Inspiratory muscle training improves maximal inspiratory pressure and may assist weaning in older intubated patients: a randomised trial

Samária Ali Cader1,4, Rodrigo Gomes de Souza Vale1,4, Juracy Correia Castro1,2, Silvia Corrêa Bacelar3, Cintia Biehl4, Maria Celeste Vega Gomes4, Walter Eduardo Cabrera4 and Estélio Henrique Martin Dantas1,4

1University Federal do Estado do Rio de Janeiro – LABIMH–UNIRIO, Brazil, 2Universidade de Trás-os-Montes e Alto Douro, Portugal, 3Grande Rio University – UNIGRANRIO, Brazil, 4Catholic University of Nuestra Senora de Asunción, Paraguay

Questions: Does inspiratory muscle training improve maximal inspiratory pressure in intubated older people? Does it improve breathing pattern and time to wean from mechanical ventilation? Design: Randomised trial with concealed allocation and intention-to-treat analysis. Participants: 41 elderly, intubated adults who had been mechanically ventilated for at least 48 hr in an intensive care unit. Intervention: The experimental group received usual care plus inspiratory muscle training using a threshold device, with an initial load of 30% of their maximal inspiratory pressure, increased by 10% (absolute) daily. Training was administered for 5 min, twice a day, 7 days a week from the commencement of weaning until extubation. The control group received usual care only. Outcome measures: The primary outcome was the change in maximal inspiratory pressure during the weaning period. Secondary outcomes were the weaning time (ie, from commencement of pressure support ventilation to successful extubation), and the index of Tobin (ie, respiratory rate divided by tidal volume during a 1-min spontaneous breathing trial). Results: Maximal inspiratory pressure increased significantly more in the experimental group than in the control group (MD 7.6 cmH2O, 95% CI 5.8 to 9.4). The index of Tobin decreased significantly more in the experimental group than in the control group (MD 8.3 br/min/L, 95% CI 2.9 to 13.7). In those who did not die or receive a tracheostomy, time to weaning was significantly shorter in the experimental group than in the control group (MD 1.7 days, 95% CI 0.4 to 3.0). Conclusions: In intubated older people, inspiratory muscle training improves maximal inspiratory pressure and the index of Tobin, with a reduced weaning time in some patients. Trial registration: NCT00922493. [Cader SA, Vale RGS, Castro JC, Bacelar SC, Biehl C, Gomes MCV, Cabrera WE, Dantas EHM (2010) Inspiratory muscle training improves maximal inspiratory pressure and may assist weaning in older intubated patients: a randomised trial. Journal of Physiotherapy 56: 171–177]

Key words: Respiration, artificial; Weaning; Aged; Intensive care; Inspiratory muscle training; Physiotherapy

Introduction

The primary reason for admission to an intensive care unit is the need for mechanical ventilation (Tobin 2001). Weaning from mechanical ventilation often accounts for a large proportion of the total time spent on the ventilator (Esteban et al 1994) and respiratory muscle weakness is a major determinant of failure to wean (Ambrosino 2005). Failure to wean increases the risk of ventilator-associated pneumonia and further respiratory muscle deconditioning (Epstein 2006). With ageing, lung elastic recoil, chest wall compliance, and respiratory muscle strength all decrease, with resultant changes in static lung volumes and regional ventilation (Kim and Sapienza 2005, Krieg et al 2007). Therefore interventions to improve the success of weaning, especially those targeting respiratory muscle strength, may be particularly important in the older population.

Inspiratory muscle strength and the index of Tobin are recognised as predictors of the success of weaning patients from mechanical ventilation (Meade et al 2001). Maximal inspiratory pressure is used widely as a test of inspiratory muscle strength (Green et al 2002). The index of Tobin is the ratio of respiratory frequency to tidal volume (Yang and Tobin 1991); it therefore quantifies the degree to which the breathing pattern is fast and shallow.

Data from several other studies support the hypothesis that inspiratory muscle training improves inspiratory muscle strength in patients who are weaning from ventilatory support and therefore results in an improvement in the likelihood of success of extubation (Chang et al 2005a, Epstein et al 2002). However, most of the clinical studies that have examined the efficacy of inspiratory muscle training in the intensive care setting have been performed with tracheostomised participants (Aldrich et al 1989, Chang et al 2005b, Martin et al 2002, Sprague and Hopkins 2003). One study with intubated patients (Caruso et al 2005) delivered the inspiratory muscle training intervention primarily while patients were still receiving controlled ventilation. The controlled ventilation was continued until approximately one day before extubation. In our experience, however, a longer “weaning period” (ie, spontaneously initiated breaths with pressure support only) is used before extubation. We are unaware of any clinical studies of inspiratory muscle training in critically ill, intubated patients during the weaning period. Therefore, the research questions were:

1. Does inspiratory muscle training during the weaning period improve maximal inspiratory pressure in intubated older patients?
2. Does it improve the index of Tobin and the time to wean from mechanical ventilation?
Research

**Method**

**Design**

A randomised trial was conducted between December 2007 and November 2008. Participants were recruited from the intensive care unit of one hospital in Brazil. After undergoing confirmation of eligibility and baseline measurements, the participants were randomly allocated into either an experimental group or a control group. The enrolling investigator contacted another investigator to request an allocation for the participant from the concealed list of random allocations that had been generated by drawing numbers from a bag. This investigator was not otherwise involved in the study. The experimental group received usual care and also underwent inspiratory muscle training twice daily throughout the weaning period. The control group received usual care only. The weaning period was defined as from the end of controlled ventilation (ie, the commencement of pressure support ventilation only) until extubation. Maximal inspiratory pressure and the index of Tobin were measured immediately before participants commenced pressure support ventilation, daily during the weaning period, and immediately before extubation (Figure 1).

**Participants**

Patients were included in the study if they were aged at least 70 years, had undergone mechanical ventilation for at least 48 hours in a controlled mode (Chang et al 2005a), had been intubated because of acute hypoxaemic (Type I) respiratory failure, and were unable to generate greater inspiratory pressure than 20 cmH₂O (Yang and Tobin 1991). Patients were excluded if they had a condition that could compromise weaning, eg, cardiac arrhythmia, congestive heart failure or unstable ischaemic cardiac disease, or that could prevent adequate performance of inspiratory muscle training, eg, neuropathy or myopathy. Patients were also excluded if they had been tracheostomised before the commencement of weaning, had a major neurological co-morbidity, were morbidly obese, or were taking medication that could cause a disorder of attention.

**Intervention**

In the experimental group, inspiratory muscle training was commenced when the participant was changed from controlled to spontaneous (ie, pressure support) ventilation. A threshold device was used because it provides resistance to inspiration through the use of a flow-independent one-way
valve, generating a linear pressure load. During expiration there is no resistance because the unidirectional valve opens, while during inspiration the valve closes, providing resistance to inspiration. The amount of resistance can be adjusted by increasing the compression on a spring mechanism in the device (Sprague and Hopkins 2003, Johnson et al 1996).

At each training session, participants were positioned supine with the backrest raised to 45 deg (Sprague and Hopkins 2003). The target regimen was to commence with a load of 30% of the participant’s maximal inspiratory pressure (Chang et al 2005b), increasing daily by 10% (absolute), with training for five minutes (Cahalin et al 1997), twice a day, seven days a week (Liaw et al 2000) throughout the weaning period. Supplemental oxygen was provided as needed (Martin et al 2002). The training session was interrupted when the treating therapist observed any of the following: respiratory rate greater than 35 breaths/min or 50% higher than at the start of the session; oxyhaemoglobin saturation less than 90%; systolic pressure greater than 180 mmHg or less than 80 mmHg; heart rate more than 140 beats/min or 20% higher than at the start of the session; paradoxical breathing; agitation; depression; haemoptysis; arrhythmia or sweating (Caruso et al 2005, Conti et al 2004). When any of these signs occurred during a training session, the load was maintained (ie, not increased by 10%) at the next session.

The control group did not undergo any training of the respiratory muscles during the weaning period. Both groups continued to receive all other usual care. This included changes in ventilatory support settings (such as positive end-expiratory pressure and supplemental oxygen) as needed by the patient, in accordance with arterial blood gas reports. Usual care also included regular physiotherapy intervention including passive to active-assisted mobilisation of the limbs, chest compression with quick release at end-expiration, aspiration of the endotracheal tube, and positioning, with manual hyperinflation and saline instillation where indicated (Blattner et al 2008, Lemes et al 2009).

**Decision to extubate:** The decision to extubate was based on the presence of: improvement in the aetiology that resulted in respiratory insufficiency; a cough reflex; haemodynamic stability; normal body temperature; no vasoactive drugs (with the exception of Dopamine 5 mg/kg/ min); stable electrolytes (mainly calcium, magnesium, and phosphate); and normal radiological evaluation (without pneumothorax, congestion, or major pleural effusion or atelectasis). In addition, the pH was required to be between 7.30 and 7.60; the partial pressure of carbon dioxide to be less than 60 mmHg; the fraction of inspired oxygen to be less than 40%; and the ratio of partial pressure of oxygen to fraction of inspired oxygen to be at least 200. Also, the participant was required not to have paradoxical breathing, use of accessory musculature, a respiratory rate over 35 br/min (or an increase of 50% compared with before the training) and sweating (Martinez et al 2003). The decision to extubate was also delayed until the patient could demonstrate maximal expiratory pressure of at least 20 cmH2O (Afessa et al 1999). The cut-off point for the index of Tobin to consider extubation was 100 br/min/L (Epstein and Ciubotaru 1996).

The protocol for extubation was to reduce the pressure support to 8 cmH2O ensuring that a minimum tidal volume of 6 ml/kg was maintained, followed by use of a T-tube for 30 minutes (Boles et al 2007). The extubation was considered a failure if the patient returned to mechanical ventilation within 48 h (Sprague and Hopkins 2003) or required a tracheostomy.

**Outcome measures**

The primary outcome was maximal inspiratory pressure, measured using a vacuum manometer according to the method of Marini and colleagues (1986), which needs little contribution from the patient. The manometer is attached to the endotracheal tube via a connector with an expiratory unidirectional valve, permitting expiration while inspiration is blocked. This causes the participant to make successive respiratory efforts as their lung volume progressively approaches residual volume. Measurement of inspiratory pressures is maintained with the valve in situ for 25 seconds to obtain the best result (Caruso et al 1999). Testing was performed once daily in both groups before any inspiratory muscle training or other physiotherapy, with participants positioned supine with the backrest raised to 45 deg (Sprague and Hopkins 2003).

Secondary outcomes were the index of Tobin and weaning time. For the index of Tobin, the participant was disconnected from the ventilator and a ventilometer measured the participant’s spontaneous ventilation for one minute (Yang and Tobin 1991). The index is calculated as the number of breaths per minute divided by the tidal volume in litres. Testing was performed once daily in both groups before any inspiratory muscle training or other physiotherapy, with participants positioned supine with the backrest raised to 45 deg (Sprague and Hopkins 2003).

Outcomes were measured or recorded by physiotherapists in the intensive care unit. Compliance with the training regimen was also noted daily.

**Data analysis**

In the absence of an established minimum clinically important difference in maximal inspiratory pressure in this population, we nominated 10 cmH2O. The best estimate of the standard deviation of maximal inspiratory pressure in a population of intubated elderly patients is 4.5 cmH2O (Yang et al 1993). A total of 10 participants would provide an 80% probability of detecting a difference of 10 cmH2O in maximal inspiratory pressure at a two-sided 5% significance level. We anticipated that a substantial proportion of these critically ill participants would die or receive a tracheostomy. We therefore increased the recruited sample to 20 participants per group to allow for this.

All participants with follow-up data were analysed according to their group allocation, ie, using the intention-to-treat principle. Statistical significance was considered as p < 0.05, therefore mean between-group differences and 95% confidence intervals are presented for maximal inspiratory pressure, the index of Tobin, and weaning time. The Kappa test was used to evaluate the agreement between the evaluators of maximal inspiratory pressure. Total intubation time was analysed using a Kaplan-Meier curve. In the event of death, tracheostomy, or self-extubation, participants were excluded from the independent t-tests of between-group differences and were treated as censored cases in the survival analysis.
Flow of participants and therapists through the trial

During the recruitment period, 198 patients were screened, of whom 67 were eligible and monitored daily to assess readiness to start weaning. Of the 67, 20 were tracheostomised, 5 died, and 1 was transferred to another centre before the start of weaning. The remaining 41 were randomised: 21 to the experimental group and 20 to the control group. The baseline characteristics, ie, on the day weaning started, of the two groups are presented in Table 1 and in the first two columns of Table 2. Four participants in each group died before extubation. Three participants in the experimental group and two in the control group were tracheostomised before extubation.

The intensive care unit had a total of 24 beds, with 8 of these dedicated to postoperative patients. The physiotherapy team comprised 11 physiotherapists working in three shifts, all with expertise in intensive care, of which two have doctoral and six have masters qualifications. Consistency between the physiotherapists for the assessment of maximal inspiratory pressure was good, with a Kappa value of 0.68.

Compliance with trial method

Participants in the experimental group underwent training on all days during their weaning period. The average training load of the participants in the experimental group increased from 3 cmH$_2$O initially to 20 cmH$_2$O at the end of the weaning period.

Effect of intervention

Group data for all outcomes at the start of weaning and at extubation for the experimental and control groups are presented in Table 2 while individual data are presented in Table 3 (see eAddenda for Table 3). Maximal inspiratory pressure increased significantly more in the treatment group than the control group (MD 7.6 cmH$_2$O, 95% CI 5.8 to 9.4). The index of Tobin increased (ie, worsened) in both groups over the weaning period, but the increase was attenuated.
Among uncensored participants (ie, those who did not die or receive a tracheostomy), the weaning period was significantly shorter in the experimental group than in the control group. The effect of inspiratory muscle training was to reduce the weaning period by 1.7 days (95% CI 0.4 to 3.0), as presented in Table 4, with individual data in Table 5 (see eAddenda for Table 5).

Prior to the weaning period, the controlled ventilation period (see Table 1) accounted for approximately half of the total ventilation period. A Kaplan-Meier analysis of the total intubation time (ie, the controlled ventilation period plus the weaning period) did not identify a significant difference between the experimental and control groups ($p = 0.72$, see Figure 2.)

### Discussion

Although we screened 198 patients in the intensive care unit, a large proportion of these critically ill patients died or were tracheostomised either before or after commencing weaning. This is typical of research in inspiratory muscle training in the intensive care setting (Caruso et al 2005, Chang et al 2005a, How et al 2007, Sprague and Hopkins 2003). This loss to follow-up was one limitation of the study. It was compounded by the wide variability in the condition of these patients, including modifications to their medication regimen, psychological state, haemodynamic stability, and degree of sepsis. Nevertheless, the sample size remained sufficient for statistically significant between-group differences to be identified on several outcomes. Another limitation of the study was the lack of blinding.

However, because informed consent was provided by the relatives of these critically ill patients, the potential for placebo and Hawthorne effects to operate within the patients was reduced.

Previous research suggests that imbalance between the ventilatory load and the strength and endurance of the respiratory muscles is an important determinant of dependence on mechanical ventilation. For example, patients who have success in weaning have a significantly higher maximal inspiratory pressure than those who do not wean successfully (Epstein et al 2002). This relationship is also reflected in our data, with the experimental group showing both a significant increase in maximal inspiratory pressure and a reduction in the weaning period when compared to the control group.

Our findings that inspiratory muscle training improved both inspiratory muscle strength and the weaning process are also similar to the findings of several other case series. Martin and colleagues (2002), Sprague and Hopkins (2003), and Chang and colleagues (2005b) delivered inspiratory muscle training to tracheostomised patients with a long-standing dependence on mechanical ventilation. All of these patients showed improved inspiratory muscle strength and almost all weaned successfully within several weeks of starting the training. However, the participants in the current study differed by being intubated and not tracheostomised, and the conclusions are more robust due to the inclusion of a randomised control group.

Our findings differ, however, from those of one randomised trial (Caruso et al 2005). In this trial, inspiratory muscle training was achieved by increasing the pressure required to trigger pressure support, and the outcomes were the

<table>
<thead>
<tr>
<th>Table 2. Mean (SD) of outcomes for each group, mean (SD) difference within groups and mean difference (95% CI) between groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>MIP (cmH2O)</strong></td>
</tr>
<tr>
<td><strong>IT (br/min/L)</strong></td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th>Table 4. Mean (SD) duration of the weaning period among uncensored participants.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Weaning period (days)</strong></td>
</tr>
</tbody>
</table>

---

MIP = maximal inspiratory pressure (cmH2O), IT = index of Tobin (br/min/L), Exp = experimental group, Con = control group, Pre-test = start of weaning, Post-test = extubation, shaded row = primary outcome
duration of the weaning period and the rate of re-intubation in critically ill patients. The experimental and control groups did not differ significantly in terms of the weaning period (p = 0.24) and the maximum inspiratory pressure final value (p = 0.34). One possible explanation for the discrepancy between the studies is that inspiratory muscle training via reduction of sensitivity of the pressure support trigger only offers an initial resistance to the opening of the valve of the system, while inspiratory muscle training with a threshold device maintains resistance to the respiratory system for the period of the inspiration. Other studies have also reported differences in the clinical efficacy of inspiratory muscle training when delivered by a threshold device versus another method (Johnson et al 1996).

The beneficial effect of inspiratory muscle training on the index of Tobin in this study indicates a more relaxed breathing pattern. This is consistent with a study of inspiratory muscle training in 23 healthy adults (Huang et al 2003). After training, a significant increase in maximum inspiratory pressure was observed, which had a significant negative correlation with the significant reduction in respiratory stimulation P0.1. These data suggest that a reduced time of P0.1 results in a reduction in the occurrence of dyspnoea.

Inspiratory muscle training in the experimental group was found to contribute to a significant increase in maximum inspiratory pressure and to a reduction in the index of Tobin. These are considered to be good predictors of weaning, which is consistent with our finding that inspiratory muscle training significantly reduces the weaning period in patients who did not die or receive a tracheostomy.

We conclude that inspiratory muscle training improves inspiratory muscle strength in older intubated patients. In patients who do not die or receive a tracheostomy, it may also reduce weaning time.

eAddenda: Tables 3 and 5 available at www.jop.physiotherapy.asn.au

Ethics: Committee of Ethics in Research Involving Human Beings of the Euro-American Network of Human Kinetics – REMH (protocol number: 005/2007). Informed consent was obtained from each participant’s relatives with no refusals, and the experimental procedures were executed in accordance with the Declaration of Helsinki from 1975.

Acknowledgements: We are grateful to the physiotherapists in the Center of Intensive Therapy for their help with measurement.

Competing interests: None declared.

Correspondence: Professor Samária Ali Cader, LABIMH, Castelo Branco University, Brazil. Email: samariacader@gmail.com

References


Kim J, Sapienza CM (2005) Implications of expiratory muscle...


