Inspiratory pressure during noninvasive ventilation in stable COPD: help the lungs, but do not forget the heart

To the Editor:

The disappointing results of the randomised trials on the use of noninvasive ventilation (NIV) in stable hypercapnic chronic obstructive pulmonary disease (COPD) patients [1] necessitates a search for the reasons for NIV inefficiency in long term treatment. WINDISCH *et al.* [2] suggested that NIV aimed at increasing maximum-tolerated inspiratory positive airway pressure and taking over patients breathing rhythm by a ventilator is a key factor in the success of NIV. The new idea proposed by WINDISCH *et al.* [3], called high intensity noninvasive positive pressure ventilation (Hi-NPPV), seems to be attractive, but requires verification. Therefore, we would like to congratulate LUKÁCSOVITS *et al.* [4] on their excellent physiological study of the short-term effects of Hi-NPPV published in the April 2012 issue of the *European Respiratory Journal*. However, we believe that some aspects of this study need to be critically discussed.

Firstly, LUKÁCSOVITS *et al.* [4] proved that Hi-NPPV decreases both arterial carbon dioxide tension (P_{a,CO_2}) values and the work of breathing, even if it is obtained at the cost of a significant reduction in cardiac output. The rate of decrease in cardiac output under Hi-NPPV was 28% *versus* spontaneous breathing and 13% *versus* low-intensity noninvasive positive pressure ventilation (Li-NPPV). A similar reduction was noted in oxygen delivery capacity under Hi-NPPV and it consisted of 250 mL of oxygen per min (*versus* spontaneous breathing). These findings raise a very interesting issue concerning adequate tissue oxygen delivery during Hi-NPPV. The authors claimed that this finding did not necessarily have an adverse effect. This statement is not supported by scientific results but rather by the intuition of researchers, and we cannot share their optimism about it. Above all, we doubt if it is worth decreasing P_{a,CO_2} by 10 mmHg at the expense of 250 ml of oxygen delivered to tissues every minute. If oxygen delivery becomes insufficient to meet peripheral oxygen consumption, the tissues have to extract more oxygen from the haemoglobin. However, a substantial reduction in oxygen delivery cannot be compensated for by increased oxygen extraction and results in anaerobic metabolism with lactic acidosis. Unfortunately, the lack of data dealing with changes in saturation of mixed venous blood under Hi-NPPV does not give us clear information about tissue oxygen extraction.

Secondly, the detrimental effects of significant falls in cardiac output are likely to have a clinical impact (*e.g.* insufficient perfusion of vital organs) in stable patients on home NPPV without known heart disease under those conditions which are associated with increased ventilatory demands. This is particularly true given the fact that high pressure level-induced cardiac output fall is more evident in COPD patients as compared to those with acute lung injury [5]. Moreover, the negative haemodynamic effects of Hi-NPPV are based on the multiple interferences between the type of mask, the level of inspiratory pressure and the external positive end expiratory pressure (PEEP) applied [5].

Thirdly, we are not convinced by the hypothesis given by the authors that considers that the cardiac output reduction reflects, at least in part, the lower metabolic demand of respiratory muscles which undergo a full rest under Hi-NPPV. Unfortunately, this speculation is not supported by the measurement of biochemical indexes of muscle energy consumption (lactate) or oxygen uptake (V'_{O_2max}).

Fourthly, LUKÁCSOVITS *et al.* [4] used transthoracic echocardiography to exclude patients with existing heart disease on the basis of an ejection fraction less than 40%. However, a normal ejection fraction does not exclude the presence of diastolic left ventricular dysfunction and pulmonary arterial hypertension with/without right heart failure, both cardiovascular conditions that are able to influence the response to NPPV in the acute setting [5].

Fifthly, in our opinion the Hi-NPPV-induced worsening pulmonary hyperinflation should be emphasised. The authors could not calculate the amount of dynamic intrinsic PEEP from the tracing of oesophageal pressure due to the full abolishment of inspiratory muscle activity. However, due to the physiological alterations occurring in COPD, causing an increased constant of time, the greater the delivered tidal volume during mechanical ventilation the higher the chance of an incomplete expiratory emptying of the lungs. A worse dynamic hyperinflation during Hi-NPPV may increase the risk of asynchrony between patient and ventilator (*i.e.* wasted efforts), barotrauma and cardiovascular interferences.

In conclusion, we would like to underline that LUKÁCSOVITS *et al.* [4] showed that Hi-NPPV is very efficient in improving gas exchange in the lung; however, it has a negative impact on oxygen delivery and therefore has to be used with caution in COPD patients with severe hypoxaemia and conditions vulnerable to ischaemia. If ''lungs'' are likely to benefit from the implementation of the Hi-NPPV philosophy, the ''heart'' seems to suffer these ''strong pressures'', which could have negative impact on oxygen delivery.

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From the authors:

We would like to thank A.M. Esquinas and co-workers for their interest in our article [1] and the accurate analysis and comments.

Our study was designed to evaluate the changes in respiratory mechanical and cardiovascular parameters during a high intensity mechanical ventilation (Hi-NPPV) lasting 30 min.

Using similar ventilatory settings to those applied by WINDISCH and co-workers [2, 3] we demonstrated that Hi-NPPV in stable chronic obstructive pulmonary disease (COPD) patients is more effective than low intensity mechanical ventilation (Li-NPPV) at acutely improving gas exchange and reducing the patient's respiratory effort but the high inspiratory positive airway pressure values induced a marked lowering in cardiac output and oxygen transport. The oxygen transport mainly depends on the cardiac output, blood haemoglobin concentration and arterial oxygen saturation. During our trial haemoglobin was likely to be constant and the inspiratory oxygen fraction was set to achieve an arterial oxygen saturation of about 90–92%, therefore the calculated oxygen transport basically went in parallel with changes in cardiac output. The harmful effect of positive pressure ventilation on cardiac output is well known from previous studies [4, 5]. The ''negative'' effects on cardiac output depend on: 1) worsening of venous return in the right atrium; and 2) increasing the pulmonary vascular resistance caused by lung tissue expansion. The most important effect is probably the former that depends on the changes in intrathoracic pressure (pleural pressure). The amount of pressure transmitted from the airways into the pleural space depends on the ratio between the lung compliance and lung plus chest wall compliance ($\Delta P_{pl}/\Delta P_{aw} = C_L/(C_L+C_T)$; ΔP_{pl}: change in pleural pressure; ΔP_{aw}: change in airway pressure; C_L: lung compliance; C_T: thorax compliance) [5]. For instance in an emphysematous patient, with high lung compliance and rigid chestwall (*e.g.* emphysema), the airway pressure will be transmitted to a higher degree than in a patient with normal chest wall compliance with restrictive pulmonary disease (*e.g.* acute respiratory distress syndrome, pulmonary fibrosis). For this reason, in different types of lung disease patients the positive airway pressure will cause different changes in cardiac output.

Contrary to our investigation, where Hi-NPPV was applied briefly and rapidly, WINDISCH and co-workers [2, 3] used a very slow increase, lasting days, in inspiratory pressure at the maximum level tolerated by the patient. It is therefore to be demonstrated that the described changes in cardiac output are of the same magnitude when increasing levels of pressure are applied slowly.

Previous articles suggested that to avoid a decrease in cardiac output, the patient must be placed in supine or Trendelenburg position [4, 5]. Our subjects were studied in a semi-recumbent position in contrast with the patients of WINDISCH and co-workers [2, 3] who used the NPPV mostly during the night, probably in supine position, in this way facilitating venous return.

There are, however, some potential advantages in lowering venous return in some chronic patients. For example, the described ''reversal'' of pleural pressure (from negative to positive during inspiration) observed with Hi-NPPV, limiting venous return and lowering left ventricular afterload, can improve the cardiac output in patients with left ventricular failure [4]. For this reason we excluded the patients with left ventricular ejection fraction lower than 40% or with any signs of acute or chronic left ventricular insufficiency.

Indeed the pressure time product of the diaphragm in COPD patients during spontaneous breathing was, on average, about three times higher than in a normal subject, which means a notable oxygen consumption. Therefore, the loss in oxygen transport was probably partly compensated by the lower oxygen consumption caused by Hi-NPPV.

We agree with A.M. Esquinas and co-workers and we have already discussed the problem that dynamic hyperinflation and patient/ventilator asynchrony may occur during Hi-NPPV, leading to poor tolerance, volutrauma, barotrauma and cardiovascular interferences. Unfortunately, objective signs of dynamic hyperinflation (*e.g.* dynamic intrinsic positive end expiratory pressure) were not measurable, because of the complete rest of the respiratory muscles observed in the majority of patients during Hi-NIPPV.

In conclusion, Hi-NNPV is more effective than the traditional settings of noninvasive ventilation in improving gas exchange and reducing patient respiratory effort. Despite its beneficial effects, through high inspiratory pressure it can provoke a pronounced decrease in cardiac output and oxygen transport, for this reason it should be used with caution in patients with pre-existing decreased cardiac output, serious anaemia or severe hypoxaemia, but probably not in those with left