
Response

To the Editor:

We thank Yang and colleagues for their interest in our recent article in CHEST (October 2010).1 We found that the number of T regulatory cells (Tregs) was increased in the BAL of patients with moderate to severe asthma. We found evidence of an association, albeit weak (R² = 0.16, P = .01), between Treg numbers and FEV₁, but no association between corticosteroid dose and FEV₁. These associations favor the possibility that disease severity has influenced Treg numbers, although our analysis by associations cannot provide a definitive answer as to whether disease severity and/or corticosteroid use are driving the increase in Treg numbers. The concern of Yang et al that our results could be due to corticosteroid use are already discussed extensively in our article. Yang states that “…there may be an inverse correlation between Treg activity and clinical manifestations of allergic disease.” We could not agree more! Our discussion clearly states that we have studied the numbers of Tregs, but this may not be indicative of functional suppressive ability. It is probable that the Tregs in the lungs of patients with moderate to severe asthma contain a subpopulation of inducible Tregs. These may have a different functional capacity compared with naturally occurring Tregs, and this is clearly an area for further study. The effects of cytokines within the local microenvironment can influence both the induction of Tregs and their functional capacity.3,4 Functional studies using Tregs from the lungs of patients with asthma are technically difficult to perform but will provide clarification of this issue.

Yang et al raise concerns about our method of quantifying Treg numbers. We used three well-cited methods: CD4+FoxP3⁺, CD4+CD25bright and CD4+CD25⁺CD127⁻. There is no consensus regarding the best method of measuring Treg numbers, so we took a comprehensive approach. Although Yang et al favor CD4+CD25⁺FOXP3 for quantifying Tregs, it should be noted that many scientists agree that CD4⁺FoxP3⁺ expression is of key importance, as we described previously. We have plotted the data using CD4⁺CD25⁺FOX3 (Fig 1), which gives a similar pattern to the analysis using CD4⁺FOXP3 (healthy vs moderate/severe, P = .003). Either approach appears valid for identifying Tregs in the airways.

Lucy J. C. Smyth, PhD
Amanda Eustace, PhD
Umme Kolsum, MSc
John Blaikely, MD
Dave Singh, MD
Manchester, England

Affiliations: From the University of Manchester (Drs Smyth, Eustace, Blaikely, Singh, and Ms Kolsum), National Institute for Health Research Translational Research Facility, Manchester Academic Health Science Centre, University Hospital of South Manchester Foundation Trust; and the University of Salford (Dr Smyth), Centre for Parasitology and Disease, School of Environment and Life Sciences, Salford, England.

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Correspondence to: Lucy J. C. Smyth, PhD, University of Salford, Centre for Parasitology and Disease, School of Environment and Life Sciences, Salford, M5 4WT, England; e-mail: l.smyth@salford.ac.uk

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REFERENCES

Noninvasive Ventilation as a Weaning Tool

To the Editor:

We read with great interest the article recently published in CHEST by Ortiz et al (June 2010) about the use of synchronized intermittent mandatory ventilation with pressure support (SIMV-PS) compared with assist-control (A/C) ventilation as the primary mode of ventilatory support using the data of an international prospective cohort study of mechanical ventilation. The authors have analyzed the SIMV-PS and A/C modes as weaning modes. Although this is a statistical study, not a clinical study, the absence of any commentary about noninvasive ventilation

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(NIV) as a weaning mode is a point of attention that should be highlighted.

Several randomized controlled trials have reported the usefulness of NIV to facilitate weaning in patients who have failed at least one spontaneous breathing trial (SBT). In the study of Nava et al, 6 patients with COPD with severe acute-on-chronic respiratory failure were included. The 50 patients who failed the T-piece SBT were randomized. Twenty-five patients were extubated to NIV delivered with an oronasal interface and an ICU ventilator in pressure-support mode, with a weaning protocol similar to that used in the invasive-ventilation group. The NIV patients had better outcomes, including shorter mechanical ventilation (10 vs 17 days) and ICU stay (15 vs 24 days). The NIV patients were more likely to succeed in weaning (88% vs 68%) and to be alive at 60 days (92% vs 72%). None of the NIV patients developed pneumonia, compared with 25% of those who remained intubated.

Ferrer et al 5 applied a different design in randomizing 43 patients (77% with chronic lung disease) who had failed at least three SBTs. NIV was applied for at least 24 h, using a bilevel mode (inspiratory pressure 10-20 cm H2O, expiratory pressure 4-5 cm H2O) delivered via nasal or oronasal interface. Compared with invasive weaning, NIV weaning was associated with significant and substantial reductions in duration of invasive ventilation, duration of ICU and hospital stay, incidence of septic shock and pneumonia, and need for tracheostomy.

Burns et al 6 have performed a metaanalysis of NIV weaning to facilitate liberation from mechanical ventilation. They have found that NIV was associated with lower mortality (risk ratio, 0.41), less ventilator-associated pneumonia (risk ratio, 0.28), and shorter mechanical ventilation (7.3 days), ICU stay (6.9 days), and hospital stay (7.3 days). NIV had no effect on the probability of weaning success. Recently, Burns et al 6 updated their metaanalysis with new studies, totaling 227 patients with COPD with pneumonia, that randomized patients after they met criteria indicating control of pulmonary infection, rather than after failure to tolerate an SBT. In addition, some of these studies differed fundamentally from other studies in that the weaning mode was different in the two groups: NIV weaning was conducted with pressure support, whereas invasive weaning was performed with synchronized intermittent mandatory ventilation plus pressure support. With these caveats in mind, this metaanalysis of 12 studies and 530 patients, principally with COPD, showed that NIV weaning significantly reduced mortality (risk ratio, 0.55; 95% CI, 0.38-0.79), nosocomial pneumonia (risk ratio, 0.29; 95% CI, 0.19-0.45), ICU stay (weighted mean difference, 6.3 days), hospital stay (7.2 days), total duration of ventilation (5.6 days), and duration of invasive ventilation (7.8 days). NIV was associated with fewer tracheostomies.

Girault et al 4 recently completed a randomized controlled trial with 208 patients in 17 centers in France. Patients were included if they had been intubated for at least 48 h with acute-on-chronic respiratory failure and had failed an SBT trial. Patients were randomized into three groups: continued intubation with conventional weaning on pressure support (n = 69), extubation to NIV (n = 69), or extubation to oxygen but without NIV (n = 70). There were no differences in weaning failure (predominantly reintubation within 7 days of extubation), complications, ICU or hospital stay, or hospital survival. Interestingly, NIV was used effectively as salvage therapy in 14 (45%) of 31 patients weaned inversely and 23 (55%) of the 40 patients extubated to oxygen alone. In agreement with Epstein and Durbin, we believe that NIV is an effective tool for facilitating weaning in patients with acute-on-chronic respiratory failure, mainly patients with COPD.

Salvador Díaz Lobato, PhD
Sagarnlo Mayoralas, PhD
Madrid, Spain

Affiliations: Pneumological Department, Ramón y Cajal Hospital (Dr Lobato); and Hospital Moncloa (Dr Mayoralas).

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Correspondence to: Salvador Díaz Lobato, PhD, Pneumological Dept, Ramón y Cajal Hospital, Carretera de Colmenar Viejo, Km 9, 100, 28034 Madrid, Spain; e-mail: sldazlobato@gmail.com

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References


Response

To the Editor:

We thank Drs Díaz-Lobato and Mayoralas for their interest in our article in CHEST (June 2010) 3 on the use of synchronized intermittent mandatory ventilation with pressure support (SIMV-PS) compared with assist-control ventilation as the primary mode of ventilatory support. Although the topic of their letter has a marginal relationship with our article, which is not an analysis of methods for weaning, we are interested in the controversy about the use of noninvasive positive-pressure ventilation (NIPPV) as a weaning method.

As the authors reference in their letter, there are now 13 reported randomized, controlled trials of NIPPV to facilitate weaning in ventilated patients. Among these studies, three have been presented only in abstract form, one is an unpublished dissertation, and four are studies published in Chinese. An additional study included intubated patients with COPD and pneumonia who were randomized to NIPPV vs SIMV-PS, but the patients had not failed a spontaneous breathing trial before being randomized. Therefore, there would only be four accessible studies 1-4 to assess the role of NIPPV as a weaning method. These studies have some design and methodologic flaws worth mentioning.