

Non-infectious approach to ventilator-associated pneumonia (VAP) in neonates: a new concept

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Definition of VAP

Ventilator-associated pneumonia (VAP) by the centers for disease control and prevention (CDC) definition is a type of hospital acquired pneumonia (HAP) among intensive care units admitted patients with a prior 48-hour continuous respiratory assistance through either tracheostomy or endotracheal tube (ETT) (1). This may increase hospital stay, treatment cost and mortality rate. Among neonates, VAP rates varies from 0.9 (birth weight <750 gr) to 2.6 (Birth weight >2500 gr) /1000 ventilator-day (2). Even as high as 37.2 cases /1000 ventilator days is reported (3).

Etiology and Diagnosis

Pathogens gain access to the respiratory tract mainly during respiratory care and via usage of equipments (e.g. ETT, suctioning and pulmonary toileting solutions) or from preceding systemic bacterial infection and frequent micro aspiration of upper gastrointestinal content, as alternative routes. According to current guidelines, any infant younger than 1 year should be worked up for probable VAP with worsening gas exchange and at least three of the following: (1) temperature instability with no other recognized

cause, (2) leukopenia (WBC <4000 /mm³) or leukocytosis (WBC ≥15000 /mm³) and left shift (≥10% band form), (3) new onset of purulent sputum, or change in character of sputum or increase in respiratory secretions or increase in suctioning requirements, (4) apnea, tachypnea, nasal flaring with retraction of chest wall or grunting (5) cough, wheezing, rales or rhonchi (6) bradycardia or tachycardia (<100 and >170 beats/min, respectively). Moreover, neonates with underlying diseases which have 2 or more x-rays with one of the following: (1) new or progressive and persistent infiltrates (2) consolidation (3) cavitations and (4) pneumatoceles (4).

Current preventive believes and concepts

Risk factor for VAP among neonates may addressed to the number of re-intubation, duration of the mechanical ventilation and NICU stay, low birth weight and prematurity, muscular blockade, preceding blood stream infection and frequency of suctioning (2,3). Various microbiological assessments are introduced with different sensitivity and specificity (e.g. tracheal aspirate culture, protected specimen brush, bronchoalveolar lavage and combination of mentioned methods) (2). Different diagnosis criteria and various confirmatory methods may ra-

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tionalize the diverse reported rates from different centers.

New concept: evidence of pros and cons

Along with many aspects of VAP-preventive bundle (e.g., caregivers hand hygiene, head of the bed or lateral decubitus positioning, peptic ulcer disease prophylaxis and staff education), preventing methods from any iatrogenic disturbance in integrity of pulmonary barriers and cellular malfunction should be better reevaluated in order to attenuate proceeding mishaps of presence of pathogens in respiratory tract (2). Repetitive alveolar collapse during ventilation phase may lead to release of inflammatory cytokines with further epithelial damage, which is the so-called *Biotrauma* or *Atelectotrauma* (4). In addition, premature neonates with respiratory distress syndrome who requires higher level of fraction of inspired oxygen (F_{iO_2}) in combination with incompetent anti oxidative system are exposed to high levels of oxidant free radicals of ongoing production through vulnerable airways. The cascade of cytokine release within respiratory system may accelerate the transition of early pneumonitis to complete pneumonia besides aggravation form systemic inflammation response syndrome (SIRS) to sepsis and ultimate multi organ failure dysfunction syndrome (MODS). This condition, may vice-versa deteriorate lung health and function.

Suggested strategies

1. Early surfactant administration with nasal CPAP while avoiding high tidal volume may preserve lung compliance at a desirable level, if started in early hours of life especially for neonates born prematurely (4). Such approach probably decreased intubation rate and probably VAP rates in NICUs.

2. Biotrauma may be prevented by keeping reasonable volume at end-expiratory phase with a sufficient PEEP (4). A sufficient PEEP may be achieved when titration of PEEP is accomplished with the aid of ABG records accompanying cautionary monitoring of real pulmonary graphs (i.e., PEEP of

2cmH₂O more than lower inflation point in pressure-volume loops).

3. Higher ventilator rates with smaller tidal volumes may reduce air leak syndrome. *Permissive hypercapnia* ($Paco_2$ as high as 55mmHg) when implemented in selected cases has many advantages (5,6). Hypercapnic acidosis inhibits activation of nuclear factor_κB (NF_κB) and down regulates adhesive molecules, IL₁ and IL₈, preventing from neutrophil invasion to the epithelial cells. Also, in acidic pH, superoxide formation, and bacterial lipopolysaccharide induced macrophage activation and oxidative burst are decreased, hence lung is protected from complications of infection (4).

4. *Permissive hypoxemia* (Spo₂ 82-88%) means accepting normal values instead of supra normal values. This technique diminishes free radical damages of respiratory system (6).

Conclusion

One should remember that these benefits should be balanced against irreversible cerebral damage following severe hypoxemia and hypercapnia (5). Briefly, selecting appropriate ventilator setups with regards for possible indication of *permissive hypoxemia and permissive hypercapnia*, would help the respiratory system to maintain its function and integrity that make it less vulnerable in the case of bacterial, fungal or viral colonization and infection, by which incidence of VAP may be reduced. Hence, in addition to infectious preventive approaches, such non-infectious approached should be considered when an optimal delivery of health care is decided.

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