Critical Review Form

Therapy

Randomized controlled comparison of CPAP, BIPAP and standard treatment in ED patients with ACPE, *Emerg Med J* 2004; 21:155-161

Objective:

"To investigate whether either CPAP or bi-level ventilation would result in faster recovery within the emergency department in the UK setting as compared with the use of standard oxygen therapy in patients with acute CPO (cardiogenic pulmonary oedema)." (p 155)

Methods:

Adults presenting to one of two university hospitals between May 2000 and September 2000 in Leads, UK with clinical evidence of CPO in the opinion of the treating physician were evaluated for enrollment. Inclusion criteria included respiratory rate > 23, pulmonary edema on CXR, and arterial pH <7.35. Exclusion criteria included systolic BP <90, temperature >38ºC, patients requiring thrombolysis for AMI, patients requiring dialysis, impaired consciousness or recognized dementia. Upon identification of eligible subjects, researchers were notified and assumed clinical care for the next two-hours with all subjects receiving 10L 0_2 per non-rebreather and standard medical therapy (furosemide nitrates, morphine) with the a priori goal to maintain oxygen saturation above 90%.

Twenty subjects each were randomized via Excel random number generator with initial allocation concealed by double opaque envelopes into standard face ask oxygen, CPAP (10cm H_2O), or BIPAP (15cm H_2O IPAP, 5cm H_2O EPAP). Various physiological parameters (BP, respiratory rate, pulse oximetry) were recorded at 10-minute intervals and every 30-minutes an unvalidated 10cm dyspnea visual analog score was compiled. Treatment failure was defined a priori as respiratory rate > 40 or < 10 or reduced consciousness associated with a falling arterial pH. Treatment success was defined a priori as respiratory rate < 23, oxygen saturation > 90% and arterial pH > 7.35. Patients were followed until hospital discharge or death. A Bonferroni test was used for repeat measures to avoid α-over inflation. Logistic regression was conducted to identify factors significantly associated with survival. No power calculation is reported.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	Yes, via an Excel random number generator and double sealed opaque envelopes (p 156)
2.	Was randomization concealed (blinded)?	Only until allocation.
3.	Were patients analyzed in the groups to which they were randomized?	Yes, data were analyzed according to original treatment assignment (p 156)
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes "the three study groups were not significantly different in any of the baseline characteristics" (p 156). Additionally subjects not enrolled during study period did not differ from those enrolled. (Table 1, p 157)
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	Yes. Blinding impossible without unethical sham NIV groups.
2.	Were clinicians aware of group allocation?	Yes, as above.
3.	Were outcome assessors aware of group allocation?	Yes, although they could have been blinded to treatment group assignment.
4.	Was follow-up complete?	No loss to follow-up was reported.
II.	**What are the results (answer the questions posed below)?**	

1.	How large was the treatment effect?	<u>Treatment Success at 2-hours</u> Control 3/20 15% **<u>NNT</u>** CPAP 7/20 35% * **5** BIPAP 9/20 45% **3** * p = 0.116 <u>Treatment Failure* *at 2-hours</u> Control 3/20 5% p=0.344 CPAP 4/20 25% BIPAP 5/20 5% **only 2 pts were actually intubated. The majority just continued on NIV. • Oxygen saturation was significantly lower than controls at 10-30 min after randomization in the CPAP group. • Resp rate decreased significantly at 10 min in the BIPAP group and 40 min in the CPAP group. • Only 55% of subjects could complete the VAS and displayed no significant differences between groups. • 5 subjects could not tolerate NIV. • No difference in MI between groups but there was a <u>non-significant trend towards increased CK-peak in the BIPAP group</u> • Pre-hospital nitrates and higher arrival systolic BP was more likely to survive but these factors lost significance in LR model. <u>Survival to Hospital Discharge</u> Control 70% CPAP 100% p=0.029 BIPAP 75%

		7-day Survival Control 85% CPAP 100% p=0.144 BIPAP 80%
2.	How precise was the estimate of the treatment effect?	No CI reported, so cannot comment on precision.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	Yes, severe CHF exacerbation with radiological pulmonary edema and respiratory acidosis.
2.	Were all clinically important outcomes considered?	Yes, mortality, treatment failure, and side-effects.
3.	Are the likely treatment benefits worth the potential harm and costs?	No cost-effectiveness analysis was performed or reported upon.

Limitation

1) **Outcome assessors not blinded.**
2) **Majority of eligible subjects not enrolled limiting external validity to all-comers presenting with acute decompensated CHF with hypoxia.**
3) **Likely underpowered study limiting reader's ability to draw any conclusions, however no power calculation was reported so readers cannot be certain.**
4) **ABG analysis is not a routine component of CHF management so endpoints not readily comparable to daily clinical care.**
5) **Two UK hospitals limit generalization to US hospitals.**

Bottom Line

Underpowered randomized trial of acute acidotic cardiogenic pulmonary edema patients presenting to one of two UK ED's demonstrating (statistically insignificant) improved two-hour treatment success with CPAP (NNT 5) or BIPAP (NNT 3), although more treatment failures were noted at two-hours in the CPAP group and a trend towards CK elevation (marker of MI?) in the BIPAP group. CPAP offers a significant advantage in survival to discharge (100%) vs. conventional oxygen (85%) or BIPAP (80%). Pre-hospital nitrates may be associated with hospital survival although Logistic Regression fails to demonstrate this observation.