

Review of Literature

Evidence for efficacy of CPAP/NIV in the treatment of COPD:

There have been a plethora of studies investigating the use of NIV in the treatment of acute exacerbations of COPD.

Karnik (1) in 2000 concluded, that there were significant benefits to using NIV in the treatment of acute COPD. These included a reduction in the need for endotracheal intubation (ETI) by 66%, a 20% reduction in mortality and a reduction in the length of ICU stay (LICUS) of 19 days. He also reported a reduction in the length of hospital stay (LHS) of 13 days.

Peters et al (2) meta-analysis, reviewed the use of NIV in the treatment of acute respiratory failure. This group found a significant reduction in the need for ETI (numbers needed to treat 6), a decrease in LHS (2.74 days) and a 45% relative risk reduction for mortality (all groups). The results for COPD on its own were more striking – they concluded that “The effects of noninvasive ventilation are most apparent in patients with acute respiratory failure secondary to chronic obstructive pulmonary disease exacerbations.”

A Cochrane systematic review and meta-analysis by Ram et al (3) in 2003 reached similar conclusions. This group showed that treatment with NPPV significantly improved physiological markers in most patients, and reduced:

- (1) The risk of mortality (0.52 RR 95% CI 0.35-0.76),
- (2) Reduced the need for ETI (.41 RR 95% CI 0.33-0.53),
- (3) Reduced the LHS by 3.24 days (95% CI 4.42 - 2.06),
- (4) and showed a reduction in the number of adverse events compared to standard medical therapy (0.38 RR 95% CI 0.24- 0.6).

A prospective cohort study by Gorini M, et al (4) investigated the use of CPAP and BIPAP together with negative pressure ventilation. This group found a reduced need for ETI and a reduction in mortality with CPAP treatment. They also found that using a combination of positive pressure with negative pressure back up was beneficial in cases of treatment failure.

Paus-Jenssen ES, et al (5) measured efficacy of NIV in a real practice situation. They specifically looked at use outside of the ICU. They reported favorably finding a mortality rate and ETI rate similar to experimental studies.

Evidence for efficacy of CPAP/NIV in the treatment of pulmonary oedema (PO):

While CPAP/NIV provides a theoretical benefit to the pulmonary oedema patient, it is important to consider whether this translates into a clinical benefit.

Bersten et al (6) reports results from a group of 39 patients with severe cardiogenic PO who were randomised to either oxygen therapy (n=20) or CPAP (n=19). The study looked at conversion to intubation, length of ICU stay and change to arterial blood gases as outcome measures.

The results showed that CPAP can result in early physiologic improvement and reduce the need for intubation and mechanical ventilation.

Holt et al (7) reports the cost benefit analysis of treating all patients with mask CPAP for those suffering severe Cardiogenic Pulmonary Oedema CPO rather than the previous practice of admitting only patients failing conventional non-CPAP treatment and requiring mechanical ventilation. Mask CPAP reduced the need for mechanical ventilation from 35% to 0%. Cost of previous estimated yearly caseload of 35 ventilated patients (\$176,925) was greater than the cost associated with an increased caseload of 100 CPAP patients (\$115,600).

Pang et al (8) in their 1998 systematic review. In this paper the researchers reviewed a large number of trials (n=497), looking for randomised controlled trials in the treatment of PO. Interestingly of the 497 trials, only three CPAP trials (one being Bernsten et al) met the criteria for study. They found only one randomised controlled trial comparing NIV to CPAP in the treatment of PO. Pang et al concluded that "a modest amount of favourable experimental evidence exists to support the use of CPAP" in the treatment of PO. They showed that CPAP reduced intubation rates and may decrease mortality. They recommended further study before NIV could be recommended.

A literature review by Mackway-Jones (9) found that CPAP decreased the ETI rate and recommended that the "Clinical bottom line is Patients presenting with severe acute pulmonary oedema should be treated with CPAP."

Trial data presented by Crane (10) compared CPAP to BIPAP as well as conventional oxygen therapy. CPAP treatment resulted in increased physiological improvement in patients and a decrease in mortality (30% reduction p=0.029). They concluded that "In this study, patients presenting with acute cardiogenic pulmonary oedema and acidosis, were more likely to survive to hospital discharge if treated with CPAP, rather than with bi-level ventilation or with conventional oxygen therapy."

L'Her et al (11) investigated the use of CPAP in the treatment of PO in the elderly. This multi center randomized trial found the following significant results:

(1) Physiological improvement (P=0.004).

- (2) A reduction in Severe complications (rate 25% of that of the O2 group $p=0.0002$).
- (3) A decrease in the 48 hour mortality of 17% ($p=0.017$).
- (4) But unfortunately, no reductions in overall mortality during follow up.

Other Cardiogenic Data:

Matte et al (12) concluded that for the majority of patients undergoing coronary artery bypass graft (CABG) intensive CPAP can significantly improve physiological indicators in the post operative period.

Squadrone et al (13) found that those patients who received oxygen plus CPAP post operatively following major abdominal surgery had lower rates of intubation, pneumonia, infection and sepsis than patients treated with oxygen alone. They also spent fewer mean (SD) days in intensive care with nil deaths, whereas 3 died in the group that was treated with just oxygen.

Other Cause of respiratory failure:

As stated above there is limited trial data for the treatment of other causes of respiratory failure.

In terms of Asthma, there are a number of small studies published. Meduri et al (14) trialed CPAP in the treatment of status asthmaticus. The patients showed significant physiological improvement after treatment but no other longer term outcomes were followed.

The use of CPAP in other causes of respiratory failure is limited. Karnik (1) reports the CPAP is ineffective in treating patients with pneumonia. CPAP does improve oxygenation but there is limited evidence to support a reduction in ETI rates.

Another cause of respiratory failure involving excess secretions is ARDS. Antonelli et al (15) reports that ARDS is significant factor in CPAP treatment failure. It would seem that the CPAP system can improve oxygenation in this subgroup of patients but has limited effect on the long term outcomes.

However Hilbert G, et al (16) reported on immuno-suppressed patients in acute respiratory failure. The study excludes COPD and PO, and focused on other causes of acute respiratory failure like the ones above. The groups results showed a significant reduction in ETI rates ($P=0.03$) and a reduction in Mortality ($P=0.03$). There was no difference in the LICUS or the mean duration of ventilation.

Antonelli M, et al (17) showed a similar set of results in a study of solid organ transplant patients in respiratory failure. In this subset of patients they showed significant PI ($P=0.03$), a reduction in the rate of ETI (? 50% $P=0.002$), a reduction in LICUS (? 3.5 days $p=0.03$) and a reduction in ICU mortality (? 30% $p=0.05$).

Pavlovich et al (18) studied the treatment of patients suffering acute respiratory failure (ARF) secondary to congestive heart failure (CHF). Of 54 patients who met the criteria for intubation, 4 required immediate intubation with the remaining 50 placed on CPAP. Of the 50 only 4 failed CPAP and required intubation. ICU admission went from 100% to 48% and average length of stay decreased from 14.8 days to 8 days.

Endotracheal Intubation ETI:

The most consistent result in all of the papers reviewed is that CPAP can reduce the need for endotracheal intubation (1, 2, 3, 4, 5, 6, 7, 8, 9, 13, 15, 16, 18). This has the effect of removing or shortening the LICUS which in turn reduces cost. Given that an ICU bed costs \$2000 (informed estimate) per day in NZ the use of CPAP can result in significant cost saving for the health system.

A study by Girou E, et al (19) also showed significant reduction in nosocomial infection rates when comparing CPAP to ETI. The study concluded that patients with acute exacerbations of COPD treated with CPAP have reduced infection rates, decreased length of stay and reduced mortality compared to ETI. A similar study by Nourine K, et al (20) showed a significant decrease in both the overall infection rate and the ventilator associated pneumonia rate.

Once patients have been intubated there can be complications at extubation which lead to ventilator dependence for some patients. CPAP has been trialed as a ventilator weaning strategy. In a review by Burns et al (21), CPAP was shown to reduce mortality, ventilator associated pneumonia and length of ICU/Hospital stay in ETI ventilated patients. Interestingly the use of CPAP did not significantly reduce the number of weaning failures.

Conclusions:

CPAP is an effective treatment for respiratory failure resulting from COPD or Pulmonary oedema. There is positive evidence to suggest that CPAP may be useful in the treatment of other causes of respiratory failure, especially in selected subgroups of patients.

CPAP has also been shown to be useful in the treatment of other conditions like recovery from CABG operations and major abdominal surgery. CPAP is an established therapy in the area of premature infant respiratory support. It is also useful in weaning patients from ETI ventilation.

CPAP treatment's greatest advantage is that it has been shown to significantly reduce the need for ETI. This has a multitude of advantages, the most significant being to the patient. ETI is an unpleasant procedure at the best of times. CPAP allows a significant percentage of patients to avoid ETI without compromising therapeutic goals. It also allows the patients to talk to their families without the interference of a tube in the throat. This is particularly important in the terminally ill whose time is even more precious.

In terms of the health system, the avoidance of ETI means that less ICU beds are utilized as CPAP can be delivered in a medical ward. CPAP is also associated with a much lower rate of nosocomial infection which means the CPAP treated patient utilizes lower volumes of antibiotic, specialist time, which in turn leads to shorter hospital stays and savings. In some cases the LICUS and LHS can be reduced as well. All of this contribute to CPAP being a cost effective treatment method which has the advantage of being patient friendly in most cases.

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