*LITERATURE REVIEW*

# Long-Term Oxygen Therapy in Chronic Obstructive Pulmonary Disease

**Yuni Ekowati**
Department of Physical Medicine and Rehabilitation, Cipto Mangunkusumo General Hospital -Faculty of Medicine, University of Indonesia, Jakarta, Indonesia

ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) affects 210 million people worldwide and is predicted to increase more than 30% in the ten following years. Long-term oxygen therapy (LTOT) is the treatment of choice nowadays and widely used to reduce mortality in COPD. LTOT in COPD can improve hemodynamic status, exercise tolerance, dyspnoea, life expectancy, quality of life, cognitive function and frequency of hospitalization.The success of LTOT depends on patient compliance, duration of therapy and the accuracy of hypoxemia correction. Although LTOT provides many benefits in COPD patients, but it also has many disadvantages. Subjective factor is the determinant factor in the success of therapy. Follow-up session is required to evaluate the therapeutic efficacy, prevent side effects and detect any clinical deterioration or hypercapnia as early as possible for an immediate referral to the hospital.

Keywords: *Long-term Oxygen Therapy (LTOT), COPD, hypoxemia,quality of life.*

## INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lungs to noxious particles or gases.[1]

Chronic Obstructive Pulmonary Disease is a major cause of morbidity, mortality and health care utilization. It affects approximately 210 million people worldwide and is expected to increase by more than 30 % in the next ten years.[2] In Indonesia, the prevalence of COPD was 1.6 % of men with aged ≥ 30 years and women was 0.9%. The increase of the cases was supported by the increase in the number of risk factors, namely life expectancy, smoking behavior and air pollution.[3]

Long-term oxygen therapy (LTOT) is a treatment of choice that has been widely used to reduce mortality in COPD.[3] The concept of oxygen consumption as a therapeutic was introduced in 1922 by Alvan Barach. In 1950, the benefit of oxygen therapy to improve exercise tolerance in the hospital was established. Petty et al. in 1968 also published about the utilization of long-term use of portable oxygen at home (domiciliary).[1,4] Supporting this, some studies suggested that LTOT in COPD can improve hemodynamic status, exercise tolerance, dyspnoea and life expectancy. LTOT was also shown to improve

*Received in March 2015 and accepted for publication in April 2015*

**Correspondence detail:**
Yuni Ekowati.
Clio Vintage Block PA8 De Latinos, BSD City, Indonesia
Email: yuniekowati93@yahoo.co.id
Phone: +62 811594771

the quality of life, cognitive function and frequency of hospitalization.[5]

The purpose of this paper is to explain the benefits of LTOT in COPD patients based on research that has been performed, including the prescription and the factors that need to be considered in the provision of LTOT in COPD patients.

## DISCUSSION

Long-term oxygen therapy (LTOT) is an oxygen therapy using low-flow (1-3 Lt/ min) for more than 15 hours / day. It is indicated for patients with chronic hypoxemia to provide oxygen supply at higher concentration compared to the outside air. It is believed can treat or prevent the symptoms and effects of hypoxia by maintaining the arterial oxygen pressure ($PaO_2$) above 60 mmHg and oxygen saturation ($SaO_2$) above 90%.[1,4]

There are many indications for LTOT admnistration, such as (1) $PaO_2 \leq 55$ mmHg or $SaO_2$ through pulse oximetry ($SpO_2$) $\leq 88\%$ at rest; (2) $PaO_2$ 56-59 mmHg or $SpO_2$ 89% with signs of pulmonary hypertension or haematocrit $\geq$ 55% or peripheral edema due to right heart failure; (3) $PaO_2 \leq 55$ mmHg or $SpO_2 \leq 88\%$ during exercise / sports; (4) nocturnal oxygen desaturation $\leq 88\%$.[4,6]

Thus, LTOT was applied in COPD patients with severe chronic hypoxemia (PaO2 $\leq$ 55 mmHg (7.3 kPa) or PaO2 between 56-59 mmHg (7.4 to 7.8 kPa) with signs of cor pulmonale, haematocrit > 55%, peripheral edema). Patients were then clinically stable in the sense that no exacerbations occured within 4 weeks.[7,8]

Prevalence of hypoxia among patients with COPD is not known yet. In the overall population of COPD, severe hypoxemia is relatively rare, with only 2% of 5993 participants in the UPLIFT (an experimental therapy or oxygen supplementation) study. Meanwhile, the National Emphysema Treatment Trial suggested almost 80% of COPD patients with advanced disease degrees using LTOT.[9]

LTOT is often used by patients with other chronic lung diseases such as ILD (interstitial lung disease). Some studies suggested that long-term use of oxygen in ILD could supress the symptoms and improve the quality of life. In addition, LTOT is also frequently used as part of palliative therapy in cancer and heart failure to ameliorate shortness of breath, either with or without hypoxemia. But there were few clinical evidences mentioning it's benefits in cancer and heart failure.[4]

LTOT may alleviate severe chronic asthma, cystic fibrosis, bronkhiektasis, pulmonary vascular disease, primary pulmonary hypertension with criteria or indication as in COPD provision.[8]

There are no absolute contraindications for oxygen therapy. Smoking may combusive due to high oxygen concentration used in therapy. Therefore, patients using LTOT are highly recommended to quit smoking.[4,8]

LTOT should be given in low-flow oxygen (1-3 Lt/ min) for > 15 hours/ day. It can be increased for about 1 Lt/ min to the regular dose at bedtime or after a meal and during exercise. It is because of the raise of metabolic rates after eating and during exercise, as well as hypoventilation occurs when sleeping.[1,4]

### Oxygen Delivery System of LTOT

Oxygen delivery system includes a conventional oxygen cylinder, an oxygen concentrator, and liquid oxygen. The conventional oxygen cylinder (Figure 1) contains compressed oxygen with a pressure of 2000-3000 pounds / inch$^2$ and equipped with a pressure regulator that allows oxygen distribution at a pressure of 50 pounds/ inch$^2$ when in used. Oxygen cylinder contains 680 Lt of oxygen which can provide oxygen for approximately 5 hours with the flow of 2 Lt/ min. A portable oxygen cylinder contains 400 Lt of oxygen that allows oxygen supply for approximately 3 hours with a flow of 2 Lt/ min.[4] Higher oxygen demands is required in patients who are immobile. This portable cylinder is relatively low-priced but it needs replacement when required.[10]

Figure 1. Oxygen Cylinder[11]

Oxygen concentrator (Figure 2) works by denitrogenation of free air atmosphere using ziolite filter to obtain 95% oxygen. Portable oxygen concentrator that provides airflow about 1 Lt/ min, weighs around 2.5 to 5 kg. It is relatively affordable, but not carriageable due to it's dependency on electricity.[4,12]

Figure 2. Oxygen Concentrator[11]

Liquid oxygen (Figure 3) is converted from gas to liquid form at -300° F and stored in a reservoir at a pressure of ± 2 Lt/ inch$^2$, which is safed to be used at home. A liter of liquid oxygen can provide 860 Lt of gas. A reservoir contains 30-40 Lt of liquid oxygen which can provides airflow around 2 Lt/ min for about 8-10 days. This is the best choice although more expensive than other systems because it offers higher improvement on patient's quality of life. It is easy to carry and can be re-filled.[4,12]

Figure 3. Liquid Oxygen[11]

**Long-term Oxygen Therapy (LTOT) Administration Guidelines** [8]

The LTOT administration algorithm is illustrated in Figure 4 below. LTOT is administered when a patient is clinically stable without an episode of exacerbation for the last 4 weeks. $PaO_2$ must be measured twice at intervals of not less than 3 weeks and before the administration of LTOT. The assessment of hypercapnia should be based on blood gas analysis primarily, not simply $SaO_2$, and the response to oxygen therapy is necessary for the safety LTOT prescription. Moreover, assessment oxygen demand should be done by a standard source of oxygen or oxygen concentrator.

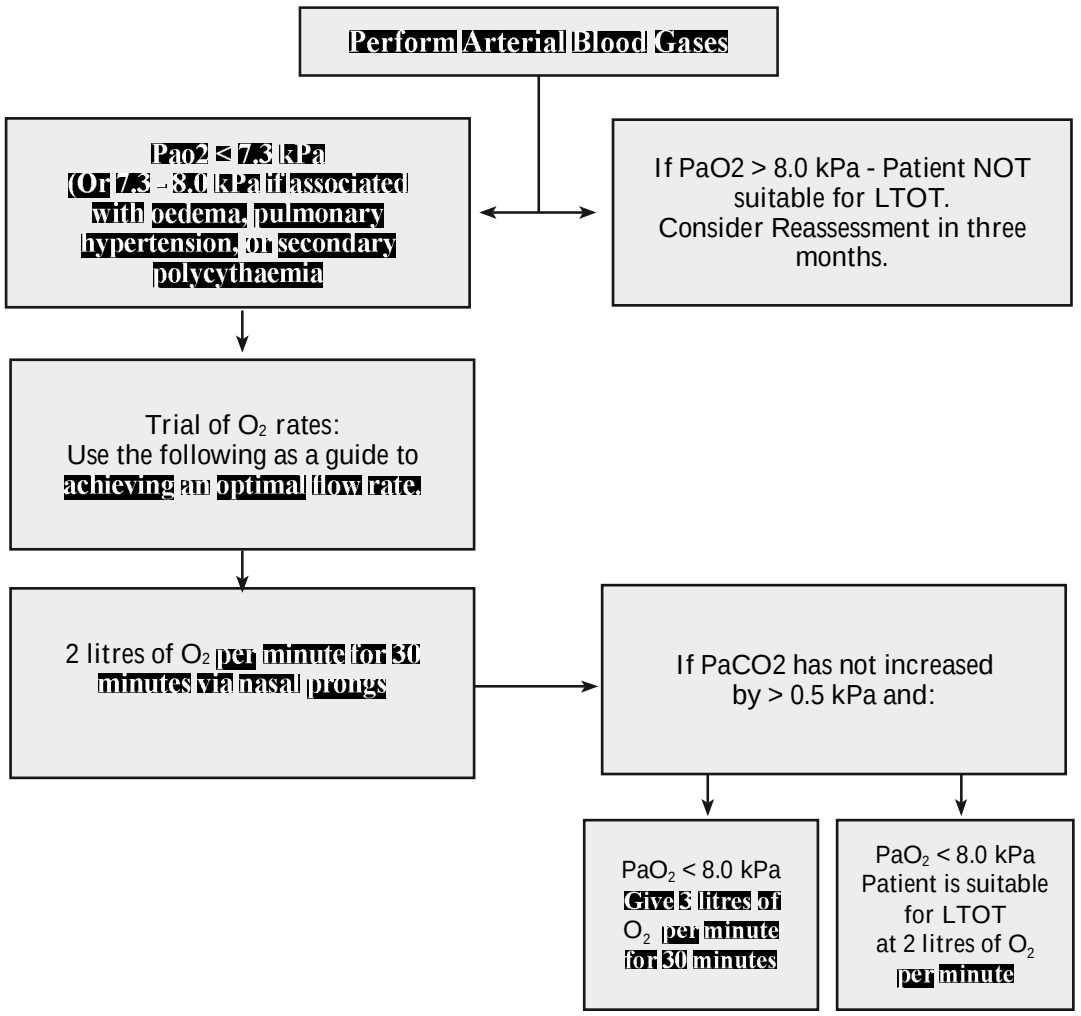


**Figure 4. Algorithm of LTOT Administration**

**LTOT Benefits in COPD Patients**

LTOT offers many advantages in COPD patients' lives, such as improving survival rate, exercise capacity, pulmonary hemodynamics, quality of life and mental status. The British Medical Research Council conducted a research in 1981 on 87 patients, with aged less than 70 years with chronic bronchitis or emphysema (FEV1 0.58 to 0.75 Lt) with severe hypoxemia ($PaO_2$ from 49.4 to 51.8 mmHg) and retention of carbon dioxide ($PaCO_2$ 56-60 mmHg). Randomly chosen to be given oxygen therapy 2 Lt/ min via nasal cannula for 15 hours/ day. Patients were followed up every 3-6 months. After 5 years, it was found that 19 out of 42 patients receiving oxygen therapy died. Meanwhile, 30 out of 45 patients died in the control group. This indicated that oxygen therapy increased survival rate although the effects of oxygen therapy versus non-treatment of the physiological variables were not statistically significant.[13]

The Nocturnal Oxygen Therapy Trial (NOTT) were also conducted a study of 203 patients with COPD with hypoxemia. There were two studied groups, a group with continuous oxygen therapy (17.7 ± 4.8 hours / day) and another group receiving nocturnal oxygen (12 ± 2.5 hours / day). They were followed up at 12 months and 24 months post therapy. Result showed 23 patients died in the continuous therapy group, and 41 died on

nocturnal therapy. In this study, a significant result on the relationship between continuous oxygen therapy with a decrease in pulmonary vascular resistance and haematocrit were absolute. [13]

Gulbas et al., conducted a research on oxygen therapy with a duration of 15 hours / day (flow rate of 1-3 l / min) using oxygen concentrator to 228 COPD patients at age of 43-89 years. Among them, 55 did not get therapy, 112 received intermittent therapy ( <15 hours/ day) and 61 had 15 hours/ day during research period. It was found that 75% died after 5 years of follow-up. The average value of the survival rate in the non-treatment group was 19.5 ± 5.6 months, the intermitten group was 32.5 ± 4.1 months and 15 hours/ day therapy group was 29 ± 2.7 months. This study suggested no significant difference in survival rate between the intermittent (<15 hours/ day) and the 15 hour / day groups.[5]

Criner and Celli suggested that oxygen therapy in COPD patients can improve ventilatory muscle functions during exercise. Oxygen consumption may prevent additional workload muscles, thereby reducing breath tightness and improve endurance.[15] Significant improvement in exercise capacity was seen in patients with mild to moderate hypoxemia. This is explained by decreasing minute ventilation, dynamic hyperinflation, vasoconstriction in lung area, and pulmonary vascular resistance, and increasing stroke volume and oxygen transport capacity.[4] Supporting these, Malgorzata et al. (2012) studied 20 COPD, 4 bronchiectasis, 3 interstitial lung disease and 3 cystic fibrosis patients receiving LTOT (first 9 hours of 1.5 Lt/ min, 7 hours later with 2 Lt/ min, and the following 4.5 hours with 3 Lt/ min) for 6 months. The average increase mileage achieved in the 6-minute walking test was 34.31 ± 15,45 m ($p<0.0001$).[14]

Moreover, oxygen therapy may improve pulmonary haemodynamics and stroke volume. LTOT administration for 2 years can reduce pulmonary artery pressure and remain stable up to 6 years. Pulmonary haemodynamic improvement occurs more frequently in patients receiving continuous oxygen therapy compared with the intermittent.[4,13]

Health status improvement via oxygen therapy in relation to the quality of life can be assessed by St. George's Respiratory Questionnaire (SGRQ). High scores were found in all aspects of SGRQ after receiving proper LTOT using oxygen concentrator or portable liquid oxygen. A greater increased in quality of life was produced by using portable liquid oxygen because patient was able to perform activities outside the home. This could be seen through significant improvement in ADL or IADL assessment.[14] This is consistent to Okubadejo et al. finding on LTOT with oxygen concentrator of 15 hours/ day in 23 COPD patients with severe hypoxemia. It was found that SGRQ score improved after 2 weeks of oxygen consumption although it was statistically insignificant. After 6 months of therapy there was a slight increase in the value of SGRQ though statistically insignificant. It was because of the utilization of oxygen concentrators which limited patients' ambulation.[16]

COPD patients with hypoxemia often suffer neuropsychological deficits, personal and mood disorders. LTOT can improve psychological status of patients by significantly improving their mood and behaviour.[4] Okubadejo et al. also found that the anxiety level of COPD patients with severe hypoxemia decreased significantly after given LTOT for 6 months. As for the level of depression found no significant difference between the group who received LTOT and the control group.[16]

Furthermore, sleep-disordered breathing is common in COPD patients and is often associated with the occurrence of nocturnal desaturation. Increased sleep latency, and decreased total sleep time, slow-wave sleep and sleep REEM are the causes of sleep problems in patients with COPD. For about 30-70% patients with COPD experience imsomnia and body weakness when wake up. It is often considered as drug side effect, airflow obstruction and hypercapnia. However, most importantly is that COPD patients often experienced nocturnal desaturation. Therefore, oxygen therapy during sleep can prevent nocturnal hypoxemia and improve sleep quality. [13,16]

Disadvantages and Side Effects of LTOT in COPD Patients

Although the use of LTOT has many benefits in COPD patients, but it also has disadvantages on its efficiencies or adverse effects. Under LTOT circumstance, patient compliance is the determining factor that influences the success of therapy. This is because of the long course of LTOT makes patients bored and often avoid to use because of fear of addiction. Besides, oxygen is flammable, so patient has to stop smoking and for about 20% of COPD patients are active smokers. A study reported that the incidence of burns were found in the use of LTOT with burn size 3.9% minimumly.[6,9]

Low-flow oxygen delivery rarely causes serious side effects. The common side effects are local irritation of the nose and eyes. More severe side effects can occur at high-flow administration, which can induce the occurrence of $CO_2$ retention and may cause hypercapnia. However, these are avoidable by maintaining $PaO_2$ at a pressure of 60-65 mmHg. The use of home oximetry will allow patients to monitor $SpO_2$ and may improve patient adherence.[4,6]

The success or clinical benefit of LTOT depends on several factors: patient compliance, duration of therapy and the accuracy of hypoxemia correction. It is suggested that the level of patient adherence to LTOT is ranging from 45% to 70%. Several factors that affect the degree of patient compliance include the disease (disease characteristics and complexity of treatment), personal/ family (demographics, function the patient/ family, cognition/ knowledge of health), shame and fear of addiction, and the presence of complications (irritation of the nose, dry nose, nosebleeds, loss of sensation sniffing/ flavor). Moreover, many patients especially the elderly with reduced endurance and strength find that portable oxygen are heavy.[7]

**LTOT Home-Follow-up**

Oxygen therapy at home can be monitored 4 weeks after prescription by an experienced nurse. The purposes of this follow-up at home are providing further education and support patients and care giver, recording the $SaO_2$ by pulse oximetry ($SpO_2$), and prescribe the flow rate, achieving correct management of hypoxemia ($SpO_2$ target 92% or above), and acquiring pulse oximetry result for hospital record and further evaluation.[8]

Every patient who is on LTOT will then be followed up within 3-6 months. During the visit, the nurse should take notes about the location of the tool/ concentrator, nasal cannulas used, the need for additional cylinder tube, patient compliance, highly encourage patient to not smoking, available contacts of oxygen providers and experienced nurses in oxygen therapy.

If the $SpO_2$ belows the expected correction, patient should be re-assessed with a blood gas analyzer for readjustment of LTOT. If patient's clnical symptoms worsen or hypercapnia occurs, patient has to be referred to the hospital immediately.

## CONCLUSION

LTOT provides many benefits in stable COPD patients with severe chronic hypoxemia. It can improve the survival rate, exercise capacity, pulmonary hemodynamics, quality of life and mental status. The success of LTOT depends on patient adherence to therapy, duration of therapy and the accuracy of hypoxemia correction. The most important thing to consider is the complexity of the tools used and the accuracy of the intervention. Understanding and investigating patient's existing problems and knowledge about oxygen therapy can help the development of new strategies and interventions.

Follow-up session is required to evaluate the therapeutic efficacy, prevent side effects and detect any clinical deterioration or hypercapnia as early as possible for an immediate referral to the hospital.

## REFERENCES

1. Global Strategy For The Diagnosis, Management, and Prevention of COPD . In : Global Intiative For Chronic Obstructive Lung Disease;2013.
2. Juliet G, Abebaw MY, Ryan W, Susan C.

'It is not going to change his life but it has picked him up': a qualitative study of perspectives on long term oxygen therapy for people with COPD. Health and Quality of Life Outcomes. 2013 ;11:1-9
3. Ana AP, Ira P, M. Agus P. Pemberdayaan Keluarga Dalam Rehabilitasi Medik Paru Pada Penderita PPOK di Balai Pengobatan Penyakit Paru-Paru Yogyakarta. Berita Kedokteran Masyarakat. 2010; 26 : 55-62.
4. Surinder KJ, Ritesh A. Long-term Oxygen Therapy. Expert Reviews Respir. Med. 2012;6:639-49.
5. Gulbas G, Gunen H, In E, Kilic T. Long-term follow-up of COPD on long-term oxygen treatment. Internal Journal Clinical Pract. 2012;66: 152-7.
6. Benedicta M, Calvin K, Christopher R, Deriyan S . Terapi Oksigen. Div. Pulmonologi FK Universitas Indonesia.2012;1-21.
7. Stamatis K, Stavros HC. Long-term Oxygen Therapy in COPD : Factor Affecting and Ways of Improving Patient Complience. Hindawi Publishing Corp. Pulmonary Medicine. 2011;1-8.
8. William MacNee. Lothian Guideline for Domiciliary Oxygen Therapy Service For COPD. NHS Lothian;2009.
9. Brian D, Patrick D, Walter T. Hypoxemia in patients with COPD: cause,effects, and disease progression.International Journal of COPD.2011;6:199-208.
10. Rasmin M. Terapi Oksigen: Mengenal Terapi Oksigen. Perhimpunan Dokter Paru Indonesia.Jakarta;2006.
11. Jones Medical Supply. Oxygen Therapy. Available on ; http : // jonesmed.com/ Oxygen.html.
12. Thomas P, Robert W, Dennis E. Long-term Oxygen Therapy (LTOT). History, Scientic Foundations and Emerging Technologies. In National Lung Health Education Program;2006.
13. Victor Kim, Joshua O, Robert A, Amir S. Oxygen Therapy in Chronic Obstructive Pulmonary Disease. Proc Am Thorac Soc. 2008;5:513-8.
14. Malgorzata C, Beata P, Anna C, Katarzyna K, Pawel J. Comparison of results of sequential home oxygen therapy in patients using stationary or portable oxygen sources. Pneumonol.Alergol. Pol.2012;8:308-16.
15. Crinner G, Celli B. Ventilatory muscle recruitment in exercise with O2 in obstructed patients with mild hypoxemia. J Appl Physiol. 1987;63:195-200.
16. Okubadejo A,Paul EA, Jones PW, Wedzicha JA. Does long-term oxygen therapy affect quality of life in patients with chronic obstructive pulmonary disease and severe hypoxemia. European Respiratory Journal.1996;9: 2335-9.