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Research Article

Mechanical Ventilation and Secondary Infections in Infants with Bronchiolitis

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Abstract

Background: In this study we evaluated mechanical ventilation (MV) and Secondary bacterial infections (SBI) in infants with bronchiolitis. **Methods:** This is a retrospective chart review analyzing the MV course, complications and SBI in bronchiolitis infants. Descriptive statistics and unpaired t-tests were used to compare the data. **Results:** There were 32 infants with mean age of 2.2 ± 2.1 months, 56% were premature, 17 (53%) had Respiratory syncytial virus (RSV) and no mortality. Pressure control (PC) ventilation was used in 22 (68%) and volume control (VC) in10 (32%) patients. Initial Peak inspiratory pressures (PIP) were 26 ± 5 cm of H_2O, Compliance was 0.4 ±0.1 ml/kg/cm of H_2O, oxygen requirement was 67 ± 26%. Average duration of ventilation was 3.9 ±2.6 days. PIP was lower in PC compared to VC ventilation (24 ± 4 versus 28 ± 5 cm of H_2O, with equivalent tidal volumes, p =0.04). MV duration was longer in preterm infants (5 ± 3.3 versus 2.9 ± 1.1 days, p =0.02). and in infants with poly-viral infections (5.3 ± 4.5 versus 3.4 ±1.6 days, p =0.09). Eighteen patients (56%) had SBI. These had longer MV compared to infants with no SBI (4.8 ± 3.1 versus 2.6 ±1.3 days, p =0.017). Hemophilus influenzae (31%), Moraxella catarrhalis (22%), Streptococcus pneumoniae (18%) were common organisms. **Conclusion:** Average duration of MV in bronchiolitis infants is 4 days with low mortality with 56% incidence of SBI. Prematurity, poly-viruses and SBI are risk factors for longer duration of MV.

Keywords: Mechanical Ventilation; Bronchiolitis; Infants; Secondary Infections; Pediatric Intensive care

Introduction

Acute viral bronchiolitis is common cause of hospitalization and accounts for 2-3% of all admissions in children < 1 year of age [1-4]. Respiratory syncytial virus is the most common of many viruses causing bronchiolitis in children and is associated with severe illness in premature infants [1-3]. Pediatric intensive care unit (PICU) admissions for bronchiolitis has increased from 16% in 2010 to 21% in 2019 and use of non-invasive mechanical ventilation (NIMV) also has increased from 1.2% to 9.5% during the same period [5]. Even though use of NIMV has increased, a significant proportion of bronchiolitis infants develop severe disease and require mechanical ventilation. Mechanical ventilation rate in bronchiolitis varies from 10 to 15 % for RSV bronchiolitis and 25% for non-RSV bronchiolitis [6,7].

The studies of mechanical ventilation in bronchiolitis infants are not many. In a recent study median duration of mechanical ventilation in bronchiolitis was 7 days with 70% incidence of secondary bacterial infections [8]. A small study looking at respiratory mechanics in bronchiolitis states that elastic component of respiratory system was more important than the resistive component in bronchiolitis infants requiring mechanical ventilation [9]. In our study of infants with severe viral bronchiolitis, we evaluated the basics of mechanical ventilator characteristics, duration of mechanical ventilation in different subset of patients and incidence and type of secondary bacterial infections.

Materials and Methods

Study design

This study was approved by the Driscoll children's hospital institutional review board. This is a retrospective chart review study of infants with bronchiolitis admitted to our 22-bed tertiary care PICU and received mechanical ventilation during the period of 10 years from January 2012 to December 2021.

Inclusion criteria

a) Primary diagnosis of viral bronchiolitis

b) Age less than one-year

c) Mechanical ventilation treatment.

Acute bronchiolitis for this study is defined as children presenting with respiratory symptoms of cough, congestion, tachypnea and increased work of breathing with a positive diagnostic viral test and absence of any other causes like cardiac disease or sepsis for presenting symptoms. Severe bronchiolitis is defined as children with bronchiolitis requiring mechanical ventilation. Pre-term infant is defined as an infant with a gestation age of 35 weeks or less

Exclusion criteria

a) Presence of cyanotic congenital heart disease or pulmonary hypertension

b) Presence of bronchopulmonary dysplasia requiring oxygen at home

c) Pre-existing tracheostomy.

Data Collection and Analysis

Demographic data, Ventilatory data with mode of ventilation, duration of ventilation, Ventilatory pressures, oxygen requirement, complications, pertinent laboratory data, infection data with culture results, blood transfusion and antibiotics use were collected for analysis.

Statistical analysis

Descriptive statistics were used to describe demographic data and hospital information. The data variables are expressed as means and standard deviation unless specified. Unpaired T-tests were done to compare the difference between the groups. Statistical analysis was performed using GraphPad Prism version 9.3.1 GraphPad software, San Diego, California, USA. Statistical significance was set at p value > 0.05

Results

There were 32 eligible infants with bronchiolitis who received mechanical ventilation during this study period and 18 infants (56%) were preterm infants (≤ 35 weeks) and none of the preterm infants in this study had oxygen requirements at home.

At the same period there were 750 infants admitted to the pediatric floor and 140 (18.6%) patients to PICU. Among 140 patients admitted to PICU, 32 (22.8%) required intubation and the remaining 108 (77.2%) of the patients were treated with High flow nasal cannula (HFNC) oxygen.

The intubation rate was 4.2% for all patients and 22.8% for PICU patients. Demographic information of the patients is shown in (Table 1) There was no mortality in our study.

Characteristics	Measures
Age	2.2 ± 2.1 months (range 2 weeks to 10 months)
Gender	18 (56%) Boys, 14 (44%) girls
Weight	4.2 ±1.6 kg
Gestational age	36 ±3 weeks, 18 (56%) were premature infants (≤35weeks)
Ethnicity	Hispanic 24 (75%), non-Hispanic 8 (25%)

Table 1: Demographic data.

Mechanical ventilation

Clinical characteristics

All patients who required intubation developed hypoxia with oxygen saturations < 85% despite being on supplemental oxygen. Infants showed hypercarbia with respiratory acidosis at the time of intubation. Initial pH on blood gas analysis at the time of intubation was 7.12 ±0.9 and PCO_2 was 55 ±17 mm hg. Oxygen requirement on initial ventilatory settings was 67 ±26%.

Ventilatory course

Pressure control (PC) ventilatory mode was used in 22 (68%) patients and Volume control (VC) in 10 (32%) patients. On the first day of ventilation, Peak inspiratory pressures were 26 ±5 cm of H_2O, Compliance was 0.40 ± 0.11 ml/kg/cm of H_2O, Tidal volumes were 7.9 ± 1.6 ml/kg. Within 24 hours of mechanical ventilation patients' clinical status improved significantly. At 24 hours of ventilation pH improved to 7.36 ±0.07, PCO_2 decreased to 49 ± 10 mm hg and oxygen requirement was < 60% (59 ± 25%)

Average duration of mechanical ventilation was 3.9 ± 2.6 days. Clinical parameters comparison at the time of intubation and extubation are shown in (Table 2). In PC mode of ventilation Peak inspiratory pressures (PIP) were lower compared to VC mode for equivalent amount of tidal volume and duration of mechanical ventilation was similar in both modes. This is shown in (Table 3).

Parameter	At intubation	At extubation
pH	7.12 ± 0.9	7.38 ± 0.9
PCO_2	55 ±17 mm hg	46 ±7 mm hg
PIP in cm of H_2O	26 ± 5 cm of H_2O	23 ± 3 cm of H_2O
Compliance	0.40 ± 0.11 ml/kg/cm of H_2O	0.52 ±0.13 ml/kg/cm of H_2O
Oxygen requirement	67 ± 26%	40 ± 13 %

Table 2: Comparison of clinical parameters at the time of intubation and extubation; PCO_2= Partial pressure of carbon dioxide, PIP= Peak inspiratory pressures.

Parameter	Pressure control (n=22)	Volume control (n=10)	P-value
Peak inspiratory pressure (PIP) in cm of H_2O	24 ± 4	28 ± 5	0.04
Tidal volume	7.9 ± 1.7	7.8 ± 1.4	0.9
Duration of mechanical ventilation in days	3.8 ± 1.65	4.5 ± 4	0.5

Table 3: Ventilatory mode comparison.

Duration of mechanical ventilation in pre-term infants (Gestational age ≤ 35 weeks) is longer by 2 days when compared to term infants and other ventilatory parameters were similar in both groups and this is summarized in (Table 4).

Measure	Preterm infants (n=18)	Term infants (n=14)	P-Value
Initial pH	7.29 ± 0.13	7.28 ± 0.14	0.8
Initial PCO_2	51 ± 17	56 ± 16	0.37
Peak inspiratory pressures (PIP) in cm of H_2O	25 ± 5	27 ± 5	0.23
Compliance (ml/kg/cm of H_2O)	0.42 ± 0.1	0.39 ± 0.12	0.45
Tidal volume (ml/kg)	7.7 ± 1.2	8.1 ± 2	0.56
Mechanical ventilation duration	5 ± 3.3	2.9 ± 1.1	0.02

Table 4: Mechanical ventilation comparison between pre-term and term infants.

Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis in both term and preterm infants. Viruses causing bronchiolitis are shown in (Table 5). Duration of MV when RSV is pathogen is 4.8 ± 3.2 days, when RSV was not present MV duration was 3.1 ±1.5 days (P=0.069). When bronchiolitis was caused by single virus MV duration was 3.4 ±1.6 days, whereas when two or more viruses were present MV duration was 5.3 ± 4.5 days (P=0.09).

Viruses	Term infants	Preterm infants	Total
Respiratory syncytial virus	8	9	17
Rhino/enterovirus	9	4	13
Metapneumovirus	1	2	3
Parainfluenza	2	1	3
Corona Virus	1	2	3
Mixed 2 or more viruses	6	2	8

Table 5: Viral pathogen causing bronchiolitis.

Blood transfusion was administered to 6 (18%) of children in this study. Four children had Hb of < 7 g/dl and other two had Hb of 9 gm/dl. Average duration of mechanical ventilation in children with blood transfusion was 6.6 ± 5 days and in children without blood transfusion was 3.2 ± 1.7 days (P=0.03). Odds ratio for blood transfusion with mechanical ventilation longer than 4 days or more is 2.6.

Secondary bacterial infections

In this cohort, 18 (56%) of infant's had associated respiratory bacterial infection with colony count in tracheal culture of > 100, 000 colony-forming units. Blood cultures were positive in two patients. One patient had fungal infection with candida albicans in the tracheal culture. Urinary tract infection (UTI) was less frequent and was found in only two patients. One patient had Escherichia coli, and another had enterococcus infection. Most children, 27 out of 32 (84%) received antibiotic covering gram-positive and gran-negative organisms (ceftriaxone or cefepime and vancomycin) after intubation. Children with secondary bacterial infections received 8-12 days of antibiotics and in children without secondary bacterial infections antibiotics were discontinued after 48 hours. White blood cell (WBC) counts were similar in both infected and non-infected groups, with WBC count of 14,700 ±12500 /µL and 12200 ± 6300 /µL respectively (P=0.5). Children with secondary bacterial infections had longer mechanical ventilation 4.8 ± 3.1 days compared to children without secondary infections 2.6 ±1.3 days (P=0.017). Pathogens causing secondary infections in these children are shown in (Table 6).

Pathogens	**Number of patients** (n=18, 100%)
Haemophilus influenzae	10 (55%)
Moraxella catarrhalis	7 (38%)
Streptococcus pneumoniae	6 (33%)
Streptococcus viridans	1 (5%)
Staphylococcus aureus, Methicillin sensitive	1 (5%)
Serratia Marcescens	1 (5%)
Pseudomon**as** aeruginosa	1 (5%)
Escherichia coli	1 (5%)
Mycoplasma Pneumoniae	1 (5%)
Candida albicans	1 (5%)
Mixed infections (2 or more)	9 (50%)

Table 6: Secondary infections in children with bronchiolitis on mechanical ventilation.

Other factors

Most children 27 (84%) had central venous line or peripherally inserted central line and 4 (12.5%) of children had arterial line placed for management. Scheduled albuterol nebulization was used in 18 (56%) of children and all children received as needed albuterol nebulization. Hypertonic saline nebulization was used in 28 (87%) of children. Intravenous methylprednisolone was used in 22 (68%)

of children. All children were fed by enteral route and all children had gastric prophylaxis with either famotidine or esomeprazole. High frequency oscillatory ventilation and veno-venous ECMO was used in one patient. Two children had pneumothorax. Only 3 patients (10%) were discharged home on oxygen.

Discussion

This is a single center limited study with small number of patients with retrospective analysis of the data. In this study we have described the clinical course of bronchiolitis infants who required mechanical ventilation and incidence of secondary bacterial infections. Children with acute bronchiolitis with respiratory distress are usually managed with high flow nasal cannula (HFNC) oxygen therapy to avoid intubation. However in children with hemodynamic instability or intractable apnea early intubation is more appropriate [10,11] and hence we undertook this study to evaluate the clinical course of mechanical ventilation in bronchiolitis. Earlier reports suggested that secondary bacterial infection rates are low (< 2%) in infants with bronchiolitis [12-14]. Subsequent studies reported higher incidence of secondary infections of 25 to 40% in infants with bronchiolitis admitted to PICU [15,16]. Therefore, we investigated the rate and type of secondary infections in ventilated bronchiolitis infants.

In bronchiolitis both PC mode and Volume control mode can be used and there is no significant difference in clinical course depending on the mode of ventilation [17]. In our study PC ventilation was used most often (68%), compared to VC. PIP was lower by 4 cm of water in PC mode compared to volume control mode. Duration of ventilation between PC and VC was similar. We could not find any study investigating these parameters to compare these facts. In our study average PIP was 26 cm of water, which is comparable to the reported PIP of 25 to 30 cm of water [9,17]. Reported duration of average days of mechanical ventilation is 4 to 7days [8,17], which is similar to the finding in our study and patients with significant comorbidities or complication may require longer duration of ventilation of > 2 weeks [17]. Mortality in bronchiolitis remains low (2.8%), and can be higher (8-10%) in in infants with co-morbid conditions like low birth weight, cardiac disease, or immune deficiency [18,19]. In our study there were no deaths.

There are many risk factors which can predispose infants with bronchiolitis for intubation and possibly prolonged ventilation. Pre-maturity, low birth weight, Cardiac disease, pre-existing genetic diseases, pre-existing neurological diseases, secondary or multiple infections and Acute Respiratory Distress Syndrome (ARDS) are some of the risk factors actors which can prolong mechanical ventilation duration of 2 weeks or more [8,17]. In our study pre-maturity and secondary bacterial infections were associated with prolonged mechanical ventilation duration by 2 days. RSV and multi-viral bronchiolitis trended towards slightly prolonged mechanical ventilation duration, but this trend was not statistically significant probably due to small number of cases. Prolonged ventilation is a risk factor for blood transfusion and in our study odds ratio for blood transfusion with MV duration of 4 days or more is 2.6

Secondary bacterial infection in PICU and ventilated patients seems to be quite significant. In our study more than 50% of the intubated patients had secondary bacterial infections. Even though overall secondary bacterial infection rate in bronchiolitis is < 2% [12,13], in PICU patients infection rate is around 40% and in intubated bronchiolitis is about 72% [8,15]. Our study shows that both gram positive and gram negatives bacterial infections are common and infection with more than one bacterium is also frequent (50%) and we did not observe any methicillin resistant staphylococcal aureus (MRSA) infections. In our study WBC count was not helpful in identifying children with secondary bacterial infection and this has been reported earlier [20]. These observations are useful for bedside physicians regarding treatment of secondary bacterial infection in infants with bronchiolitis.

American Academy of Pediatrics practice guidelines for pediatrics [21], does not recommend routine use of inhaled albuterol and systemic steroids. It does suggest administration of hypertonic saline in hospitalized children only. In our study scheduled albuterol nebulization use was frequent (56%) and almost all children received at least one dose of albuterol, and systemic steroid use was also frequent (68%) even though systemic steroids are not recommended in bronchiolitis and majority (87%) received hypertonic saline. This shows variability of practice in severe bronchiolitis children. In our study most children were fed by an enteral route.

In summary, mechanical ventilation in children with severe viral bronchiolitis is effective and safe. In PC mode PIP is lower compared to VC mode and duration of ventilation is similar in both modes and average duration of mechanical ventilation is 4 days. Secondary bacterial infection rate is high (56%) in ventilated children. Prematurity and secondary bacterial infections prolonged ventilation by at least two days. RSV and poly-viral bronchiolitis may prolong duration of mechanical ventilation. Mortality is very low in bronchiolitis infants treated with mechanical ventilation.

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