Un bout de souffle: ventilatory support for pulmonary oedema

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What is the best treatment for acute pulmonary oedema? There is a wealth of large scale randomized studies conducted in chronic stable heart failure which informs the management of the condition and has helped in drawing up guidelines. In contrast, there have been very few trials of treatment for acute pulmonary oedema.

Pulmonary oedema is an appalling experience. For many patients, it is the most distressing thing they ever experience. The pathophysiological model that best appears to describe the syndrome is the straightforward haemodynamic model: left ventricular filling pressure rises, causing a rise in pulmonary venous and pulmonary capillary pressure. The pressure exceeds the colloid osmotic pressure in the vessels and oedema fluid accumulates in the air spaces; the rate of accumulation exceeds the rate of lymphatic drainage, and the patient starts to drown.

Traditional management has focussed on the need to reduce ventricular filling pressures, principally with nitrates, and on inducing a diuresis with loop diuretics. Oxygen at high flow rates is given. In passing, there is a certain lack of logic to this approach: in acute pulmonary oedema, there has been little time for the patient to develop fluid overload, and the problem is mainly haemodynamic. Circulatory support with positive inotropic drugs is sometimes-needed. Intubation and positive pressure ventilation is the last resort and offers the distressed and tiring patient almost immediate relief of symptoms, whilst buying time for pharmacological treatment to work.

Data are slowly accumulating on the possible role of non-invasive respiratory support but the techniques and equipment are fertile areas for confusion. Continuous positive airway pressure (CPAP) should be distinguished from non-invasive positive pressure ventilation, although both can be applied with similar looking nasal or full-face masks. Patients on CPAP are breathing spontaneously and determine the depth and frequency of their breaths. The pressure is communicated to the airway at a constant level throughout the respiratory cycle and is positive in relation to atmospheric pressure at the end of expiration.

In contrast, positive pressure ventilation blows air and entrained gases into the lung. Gas flow is primarily determined by the ventilator and the pressure changes phasically throughout the respiratory cycle. Continuous positive airway pressure can be used in an intubated ventilated patient — when it is usually called PEEP (positive end expiratory pressure) — and means that after the high pressure inspiratory breath inflates the lung, the passive expiratory breath takes place against a resistance which stops airway pressure from going back to atmospheric pressure at the end of the breath. This process is known as bi-level ventilation and is now widely used with both invasive and non-invasive ventilators in a variety of settings. CPAP is commonly used as treatment for obstructive sleep apnoea. In this situation, it functions by splinting open the upper airway and preventing the repetitive pharyngeal collapse that causes sleep fragmentation and day time sleepiness. In critical care settings, CPAP has a well established role in the treatment of hypoxaemic respiratory failure. Of necessity, the equipment is more sophisticated than that used for domiciliary CPAP: it must be able to deliver sufficiently high flows to prevent the pressure drop in the airways in tachypnoeic patients with high minute volumes and short inspiratory times. The mechanism of action is different, too, and is believed to be mediated through an increase in functional residual capacity. The effects include recruitment of collapsed alveoli, increased lung compliance, prevention of atelectasis, improved oxygenation and reduced work of breathing.

How might CPAP improve outcomes in cardiac failure? One paradox that needs explanation is that in the normal heart PEEP, and to a lesser extent CPAP, seems to decrease cardiac output through decreased venous return, increased right ventricular afterload and decreased contractility. However, in the dilated failing left ventricle, CPAP somehow reduces left ventricular transmural pressure and wall stress (and hence afterload) and results in an increase in stroke volume[1]. Other mechanisms are also likely to be important: in chronic heart failure the inspiratory muscles need to generate a greater force — presumably because of reduced lung compliance — and CPAP is capable of unloading these muscles and perhaps reducing their metabolic demands.

Three randomized controlled trials have compared CPAP with medical therapy for pulmonary oedema alone. Rasanen et al.[2] showed a more rapid improvement in ventilation and reduction in the need for intubation in a randomized study of 40 patients.
Bersten et al.\textsuperscript{[3]} and Lin et al.\textsuperscript{[4]} showed similar results, although none of the studies was able to show an improvement in eventual mortality.

In the study reported in this issue\textsuperscript{[5]}, the 27 patients randomized to CPAP had a convincingly more rapid reduction in symptom scores, respiratory rate and acidosis compared to the 31 randomized to oxygen alone. There was a suggestion of a survival benefit. Additionally, noradrenaline levels were shown to be mildly raised at presentation, but there was a much more dramatic elevation of B-type natriuretic peptide (more than 10 times the upper limit of normal). Higher neurohormonal levels were associated with death or myocardial infarction.

Importantly, patients so unwell they were unable to speak and maintain their own airway were excluded from these studies\textsuperscript{[2–5]}. Bi-level positive pressure support (which might be expected to mimic conventional ventilation more closely) was associated with a worse outcome in a study of patients with very severe pulmonary oedema\textsuperscript{[6]}. In this study, patients were managed initially in mobile intensive care units, so that very ill patients who might otherwise have died before reaching hospital were included.

A small study has suggested that bi-level ventilation may be beneficial\textsuperscript{[7]}, but the control and intervention groups were not well matched. Other studies have confirmed that there may be a problem with bi-level ventilation. In a study comparing bi-level and CPAP\textsuperscript{[8]}, the trial had to be stopped early because of an increased rate of myocardial infarction in those receiving bi-level ventilation. Other series have also suggested an adverse interaction between bi-level ventilation and acute myocardial infarction\textsuperscript{[9]}

Why are there so few data on the treatment of acute pulmonary oedema? Part of the problem is the nature of the condition. Patients tend to present in the early hours of the morning, and in a condition where obtaining informed consent is next to impossible. It is difficult to define a uniform population of patients to study; most will have some acute precipitant to the pulmonary oedema which will itself have a major bearing on outcome. In the study of Mehta et al, for example, although bi-level ventilation was found to improve respiratory variables more, it was associated with an increased risk of myocardial infarction\textsuperscript{[8]}. However, more patients with chest pain were randomised to this form of treatment. In the study suggesting benefit for bi-level ventilation, more patients with acute infarction were randomized to the control group\textsuperscript{[7]}

A meta-analysis of three small studies (total 179 patients) has suggested a decrease in the need for intubation and a less clear cut trend towards survival benefit for CPAP\textsuperscript{[10]}. The data on the use of positive pressure ventilation was too sparse to combine and no conclusions were reached. Despite a comprehensive search strategy, there must be a likelihood of publication bias whereby small negative trials are not reported and inevitably, there were variations in the regimes used. However, if respiratory support can reduce distressing symptoms more rapidly than conventional therapy, that is a worthwhile end in itself, as long as there is no cost in terms of an excess mortality. CPAP seems a safe and effective therapy which the present study shows can be safely initiated in the Accident and Emergency Department\textsuperscript{[5]}. Three studies have, however, sounded a note of caution. More aggressive therapy with bi-level ventilation seems to be associated with a worse outcome in some\textsuperscript{[6,8,9]}, but not all studies\textsuperscript{[7]}

It is traditional for editorials to call for more research into the area under discussion. There is already reason to believe that CPAP should be considered in the management of patients with severe pulmonary oedema, but there is no hard evidence for its effects on mortality. A large randomized study would answer this question. The role of non-invasive bi-level ventilation is more difficult to define because of safety concerns but might usefully be compared with invasive ventilation for a particularly severely affected subgroup in whom CPAP has failed. CPAP treatment for heart failure was first described 65 years ago\textsuperscript{[11]}; shouldn’t we understand its role by now?

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References


