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Importance of the $PaCO_2$ from 3 to 6 months after initiation of long-term non-invasive ventilation

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Summary
Background: The level at which arterial carbon dioxide tension ($PaCO_2$) a few months after introduction of long-term non-invasive positive pressure ventilation (NPPV) is associated with a favorable prognosis remains uncertain.
Methods: Data on 184 post-tuberculosis patients with chronic restrictive ventilatory failure who were receiving long-term domiciliary NPPV were examined retrospectively. Average $PaCO_2$ 3–6 months after NPPV (3- to 6-mo $PaCO_2$) and potential confounders were analyzed with discontinuation of long-term NPPV as the primary outcome. The effects of 3- to 6-mo $PaCO_2$ on annual hospitalization rates due to respiratory deterioration from 1 year before to 3 years after the initiation of NPPV were examined. The effect of the difference between the $PaCO_2$ value at the start of NPPV (0-mo $PaCO_2$) and the $PaCO_2$ value 3- to 6-mo later (d-$PaCO_2$) on continuation rates for NPPV was also assessed in patients who initiated NPPV while in a chronic state.
Results: Patients with relatively low 3- to 6-mo $PaCO_2$ values maintained a relatively low $PaCO_2$ 6–36 months after NPPV ($p < 0.0001$) and had significantly better continuation rates ($p < 0.03$) and lower hospitalization rates from the 1st to 3rd year of NPPV ($p = 0.008$, 0.049, 0.009,

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respectively) than those with higher levels. The 0-mo $PaCO_2$ ($p = 0.26$) or d-$PaCO_2$ ($p = 0.86$) had no predictive value.
Conclusion: A relatively low 3- to 6-mo $PaCO_2$ value was predictive of long-term use of NPPV. The target values for 3- to 6-mo $PaCO_2$ may, therefore, be less than 60 mmHg in post-tuberculosis patients, although more studies are needed.

Introduction

Domiciliary non-invasive positive pressure ventilation (NPPV) has been widely used in the treatment of patients with chronic hypercapnic respiratory failure.[1–7] NPPV has been shown to improve gas exchange, probably due to increased ventilatory response to carbon dioxide (CO_2) in patients with chronic obstructive pulmonary disease (COPD)[8] and restrictive thoracic disease (RTD) including pulmonary tuberculosis sequelae.[9,10] Arterial blood gases (ABGs) were reported to be stabilized a few months after NPPV and maintained over several years in patients with COPD[1] and RTD.[1,3,4,11] In patients with RTD, a higher nighttime $PaCO_2$ measured before the start of long-term NPPV was shown to be a significant independent predictor of mortality.[12] In contrast, a higher daytime $PaCO_2$ at the start of NPPV (0-mo $PaCO_2$) was not associated with a poor prognosis in patients with RTD[12] or COPD.[13]

Generally, ABG values and the general condition are unstable in patients during the pre-NPPV period even in those who started NPPV while in a chronic state. However, gas exchange and the clinical state markedly stabilize after institution of long-term NPPV. According to our clinical experience, medication and ventilator settings seldom needed to be changed after the clinical condition of patients was stabilized by NPPV treatment. Therefore, as prognostic factors, parameters after a few months of NPPV seem to be more important and reliable than those before starting NPPV. However, to the best of our knowledge, no report has assessed $PaCO_2$ a few months after the introduction of long-term NPPV as a possible prognostic factor.

We hypothesized that patients with a relatively low mean value of $PaCO_2$ measured between 3 and 6 months after introduction of long-term NPPV (3- to 6-mo $PaCO_2$) would have higher continuation rates of NPPV and lower hospitalization rates than those with a relatively high 3- to 6-mo $PaCO_2$. We retrospectively examined the effects of the 3- to 6-mo $PaCO_2$ level on continuation of NPPV in post-tuberculosis patients. Thus, we wanted to determine which levels of $PaCO_2$ after a few months of NPPV were suitable for those patients.

Methods

Patients

All post-tuberculosis patients who had started NPPV at 6 hospitals affiliated with Kyoto University Hospital and the National Tokyo Hospital from June 15, 1990 to August 2, 2007 were included in this retrospective study. All patients had chronic respiratory failure with hypercapnia. The NPPV therapy was begun either after an acute episode or during the chronic state. The decision for initiation of NPPV was based on clinical symptoms with persistent hypercapnia during daytime ($PaCO_2 > 45$ mmHg) and/or nocturnal hypoventilation and/or clinical instability with recurrent hospitalizations. Patients with other causes of chronic respiratory failure such as neuromuscular disorders, obesity hypoventilation syndrome, bronchiectasis, idiopathic scoliosis, or COPD were excluded.

The patients were followed until November 30, 2007. Clinical assessments were performed at the end of every year from 1995 to 2002, in December 2004 and in December 2007.

The patients were divided into 3 groups according to 3- to 6-mo $PaCO_2$ levels (Group-1, 60 mmHg$>$, $n = 79$; Group-2, 60-70 mmHg, $n = 61$; Group-3, $>$70 mmHg, $n = 23$). Measurement of 3- to 6-mo $PaCO_2$ could not be performed in 19 other patients who otherwise met criteria for study entry because of clinical instability at the time or because they did not attend outpatient clinic. The patients who started long-term NPPV while in a chronic state were divided into 3 groups according to the difference between 0-mo $PaCO_2$ and 3- to 6-mo $PaCO_2$ (d-$PaCO_2$) (Group-d1, $>$16 mmHg, $n = 33$; Group-d2, 8—16 mmHg, $n = 29$; Group-d3, 8 mmHg$>$, $n = 28$). Patients in the present study were also subjects of our previous study concerning ventilator modes.[7]

Measurements

Data on age at the start of NPPV, gender, presence of pulmonary lesions, duration of long-term oxygen therapy (LTOT) before the start of NPPV, status on introduction of NPPV (i.e., acute or chronic state), ventilator mode (assisted or controlled mode), other ventilator settings such as inspiratory positive airway pressure (IPAP), expiratory positive airway pressure (EPAP), respiratory rate (f_R), and tidal volume (V_T), body-mass index (BMI), vital capacity (percentage of predicted), forced expiratory volume in 1 s over forced vital capacity (FEV_1/FVC), and concurrent use of LTOT after the start of NPPV were all examined and/or documented for determination of risk factors. Annual number of hospitalizations due to respiratory deterioration (acute bronchitis, pneumonia, spontaneous pneumothorax, chronic disease progression, etc.) beginning from 1 year before to 3 years after the start of NPPV was also included in this analysis.

Information on daytime ABGs was analyzed from 12 months before the start of NPPV to the observable endpoint if available. Determinations of ABGs were made with the patient in the supine position breathing room air or prescribed oxygen without NPPV support. ABGs were obtained in patients who were in a stable condition without exacerbation except for those obtained at the start of NPPV from patients who had begun administration of NPPV during an acute state.