**Is It Safe for Patients With Chronic Hypercapnic Respiratory Failure Undergoing Home Noninvasive Ventilation To Discontinue Ventilation Briefly?**

Sait Karakurt, MD; Francesco Fanfulla, MD; and Stefano Nava, MD

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**Study objectives:** A brief discontinuation (< 1 week) of long-term ventilation may be necessary in patients who are not totally ventilator-dependent in cases of technical problems, intolerable nasal irritation, upper airway congestion, or travel. We examined the incidence, timing, and causes of possible clinical deterioration after a brief withdrawal of ventilation in patients with chronic respiratory failure (CRF) who were well-established on long-term noninvasive mechanical ventilation (NIMV).

**Study design:** Prospective clinical study.

**Patients:** Eleven inpatients in clinically stable condition (COPD, 6 patients; and restrictive thoracic disease [RTD], 5 patients) who had severe CRF ($Paco_2 > 50$ mm Hg) and had been receiving NIMV for (mean ± SD) 19.3 ± 5.3 months were enrolled.

**Interventions and measurements:** Arterial blood gas (ABG) levels, maximal inspiratory pressure ($P_{max}$), breathing pattern, dyspnea rating, and life symptoms (measured by a questionnaire) were recorded daily after NIMV withdrawal for 6 days or until the patients showed clinical and/or ABG level deterioration. Pulmonary function tests were performed and neuromuscular drive was measured at the beginning and the end of the study.

**Results:** Five of the 11 patients (45.4%) [COPD, 3 patients; and RTD, 2 patients] were reconnected to a ventilator before the scheduled time because of ABG level deterioration. Despite these changes, none of the patients reported severe worsening of symptoms or other medical complications. The patients whose ABC levels worsened had statistically significant decreases in tidal volume and $P_{max}$, suggesting that the development of alveolar hypoventilation was related to respiratory muscle weakens.

**Conclusions:** A brief discontinuation of NIMV in patients who were affected by chronic hypercapnic respiratory failure and were well-established on NIMV is associated with a relatively high incidence of ABG level worsening due to the development of alveolar hypoventilation. If NIMV must be briefly interrupted for clinical reasons, the patient should be monitored closely for abrupt worsening, and prompt technical intervention should be provided if a ventilator fails.

**Key words:** COPD; hypoventilation; noninvasive mechanical ventilation; respiratory insufficiency; restrictive thoracic disease; ventilator failure

**Abbreviations:** ABG = arterial blood gas; CRF = chronic respiratory failure; NIMV = noninvasive mechanical ventilation; $P_{max}$ = maximal inspiratory pressure; RR = respiratory frequency; RTD = restrictive thoracic disease; $T_i$ = inspiratory time; $T_{TOT}$ = total breathing cycle time; $V_t$ = tidal volume

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Long-term mechanical ventilation has been used over the last few decades both as a life-support procedure and as a life-sustaining measure. The former is reserved for patients affected by chronic respiratory failure (CRF) requiring mechanical ventila-

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The efficacy of the long-term administration of NIMV to patients with COPD is still controversial, but it seems that selected populations of severely hypercapnic patients with COPD may show satisfactory clinical and physiologic responses.

Most patients affected by CRF live at home, where they are periodically observed by a specialized team in charge of the home-care program. It has been reported that some technical problems, such as
defective and malfunctioning equipment and the improper use of the ventilator by caregivers, might cause a temporary suspension of mechanical ventilation. As a matter of fact, about 60% of patients enrolled in a home ventilatory program will sooner or later experience one of these problems. Furthermore, a brief (<1 week) interruption of long-term ventilation may be necessary in patients who are not totally ventilator-dependent, in cases of intolerable nasal irritation and upper airway congestion due to respiratory infection, and in the event of travel. The brief withdrawal of NIMV may be associated with a worsening in clinical status and may lead to secondary aim of the study was the identification of simple physiologic indexes that possibly were associated with the clinical response.

**Materials and Methods**

Eleven patients in clinically stable condition with severe CRF were included in this study. Clinical stability was defined as a lack of hospital admissions and exacerbations requiring supplemental medical therapy and no variations in ABG levels (ie, no changes ≥5% in pH, PaCO₂, and PaO₂) or ventilator settings in the 3 months preceding the study. All the patients had been successfully seen the next section) established on home mechanical ventilation for at least 12 months, and all of them were receiving supplemental oxygen therapy at various flow rates that were kept constant during the daytime and eventually were adjusted during nighttime NIMV, as illustrated below. Six patients were affected by COPD, which was defined according to the American Thoracic Society standard, and five patients were affected by RTD (chest wall disease, four patients; obesity-hypoventilation syndrome, one patient). The individual patient characteristics that are pertinent to the study are shown in Table 1. Patients gave oral informed consent to their participation in the study, which was approved by the Ethics Committee of the S. Maugeri Foundation and was conducted in accordance with the Declaration of Helsinki.

**Criteria for Home NIMV Enrollment**

The 11 patients were established on home mechanical ventilation following the flow-chart used in our institution (Fig 1). Briefly, drawing on the clinical and scientific evidence, we enrolled only patients with pH > 7.35 and PaCO₂ > 50 mm Hg. A prolonged (ie, 3 to 4 weeks) in-hospital trial of nocturnal NIMV was employed thereafter to assess individual responses; if daytime hypercapnia improved (>6% from baseline), we withdrew ventilation for about 30 days and then reassessed the patient's ABG levels. If the patient had been able to maintain the same level of PaCO₂ that was recorded at hospital discharge, we did not.

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<th>MVD, mo</th>
<th>FEV₁, % pred</th>
<th>FVC, % pred</th>
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<th>RV, mL</th>
<th>TLC, mL</th>
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prescribe long-term NIMV. If, on the other hand, overt hypercapnia developed again or if pH decreased significantly during the 4-week observation period, long-term NIMV was prescribed. Table 1 illustrates the time that elapsed from the institution of NIMV, the results of pulmonary function tests (PFTs), and the ABG levels of the patients at enrollment into the home-care program. All the patients received bilevel ventilation with a mean (± SD) inspiratory aid of 15.3 ± 2.1 cm H₂O and a mean expiratory aid of 2.5 ± 1.0 cm H₂O with a backup rate of 8 breaths/min. The levels of aid in our clinical practice are individually titrated using the recordings of transdiaphragmatic pressure as follows. Inspiratory positive airway pressure values were titrated in order to achieve a minimum reduction of 50% from the transdiaphragmatic pressure measured during spontaneous breathing, while a level of expiratory positive airway pressure was set to 70 to 80% of the dynamic positive end-expiratory pressure that was recorded during spontaneous breathing.

Oxygen saturation was recorded continuously in all patients during the first few nights of NIMV to determine the minimal oxygen flow necessary to achieve an arterial oxygen saturation of > 90% for at least 90% of the total sleep time, and most of the patients (9 of 11) also underwent a complete sleep study to exclude the presence of obstructive sleep apnea syndrome (which, indeed, was found to be present in the obese patient). At the time of enrollment into the study, the patients had been receiving NIMV for a mean duration of 19.3 ± 5.3 months (inspiratory positive airway pressure, 14.2 ± 3.6 cm H₂O; expiratory positive airway pressure, 3.9 ± 1.8 cm H₂O) and were averaging 6.4 ± 1.1 h of use nightly, as assessed by the ventilator clock. None of the patients used NIMV during the day, except patient 9 who also received ventilation for approximately 2 to 3 h during the day. The patients in our ventilatory home-care program are periodically (usually every 3 months) admitted to our institution for a complete check-up.

**Measurements**

ABG levels were obtained from the radial artery and were analyzed using an automatic analyzer (550 Radiometer; ABL; Copenhagen, Denmark). The result of PFTs for static and dynamic lung volumes were recorded with the patient sitting, using a body plethysmograph (MasterLab; Jaeger; Hochberg, Germany).

The measurement of maximal inspiratory pressure (Pimax) was obtained at functional residual capacity using a hand-held manometer that was connected to a rigid mouthpiece, with a small air leak to prevent glottic closure, while the patient was wearing a noseclip. The best of three efforts not varying by > 5% was chosen for data analysis.²

Airflow was measured with a heated pneumotachograph (Screenmate box; Jaeger) that was positioned immediately beyond the mouthpiece when the patient was breathing spontaneously or between the ventilator circuit and the facemask when the patient was receiving mechanical ventilation.

Airway pressure during mechanical ventilation was measured through tubing connected to a differential pressure transducer (± 300 cm H₂O; Honeywell; Freeport, IL). Tidal volume (VT) was obtained by integration of the flow signal. The inspiratory time (Ti), expiratory time, total breathing cycle time (Ttot), respiratory frequency (RR), and duty cycle (Ti/Ttot) were calculated as the average values of 10 consecutive breaths after 5 min of breathing or in the presence of a monotonous breathing pattern.

The airway pressure developed in the first 100 ms after the onset of inspiration made after end-expiratory occlusion (ie,
neuromuscular drive \([P_{0.1}]\) was obtained, as described in detail by Withelaw et al. The resting dyspnea was quantified using a modified Borg scale, with 0 being the lowest level and 10 the highest level.

The patients were asked to answer a brief questionnaire daily about their level of sleepiness and to keep a diary of symptoms. A physician who was unaware of the aims of the study administered the questions.

**Study Protocol**

On day 0, the patients' ABG levels and breathing patterns were measured during ventilation after a night of receiving NIMV. Then, approximately 3 h later, the measurement of ABG levels and breathing patterns was repeated during spontaneous breathing, and PFTs, \(P_{\text{rmax}}\), \(P_{0.1}\), dyspnea rating, and answers to the questionnaire were recorded (baseline). The patients then discontinued NIMV. All the measurements, with the exceptions of PFTs and \(P_{0.1}\), were recorded each day at the same hour, except on day 1 when the measurements also were repeated, for reasons of safety, approximately 10 h after discontinuing NIMV (5 pm). On day 7, the recordings were performed in the same order as for day 0, and the trial was concluded. If the patients required early resumption of NIMV before the scheduled time because of interrupting criteria, the last measurements were recorded before the reinstitution of NIMV. At day 7, in all patients “surviving without NIMV,” nighttime ventilation again was applied.

The objective criteria for interrupting the experimental protocol were the presence of one or more of the following: (1) \(pH < 7.35\); (2) change in \(P_{\text{aCO}_2}\) of > 6% from baseline; (3) decrease in \(P_{\text{aO}_2}\) of ≥ 6% from baseline; (4) morning symptom worsening (ie, constant headache, general weakness, or tiredness); and (5) dyspnea of ≥ 6 on the Borg scale and/or a respiratory rate of ≥ 35 breaths/min.

**Data Analysis**

The flow and the pressure signals were fed into a microcomputer through an analog/digital board and were processed with appropriate software (Labdat and Anamat; RHT-InfoDat Inc; Montreal, Quebec, Canada).

Results are expressed as mean ± SD. A \(t\) test for dependent samples was used to assess differences between the data collected at baseline and at the end of the study. A \(t\) test for independent samples was used to assess differences between the two groups of patients considered (ie, those whose conditions deteriorated and those whose conditions did not). Forward stepwise multiple-regression analysis was performed to identify the physiologic variables collected at baseline that best identified patients who then went on to deteriorate clinically. Statistical significance was defined as a two-tailed \(p\) value < 0.05.

**RESULTS**

Figure 2 illustrates the proportion of patients over time who were able to remain stable without receiving NIMV. Five of the 11 patients (45.4%) met one of the five criteria for immediate reconnection to a ventilator before the scheduled time. The reasons for reconnection were the following: an increased \(P_{\text{aCO}_2}\) level (one patient on day 4); a simultaneous increase in \(P_{\text{aCO}_2}\) and decrease in \(pH\) to < 7.35 (two patients on days 3 and 5); and a simultaneous increase in \(P_{\text{aCO}_2}\) with a dyspnea score of > 5 (one patient on day 6). Despite these changes, none of the patients, with the exception of patient 5 who had substantial dyspnea, reported severe worsening of symptoms such as general fatigue or headache, and no other medical complications developed. For subsequent analysis, the patients then were divided into those in whom withdrawal was not followed by deterioration (six patients) and those in whom it was (five patients). The underlying pathologies in the patients whose conditions did not deteriorate were COPD (three patients) and chest wall restrictive disease (three patients), while in the group that needed early reconnection the underlying pathologies were COPD (three patients), chest wall restrictive disease (one patient), and obesity-hypoventilation syndrome (one patient). At enrollment, the two groups of patients (those whose conditions deteriorated and those that did not) had similar ABG levels, PFT results, and other physiologic variables (Table 2).

Figure 3 illustrates the individual changes in \(P_{\text{aCO}_2}\) (top) and \(pH\) (bottom) from enrollment to the end of the study. Overall, the mean \(P_{\text{aCO}_2}\) \(P_{\text{aO}_2}\), and \(pH\) levels did not vary significantly \((P_{\text{aCO}_2}\) variance, 51.6 ± 6.6 to 55.3 ± 10.6 mm Hg; \(P_{\text{aCO}_2}\) variance, 55.4 ± 5.0 to 56.1 ± 3.7 mm Hg; and \(pH\) variance, 7.39 ± 0.02 to 7.37 ± 0.04), but the patients who needed to be reconnected to NIMV (represented by solid lines) clearly showed a significant decrease in \(pH\) \((p = 0.004)\) and an increase in \(P_{\text{aCO}_2}\) \((p = 0.008)\) but not a decrease in \(P_{\text{aO}_2}\) \((p = 0.25)\).

Table 3 shows the pattern of breathing, dyspnea score, \(P_{\text{rmax}}\) level, \(P_{0.1}\) level, and PFT results at enrollment and at the end of the study for the whole group of patients. No statistical significance was observed in the mean data or when the patients were divided into the two groups according to the clinical response to NIMV withdrawal, with the exception of \(V_t\) and \(P_{\text{rmax}}\) levels, which were statistically lower \((p < 0.05\) for both parameters) only in the group
needing early reconnection vs that not needing it (Vt, 602.4 ± 218.9 vs 468.4 ± 180.1 mL; Pimax, 56.6 ± 21.6 vs 41.0 ± 16.3 cm H2O, respectively).

In an attempt to find any variables (including the level of inspiratory support) that were associated with the occurrence of clinical deterioration, a stepwise regression analysis was performed. As shown in Table 4, the level of the baseline Vt/Ti ratio and the level of the changes in PaCO2 recorded while patients were receiving NIMV and during the baseline measurement during spontaneous breathing were significantly associated with the clinical deterioration and the need to recommence NIMV. Patients with more marked increases in PaCO2 during baseline spontaneous ventilation (expressed as a percentage of the baseline values during spontaneous breathing) and with higher baseline mean inspiratory flow were those who required reconnection to NIMV.

**DISCUSSION**

In this prospective study, we have shown that briefly interrupting NIMV in patients with chronic hypercapnic respiratory failure who had been successfully established in a home-care program for > 1 year causes clinical and ABG deterioration in > 40% of those patients. Sporadic discontinuation from long-term ventilation, either intentional or unintentional, is quite a common problem in clinical practice. It has been shown, for example, by Srinivasan et al16 that in the Greater Los Angeles Branch of National Medical Homecare, 74% of the ventilator-dependent patients and 45% of those receiving nighttime ventilation alone had episodes of ventilator failure. The main causes of failure were related to defective equipment, improper care, damage, or tampering by caregivers and by incorrect use of the machine. The authors claimed that 99% of the problems could be solved in the home and did not have an adverse clinical effect on the large majority of the patients. Interestingly enough, in 140 of the

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<td>53.4 ± 8.3</td>
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<td>RR, breaths/min</td>
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*Values given as mean ± SD. p > 0.05 for all the considered variables. See Table 1 for abbreviations not used in the text.

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<td>0.486 ± 0.129</td>
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*Te = expiratory time. p > 0.05 for all the considered variables. Values given as mean ± SD.
189 cases of ventilator failure a backup ventilator was available at the patient’s home, so that ventilation was promptly restored. The choice of allocating a second ventilator to be kept at home is usually made in most countries only if the patient is totally ventilator-dependent, while it is very uncommon if the patient needs only partial ventilatory support, based on the common-sense assumption that these latter patients may discontinue NIMV for a few days without any major discomfort.

Technical failure of the machine is not the only cause of brief discontinuation of NIMV or poor compliance. For example, ventilators usually are removed electively from a home for a complete maintenance overhaul at the factory after every 5,000 h of use, and this maintenance may not necessarily be accompanied by the use of a substitute ventilator. More important, the patient may choose voluntarily to suspend NIMV in the case of nasal irritation due to cold or poor humidification, rhinitis or aerophagia, and discomfort from the mask or headgear; these problems have been shown to be present in, respectively, 23%, 13%, and 8% of patients for 3 weeks while in the hospital. This was not performed in the study by Hill et al19 and highlights the possible limitations of applying our findings to other populations of patients in whom NIMV has been initiated using different criteria. Last, and perhaps most important, our symptom questionnaire was focused on resting dyspnea, sleeplessness, and morning headaches, while the American study19 also focused on the assessment of energy and fatigue. Despite these possible differences, the common point of both studies was that a relatively high incidence of clinical problems develops a few days after NIMV discontinuation. This suggests that the temporary interruption of NIMV in stable patients with hypercapnia may not be safe in all patients, and, if ventilation is suspended for any reason, close monitoring of symptoms and gas exchange should be done, preferably in a more protected environment than the home. Prompt intervention in the case of ventilator failure is mandatory. This is readily achievable for patients who are provided with a second back-up ventilator, but this may

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*ΔCO₂ = variation of PaCO₂ between spontaneous breathing and mechanical ventilation recorded at the entry of the study (expressed as % of baseline value). r = 0.76; SEE (standard error of the estimate) = 0.38; p < 0.05.
be an unnecessary expense for patients who are not totally ventilator-dependent. Our data also suggest that every effort should be made by the home-care team and the caregiver to avoid the development of problems that could interfere with the daily use of NIMV. In particular, great care should be taken to minimize the problem of nose irritation, either by adequately protecting the bridge of the nose, varying the site of mask friction, or periodically changing the type or size of the mask.23 Adequate humidification and heating also should be considered as measures to avoid rhinitis and abnormal increases in nasal resistances.24

This study was designed primarily to record any clinical deterioration subsequent to NIMV suspension and not the physiologic mechanisms underlying such an event. Nevertheless, we observed that in the subjects who needed to be reconnected to the ventilator, VT and Pmax decreased significantly. This is not surprising since, in these clinically stable patients, variations in PaCO₂ are mainly determined by alveolar ventilation rather than by CO₂ production. If the RR is kept constant, alveolar ventilation is almost totally dependent on changes in VT. As a matter of fact, VT was decreased only in the patients whose gas exchange levels deteriorated. Concomitantly, a decrease in Pmax indirectly suggests that the mechanism of reduced PaCO₂ clearance may, at least in part, be due to the theory of ventilatory muscle rest.7 The removal of periodic resting of the diaphragm and other inspiratory muscles was probably associated with a quick worsening of their inotropic characteristics. If this is true, then, hypothesizing that the inspiratory resistive and elastic loads are constant, the decrease in Pmax leads to a load/capacity (ie, the pressure generated per breath over the maximal pressure generated) imbalance. The patients then may choose to behave like “wise fighters,” reducing the pressure generated per breath, and therefore the VT, and becoming more hypercapnic, rather than approaching close to the so-called fatigue threshold.25 Our results also seem to suggest that patients with a more pronounced increase in PaCO₂ briefly after NIMV suspension (ie, 3 h) and an increase in the mean resting inspiratory flow pattern may be more prone to developing clinical deterioration a few days after disconnection from NIMV. Therefore, we suggest considering the PaCO₂ response occurring shortly after NIMV suspension as a possible indicator of alveolar hypoventilation development in the case of forced withdrawal, since the recording of the VT/Ti ratio is sometimes impractical. Indeed, our observations support the theory, already suggested by other authors,10,13 that the individual responses to long-term NIMV may differ and, therefore, also that the removal of NIMV may result in two subsets of patients (ie, those who deteriorate and those who do not). Further larger prospective studies on this issue are needed to confirm this hypothesis.

The present study has some inherent limitations. First, there was not a control group, and, therefore, the study was not randomized. Keeping in mind that each patient served as his or her own control subject, the random withholding of NIMV for several weeks was not accepted by our local ethics committee, since the patients had more severe ABG abnormalities and symptoms before the establishment of the home-care program than after the enrollment (Table 1). The results of the study also support the idea that NIMV removal, even for a brief period, may be dangerous.

Another limitation was the lack of assessment of the sleep architecture, which might have afforded a better understanding of the mechanism of ABG deterioration during the daytime. We have emphasized already that the primary outcome of the study was to determine the incidence of problems linked to NIMV discontinuation rather than the underlying physiologic mechanisms. However, it has been suggested that the resetting of respiratory centers due to an improvement of nocturnal hypoventilation and sleep quality should increase the P0.1 (the index of neuromuscular drive) in the case of a rise in PaCO₂. As a matter of fact, P0.1 remained unchanged, even in the group that showed clinical worsening.

The third limitation was the selection of a heterogeneous group of patients. It has been claimed that patients affected by restrictive thoracic disease respond better to the chronic administration of NIMV than do COPD patients. However, the enrollment criteria for this study clearly stated that only patients who had been successfully receiving ventilation (in terms of ABG) for at least 1 year were eligible for inclusion in the study, so we were confident of selecting only the category of patients who were responders to ventilation. Indeed, the proportion of patients with COPD and RTD whose gas exchange levels deteriorated after the brief withdrawal was similar.

In conclusion, we have shown that a brief discontinuation of NIMV in patients who have chronic hypercapnic respiratory failure and are well-established on NIMV is associated with a relatively high incidence of ABG level and symptom worsening. The deterioration in ABG level seems to be related to the development of alveolar hypoventilation and may due to the mechanism of chronic fatigue of the respiratory muscle. If NIMV must be briefly interrupted for clinical reasons, close monitoring should be performed to pick up signs of clinical worsening.
quickly, while in the case of ventilator failure prompt technical intervention should be provided.

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