TIME SPENT OUTDOORS IN PATIENTS UNDERGOING LONG-TERM OXYGEN THERAPY AND THE CORRELATION BETWEEN DEMENTIA AND DEPRESSIVE STATE.

Megumi Mikuniya, Kunihiko Nakamura, Koichi Okudera, Shingo Takanashi, Akihito Hayashi, Takeshi Morimoto, Kageaki Taima, Jyunichi Dempoya and Ken Okumura

Abstract  Few studies have reported the time spent outdoors in patients undergoing long-term oxygen therapy (LTOT). Also, few have determined whether time spent outdoors was influenced by psychological impairments. The aim of the present study was to examine the usage of oxygen cylinders to assess the time spent outdoors of patients receiving LTOT, and to evaluate the prevalence of dementia and depressive states and determine the correlation between these disorders and time spent outdoors. Fifty-four LTOT patients were enrolled in the present study, and dementia and depressive states were investigated using specific questionnaires. Among them, 23 patients were reassessed one year after the initial evaluation. There was a large variation in time spent outdoors among LTOT patients, and the median number was one hour per day. Measured by the Hasegawa Dementia Scale-Revised (HDS-R), dementia was observed in 41% of the patients. Depressive state, measured by the Self-Rating Depression Scale (SDS), was observed in 24%. There were no correlations between time spent outdoors and psychological impairments. The percentage of patients in depressive states was statistically higher in the 2nd assessment. More attention must be given to LTOT patients’ usage of oxygen cylinders, and dementia and depressive state should be periodically assessed.

Key words: long-term oxygen therapy; time spent outdoors; dementia; depressive state; activity of daily living.

ORIGINAL ARTICLE

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Key words: long-term oxygen therapy; time spent outdoors; dementia; depressive state; activity of daily living.

在宅酸素療法患者における携帯酸素使用時間の評価および、携帯酸素使用時間と認知症・うつ状態との関連

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抄録  慢性閉塞性肺疾患患者の増加に伴い、在宅酸素療法（LTOT）を要する患者の増加が予測される。LTOT 患者の携帯酸素ポンベ使用量から携帯酸素使用時間に評価した研究は少ない。LTOT 患者54名において、携帯酸素ポンベ使用量から外出時間の算定を、また認知症・うつ状態の割合の評価と携帯酸素使用時間との関連性を検討した。認知症は改訂長谷川式簡易知能評価スケールを、うつ状態は自己評価記五つ尺度を用いて評価した。また23名において1年後の再評価を行った。携帯酸素使用時間はばらつきが大きく、平均使用時間は1日1時間であった。LTOT 患者の41%に認知症を、24%にうつ状態を認めた。携帯酸素使用時間と認知症・うつ状態に関連は認めなかった。1年後の再評価では、うつ状態の割合に有意に上昇していた。LTOT 患者の携帯酸素使用時間に留意し、認知症・うつ状態の評価を終時的に行う必要がある。

キーワード：在宅酸素療法；外出時間；認知症；うつ状態；日常生活動作。
Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality in the whole world, and the number of cases continues to rise\(^1\). COPD prevalence data obtained by the Nippon COPD Epidemiology (NICE) study suggested that COPD incidence is under-reported, and estimated that about 5.3 million Japanese currently suffer from COPD\(^4\). COPD is the most common cause for long-term oxygen therapy (LTOT) and accounts for 45% of the cases undergoing LTOT\(^5\). Thus the number of patients requiring LTOT is expected to be increased. The main complaints requiring the implementation of LTOT were dyspnea at rest, dyspnea on exertion, marked decrease in the level of activity of daily living (ADL) and cyanosis. Because dyspnea or hypoxemia on exertion can be improved with the implementation of LTOT, it is important to use oxygen cylinders appropriately when patients are outside of the home because more oxygen inhalation is needed to account for the increased ADL. According to the “Japanese White Paper on Home Respiratory Care 2010”\(^5\), 82% of the patients undergoing LTOT reported that they were using oxygen cylinders outside the home. It is possible that cylinder usage could represent the time spent outdoors and indicate outdoor activity. To the best of our knowledge, however, no study has reported the time spent outdoors calculated from the usage of oxygen cylinders. In addition, few studies have addressed the factors that affect the time spent outdoors among LTOT patients. Generally, patients receiving LTOT are elderly, and psychological impairments such as dementia and a depressive state readily may develop in the elderly patients. In addition, elderly patients typically show a decreased ADL. Thus, we hypothesized that the time spent outdoors would be influenced by the psychological impairments in LTOT patients. The aim of this study was to assess the number of hours that LTOT patients spent outdoors by monitoring the usage of oxygen cylinders. A secondary objective was to evaluate the prevalence of psychological impairments (dementia and depressive state) in patients receiving LTOT and determine whether there is a correlation between psychological impairments and the time spent outdoors.

Methods

Study subjects

This study was conducted between September 2008 and December 2009. We examined 54 patients (40 male and 14 female; mean age, 75 ± 10 years, ranging from 34 to 89) who were receiving LTOT with oxygen cylinders. All patients were followed up at clinic of Hirosaki Chuo Hospital. These patients had been receiving LTOT for 29 ± 41 months (27 ± 41 months in male and 34 ± 41 in female). The underlying diagnoses are listed in Table 1. The most common diagnosis was COPD (33%), which was followed by idiopathic interstitial pneumonia (26%), a sequence of tuberculosis infections (13%), and lung cancer (13%); other

<table>
<thead>
<tr>
<th>Table 1 Underlying diseases in patients in the study</th>
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<td>n=54 (M/F)</td>
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<tr>
<td>Chronic obstructive pulmonary disease</td>
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<td>Idiopathic interstitial pneumonia</td>
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<td>Sequence of tuberculosis infections</td>
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<td>Lung cancer</td>
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<td>Others</td>
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Calculation of time spent outdoors in each patient

Time spent outdoors was calculated from the amount of oxygen cylinder usage per month and each patient’s oxygen flow rate when going outside.

Psychological impairments

Dementia

In the present study, the Hasegawa Dementia Scale-Revised (HDS-R) was used for the evaluation of dementia. The HDS-R is frequently used for dementia screening in Japan. Patients with a total score greater than 20 points were judged as “non-dementia”, and patients with a score of 20 or less were classified as “dementia”. Using this cut-off score, the sensitivity and specificity of HDS-R for the diagnosis of dementia were reported to be 90% and 82%, respectively.

Depressive state

The Self-Rating Depression Scale (SDS) was used for the evaluation of a depressive state. The SDS is a questionnaire that consists of 20 questions to measure depressive symptoms using four-point scales. This questionnaire has previously been translated and validated in Japan. Psychometric research has provided substantial evidence for the reliability and validity of the SDS with normal subjects and patients with depressive disorders. The SDS scores were used to define four categories of the severity of depression: 1) within normal range or no significant psychopathology (below 40 points), 2) presence of minimal to mild depression (40-47 points), 3) moderate to marked depression (48-55 points) and 4) presence of severe to extreme depression (56 points and above). The ranges of these scores were based on the study results by Zung and Barrett et al. Patients suffering from severe to extreme depression were excluded from the study because it is difficult to evaluate the degree of depressive state appropriately by self-rating questionnaire.

Twenty-three of the 54 patients were re-assessed approximately one year after the initial evaluation.

Statistical analysis

Analysis was carried out using the Statistical Package for Social Sciences (SPSS 18.0, SPSS Japan, Tokyo, Japan). The results are expressed as the mean ± one standard deviation or median with range as appropriate. Parameters measured at the beginning of the study and at one year later were compared using the Wilcoxon’s signed rank test. Statistical significance was accepted at a p-value less than 0.05.

Results

Initial evaluation

Time spent outdoors

There was a large variation in the time spent outdoors and the distribution of the time spent outdoors is shown in Figure 1. The average time of oxygen cylinder usages was 43 ± 44 hours (median 30, ranging from 0 to 180) per month. Twenty-five patients (46%) used oxygen cylinders for less than 30 hours (less than one hour per day), and 42 patients (78%) for less than 60 hours per month (less than two hours per day). No significant differences were observed between the time spent outdoors and the age distribution or gender. Also, there were no significant differences between the time spent outdoors and the underlying disease.

Psychological impairment (Fig. 2)

Dementia

The median value of the HDS-R scores was 23.5, ranging from 10 to 29. Twenty-one
out of 54 patients (41%) were diagnosed with dementia (i.e., scores less than 20 points).

**Depressive state**

The median value of the SDS scores was 35, ranging from 20 to 53. The prevalence of depressive disorders was 13 out of 54 (24%). Five patients were moderately depressed, and forty-one patients (76%) scored less than 40 points (within normal range or no significant
psychopathology). There were four patients with both dementia and a depressive state.

**Relationship between time spent outdoors and psychological impairments (Fig. 3a and b)**

As shown in Figure 3a, there was no correlation between time spent outdoors and HDS-R score. The relationship between time spent outdoors and SDS score is shown in Figure 3b. Similarly, there was no correlation between SDS
score and time spent outdoors.

*Follow-up evaluation (Fig. 4)*

One year after the initial evaluation, 23 of the 54 patients who were alive and would still participate in the study were re-assessed. We did not observe any differences in either time spent outdoors or HDS-R score between the first and second assessments. In the 23 patients, the SDS score at the second assessment (median 42, ranging from 24 to 55), however, was significantly higher than the score from the first assessment (median 39, ranging from 23 to 53) \( p<0.05 \). The percentage of the patients in the depressive state increased to 61% (14/23) in the second assessment compared with 22% in the first assessment (5/23). Out of the 14 patients who were in a depressive state (i.e., 14/23), a half of them were moderately depressed.

*Discussion*

The present study showed that in patients undergoing LTOT, there was a large variation in the use of oxygen cylinders outdoors, and some of the patients did not use oxygen cylinders at all. Furthermore, the time spent outdoors calculated from oxygen cylinders was lower than expected. Interestingly, the median number of time spent outdoors was one hour per day. These findings suggest that ADL decreased considerably among LTOT patients, which could be attributed to non-compliance with the recommended prescription of oxygen flow rate or less interest in the use of oxygen outside the home. In addition, approximately 20% of the patients in the LTOT group reported that they were restricted to their homes because of problems with the portable oxygen cylinders (i.e., fear of development of breathless (55%) and lack of confidence of being alone.
(42%)\(^5\). The most common concern about the oxygen cylinder was its portability and weight. Therefore, further technical improvements of oxygen cylinder devices are required to enhance patient usage and increase the ADL in patients receiving LTOT. In addition, instructions on the appropriate use of oxygen cylinders and how to check the used hours outside the home would be important to evaluate accurate ADL of patients receiving LTOT.

It was demonstrated that dementia was observed in 41% of LTOT patients. Interestingly, the average age of LTOT patient in Japan was reported to be 71 years, and this number has been increasing in recent years. In Japan, the prevalence of dementia in the age-matched general population is 7.1%. Compared with the general population, the percentage of LTOT patients suffering from dementia was considerably high. Several reports\(^\text{13-19}\) have demonstrated decreased ADL in patients receiving LTOT and restrictions of mobility and personal and social activities in aged LTOT patients may contribute to high prevalence of dementia. In addition, LTOT itself may be one of the factors accelerating dementia. The prevalence of cognitive impairment in LTOT patients, however, is still unknown. Therefore, epidemiological studies are required to determine whether LTOT influences cognitive function.

We found that 24% of the patients were in a depressive state. Interestingly, previous studies found that the prevalence of depressive states undergoing LTOT patients ranged from 21.7% to 75\%\(^\text{16-21}\). In the present study, the percentage of patients in a depressive state was statistically higher in the second assessment. Janssens et al.\(^\text{20}\) reported depressive disorders in 27% of LTOT patients, and the prevalence was unchanged during one year period. In addition, Muramatsu et al.\(^\text{21}\) reported that 16.6-36.4% of LTOT patients were in a depressive state, and the average scores did not change throughout a three-year observation period. The variation in the prevalence can be partly attributed to the use of different measures for depression.

Contrary to our hypothesis, there were no correlations between time spent outdoors and psychological impairments. Although we have no clear explanation about these findings, time spent outdoors may not be determinant of psychological factors, but of by some multiplex factors. For another plausible explanation, patients with severe psychological impairments might have performed incorrect operation of the oxygen cylinders. In addition number of subjects might not be enough to detect the associations.

To investigate the factors other than dementia and depressive state that could be affecting the time spent outdoors, we examined the utilization of physical disability welfare and long-term care insurance services. However, we did not find any correlations between the services and the time spent outdoors (data not shown). We also measured the arterial oxygen saturation under prescribed oxygen flow rates, but no correlation was found (data not shown).

Furthermore, evaluation of the self-rating ability is important in the patients with both dementia and depressive state, since severe cognitive impairment may influence the results of self-rating questionnaire. Four patients with both dementia and depressive state were included in the study. However, data of these patients were available because psychological impairments of the patients were all mild to moderate.

We should mention the limitations of the present study. First, the number of subjects might not be enough to detect the associations. Second, we evaluated depression through self-rating questionnaire, but did not do a structured measure such as Hamilton Depression Rating Scale (HAM-D) or Montgomery and Asberg Depression Rating Scale (MADSR). Because
the SDS is a subjective evaluation method for depressive state, the possibility that the event occurred just before the evaluation influence the results of the study cannot be excluded. Therefore, further studies with large number of samples and using subjective and objective measures are required to confirm our findings.

In conclusion, there was a large variation in the time spent outdoors among LTOT patients, and the number of the time spent outdoors calculated from oxygen cylinders was less than we originally expected. We expected that decreased time spent outdoors would be influenced by the patients’ psychological impairments. In the present study, however, dementia and depressive state did not directly affect the time spent outdoors of LTOT patients, and we did not observe any correlations. The number of time spent outdoors may also be explained by factors unrelated to psychological problems. More attention must be given to LTOT patients’ usage of oxygen cylinders, which shows their time spent outdoors and provides an estimate of their ADL outside the home. In addition, the results of the present study suggest that dementia and depressive state should be periodically assessed in LTOT patients.

Reference


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THE INTERACTION OF PHOTOPROTECTIVE EFFECTS BETWEEN KERATINOCYTES AND MELANOCYTES VIA ENDOTHELIN-1/STEM CELL FACTOR SIGNALINGS

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Abstract Ultraviolet (UV) radiation is one of the important etiologic factors for skin cancer. Pigmentation of the skin is the major photoprotective mechanism against UV radiation on human skin. Pigmentation depends on the function of melanocytes, which produces melanin and transfers melanosomes to surrounding keratinocytes. Endothelin-1 (ET-1), and stem cell factor (SCF) are cytokines secreted by UVB-exposed keratinocytes, playing pivotal roles in regulating the melanogenesis in normal human melanocytes (NHM). In this study, we demonstrated that treatment with ET-1 and/or SCF not only stimulated melanogenesis but also significantly suppressed the UV-induced cell death in NHM. In addition, we revealed that expression of heme oxygenase-1 (HO-1), an anti-oxidative protein, is up-regulated by ET-1 or SCF in NHM. Taken together, ET-1/SCF, secreted by UV-irradiated keratinocytes, increases HO-1 expression, thereby protecting melanocytes from UV-induced apoptosis, and stimulates melanin synthesis in melanocytes to protect keratinocytes from UV-induced cell damage. It can be regarded as the interaction of photoprotective effect between keratinocyte and melanocyte.

Key words: Heme oxygenase-1; Endothelin-1; Stem cell factor; melanocyte; photoprotection.