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## ROLE OF NONINVASIVE VENTILATION IN HYPERCAPNIC RESPIRATORY FAILURE

Over the last two decades, noninvasive positive pressure ventilation (NIPPV) has developed as an exciting tool for management of respiratory failure without endotracheal intubation. Though initially developed for the domiciliary management of chronic hypercapnic ventilatory failure in preference to negative pressure ventilation, this technique has subsequently been used successfully for in-hospital management of acute or chronic respiratory failure.

### I. Noninvasive ventilation in type II respiratory failure

- A. Chest wall deformity : Early onset scoliosis  
Thoracoplasty/sequelae of TB
- B. Non/Slowly progressing neuromuscular conditions
  - Central hypoventilation syndrome
  - Spinal cord injury : Tetraplegia
  - Poliomyelitis
  - Diaphragmatic palsy
  - Metabolic myopathies, congenital myopathies
  - Spinal muscular atrophy
- C. Progressive neuromuscular disorders
  - Duchenne muscular dystrophy
  - Motor neuron disease
- D. Obstructive lung disease - Chronic obstructive airway disease (COAD)
  - Bronchiectasis
  - Cystic fibrosis

### II. Role of noninvasive ventilation in COAD

- a. **Severe stable COAD** : Large long term retrospective or uncontrolled trials have shown that the survival benefit with noninvasive positive pressure ventilation (NIPPV) is comparable to long term oxygen therapy (LTOT) and a combination of NIPPV and domiciliary therapy is probably better than domiciliary oxygen alone.

The following objective outcomes have been shown with the use of NIPPV:

- Improved daytime PaO<sub>2</sub> and PaCO<sub>2</sub> : correlated with improvement in mean overnight PaCO<sub>2</sub>
- Total sleep time

- Sleep efficiency
- Quality of life

At the present time, with the available evidence, the use of NIPPV is indicated in the following patients with severe COAD :

1. Symptoms of ventilatory failure
2. Physiologic criteria - one of the following :
  - i. PaCO<sub>2</sub> < 55 mmHg
  - ii. PaCO<sub>2</sub> of 50-54 mmHg + Nocturnal desaturation (SPO<sub>2</sub> < 88% for > 5 min on O<sub>2</sub> 2L/min)
  - iii. PaCO<sub>2</sub> of 50-54 mmHg and hospital admissions related to recurrent episodes of hypercapnic respiratory failure (2 or more in 12 month period)

Other indications for use of NIPPV are -

1. Patients who cannot tolerate LTOT
2. Patients with intractable right heart failure and peripheral odema.

There is no place for nocturnal NIPPV in patients of COAD without sustained day time hypercapnia.

### **B. Exacerbations of COAD and acute respiratory failure**

16-35% of acute exacerbations need assisted ventilation with an overall mortality of 12-20%.

#### **1. Advantages of NIPPV**

- a. Better outcome than conventional management
- b. Lesser complications as compared to endotracheal intubation and ventilation
- c. Can be offered even to patients with severe COAD who otherwise are not considered for intubation
- d. Gives the patient time to make his choice regarding intubation and ventilation
- e. Hypoxemia can improve without worsening of acidosis
- f. Can be applied in general ward or emergency room
- g. Clinical improvement is sustained - re-admission to ICU is rare
- h. Significant reduction in duration of ventilation and stay in ICU

#### **2. Selection criteria :** the following are widely followed

- a. PH < 7.35 and PaCO<sub>2</sub>>45 mmHg
- b. RR > 30/min

- c. PaO<sub>2</sub> on room air < 50 mmHg

#### **3. Speed of response**

- a. pH can be significantly improved at 1 hr.
- b. Significantly decreased encephalopathy score at 1 hr.
- c. Decreased respiratory rate at 1 hr. suggesting decreased work of breathing.

#### **4. Exclusion criteria**

- a. Patients requiring immediate endotracheal intubation
- b. Recent cardiac arrest
- c. Patients requiring other specific treatment for deterioration - myocardial infarction, pulmonary thromboembolism, septic shock

#### **5. Factors predicting outcome :** Following are bad prognostic factors :

- a. Pneumonia and pulmonary oedema as causes of exacerbations
- b. Underweight
- c. Greater level of neurological deterioration
- d. Higher APACHE II score. Reduced level of compliance and NIPPV.

Baseline pH has significant independent predictive value of eventual success. Improvement and absolute value of pH and PaCO<sub>2</sub> after initial trial of NIPPV also predict success.

#### **6. Mode of ventilation :**

Both volume cycled and pressure limited NIPPV have been used successfully in COAD patients with acute exacerbations and respiratory failure. Ventilators which are used should have a sensitive trigger as these patients have an irregular breathing pattern and intrinsic PEEP reduce the effective trigger sensitivity.

#### **7. Duration of ventilation :**

Reported studies have used NIPPV between 4-8 days from admission. First 24 hour treatment is most important for reversal of acidosis. A useful strategy will be to use NIPPV as much as possible for first 24 hours and then to continue NIPPV overnight for 7 days or until improvement occurs. Weaning difficulties have not been reported with the use of NIPPV.

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## C. NIPPV and weaning of patients from mechanical ventilation :

NIPPV has been successfully used in some studies to decrease the period of weaning from mechanical ventilation by deliberate early extubation followed by institution of NIPPV. However, more evidence is required before this practice is routinely followed.

## III. NIPPV in chest wall disorders and neuromuscular diseases :

Substantial evidence is there to support the beneficial role of NIPPV in these disorders

### Indications for use:

1. Symptoms of hypoventilation (such as fatigue, dyspnoea, morning headache etc.); and
2. Physiologic criteria (one of the following)
  - a. PaCO<sub>2</sub> > 45 mmHg
  - b. Nocturnal oximetry demonstrating oxygen desaturation < 88% for 5 consecutive minutes.
  - c. For progressive neuromuscular disease, maximal inspiratory pressure < 60 cm H<sub>2</sub>O or Forced Vital Capacity (FVC) < 50% predicted.

In patients with rapidly progressive neuromuscular diseases, NIPPV prolongs survival but there are a number of possible problems related to extending life by mechanical

ventilation :- (i) life of marginal quality, (ii), loss of dignity, (iii) inability to communicate, (iv) disruption of life of other family members and, (v) difficulty in stopping high technology life sustaining care once it has been started. All these ethical issues should be considered and discussed with the patient and the family before starting NIPPV.

## IV. NIPPV in patients with alveolar hypoventilation e.g. Idiopathic central sleep apnoea

Central alveolar hypoventilation  
Obesity hypoventilation syndrome  
Obstructive sleep apnoea

### Indications for usage

- a. Documented diagnosis
- b. Failure to respond to first line therapy in mild cases of hypoventilation (including CPAP in OSA)
- c. Moderate to severe hypoventilation

**Ref.:** 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).

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## SLOWLY RESOLVING PNEUMONIAS

Slowly resolving pneumonias constitute a variant of clinical pattern of community acquired pneumonias (CAP) which all clinicians must be familiar with. Non resolution or slow resolution may reflect a host of factors which have to be considered. When should these alternatives be considered, how long to wait before embarking on further investigations, what is the expected time course of resolution - these are some of the questions which have to be answered when confronted with a patient with a slowly resolving pneumonia.

**Definition:** "Non resolving" and "slowly resolving" are terms which have been used interchangeably. They refer to the condition when in the setting of a community acquired pneumonia, radiographic abnormalities persist

beyond the "expected time course of resolution". The expected time course is quite arbitrary and subject to controversy. The various definitions used in the past had been: (1) Pulmonary consolidation persisting for more than 21 days; (2) Focal infiltrates which begin with some pulmonary infection and do not resolve in expected time<sup>2</sup> ; (3) Patients of CAP who have improved clinically, defervesced with antibiotics showing <50% clearing by two weeks or less than complete clearing at four weeks on the CXR<sup>3</sup>.

### Predisposing factors

#### a. Host factors :

1. **Age** - Several studies have unequivocally demonstrated higher incidence in the elderly age group<sup>4</sup>. In one study, it was the

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persistence of radiological infiltrates at 4 wks (24.5% in patients of >50 years age Vs 6.6% in the younger) which was statistically significant. There is age related impairment of several components of host defences. As the lung ages, it loses elasticity, tracheal mucus velocity declines, respiratory muscles weaken and the strength of the cough declines.

**2. Co-morbid illness** - leads to an atypical response to a common infection resulting from an abnormality of host defense. In one study of slowly resolving CAP, associated diseases were found in 96% patients. Associated co-morbid illnesses are : COPD (emphysema and chronic bronchitis), pneumoconiosis, bronchial asthma, diabetes mellitus, heart failure, ethanol abuse, obstructive lesions, cerebrovascular disease and cigarette smoking.

**3. Immune status of patient** - Chronic corticosteroid therapy, immunosuppressive therapy, underlying malignancy.

**b. Agent factors :**

Depending on the micro-organism, the expected time course of resolution will vary. Mycoplasma and clamidia resolution is the earliest at around 2-6 wks, longest in Legionella infection i.e. 16-24 wks. In S. pneumonia infection, follow up CXR is recommended at 6 wks; complete resolution usually occurs at 4-6 mths and bacteraemia leads to a slower resolution.

**c. Extent of disease :** Single Vs multi lobar involvement, presence of absence of bacteremia, pleural involvement, abscess formation and radiological deterioration for the first 1-2 wks are factors contributing towards slow resolution.

**EVALUATION OF NON RESOLVING / WORSENING PNEUMONIA**

- ◆ Reconsider diagnosis - a host of pneumonia mimics are to be considered.
- ◆ Reconsider aetiologic diagnosis.
- ◆ 10% of CAP are polymicrobial.
- ◆ Are you dealing with a resistant micro-organism ?
- ◆ Is the antibiotic appropriate ?
- ◆ Consider tuberculosis / actinomycosis / nocardia.
- ◆ Is it a sequestered infection ?

- ◆ Has the patient developed a post-obstructive pneumonia ?
- ◆ Has a metastatic infection occurred ?
- ◆ Always consider drug fever.

**Non infectious aetiology :** Consider a non-infectious aetiology when the course of disease is indolent, there is a less startling presentation, cough is non-productive or if expectoration is not purulent. Some of the non-infectious pneumonia mimics are listed below :

- BOOP (Bronchiolitis Obliterans with Organizing Pneumonia).
- Hypersensitivity pneumonitis
- Drug induced pneumonia
- Eosinophilic pneumonia
- Lupus pneumonitis
- Pulmonary vasculitis
- Alveolar haemorrhage syndrome
- Connective tissue disorders
- Chronic granulomatous disease
- Radiation pneumonitis
- Pulmonary neoplasms

Pulmonary neoplasms are to be suspected when the clinical setting is appropriate. Pulmonary neoplasm should be considered in the differential diagnosis of a non-resolving pneumonia especially in the following situations:

- endobronchial occlusion
- bronchioloalveolar carcinoma
- primary-pulmonary lymphoma
- lympho-proliferative disorders

**MANAGEMENT**

The question which arises in the clinical situation of a slowly resolving pneumonia is when to and when not to pursue an aggressive diagnostic workup which may be expensive as well as invasive.

Patient may be safely observed for 4-8 wks when

- The presentation is typical.
- Symptomatic improvement is present
- "At risk" factors are identified

Investigate further when

- No risk factors are present
- Suspicion of non-infectious aetiology
- Lack of at least partial resolution even in asymptomatic patient at <6 wks. Further investigative work up has to be individualized. It may vary from non-invasive serological tests,

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and CT scan to an open lung biopsy. It should be remembered that a slowly resolving pneumonia is not an indication for prolonging antibiotic therapy. Pulmonary tuberculosis is always to be strongly considered in our setting. The mortality rate is low, comparable to that of CAP.

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## MUCOCILIARY DYSFUNCTION : TREATMENT (Part II)

**1. Beta adrenergic agonists and methyl xanthines** : These agents increase the intracellular CAMP which in turn increases ciliary beat frequency and mucus secretion. This effect may not be sustained overtime. A number of studies reported that short and long term treatment with aminophylline or theophylline improves mucociliary clearance in patients with airway obstruction.

**2. Gluco corticosteriods** : There is improvement of peripheral mucociliary clearance in asthmatics after treatment with oral prednisolone for a total of 4 weeks. In a short term trial however, beclomethasone did not stimulate mucociliary clearance in patients with obstructive lung disease. The mechanism of glucocorticoid action is by improvement in airway inflammation.

**3. Mucolytic agents** : These agents are used to facilitate ciliary and cough clearance of excessive lower airway secretions by optimizing the rheological properties.

**a. N-acetyl Cysteine** : Break disulfide bonds by depolymerizing the glycoconjugate molecule and thereby reducing mucus viscosity. This was effective in liquefying mucus in vitro but no controlled studies exist showing that N-acetyl cysteine improves mucociliary clearance in humans. Furthermore, N-acetyl cysteine can cause significant bronchospasm in patients with airway disease when delivered by inhalation. Also, N-acetyl cysteine penetrates poorly into sputum when given systemically.

In 1985, the British Thoracic Society issued a statement after reviewing data on the use of

oral N-acetyl cysteine in patients with severe COPD and concluded that N-acetyl cysteine may prevent one half to one exacerbation per patient per winter and that the cost and inconvenience of taking this medication did not seem to justify its routine use in patients with severe COPD. S-carboxy methyl cysteine, another disulfide bond-breaking drug has no demonstrable effect on radioaerosol clearance in patients with chronic bronchitis or on tracheal mucus velocity.

**b. Iodinated glycerol** : It is secreted by epithelium into airway lumen, thereby increasing the water content of the airway lumen and the airway surface liquids and thus decreasing mucus viscosity. Although some symptomatic improvement occurs, there are no controlled studies to demonstrate the effects by more objective measures on mucociliary clearance or mucus rheology.

**c. Guaifenesin** : Used as expectorant, the drug is detectable in sputum after oral administration. Mucus clearance is shown to increase in bronchitis patients. This has been challenged in another study where it is found that guaifenesin given to patients with chronic bronchitis, was ineffective in improving symptoms, mucus rheology or lung function.

**d. Aerosolized detergents** : These are used in the hope that they would improve the rheology of mucus and facilitate its clearance by

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cough. Oxymix (a mixture of ascorbic acid, copper sulfate and sodium percarbonate) has been reported to decrease sputum viscosity. But other studies have failed to confirm the effects.

**e. Bromhexine** : It fragments acid mucopolysaccharide. Some trials have shown that patients receiving bromhexine had a somewhat greater reduction in sputum volume and less difficulty in expectoration when compared to those treated with placebo.

Ambroxol, a bromhexine metabolite, failed to improve mucociliary clearance, pulmonary function and overall symptoms in placebo controlled trials.

**f. Nebulized indomethacin** : has been shown to decrease sputum volume. But this data need confirmation.

In summary, the current scientific evidence do not seem to justify the use of any of these mucolytic drugs in clinical practice. Rare exception might be the local application of N-acetyl cysteine through the working channel of a bronchoscope to liquify mucus plugs.

**4. DNAase** : DNA released from degenerating neutrophils and shed epithelium accumulate in the sputum of patients with cystic fibrosis and bronchiectasis, DNA induces significant changes in mucus rheology, increasing its viscosity dramatically. Human DNAase is well tolerated and it improves symptoms and lung function. A decrease in number of respiratory tract infections has been associated with this therapy in patients with cystic fibrosis.

**5. Bland aerosols** : Although mist therapy is commonly used to treat children with upper airway infection, there is no evidence that aerosol therapy is superior to air humidification. Hypertonic saline is used to induce sputum in patients who do not have productive cough but it does not improve lung function.

## **6. Physical Therapy**

**a. Postural drainage** : In patients with expectoration, postural drainage alone will improve overall mucus clearance by moving secretions to the central airways where cough clearance is more effective. A 20° - 40° head down position is used. Postural drainage on its own is not particularly useful if cough is suppressed. It has to be combined with other

physical therapy modalities.

**b. Forced expiration technique and directed cough** : This involves forced expiration manoeuvre repeatedly from mid to low lung volumes. The achieved gas liquid interactions are sufficiently effective to increase overall clearance of mucus.

Directed cough in which patient is trained and encouraged to perform deep coughs, is an efficacious and cost-effective method to improve mucociliary clearance.

Rapid inhalation combined with directed coughing has also been shown to increase mucociliary clearance.

**c. Oscillation** : Oscillation manoeuvres displace mucus from airway wall by vibration. This increases the volume of expectorated sputum. But studies have failed to detect advantages of chest percussion/vibration over postural drainage/forced expiratory manoeuvres in patients with cystic fibrosis. The failure of manual percussion may be due to the relatively low frequencies achieved with this technique.

Higher frequencies can be achieved by mechanical devices. One of the device is the Flutter which generates air flow oscillations at the airway opening.

Although Flutter treatment increases the amount of sputum which is expectorated, there are no proven benefits of this device on lung function or on radio aerosol clearance.

Mechanical chest wall oscillation devices with optimal frequency around 15 Hz have been shown to effectively increase mucus clearance. Forced oscillations with expiratory flow hold great promise but further investigations are needed before they can be recommended for routine chest physiotherapy.

**Conclusions** : Both drug therapy (e.g. inhaled beta adrenergic agonist) and physical therapy seem to benefit patients with impaired ciliary clearance but none of these modalities is effective alone. Most patients should receive combinations of the two. Nevertheless, the present day therapy for mucociliary dysfunction remains unsatisfactory.

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