Is there a role for Home NIV in COPD patients?

Dr C M Chu
MD, MSc (Lond), FRCP (Lond, Edin, Glasg), FCCP
President
American College of Chest Physicians
(Hong Kong & Macau Chapter)

Topics

1. Acute NIV in hypercapnic exacerbation of COPD
2. What happens afterwards?
3. Chronic NIV in COPD – review of RCTs
4. Critique
5. Design of an RCT of chronic NIV in COPD
6. An approach to home NIV for COPD

NIPPV in acute hypercapnic respiratory failure of COPD

Standard first line treatment in suitable patients

Evidence base for acute NIV

- Randomised controlled trials – reduced intubation, mortality
  - Bott J, et al. Lancet 1993;341:1555.
  - Brochard L, et al. NEJM 1995;333:817.
  - Kramer N, et al. AJRCCM 1995;151:1799.
  - Angus RM, et al. Thorax 1996;51:1048.
  - Celikel T, et al. Chest 1998;114:1636.
  - Martin TJ, et al. AJRCCM 2000;161:807.
  - Plant PK, et al. Lancet 2000;355:1931.

Meta-analyses

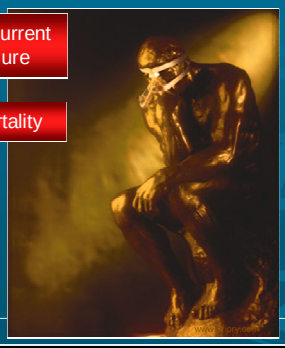
- COPD acute exacerbations with respiratory failure
- NIV is associated with:
  - Lower mortality (RR = 0.41)
  - Lower intubation rate (RR = 0.42)
  - Lower treatment failure (RR 0.32)
  - Greater improvement in pH, PaCO2, resp rate at 1 hr
  - Fewer complications (RR = 0.51)
  - Shorter hospital stay (weight mean difference = - 3.24 days)

What happens after acute NIPPV?

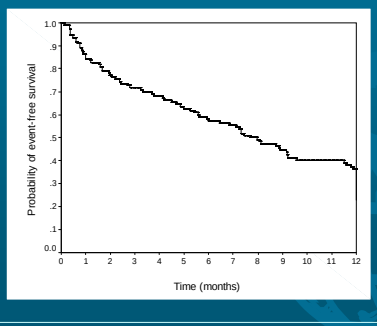
Problem of the Survivor

High rates of recurrent respiratory failure

High mortality



Probability of Event-free Survival



Recurrent AHRF: 63% in 1 year

Death ~ 50%

Chu CM, et al. Thorax 2004;59

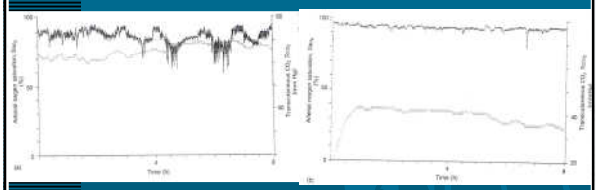
Theoretical benefit of Home (nocturnal) NIV in COPD

NIPPV reverses nocturnal hypoventilation

- Improve atelectasis
- Improve respiratory muscle fatigue
- Resetting of CO2 set-point - ↑ventilatory response to CO2 **
- Reverse daytime respiratory failure as well
- Splint upper airway (CPAP) for OSA

Nickol AH, et al. Thorax 2005;60:754.

Nocturnal Hypoventilation



Long term NIV at home

- Attractive option for chronic respiratory failure
- Acceptability of face mask and Bi-level machine
- Cheaper machines
- Obviates tracheostomy

Sleeping with non-invasive ventilation

Long term dependency on NIPPV after ARF

[Cuvelier A, et al. ERJ 2005;26:289.]

- 100 ARF due to COPD (42%) and non-COPD (58%: chest wall deformities, obesity, old TB, bronchiectasis, neuromuscular disease)
- Overall 31% required home NIPPV (39% in non-COPD; 19% in COPD)
- Lower pH on admission and non-infectious cause of ARF predicts long term dependency on NIPPV

50% home NIV in HK are for COPD

Chu CM, et al. ERJ 2004

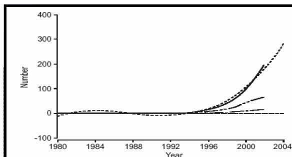


Fig. 1.–New cases (— - - - — cumulative number of home ver (- - -)).

Diagnosis	
Restrictive thoracic disorders	
Thoracic cage disorders	38 (15.3)
Post-tuberculous fibrothorax	9 (3.6)
Neuromuscular disorder	30 (12.0)
Mixed pathologies and miscellaneous	8 (3.2)
Complicated OSA/OHS	
OHS	11 (4.4)
COPD: OSA overlap syndrome	22 (8.8)
Severe OSA, intolerant to CPAP	10 (4.0)
COPD	121 (48.6)

Data are presented as n (%). OSA: obstructive sleep apnoea; OHS: obesity hypoventilation syndrome; COPD: chronic obstructive pulmonary disease; CPAP: continuous positive airway pressure. Percentages add up to 99.9% because of rounding.

Evidence in favour of home NIPPV for COPD

Uncontrolled trials

1. Jones SE, et al. Thorax 1998;53:495-498

- Home NIV in 11 severe stable COPD patients with chronic symptomatic hypercapnia
- Mean age 60, FEV_1 34.5%, PaO_2 6 kPa, $PaCO_2$ 8 kPa, followed for 24 months
- Hospital admissions, duration of stay and clinic visits were halved in the subsequent year
- a sustained improvement in arterial blood gases, ↓somnolence

2. Tuggey JM, et al. Thorax 2003;58:867−871.

- 13 COPD patients with acidotic exacerbation of COPD requiring NIPPV
- Continued with NIPPV at home, supported by nurse specialist
- Mean age 55 (7.5), pH 7.31, FEV_1 0.58L
- Mean no of admission from 5 to 2 (p = 0.007), days hospitalised from 78 to 25 (p = 0.004), ICU days 2 to 0.3, outpatient visit from 5 to 4
- Cost saving of £ 8,254 per patient (p = 0.002)

3 Positive RCTs

1. Meecham-Jones DJ, et al. AJRCCM 1995;152:538

- 14 stable COPD: median age 69, FEV1 32%, PaO2 45 mmHg, PaCO2 55.8 mmHg
- Randomised cross-over LTOT vs LTOT+NIPPV, 3 month each
- Median IPAP 18 cm H20, EPAP 2 cm H2O
- 1/14 did not tolerate NIPPV
- ↓$PaCO_2$ 4.5 mmHg, ↑PaO_2 5.9 mmHg, ↑sleep time 56 min and efficiency 8%, SGRQ score
- Improvement of $PaCO_2$ correlates with control of $TcCO_2$ at night

Improvement of ABG, sleep, HRQoL at 6 month in NIIV + LTOT group

2. Casanova C, et al. Chest 2000;118:1582

- Randomised, parallel group x 1 year; severe stable COPD
- NIPPV (n = 20) vs. standard Rx (n = 24)
- FEV_1 30%, $PaCO_2$ 51 mmHg
- IPAP 12, EPAP 4
- ↓ no. of hospital admission at 3 month (5% vs. 15%, p < 0.05), effect lost at 1 year
- Improved dyspnoea and psychomotor coordination
- No survival benefit

NIV ↓ Hospital admission at 3 mths but not > 6 mths, improves dyspnoea and psychomotor function

3. Clini E, et al. ERJ 2002;20:529

- Prospective, multicentre, randomised, parallel groups, 2 years
- 122 stable severe COPD: FEV1 29% PaCO2 54 mmHg
- NIPPV+LTOT (n = 43) vs LTOT (n = 47)
- IPAP 14, EPAP 2, 9 hour/night
- Survival same

NIV + LTOT - Improved $PaCO_2$ (5 mmHg), dyspnoea, HRQoL

Trend to reduce ICU admission from -20% to -75%

3 Negative RCTs

1. Strumpf DA, et al. ARRD 1991;144:1234.

- Randomised crossover, 3-month each
- NIPPV vs standard care
- 39 screened, 11 declined, 5 AECB, 23 enrolled, 16 withdrawn, 7 due to intolerance
- Only 7 complete both arms
- FEV_1 0.54L, 33%; $PaCO_2$ 46 mmHg
- IPAP 15, EPAP 2

No improvement in all outcome variables:

ABG, PFT, MIP, MEP, 6MWT, dyspnoea, walking time, neuropsychological

2. Gay PC, et al.Mayo Clin Proc 1996;71:533.

- Randomised, parallel, 3 month
- NIPPV (n = 7) vs. sham (n = 6)
- IPAP 10/2 vs 2/2
- Only 4/7 in NIPPV group complied
- Only 1 patient in NIPPV gp lower $PaCO_2$ from 50 to 43 mmHg

No change in PFT, ABG, PSG, O/N SaO_2

3. Lin CC. AJRCCM 1996;154:353.

- Randomised, crossover, 2 weeks
- 17 severe COPD
- NIPPV+ O_2 vs O_2
- IPAP 12 EPAP 2
- Age 65, PaC O_2 50.5 mmHg

No improvement in O/N SaO_2, ABG, heart function, PSG

Sleep poorer in NIPPV

Meta-analysis

Wijkstra PJ, et al.Chest 2003;124:337

- 164 publications + 8 abstracts
- 10 potential articles: 4 excluded (not RCT, NIPPV < 5 hr/N, training < 3 weeks); 2 unpublished
- Included 4 trials: Gay, Strumpf, Meecham-Jones, Casanova
- No improvement in: ABG, 6MWD, PFT, Sleep efficiency
- Small improvement in PImax

Critiques of RCTs on NIPPV

Author	Result	$PaCO_2$	I/E	Duration	Effect
Meecham-Jones	positive	56	18/2	3mth	ABG, sleep, SGRQ
Casanova	positive	51	12/4	1 year	3mth admission, dyspnea
Clini	positive	54	14/2	2 years	PaCO2, MRC, HRQL
Strumpf	negative	46	15/2	3 months	negative
Gay	negative	55	10/2	3 months	negative
Lin	negative	51	12/2	2 weeks	negative

Inconclusive evidence on the use of long-term NIV in COPD patients

Critique of RCTs on NIPPV

- Variable design, duration, outcome measurements
- All stable COPD
- $PaCO_2$ not high enough?
- Duration not long enough?
- Low IPAP/EPAP?
- No sham ventilation
- Poor compliance/tolerance in early studies
- In-hospital acclimatization important
- Relevant outcomes: ICU admissions, hospital admissions – not examined or not powered to examine

Considerations for RCT of home NIPPV in COPD

- Patients who survived an episode of acidotic exacerbation treated by acute NIPPV
- Already acclimatised to NIPPV
- Optimal IPAP and EPAP
- Powered to examine relevant outcomes: recurrent AHRF, hospital admission, survival, cost-effectiveness
- Sham NIPPV in control group

RCT of continuation of home NIV vs. Sham ventilation in survivors of AHRF in COPD (Supported by the HKLF)

Division of Respiratory
Dept. of M&G, UCH

An RCT of Home NIV vs Sham Ventilation for COPD after 1st episode of AHRF (UCH, HK)

- Subject – COPD + AHRF treated by acute NIV (already acclimatized)
- Exclude non-COPD causes of AHRF
- Exclude OSA
- Randomised to
  - NIPPV
  - Sham (CPAP 5 cm H_2O)
- Primary outcome – recurrent AHRF or death

Study objective

To test whether:

- continuation of home non-invasive ventilation (NIV) would
- reduce recurrent acute hypercapnic respiratory failure (AHRF)
- in survivors of chronic obstructive pulmonary disease (COPD)
- who survived an episode of AHRF treated by acute NIV

Methods

Screening

- COPD patients who survive after an episode of AHRF treated with acute NIV
- Intubated patients eligible if also treated by NIV before/after intubation
- All patients has PSG to exclude significant OSA of AHI ≥ 10/hr
- All patients received long-acting bronchodilator, inhaled steroid (equiv to fluticasone 1,000μg/day), up-to-date vaccination (pneumococcal + flu) ± LTOT as per standard indication
- Weaned from NIV or ventilator ≥ 48 hours

Randomisation

- Random numbers in sealed envelope
- Kept by non-study personnel

Intention-to-treat analysis

Sample size

- Assume event rate: sham group = 0.7, NIV group = 0.2
- Assume drop-outs 15%
- Sample size = 23 per arm to detect 50% difference (power 0.8, significance = 0.05)

Trial Registration: www.clinicaltrials.gov [NCT00429156]

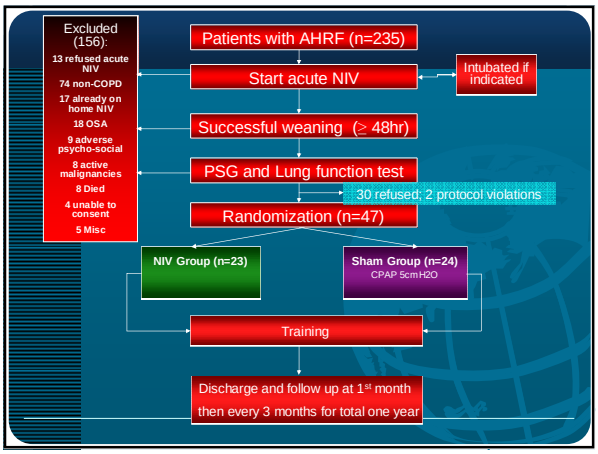
Treatment groups

Sham Ventilation

- Necessary as strong placebo effect of NIV ("Breathing machine") in a breathless patient who just experienced a life-threatening event [Elliot M, Thorax 2004]
- CPAP 5 cm H_2O
  - No change in RR, Vt, Ti, Te, SaO_2, $TcCO_2$ [Petrof BJ et al. ARRD 1991]
  - No worsening of ABG vs. NIV group [Krachman SL, et al. Chest 1997]
- O_2 as required to achieve SpO_2 > 90%

NIV group

- EPAP 5 cm H_2O
- IPAP 10 – 20 cm H2O based on pressure settings during acute NIV – max tolerated pressure to achieve Vt of 7 – 10 mL/kg
- Backup rate 14/min; Ti 1s
- O2 as required to achieve SpO2 > 90%



End-points

- Primary end-point = recurrent AHRF
- Other end-points:
  - Deaths
  - SAE
  - Compliance (build-in counter)
  - ABG
  - Health care utilization, readmissions
  - Withdrawn from the study

Baseline Characteristics

Baseline Characteristics	Group	Mean	SD	*p*
Age	Sham	71.0	7.7	0.52
	NIV	69.5	7.8	
APACHE II	Sham	16.4	3.7	0.49
	NIV	15.7	3.6	
BMI	Sham	19.7	3.5	0.59
	NIV	19.1	3.8	
FEV1 (%) within 6 months	Sham	31.3	9.3	0.24
	NIV	28.1	8.5	
Previous episode of AHRF	Sham	1.5	2.5	0.69
	NIV	1.8	2.4	
ABG pH on admission	Sham	7.25	0.06	0.06
	NIV	7.28	0.05	
ABG $PaCO_2$ on admission	Sham	80.3	24.6	0.58
	NIV	76.6	20.0	

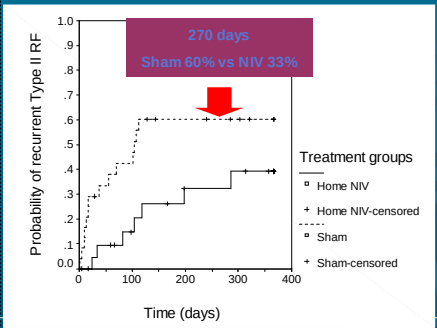
No difference in sex, MRC dyspnea score, Katz ADL score, ABG on randomisation, comorbidity, LOS, LTOT use, smoking history

Results – Compliance

Compliance (hours/night)	Group	No	Mean	SD	*p*
1st Follow-up	Sham	18	7.7	2.2	0.69
	NIV	21	7.4	2.3	
2nd Follow-up	Sham	11	7.3	2.9	0.38
	NIV	14	8.1	1.8	
3rd Follow-up	Sham	7	8.2	1.6	0.74
	NIV	12	8.5	2.2	
4th Follow-up	Sham	6	8.0	1.4	0.33
	NIV	10	8.9	2.0	

No significant difference in compliance between the two groups

Recurrent AHRF (Interim at 270 days)



Current status

- Interim data - trend for better outcome
- Currently 2 active cases still under follow-up
- Final results should be available in March 2009

Home NIPPV for COPD - Current status

Home NIPPV for COPD

consensus conference

Clinical Indications for Noninvasive Positive Pressure Ventilation in Chronic Respiratory Failure Due to Restrictive Lung Disease, COPD, and Nocturnal Hypoventilation—A Consensus Conference Report*

(CHEST 1999; 116:521–534)

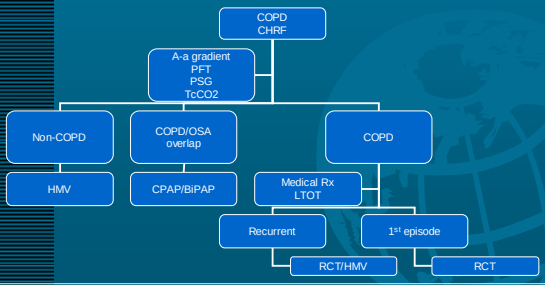
Consensus criteria for Starting Home NIPPV in COPD

SELECTION GUIDELINES: LONG-TERM NONINVASIVE VENTILATION FOR OBSTRUCTIVE LUNG DISEASES

1. Symptoms:
   Fatigue, hypersomnolence, dyspnea, etc. and
2. Gas exchange abnormalities:
   Pa_{CO_2} ≥ 55 mm Hg or
   Pa_{CO_2} 50 to 54 mm Hg and O_2 sat < 88% for > 10% of monitoring time despite O_2 supplementation and
3. Failure to respond to optimal medical therapy:
   Maximal bronchodilator therapy and/or steroids
   O_2 supplementation if indicated
4. Failure to respond to CPAP therapy if moderate to severe obstructive sleep apnea
5. Reassess after 2 mo of therapy; continue if compliance is adequate (> 4 h/24 h), and therapeutic response is favorable.

COPD
Chronic Hypercapnic Respiratory Failure

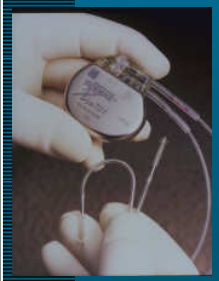
Not all patients with chronic respiratory failure are due to COPD!!



Conclusion

- Acute NIV is the standard of care in AHRF of COPD without contraindications
- In COPD, acute NIPPV does not prevent recurrent respiratory failure
- Throughout the world, tremendous rise in home NIPPV (no. and $)
- Urgent need for RCT of long term NIPPV in COPD

Pacemakers for chronotrophic failure



ICD

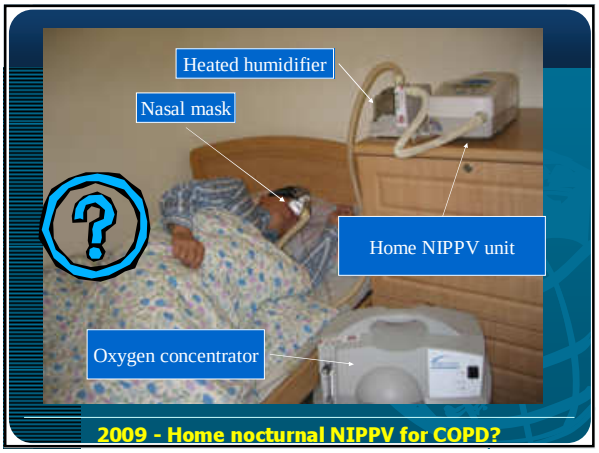
Pacemakers

Dialysis for renal failure

Cycler PD

HD

CAPD



2009 - Home nocturnal NIPPV for COPD?

Thank you