Original Articles

ASSISTED VENTILATION FOR HYALINE MEMBRANE DISEASE

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ABSTRACT

***Objectives**: To study the outcome and complications of assisted ventilation in neonates with hyaline membrane disease (HMD).*

***Design**: Retrospective study.*

***Setting**: Hospital based.*

***Subjects**: Seventy five premature neonates with HMD needing assisted ventilation born over a period of five years.*

***Main outcome measures:** Survival rate among those ventilated and complications of assisted ventilation.*

***Results**: Survival on assisted ventilation improved from initial 22.2% in 1989 to 77.8% in 1993. Of 19 babies weighing between 750-1000 g, 8(42.1%) survived. Twelve of 27 babies (44.4%) with a gestation of less than 28 weeks survived. Survival rates in babies with gestation of more than 33 weeks was 94%.*

Intraventricular hemorrhage was the leading cause of death in 52% babies. Nosocomial infections were common and occurred in 50.6% of infants on ventilation and accounted for one-third of deaths. Pneumothorax occurred in one-fifth of babies and was responsible for 3 deaths. Pulmonary interstitial emphysema was observed in 6 babies. Six babies developed bronchopulmonary dysplasia while 7 had retinopathy of prematurity.

***Conclusions:** Outcome of neonates needing assisted ventilation for HMD has shown consistent improvement over the period of study. Nosocomial infections continue to be a major complication of assisted ventilation in neonates.*

***Key Words:** Hyaline membrane disease, Prematurity, Inermittent positive pressure ventilation.*

Respiratory distress due to variety of causes afflicts 5-7% of neonates(l). Most of these are due to hyaline membrane disease (HMD) (33.5%) which affects 14.1% of preterm babies(2). These figures are comparable to the incidence reported from the West. The reported low incidence from India is probably due to frequent occurrence of intrauterine growth retardation and failure of recognizing the condition.

The first description of providing patient controlled ventilation to newborns was made by Donald and Lord(3). Stahlman *et al.* described the use of positive pressure ventilation in treating HMD(4). Since then, assisted ventilation has revolutionized the care of preterm newborns in intensive care units. HMD

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remains a common indication of ventilation in preterm neonates(5-8). Ventilation in HMD aims to reduce the work of breathing and maintain oxygenation using the minimum pressures and oxygen concentration so as to avoid pulmonary air leaks, retinopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD). This study was undertaken to evaluate the survival, mortality and complications related to ventilation in neonates requiring assisted ventilation for HMD.

Subjects and Methods

All babies born between 1st January 1989 and 31st December 1993 and diagnosed to have HMD were included. A diagnosis of HMD was made when a preterm baby (<37 weeks) developed increasing respiratory distress with tachypnea, retractions and grunting(9). Negative gastric aspirate shake test and suggestive chest roentgenograms supported the diagnosis. Post-mortem studies showing atelectasis in, an unaerated area, and/or eosinophilic hyaline membranes in the aerated areas confirmed the diagnosis.

All babies were examined at birth and information regarding birth weight, gestational age, mode of delivery, Apgar score and maternal infections were recorded. Gestation was assessed clinically by a scoring system particularly in babies born to mothers with uncertain duration of gestation. For recording weight, an electronic weighing scale with an accuracy of 1 g was used. All babies were born in our hospital and all deliveries were attended by a trained pediatrician. Infants requiring ventilation for severe birth asphyxia, birth weight <750 g, congenital malformations, septicemia and hydrops fetalis due to rhesus isoimmunization were excluded.

All babies with increasing respiratory distress and hypoxemia were given assisted ventilation in the form of continuous positive airway pressure (CPAP) or intermittent positive pressure ventilation (IPPV). The newborn was initiated on CPAP (nasal or endotracheal) if he was unable to maintain arterial blood gases despite ambient FiO_2 of 0.6 (ph <7.25, and/or PaO_2 <50 mm Hg, and/or $PaCo_2$>60 mm Hg). The initial settings for CPAP mode at the time of diagnosis was 5-6 cm water with FiO_2 of 0.5(10). Endotracheal CPAP was preferred in babies <1.0 kg, as these infants frequently progressed to require IPPV.

CPAP was increased in increments of 2 cm water and FiO_2 in increments of 0.1 while monitoring blood gases. The arterial blood gases were maintained at pH between 7.35-7.45, $PaCo_2$ 35-45 mm Hg, and PaO_2 between 50-80 mm Hg. If despite using CPAP of 10-12 cm water (nasal), or 8-10 cm water (endotracheal) with FiO_2 of 0.8, the newborn had hypoxemia or hypercarbia, it was considered an indication to institute IPPV. If clinical condition improved with disappearance of cyanosis and normal arterial blood gases, CPAP was gradually reduced in steps by 1 cm water under constant monitoring to 3 cm water and the child was weaned off to oxygen by hood with a FiO_2 of 0.5. Patients on nasal CPAP had continuous orogastric drainage for deflation of stomach and no oralfeeds were instituted.

Infants with severe HMD as evidenced by marked tachypnea (rate >80/

min), severe chest retractions or cyanosis under CPAP with a FiO_2 0.8, $PaCO_2$ >50 mm Hg and pH <7.20 were put on IPPV. Extremely premature neonates (<1 kg) with severe HMD were initiated on IPPV before the appearance of severe abnormalities on blood gases and acid-base parameters.

Time cycled, pressure limited, continuous flow infant ventilator (Sechrist-100 B infant ventilator) with varying peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), flow rates, inspiratory time (Ti) and FiO_2 were used. Typical initial settings used at the time of diagnosis of HMD in a preterm infant weighing <1.5 kg were PIP 18-20 cm, PEEP 5 cm, flow rate 5-8 L/min, FiO_2 0.6, Ti 0.5 sec and respiratory rate 50-60/min. All babies were nursed under servo-controlled open care system. Radial or umbilical artery or arterialized capillary blood gases were measured. In 12 cases, low umbilical artery lines were put to record continuous blood pressure and for taking blood samples. All babies had continuous oxygen saturation monitoring (Ohmeda-Biox, *In vivo,* Criticare) and oxygen saturation was maintained between 87-95%. Continuous heart rate or electrocardiographic monitoring was done in all babies.

After initial stabilization over 2 days, babies on IPPV received enteral feeds (mostly expressed breast milk). It was gradually stepped up over several days and stopped 6 h prior to extubation. In the event of intolerance to feeds or suspicion of necrotizing enterocolitis (NEC), parenteral nutrition was resorted to. Enteral feeds were not given to babies on CPAP.

The aim of assisted ventilation was to maintain normal blood gases at minimal pressures and for a minimum duration. Weaning in patients of HMD was attempted on the third or fourth day especially at a time when maximum diuresis was observed. The patients were gradually weaned off to intermittent mandatory ventilation mode (rate 10-15/min; FiO_2 0.4, PIP 13-15 cm, PEEP 3-4 cm, Ti 0.3 sec). Following extubation they were placed under hood with FiO_2 0.5. Aminophylline was initiated 24 h prior to the expected time of extubation. Dexamethasone was used in babies when extubation became exceedingly difficult or those requiring reintubation and if BPD was suspected.

All babies were monitored during ventilation for evidences of pulmonary air leaks, congestive heart failure secondary to PDA, sepsis, chest infection and intraventricular hemorrhage (IVH). All babies on IPPV received antibiotics. If septic screen (C-reactive protein, total leucocyte count, band count and micro-ESR) was positive or there were predisposing factors for development of infection, antibiotics were changed depending on the prevalent bacterial flora. Skiagrams of chest were obtained after each endotracheal tube change or whenever sudden deterioration occurred or routinely every day during first seven days and then as required. Chest physiotherapy, with frequent postural changes was done in patients with atelectasis. Endotracheal suction was done routinely after 48 h of intubation every 4-6 h with complete aseptic precautions.

The cause of death was assigned by a team of atleast two consultants after obtaining the autopsy report(11).

Results

Seventy five neonates *were* ventilated for HMD during the 5 years of study. In 1992-93, IPPV was preferred over CPAP *(Table I)* as a mode of ventilation in preterm newborns as compared to 1989-1991. Survivals on IPPV showed a dramatic improvement from 22.2% in 1989 to 77.8% in 1992 and 1993 *(Table* I). Forty eight babies (64%) survived with the help of ventilatory support with CPAP survival of 66.6% and IPPV survival of 63%. The success rate of ventilation in babies with a birth weight above 1.5 kg *(Table II)* was 89%. Babies weighing between 1000 to 1500 g showed a survival of 56.2%. Neonates below 1.0 kg fared badly and only 42.1% survived.

Survival in babies with a gestation of more than 33 weeks was above 90% *(Table III)*. The survival in babies with a gestational age between 29 and 32 weeks was 63%; 44% neonates below 28 weeks survived. Most babies with HMD required ventilation for more than 48 h and were weaned off between 3-7 days. Only 12 babies required ventilation for more than 10 days primarily because of extreme prematurity, BPD and occurrence of nosocomial infection.

TABLE I–*Survival Rates and Mode of Ventilation*

	1989	1990	1991	1992	1993	Total
IPPV	2/9 (22.2)	5/9 (55.5)	6/7 (85.7)	7/11 (63.6)	14/18 (77.8)	34/54 (63)
CPAP	6/7 (85.7)	4/9 (44.4)	2/3 (66.6)	– –	2/2 (100)	14/21 (66.6)
Total	8/16 (50)	9/18 (50)	8/10 (80)	7/11 (63.6)	16/20 (80)	48/75 (64)

Figures in parentheses indicate percentages.

TABLE II–*Birth Weight-Specific Survival Rates with Ventilation*

Birth weight (g)	1989	1990	1991	1992	1993	Total
≥750-<1000	0/6	3/4	2/2	1/4	2/3	8/19 (42.1)
>1000-1500	2/4	3/9	4/6	2/3	7/10	18/32 (56.2)
>1500-2500	4/4	2/4	2/2	2/2	6/6	16/18 (88.8)
>2500	2/2	1/1	–	2/2	1/1	6/6 (100)

Figures in parentheses indicate percentages.

Nosocomial infections *(Table IV)* were the commonest complication of assisted ventilation and occurred in 38 babies; 50.6% were culture proven sepsis. Eighteen babes also had superadded pneumonia in addition to septicemia. Pneumothorax was found in one-fifth neonates. BPD, defined as chronic lung disease in babies requiring prolonged ventilation and oxygen dependency

TABLE III-*Gestational Age-Specific Survival Rates with Ventilation*

Gestation (weeks)	1989	1990	1991	1992	1993	Total *(%)*
<28	0/6	*417*	5/6	1/3	2/5	12/27 (44.4)
29-30	1/3	0/1	1/1	1/3	6/6	9/14 (64.2)
31-32	1/1	2/6	2/3	-	5/6	10/16 (62.5)
33-34	5/5	2/3	-	5/5	2/2	14/15 (93.3)
35-36	1/1	1/1	-	-	1/1	3/3 (100)

TABLE IV-*Complications of Assisted Ventilation*

	1986	1990	1991	1992	1993	Total (%)
No.	(16)	(18)	(10)	(11)	(20)	(75)
Sepsis						
Total	5	10	5	9	9	38 (SO.6)
Probable	1	3	3	6	5	18 (24.0)
Proven	4	7	2	3	4	20 (26.6)
Pneumonia*	1	3	2	7	5	18 (24.0)
Pneumothorax	4	4	1	-	6	15 (20.0)
Pneumomediastinum		2	-	-	-	2 (2.6)
PIE	2	2	1	1	-	6 (8.0)
BPO**	-	2		2	3	7 (14.5)
PDA	2	4	4	4	6	20 26.6)
ROP**	2	-	-	2	3"	7 (14.5)

* All patients with pneumonia had sepsis.

** Calculated in surviving patients.

beyond 28 days was seen in 7 babies. ROP was recognized as a serious problem in seven babies. Neonates showing BPD or ROP were <1300 g and <30-32 weeks gestation, and required prolonged oxygen therapy.

Patent ductus arteriosus (PDA) was a common problem, and occurred in 20 babies. Oral indomethacin in a dose of 0.2 mg/kg/dose for 3 doses in 10 patients who did not respond to the initial management of fluid restriction resulted in closure of the PDA.

IVH was the main immediate cause of death in 14 (51.8%). Sepsis-related mortality accounted for 10 (37 %) deaths. There were no deaths due to pneumothorax during the last 3 years of ventilation while during the first two years they accounted for 3 deaths.

Discussion

While assisted ventilation is an accepted mode of treatment of newborns in the developed countries(7-10,12,13), majority of hospitals attached to medical colleges in India lack the basic infrastructure to ventilate critically sick neonates. There is, therefore, scanty data on HMD and ventilation from our country(l,5). We first initiated ventilation at our NICU in 1984 but only after 1989 we were able to successfully treat patients with HMD(14). Experience over the last 5 years has shown that CPAP trial should be given to HMD babies weighing between 1.0-1.5 kg before shifting them to IPPV mode(14). Babies above 1.5 kg do fairly well on CPAP alone if they have mild to moderate HMD. Survival rates above 90% for HMD in babies with a birth weight of >1.5 kg on CPAP alone supports the above recommendation. Babies below 1.0 kg invariably failed on CPAP mode due to severe disease and required TPPV.

Babies with gestational age between 29-32 weeks and birth weight between 1.0-1.5 kg stand to gain maximum from assisted ventilation with good chances of normal long term outcome. It would therefore, be worthwhile to make concerted efforts to improve survival in this group of babies.

Sepsis, however, continues to be a preventable and treatable cause of ventilation-related mortality and urgent efforts should be made to reduce nosocomial infections in any unit undertaking assisted ventilation. Pulmonary air leaks were detected as pneumothorax in 20% of our patients. Various other centers have reported the incidence of pulmonary air leaks ranging from 16 to 48%(15-17). Since air leaks are related to pressures used in ventilation, IPPV should aim at using the minimum pressures to maintain normal blood gases.

BPD is the major chronic complication associated with prolonged ventilation in the neonates(18). Most centers report 10-20% incidence of BPD among survivors of HMD receiving IPPV(19-21). Of 48 of our babies surviving assisted ventilation, 7(14.5%) developed BPD which is comparable to reports from other centers. The most effective means of preventing BPD would be to reduce the incidence or severity of HMD. Currently available preventive measures include administering tocolytic agents to arrest preterm labor and corticosteroids for enhancing synthesis of surfactant *in utero.*

ROP is a complication found exclu-

sively in newborn preterm babies receiving ventilation (22). Cicatricial disease (severe ROP) develops in about 22-42% of babies weighing <1000 g (22). Seven of 48 (14.5%) surviving babies with HMD and ventilation developed ROP. All preterm babies below 32 weeks and all neonates requiring ventilation should be screened for ROP.

With improving standards of supportive care and enhanced confidence in using IPPV, the survival rates have improved from 22.2% in 1989 to 77.8% in 1993. Babies below 1.0 kg and below 28 weeks continue to do badly despite ventilation. In view of limited resources, treatment with assisted ventilation should focus on babies weighing between 1.0-1.5 kg. Nosocomial infections continue to be a major problem in sick preterm neonates and their early detection and prompt treatment is essential. The success of assisted ventilation depends on the devotion, continuous involvement and commitment of trained and skilled nurses, resident doctors, and supporting staff.

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