Respiratory Medicine (2014) xx, 1–9

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Ambulatory adaptation to noninvasive ventilation in restrictive pulmonary disease: A randomized trial with cost assessment

Mercedes Pallero [a,b,c,1], Carme Puy [d], Rosa Güell [d], Caridad Pontes [e], Sergi Martí [a,b,c,*], Ferran Torres [e], Antonio Antón [d], Xavier Muñoz [a,b,c,f]

[a] *Respiratory Medicine Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain*
[b] *CIBER de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain*
[c] *Departament de Medicina, Universitat Autònoma de Barcelona (UAB), Barcelona, Spain*
[d] *Respiratory Medicine Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*
[e] *Biostatistics and Data Management Platform, IDIBAPS, Hospital Clínic, Biostatistics Unit, School of Medicine, Universitat Autònoma de Barcelona (UAB), Barcelona, Spain*
[f] *Department de Biologia Celular, Fisiologia, Inmunologia, Universitat Autònoma de Barcelona (UAB), Barcelona, Spain*

Received 22 November 2013; accepted 20 April 2014

KEYWORDS
Ambulatory adaptation;
Noninvasive ventilation;
Neuromuscular disease;
Chest wall disease

Summary
Background: Home mechanical ventilation is usually initiated in hospital. However, cost-effectiveness of inpatient set up has never been compared to outpatient adaptation in a randomized design. A Prospective, multicenter, non-inferiority trial was conducted comparing the effectiveness of adaptation to noninvasive mechanical ventilation (NIMV) performed in the ambulatory or hospital setting in patients with chronic respiratory failure secondary to restrictive thoracic disease, obesity-hypoventilation syndrome or neuromuscular disease.
Methods: The study included 53 candidates for NIMV, randomized to ambulatory adaptation (AA) ($n = 27$) or hospital adaptation (HA) ($n = 26$). The patients' characteristics were recorded before establishing ventilation and at 1 and 6 months after. The main outcome variable was $PaCO_2$ decrease at 6 months following initiation of NIMV. The direct costs of the two interventions were compared.
Results: Before starting NIMV, $PaCO_2$ was 50.4 ± 6.8 mmHg in the AA group and 50.3 ± 5.7 mmHg in the HA group. At 6 months of NIMV use, a significant improvement in $PaCO_2$

* Corresponding author. Respiratory Medicine Department, Hospital Universitari Vall d'Hebron, Passeig Vall d'Hebron 119-129, 08035 Barcelona, Spain. Tel.: +34 93 2746157; fax: +34 93 2746083.
E-mail addresses: pneumo@vhebron.net, smarti@vhebron.net (S. Martí).

[1] This study is a part of the doctoral thesis of Mercedes Pallero. This work was supported by a grant from Catalan Foundation of Pneumology (FUCAP) 2003-2004.

http://dx.doi.org/10.1016/j.rmed.2014.04.016

relative to baseline was found in both groups: mean (95% CI) $PaCO_2$ decrease was 4.9 (2.3; 7.4) mmHg in AA and 3.3 (1.4; 5.1) mmHg in HA. The direct calculated cost was 1500 euros per patient in AA and 2692 euros per patient in HA.

Conclusions: Adaptation to NIMV in the ambulatory setting is not inferior to hospital adaptation in terms of therapeutic equivalence in stable patients with chronic respiratory failure secondary to restrictive thoracic disease, obesity-hypoventilation syndrome or neuromuscular disease. Outpatient adaptation may represent a cost saving for the healthcare system.

Clinical Trial: Identifier number NCT00698958 at www.clinicaltrials.gov.

Introduction

Restrictive thoracic disease, obesity-hypoventilation syndrome and neuromuscular disease are important causes of chronic hypercapnic respiratory failure [1]. Although there are no long-term randomized controlled studies investigating noninvasive home mechanical ventilation (NIMV in patients with these conditions, it is considered the treatment of choice in cases of established hypercapnic respiratory failure [2]. NIMV improves the patient's blood gas status, health-related quality of life (HRQL), and physical activity, and results in increased survival as compared to historical cohorts [3—8].

The process by which a patient initiates and adapts to NIMV is complex and involves a series of decisions that can determine the success of this therapy. Some of the most important choices are the type and the characteristics of the ventilator, and the setting where adaptation will be carried out. Regarding this latter factor, it is well recognized that patients with acute disease should undergo adaptation during hospital admission [9], but other options have been proposed for patients initiating ventilation in a stable phase of disease.

Patients are often hospitalized when NIMV is started [10] to enable better monitoring of the adaptation process. However, hospitalization is expensive, there may be waiting lists, and it has not been conclusively demonstrated that this policy leads to better compliance with the prescription [11,12]. Thus, some authors prefer to carry out NIMV adaptation in the sleep laboratory [13,14], whereas others advocate ambulatory adaptation in an outpatient clinic or the patient's home [11,12,15].

Because few studies have evaluated the superiority of one setting over another for adapting to NIMV, the choice has been based on the preferences or possibilities of each team of health professionals. The aim of the present study is to evaluate whether the effectiveness of adaptation to NIMV on an ambulatory basis is comparable to hospital adaptation in patients with chronic respiratory failure secondary restrictive thoracic disease, obesity-hypoventilation syndrome or neuromuscular disease and to analyze the associated cost of these two approaches.

Patients and methods

Study design

This is a prospective clinical trial (identifier NCT00698958 at www.clinicaltrials.gov) with randomized assignment of patients to two parallel groups. The study evaluated noninferiority in terms of effectiveness and associated cost of ambulatory or hospital-based NIMV adaptation in patients with chronic respiratory failure secondary to restrictive thoracic disease, obesity-hypoventilation syndrome or neuromuscular disease in two teaching hospitals in Barcelona (Spain). The study protocol (03-0222) was approved by the Ethics Committees for Clinical Research of the participating centers and by the Spanish Agency for Medicines and Healthcare Products.

Patients

In the period of 2004—2008, all patients 18—80 years of age with chronic respiratory failure secondary to restrictive thoracic disease, obesity-hypoventilation syndrome or slowly progressive neuromuscular disease and having an indication for NIMV were informed of the study. All those who gave consent to participate were included and randomly assigned to one of two parallel groups: ambulatory adaptation (AA) or hospital adaptation (HA).

The indication for NIMV was based on consensus conference criteria [16] and Spanish guidelines [17]. Briefly, the criteria included clinical symptoms (dyspnea, fatigue, orthopnea, and morning headache) and one of the following: 1) chronic hypercapnia ($PaCO_2 > 45$ mmHg) in a stable patient, or 2) nocturnal oxygen saturation $<90\%$ (CT90) during at least 30% of the night. Patients in whom NIMV was contraindicated [17], those with acute disease, and those requiring invasive airway access through a tracheostomy were excluded. Patients who were residing more than 50 km from the participating hospitals were also excluded.

Sample size calculation: with 26 evaluable patients per group, the study had an 80% power to test the noninferiority of ambulatory adaptation against hospital adaptation for the main effectiveness variable, post-adaptation $PaCO_2$ decrease at 6 months.

Outcome variables

The main outcome variable was reduction in $PaCO_2$ at 6 months following the start of NIMV with respect to $PaCO_2$ baseline value before starting NIMV. The secondary variables considered were pharmacoeconomic assessment and health-related quality of life.

Please cite this article in press as: Pallero M, et al., Ambulatory adaptation to noninvasive ventilation in restrictive pulmonary disease: A randomized trial with cost assessment, Respiratory Medicine (2014), http://dx.doi.org/10.1016/j.rmed.2014.04.016