LTOT) provides support for children experiencing chronic hypoxemia due to various causes, including chronic neonatal lung disease (CNLD), cystic fibrosis (CF), interstitial lung disease (ILD) and neurodisability (1). Despite the heterogeneous and distinct nature of pediatric chronic respiratory conditions, guidelines and diagnostic criteria are frequently borrowed from adult protocols, primarily centered on patients with chronic obstructive pulmonary disease (COPD) (2, 3). A multidisciplinary panel assembled by the American Thoracic Society (ATS) recently issued valuable clinical recommendations for home oxygen therapy tailored to pediatric chronic lung diseases and pulmonary vascular diseases (4). However, authors emphasized the scarcity and low quality of available evidence in particular about the pediatric population, with limited data about implementation, efficacy,

monitoring, and discontinuation of LTOT across various age groups and clinical conditions. Given the potential harms and costs, it is essential to obtain data on the number of children receiving home oxygen therapy and their characteristics. In fact, only a few national experiences have been reported, providing prevalence rates of children undergoing LTOT. Balfour-Lynn and colleagues aggregated data from a cross-sectional survey and a dedicated database in England and Wales (5). They estimated a prevalence of 1.08 per 1000 in the first year of life and 0.33 per 1000 in children older than one year of age, with chronic neonatal lung disease (CNLD) being the primary cause, followed by neurodisability (5). Other prevalence studies of national registers from Scandinavian countries dealt with pediatric population only partially and are more than twenty years old (6-8).

The Study Group "Chronic Respiratory Failure and Long-Term Ventilation" within the Italian Society of Pediatric Respiratory Disease (Società Italiana per le Malattie Respiratorie Infantili, SIMRI) conducted a research project to offer an overview of the Italian scenario and lay the foundation for future implementation projects.

METHODS

The Study Group "Chronic Respiratory Failure and Long-Term Ventilation" devised a survey questionnaire through a multistage process. A task force of four pediatric pulmonologists within the Study Group formulated the study protocol, identifying various aspects of interest for each center, including: geographic location, medical subspecialties of the prescriber, number of patients cared for at each center, diagnostic tools utilized, oxygen delivery devices and monitoring methods employed, clinical conditions, and follow-up procedures. The task force formulated a questionnaire which underwent revision by the Study Group in two dedicated meetings. A final version was subsequently approved by the entire Study Group.

The survey questionnaire was distributed via email invitation, along with a link to an online platform, to regional representatives of SIMRI and SIN (Italian Society of Neonatology), starting from July 10th, 2023. We selected the regional representatives with the aim of giving the most complete national picture and of avoiding specialty-based sampling bias.

Following a second email reminder, responses received up to June 1st, 2024, were assessed.

Dichotomous and categorical variables were presented as numerical values and percentages. Most of the percentages represent the distribution across prescribing centers, with any exceptions to this explicitly noted. Continuous variables were reported as either the mean and standard deviation (SD) if normally distributed, or as the median with the first and third quartiles if not normally distributed. The normality of the data was evaluated both visually and through the Shapiro-Wilk test.

RESULTS

Email invitations were sent to 200 SIMRI and SIN representatives between July 2023 and June 2024. Forty-two centers (21%) replied; 32 centers (32/40, 76% of the participating centers) reported prescribing LTOT. Ten centers (10/42, 24%) participated in the survey as non-prescribing centers: 3 Tertiary referral Pediatric Hospitals, 3 Neonatology Units and 6 Secondary Pediatric hospitals.

Eight centers (25% of the prescribing centers) reported following more than 30 patients in LTOT, three centers (9%) between 20 and 30 patients, 9 centers (28%) between 10 and 20 and 12 centers (37%) less than 10 patients (**Figure 1**).

Figure 1 regarding the start of LTOT, 20 centers (20/32, 63%) reported using blood gas test (BGT). Seven centers (7/32, 22%) used daytime and/or nighttime pulse oximetry (**Figure 2**) and five used both (5/32, 16%).

EQUIPMENT

All but one center prescribed liquid oxygen; 28 centers (28/32, 87%) prescribed oxygen gas and 22 centers (22/32, 69%) oxygen concentrators. Twenty-two prescribing centers (22/32, 69%) prescribe high-flow oxygen, of which 8 (8/22, 36%) to more than five patients/year and the remaining (14/22, 64%) to less than five patients/year.

Patients receiving high-flow oxygen therapy were: patients with bronchopulmonary dysplasia (10/26, 38%), neurological disease (6/26, 23%), interstitial disease (6/26, 23%), oncological disease (2/26, 8%) or cystic fibrosis (2/26, 8%).

DISCUSSION

The last twenty years have been characterized by a profound change in the landscape of pediatric patients with respiratory insufficiency and complex clinical needs (9), with a remarkable increase in the number of these patients. Despite the relative availability of data on non-invasive ventilation, our study represents the first report on long-term oxygen therapy (LTOT) in the pediatric population published in the last twenty years and the very first in Italy. There is only one European survey that analyzed the pattern of LTOT prescriptions in children (5).

Similar to non-invasive ventilation, the availability of LTOT is scattered throughout the territory of Italy, with most centers reporting the care of only a few dozen patients.

Available recommendations on LTOT are based on poor data quality (10). Regarding prescriptions, the ATS task force recommend pulse oximetry to define hypoxemia; surprisingly, in our report almost all the centers (87%) based LTOT prescriptions on arterial blood gas test, even if it is neither practical nor reliable for routine assessment in pediatric patients due to factors such as crying, procedural pain, and technical challenges.

On the other hand, overnight pulse oximetry was reported to be available for outpatient assessment and monitoring, but its use to prescribe LTOT appears to be limited to a few centers (26%). We consider it a rather contradictory approach, that could be due to adult guidelines where measurement of arterial PaO2 is critical for oxygen therapy. The use of pulse oximetry is cost-effective and non-invasive, whereas blood gas analysis is painful, often inaccurate when performed during crying, and therefore limited to the intensive care setting. Given that pulse oximetry is a painless, accurate, and non-invasive method for diagnosing hypoxemia in children, we fully support its use, instead of the blood gas test, as the preferred diagnostic tool.

This recommendation is backed by other guidelines about hypoxemia and by the fact that the use of BGT is increasingly limited even in acute settings, with a preference for using the peripheral oxygen saturation to the fraction of inspired oxygen ratio (SpO2/FiO2) instead of the arterial oxygen tension to the fraction of inspired oxygen ratio (PaO2/FiO2). This shift in approach is highlighted in the latest update regarding pediatric acute respiratory distress syndrome (PARDS) guidelines (11).

Moreover, the use of pulse oximetry perfectly aligns with the philosophy of telemedicine and home monitoring, as it is easily implementable in various settings and has been integrated into medical practice for several years now (12).

Similar to the findings of Balfour-Lynn and colleagues, LTOT prescriptions were primarily given to children with BPD. Prescriptions of LTOT for BPD are followed by those for patients with neurodisability (5). If this finding was once considered surprising, it is no longer so nowadays, given the increasing number of children with neurodisability observed over the past decades. In such patients, the clinical rationale of LTOT is not always clearly evident. Actually, in such patients, LTOT may be prescribed to enhance the quality of life of patients and their families rather than to reach saturation targets. In such a setting oxygen may be necessary exclusively during intercurrences and exacerbations. This approach is supported also by the British Thoracic Society (BTS) guidelines referring to these aspects with the term “special situation” (13).

Our research has several limitations. Despite invitations to all the representative members of the two societies, only a small proportion of members responded. Consequently, we can offer only a partial picture derived from results potentially contaminated by respondent bias.

About 50% of responses resulted from centers located in Northern Italy and data from some central regions are missing. Nevertheless, we still got response from 8 centers (8/32, 25%) located in Southern Italy and from 8 centers (8/32, 25%) in Central Italy.

The lack of data for some smaller regions in central Italy may be due to the actual absence of prescribing centers. Moreover, given the phenomenon of healthcare migration, many patients travel to larger centers in neighboring regions (14).

Furthermore, we did not collect data regarding clinical conditions or comorbidities nor patients’ age or SpO2 measurements as well. Lastly, we did not provide any information about discontinuation.

We hope this research raises awareness and interest in pediatric pulmonologists in order to pave the way for a national dataset. Further data collection is warranted based on a more comprehensive survey and involving oxygen providers. Future efforts of the Study Group will be directed towards standardization in providing LTOT, promoting non-invasive assessment and monitoring and optimizing the care of children with respiratory conditions on a more general perspective.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests

The Authors have declared no conflict of interests.

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Ethical approval

Human studies and subjects

The study followed the ethical standards established in the Declaration of Helsinki.

Animal studies

N/A.

Data sharing and data accessibility

Data are available upon motivated request to the Corresponding Author.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

All the data corresponds to the real.

REFERENCES

1- Balfour-Lynn IM, Primhak RA, Shaw BN. Home oxygen for children: who, how and when? Thorax. 2005 Jan;60(1):76-81. doi: 10.1136/thx.2004.031211. PMID: 15618588; PMCID: PMC1747170.

2- Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. Nocturnal Oxygen Therapy Trial Group. Ann Intern Med. 1980 Sep;93(3):391-8. doi: 10.7326/0003-4819-93-3-391. PMID: 6776858.

3- Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. Report of the Medical Research Council Working Party. Lancet. 1981 Mar 28;1(8222):681-6. PMID: 6110912.

4- Hayes D Jr, Wilson KC, Krivchenia K, Hawkins SMM, Balfour-Lynn IM, Gozal D, Panitch HB, Splaingard ML, Rhein LM, Kurland G, Abman SH, Hoffman TM, Carroll CL, Cataletto ME, Tumin D, Oren E, Martin RJ, Baker J, Porta GR, Kaley D, Gettys A, Deterding RR. Home Oxygen Therapy for Children. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2019 Feb 1;199(3):e5-e23. doi: 10.1164/rccm.201812-2276ST. PMID: 30707039; PMCID: PMC6802853.

5- Primhak RA, Hicks B, Shaw NJ, Donaldson GC, Balfour-Lynn IM. Use of home oxygen for children in England and Wales. Arch Dis Child. 2011 Apr;96(4):389-92. doi: 10.1136/adc.2009.180653. Epub 2010 Jun 3. PMID: 20522469.

6- Ringbaek TJ, Lange P, Viskum K. Geographic variation in long-term oxygen therapy in Denmark : factors related to adherence to guidelines for long-term oxygen therapy. Chest. 2001 Jun;119(6):1711-6. doi: 10.1378/chest.119.6.1711. PMID: 11399695.

7- Ström K, Boe J. A national register for long-term oxygen therapy in chronic hypoxia: preliminary results. Eur Respir J. 1988 Dec;1(10):952-8. PMID: 3224692.

8- Schaanning J, Strøm K, Boe J. Do patients using long-term liquid oxygen differ from those on traditional treatment with oxygen concentrators and/or compressed gas cylinders? A comparison of two national registers. Respir Med. 1998 Jan;92(1):84-7. doi: 10.1016/s0954-6111(98)90037-3. PMID: 9519230.

9-Caggiano S, Pavone M, Cherchi C, Paglietti MG, Schiavino A, Petreschi F, Chiarini Testa MB, Cutrera R. Children with medical complexity and pediatric palliative care: Data by a respiratory intermediate care unit. Pediatr Pulmonol. 2023 Mar;58(3):918-926. doi: 10.1002/ppul.26278. Epub 2022 Dec 20. PMID: 36510441.

10- Hayes D Jr, Wilson KC, Krivchenia K, Hawkins SMM, Balfour-Lynn IM, Gozal D, Panitch HB, Splaingard ML, Rhein LM, Kurland G, Abman SH, Hoffman TM, Carroll CL, Cataletto ME, Tumin D, Oren E, Martin RJ, Baker J, Porta GR, Kaley D, Gettys A, Deterding RR. Home Oxygen Therapy for Children. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2019 Feb 1;199(3):e5-e23. doi: 10.1164/rccm.201812-2276ST. PMID: 30707039; PMCID: PMC6802853.

11- Emeriaud G, López-Fernández YM, Iyer NP, Bembea MM, Agulnik A, Barbaro RP, Baudin F, Bhalla A, Brunow de Carvalho W, Carroll CL, Cheifetz IM, Chisti MJ, Cruces P, Curley MAQ, Dahmer MK, Dalton HJ, Erickson SJ, Essouri S, Fernández A, Flori HR, Grunwell JR, Jouvet P, Killien EY, Kneyber MCJ, Kudchadkar SR, Korang SK, Lee JH, Macrae DJ, Maddux A, Modesto I Alapont V, Morrow BM, Nadkarni VM, Napolitano N, Newth CJL, Pons-Odena M, Quasney MW, Rajapreyar P, Rambaud J, Randolph AG, Rimensberger P, Rowan CM, Sanchez-Pinto LN, Sapru A, Sauthier M, Shein SL, Smith LS, Steffen K, Takeuchi M, Thomas NJ, Tse SM, Valentine S, Ward

S, Watson RS, Yehya N, Zimmerman JJ, Khemani RG; Second Pediatric Acute Lung Injury Consensus Conference (PALICC-2) Group on behalf of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Executive Summary of the Second International Guidelines for the Diagnosis and Management of Pediatric Acute Respiratory Distress Syndrome (PALICC-2). Pediatr Crit Care Med. 2023 Feb 1;24(2):143-168. doi: 10.1097/PCC.0000000000003147. Epub 2023 Jan 20. PMID: 36661420; PMCID: PMC9848214.

12- Sotirios Fouzas, Kostas N. Priftis, Michael B. Anthracopoulos; Pulse Oximetry in Pediatric Practice. *Pediatrics* October 2011; 128 (4): 740–752. 10.1542/peds.2011-0271

13- Balfour-Lynn IM, Field DJ, Gringras P, Hicks B, Jardine E, Jones RC, Magee AG, Primhak RA, Samuels MP, Shaw NJ, Stevens S, Sullivan C, Taylor JA, Wallis C; Paediatric Section of the Home Oxygen Guideline Development Group of the BTS Standards of Care Committee. BTS guidelines for home oxygen in children. Thorax. 2009 Aug;64 Suppl 2:ii1-26. doi: 10.1136/thx.2009.116020. PMID: 19586968.

14- De Curtis, M., Bortolan, F., Diliberto, D. et al. Pediatric interregional healthcare mobility in Italy. Ital J Pediatr 47, 139 (2021). https://doi.org/10.1186/s13052-021-01091-8

Figure 1: Numbers of patients in LTOT followed by prescribing centres.

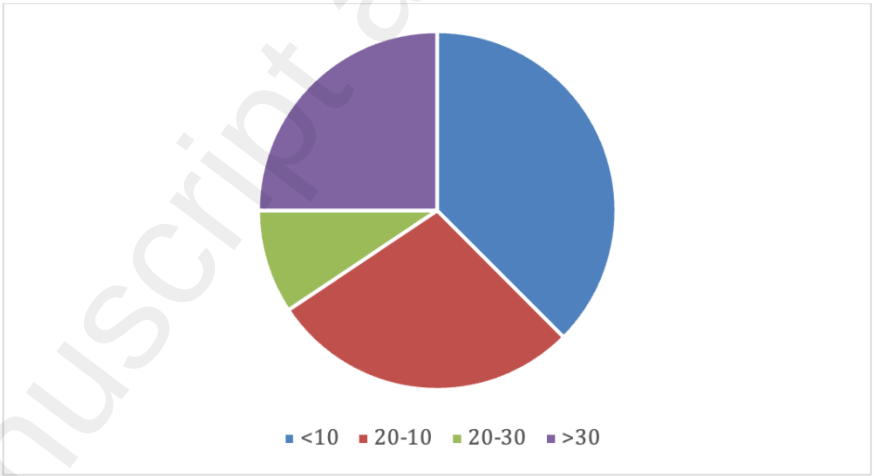

Figure 2: Diagnostic tests. BGT = Blood Gas Test.