



LETTERS / CORRESPONDANCE

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TREATMENT OF ACUTE CARDIOGENIC PULMONARY EDEMA

To the Editor:

I read with interest the article titled "Rural treatment of acute cardiogenic pulmonary edema"¹ in the summer 2008 issue of *CJRM*. It was a very helpful look at what works and what doesn't, and I was about to generate a big change in my practice, starting with continuous positive airway pressure (CPAP) (though that's difficult in my hospital as only a few nurses know how to set it up), moving to nitro and sublingual captopril, with furosemide as a third-line drug and avoidance of morphine.

A few days later, I received an email summary of a study: "Non-invasive ventilation in acute cardiogenic pulmonary edema."² The authors demonstrated symptomatic improvement but no impact on short-term mortality or the need for intubation.

This leaves me wondering how strong the evidence is? Should I change from my usual practice of beginning with morphine and furosemide to that outlined in the *CJRM* paper?

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[The author replies:]

The evidence for noninvasive ventilation (NIV) in acute cardiogenic pulmonary edema (CPE) has been inferred from 4 meta-analyses,¹⁻⁴ the largest containing 938 patients. So convincing was the evidence for reduced intubation and in-hospital mortality that there was some opinion that it might be "unethical" to conduct further studies containing an oxygen-only arm.^{2,5} The new study⁶ is a megatrial of over 1000 patients, which, contrary to the best previous evidence, fails to support findings of reduced rates of endotracheal intubation and reduced mortality using NIV. It does, however, reinforce the value of NIV in earlier symptom improvement and early improvement of physiologic parameters, such as respiratory rate, oxygenation, acidosis and hypercapnia.

The new study by Gray and colleagues had very high recruitment rates and fewer exclusions than most of the studies included in the meta-analyses. Patients with chronic obstructive pulmonary disease and acute myocardial infarction were included. The patient population was generally older than that of some of the smaller studies. The study population was therefore somewhat different. Management seemed to be different as well, as demonstrated by an extremely low intubation rate in all groups — only 2.8% as compared with 10%–25% in the meta-analyses. Similarly, death rates in hospital were 9.5%

as compared with 10%–20% in the meta-analyses. Although an intention-to-treat analysis was followed, there was a rather large crossover in this study of 19%, mainly because of the failure of oxygen-only to improve clinical status and intolerance to the biphasic positive airway pressure (BiPAP) arm of the NIV group. No mention is made in this study as to how quickly the interventions were applied and whether there was a difference in early mortality (0–48 hr).

The study confirms that patient symptoms and physiologic parameters improve more quickly with the use of NIV. It also shows that CPAP is better tolerated than BiPAP, and that both modalities are safe. A recent retrospective analysis of the massive Acute Decompensated Heart Failure National Registry (ADHERE) of patients in acute decompensated heart failure shows that patients managed with NIV in fact have better outcomes than similar patients managed by endotracheal intubation.⁷ It may be that we cannot expect a short-term intervention to have an effect on long-term mortality, and that our anticipated end points with this intervention need to be different. Improvement in dyspnoea and physiologic parameters without adverse effect on longer term morbidity and mortality is probably a reasonable objective in early goal-directed therapy.⁸ One similar NIV study of over 100 elderly patients showed a significant 48-hour

mortality difference, but ultimately no change in longer term mortality.⁹ These early, short-term advantages cannot be discounted when initially managing these patients in small centres.

A parallel set of smaller prospective studies considers the use of NIV in the prehospital setting. A number of these again show a dramatic reduction in intubation rates and in-hospital mortality.¹⁰⁻¹² These findings suggest that the early use of CPAP in CPE may produce dramatic benefit, particularly if the diagnosis is in doubt.

There is now a simplified apparatus for administration of CPAP, especially in the prehospital setting. The Boussignac single-use system requires only an oxygen regulator that can supply 25 L/min to achieve a positive pressure of 10 cm water. There are several papers attesting to the effectiveness of this device in settings with minimal staff training and experience.^{13,14} This device should greatly simplify the process of administration and make it possible to apply the intervention early with the limited pairs of hands available in a rural emergency department.

When faced with a patient with CPE in a setting with limited resources, we have excellent evidence that there is a simple means of administering early CPAP, and that it will produce more rapid symptom relief and improved physiology. Because of this new paper, we can be less sure that rates of intubation or death will be reduced, but we can be reasonably confident that a choice for NIV will produce a better result than a choice for intubation, even if intubation is

eventually required.⁷ It seems likely that NIV should be applied early for best results, and that there are subgroups such as those with the highest presenting blood pressure^{7,8} and those with severe acidosis or hypercapnia⁴ who may selectively benefit from early intervention in terms of reduced intubation and in-hospital mortality. Another megatrial may be required to establish whether such benefit truly exists.

The evidence remains strong for early use of high-dose nitroglycerine. Furosemide remains an adjunct, bearing in mind that not all patients in CPE are volume overloaded. There was never good evidence for morphine. There is now a retrospective analysis of the ADHERE registry,¹⁵ which indicates increased intubation, intensive care unit admission, hospital length of stay and death with use of morphine. Morphine is, in fact, an independent predictor of death in CPE, even after risk adjustment and exclusion of ventilated patients, with an odds ratio of 4.84.¹⁵ Benzodiazepines work well if sedation is required.

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