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International approaches to the prescription of long-term oxygen therapy

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International approaches to the prescription of long-term oxygen therapy. P.J. Wijkstra, G.H. Guyatt, N. Ambrosino, B.R. Celli, R.Güell, J.F. Muir, C. Préfaut, E.S. Mendes, I. Ferreira, P. Austin, B. Weaver, R.S. Goldstein. ©ERS Journals Ltd 2001.

ABSTRACT: While there is broad agreement about who should receive long-term oxygen therapy (LTOT), there is little information available on how clinicians should decide on the oxygen prescription itself, at rest, during sleep and during exercise. The authors describe the results of an international survey that was undertaken to compare how respirologists prescribed oxygen.

A questionnaire was sent to 100 respirologists in each of seven countries. The questionnaire identified whether resting flow rates were derived in a standard manner or by individualized patient testing. Test targets were ascertained for rest, exercise and sleep, as was the percentage of time that each test target had to reach for the test to be accepted.

The majority of respondents individualized the oxygen prescription at rest (81%). Resting arterial oxygen saturation (S_{a,O_2}) was most commonly targeted at 90–91%. The approach to night prescription varied (p<0.001). Respirologists in Canada and the USA increased the resting S_{a,O_2} by 1–2 L·min^{-1} during sleep, while those in Spain used the resting (awake) flow for the night prescription (62%). Respirologists in the Netherlands, France, and Italy individualized the night prescription more frequently. Although oxygen during exercise was individualized in most countries (74%), significant differences remained among countries (p<0.001). The majority of respirologists (62%) aimed to achieve an S_{a,O_2} of 90–91% during exercise, while 70% of all respirologists tried to achieve the desired S_{a,O_2} for 90% of the test.

There were substantial differences among countries as to how the oxygen prescription was written. This survey highlights the need for multicentre studies that improve the effectiveness of long-term oxygen therapy utilization.

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Long-term oxygen therapy (LTOT) has been shown to improve survival in patients with chronic obstructive pulmonary disease (COPD), especially when used for >15 h a day [1, 2]. Many professional organizations, including the American Thoracic Society (ATS) and the European Respiratory Society (ERS), base their guidelines for the use of LTOT in COPD on two classic multicentre studies [3, 4]. In most jurisdictions, oxygen is recommended for patients with COPD if their resting awake oxygen tension in arterial blood (P_{a,O_2}) is <7.3 kPa (55 mmHg), or if it is 7.3–7.9 kPa (55–59 mmHg) in the presence of an elevated haematocrit (55%) or electrocardiogram evidence of an elevated right ventricular pressure. The goal of LTOT is to maintain the P_{a,O_2} at >8.0 kPa (60 mmHg) or the arterial oxygen saturation (S_{a,O_2}) at 90%.

The benefits of LTOT to all hypoxaemic respiratory patients have been extrapolated from the evidence of its life-saving effects in COPD, and many countries have extended programmes for domiciliary oxygen to include patients with other chronic respiratory conditions. In a review of LTOT in 12 European countries, ZIELINSKI [5] identified that a P_{a,O_2} of <7.3 kPa (55 mmHg) was the primary indication of the need for LTOT. A P_{a,O_2} of 7.3–8.0 kPa (55–59 mmHg), in combination with evidence of target organ involvement, was considered as a secondary indication. Some countries included transient nocturnal desaturation or transient exercise hypoxaemia as a tertiary indication [5].

While there is broad agreement, based on resting P_{a,O_2}, as to who should receive LTOT, there is little information on how clinicians should choose the flow rates patients should receive at rest, during sleep and during exercise. Some jurisdictions apply the nocturnal oxygen therapy trial (NOTT) [1] recommendations, increasing oxygen by 1 L·min^{-1} above the resting prescription for sleep and exercise, whereas others make no recommendation at all.

The number of individuals who receive LTOT is increasing in Europe, North America and Asia [6]. A standardized approach to assessing potentially eligible patients and established protocols for measuring and prescribing oxygen would allow better evaluation of the many outstanding clinical questions and cost issues associated with oxygen therapy. The World Health Organization and the National Heart, Lung and Blood Institute are showing a growing interest in promoting a global consensus among healthcare professionals in the management of chronic respiratory conditions (Global Obstructive Lung Disease initiative (GOLD)) [7]. One of the first steps in achieving consensus is to understand the existing degree of variability in practice. The present authors undertook a survey to compare how respirologists in seven countries prescribed oxygen for domiciliary use.

Methods

Sample selection and questionnaire administration

In each of seven countries (Brazil, Canada, France, Italy, Spain, the Netherlands and the USA), a respirologist, who had agreed to coordinate the survey, mailed questionnaires to 100 respirologists randomly selected from a list of respiratory specialists belonging to their professional organization (for example, the Canadian Thoracic Society). If the questionnaire was not returned within 2 weeks, it was re-sent to the same individuals with a polite reminder. Those who had not replied in a further 2 weeks were contacted by telephone. If they did not respond after the phone call, the questionnaire was classified as "not returned". A returned questionnaire was accepted as completed if the demographics and key questions had been answered (even if some questions were not completed). A file was considered as incomplete if only the demographics were completed.

Questionnaire

Characteristics of the respirologists. Respirologists were requested to provide their date of birth, how many years they had been practising respiratory medicine and the number of patients for whom they prescribed oxygen for the first time or for renewal purposes over the previous month.

Prescription of oxygen at rest. Respondents were asked whether they prescribed a standard oxygen flow rate for all their patients or whether they individualized flow rates with or without specific testing of each patient. Respondents were then asked how the recommended oxygen flow at rest was chosen (either tested at rest or tested during exercise). They were also asked to indicate the position (sitting, semirecumbent, supine) in which the patients were tested. Finally, the respondents were asked to identify the target level of S_{a,O_2} used to establish an oxygen prescription and the percentage of time during the measure in which this target had to be achieved (*i.e.* S_{a,O_2} had to be maintained at a particular target for a certain percentage of the test).

Prescription of oxygen during sleep and exercise. Respondents were asked how they prescribed oxygen during sleep and exercise. They were asked to identify the type of exercise test (walking, laboratory testing) used to establish the exercise prescription. Finally, they were asked to identify the target level of saturation during exercise and the percentage of time during the test in which this target had to be achieved.

Statistics

Continuous variables were expressed as mean±SD. Comparisons among countries were made using analysis of variance (ANOVA) for continuous variables and Pearson's Chi-squared test for categorical variables. All statistical tests were two-tailed with $\alpha=0.01$.

Results

Responses

Table 1 summarizes the response rate. The number of questionnaires returned by Brazil was below the minimum of 50, and therefore, the responses were excluded from further statistical analysis. Two hundred questionnaires were sent out by mistake in the USA (2-week reminders went to a second group of respirologists with some overlap between the first and second group), of which 64 were returned. As the absolute number was comparable to the number returned from other countries, the questionnaires were

Table 1. – Number of returned and completed questionnaires across all countries

Country	Returned	Completed	%#
Brazil	33	27	5.7
Canada	98	81	17.1
France	99	99	20.9
Italy	62	62	13.1
Spain	75	74	15.6
The Netherlands	72	72	15.2
USA	64	59	12.4
Total	503	474	100

#: percentage of total completed questionnaires. Return rate is significantly different between the countries ($p<0.001$).

Table 2. – Testing requirements for oxygen at rest

Country	Target S_{a,O_2} level during test				Time during which target S_{a,O_2} must be achieved		
	n#	<90%	90–91%	>91%	n#	>90%	<80%
Canada	56	6	40	10	51	41	10
France	63	1	39	23	62	46	16
Italy	46	1	33	12	28	24	4
Spain	34	1	21	12	22	20	2
The Netherlands	50	1	34	15	47	34	13
USA¶	42	8	30	4	39	36	3
Total	291	18	197	76	249	201	48

S_{a,O_2}: arterial oxygen saturation; n: number of responders. #: the number of responders decreased throughout the test; ¶: was not included in the statistical analysis; There were significant differences between all countries for target S_{a,O_2} level at rest ($p<0.001$), while time during which target level S_{a,O_2} must be achieved was not significantly different between all countries ($p=0.105$).

included in the survey. However, due to a significantly lower return rate (32%) the authors excluded the USA from the statistical analysis between countries. Countries differed in their questionnaire return and completion rates. Reasons for not completing the questionnaires (the difference between returned and completed) were: no reason given (Canada 3, USA 1); questionnaire sent to physician other than a respirologist (Canada 8, Brazil 2); physician no longer practising (Canada 4, USA 2); no patients receiving oxygen (Canada 2, Brazil 3); unclear translation (Spain 1); incorrect address (USA 2); and insufficient patients with ambulatory oxygen (Brazil 1). Since the respirologists did not answer all of the questions, the tables show different numbers of responses depending on the particular question.

Characteristics of the respirologists

The mean age of the respirologists was 45.9±7.7 yrs, with no differences between the countries ($p=0.14$). The majority of the respirologists (80.2%) prescribed oxygen for more than one patient per month. The majority of respirologists individualized the oxygen prescription by testing each patient (82%), although there were significant between-country differences, with more respondents in France (22%) and Spain (38%) who did not specifically test each patient for resting flow rates. Almost all respirologists (93%) prescribed the resting flow rate for oxygen based on the identified resting requirements (rather than assuming a resting prescription based on the exercise requirements). The flow rate in Brazil was individualized by 15 out of 25 respirologists (60%).

Prescription of oxygen at rest

Although the majority of respirologists required that the patients be in a sitting position during testing, there were differences between countries ($p<0.001$). In France, Italy and especially the Netherlands, a substantial number of patients were tested lying down or semirecumbent; 23%, 36%, and 37%, respectively. Almost 10% of respirologists indicated that the patient's position varied (rather than having a fixed position for testing in each case). Most respirologists chose a target S_{a,O_2} of $\geqslant$90% (table 2). However, there were significant differences between countries ($p<0.001$). In the Netherlands, Spain, and Italy, some respirologists tried to achieve a level of $\geqslant$92%; 30%, 35%, and 36% of them, respectively. Most of the physicians required that this target S_{a,O_2} be achieved for $\geqslant$90% of the time of the test. Most Brazilian respirologists (92%) preferred the patient to be seated whilst testing, and most (69%) chose a target resting S_{a,O_2} of 90–91%.

Prescription of oxygen during sleep and exercise

There were significant between-country differences in the way oxygen was prescribed during sleep. In Canada and the USA, respirologists preferred to increase the resting flow rate by 1 or 2 $L \cdot min^{-1}$ during sleep, whereas other countries preferred to prescribe the resting flow for sleeping or to test the patients individually (table 3). Respirologists in the Netherlands and France used both the resting flow and the individualized prescription in approximately the same number of cases, while those in Spain preferred to use the resting flow (62%). In Italy, most respirologists (67%) attempted to individualize the patients' prescription by testing them during sleep.

Table 3 also shows that clinicians in all countries preferred to individualize oxygen during exercise by testing each patient ($\geqslant$74% of respirologists). There were significant international differences. Fifteen per cent of the respirologists in the Netherlands, 13% in Spain and 20% in France added 1–2 $L \cdot min^{-1}$ to the resting flow rate. In addition, 21% in the Netherlands and 29% in Spain used the same flow rates as at rest. Walking tests were the most commonly used exercise tests in most countries. However, in the Netherlands almost the same number of laboratory tests as walking tests were used. The majority of respirologists aimed to achieve an S_{a,O_2} of 90–91% during exercise (significant differences between countries, $p<0.001$; table 4). All countries tried to achieve this level of S_{a,O_2} for $\geqslant$90% of the test duration (nonsignificant differences between countries, $p=0.39$).

Table 3. – How oxygen prescription during sleep and exercise was determined

Country	Sleep				Exercise			
	n[#]	Resting	Resting flow 1 or 2 L·min^{-1}	Individually tested flow	n[#]	Resting flow	Resting flow plus 1 or 2 L·min^{-1}[¶]	Individually tested flow
Canada	56	16	23	17	54	6	5	43
France	60	25	2	33	61	5	12	44
Italy	46	8	7	31	46	0	3	43
Spain	37	23	9	5	38	11	5	22
The Netherlands	51	26	2	23	48	10	7	31
USA[+]	35	11	13	11	41	1	0	40
Total	285	109	56	120	288	33	32	223

#: the number of responders decreased throughout the test; ¶: also contains the number that prescribed the same rate as during exercise; +: was not included in the statistical analysis. Significant difference between all countries (p<0.001).

Discussion

The information in this survey is likely to be representative of the current specialist practice of the countries surveyed, as the sample of clinicians was randomly chosen. They had been practising for many years and 80% prescribed oxygen for at least one patient per month.

Although flow rates were individualized in most instances, countries differed. In most countries, only 12% of the respirologists did not individualize flow rates, but in France and Spain the percentages were much higher (22% and 38%, respectively). The absence of standardization of posture makes comparisons between studies difficult. Although most respirologists targeted the resting S_{a,O_2} to reach 90–91%, many targeted the S_{a,O_2} at 92%. These inconsistencies occurred, at least in part, because of the absence of evidence that would enable clinicians to know the S_{a,O_2} most likely to optimize the benefits of LTOT for their patients.

The evidence that oxygen is of value during sleep alone (in the presence of normoxia during wakefulness) is equivocal [8–10]. Clinicians prescribe oxygen during sleep for patients who have resting hypoxaemia, to achieve normoxia for as much of the 24-h cycle as possible. PLYWACZEWSKI *et al.* [11] reported that 48% of the patients who received LTOT without flow adjustment during sleep still desaturated during the night. In this study, there were substantial differences with regard to how oxygen was prescribed during sleep. In Spain, the resting (awake) flow was used quite frequently (62%) for the night prescription, whereas in Canada and the USA, in keeping with ATS guidelines, there was a tendency to increase the resting awake flow rate by 1–2 L·min^{-1} during sleep [4]. Clinicians in the Netherlands (45%) and France (55%) individualized the night prescription, whereas in Italy, almost 67% of respirologists tested patients during sleep. The differences in Europe may be related to the fact that guidelines for night prescription do not exist in the European countries included in this study, thus leading to different approaches. These countries are likely to follow the guidelines of the ERS (and the Medical Research Council), which do not provide clear recommendations for sleep adjustment.

Most respirologists individualized the oxygen flow rate during exercise, aiming for a target S_{a,O_2} of 90–91%. The ATS guidelines for oxygen during exercise (based on the NOTT study) recommend that the resting flow rate be increased by 1 L·min^{-1} to maintain the P_{a,O_2} at >8.0 kPa (60 mmHg) or the S_{a,O_2} at >90%. Again, the European guidelines do not provide specific recommendations about oxygen prescription during exercise [3].

Standardization of the LTOT prescription is especially important in the context of the resources allocated to oxygen throughout the world [6]. The countries involved in this survey have substantial numbers of patients receiving oxygen. Approximate

Table 4. – Testing requirements for oxygen during exercise

Country	Target S_{a,O_2} level during test				Time during which target S_{a,O_2} must be achieved		
	n[#]	87–89%	90–91%	>91%	n[#]	>90%	<80%
Canada	42	14	25	3	39	31	8
France	44	2	30	12	43	31	12
Italy	43	4	25	14	27	24	3
Spain	20	2	12	6	14	11	3
The Netherlands	31	6	19	6	27	22	5
USA[¶]	40	16	21	3	38	34	4
Total	220	44	132	44	188	153	35

S_{a,O_2}: arterial oxygen saturation; n: number of responders; #: the number of responders decreased throughout the test; ¶: was not included in the statistical analysis. There were significant differences between all countries for target S_{a,O_2} level (p<0.001), while time during which target level S_{a,O_2} must be achieved was not significantly different between all countries (p=0.39).

numbers, with costs converted to $US, are as follows: Canada 50,000 at $300 per person (pp)·month^{-1}, France 50,000 at $550 pp·month^{-1}, Italy 40,000 at $225 pp·month^{-1}, Spain 69,000 at $90 pp·month^{-1} (less because only 10% are on liquid oxygen), the Netherlands 8,000 at $500 pp·month^{-1}, USA 800,000 at $400 pp·month^{-1}. Remarkably, although evidence-based guidelines for LTOT exist, a large number of individuals receive supplemental oxygen for a variety of conditions other than those for which evidence of effectiveness has been established. A French study showed that 18% of 7,700 patients who were on LTOT had a P_{a,O_2} >8.0 kPa [12]. A UK study suggested that a substantial percentage of costs attributed to domiciliary oxygen were allocated to conditions not consistent with the evidence that LTOT was life prolonging [13]. Therefore, it is important to establish whether the substantial health resources directed towards providing oxygen for transient nocturnal or exercise desaturation and the extrapolation from observations on COPD to other diagnostic categories are actually of value to the healthcare systems.

In summary, although there is strong agreement between clinicians about which patients should receive long-term oxygen therapy, substantial between-country differences remain about how the actual prescription should be written. This survey highlights the potential for consensus conferences and multicentre studies to improve the effectiveness of long-term oxygen therapy use, while minimizing the cost of domiciliary oxygen programmes.

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