Original Articles

A prospective study of ventilated neonates in a tertiary care hospital in Sri Lanka compared to retrospective data from the same unit

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Abstract

Objectives: To prospectively study several aspects of ventilated neonates at the neonatal intensive care unit (NICU) of Sri Jayawardenepura General Hospital (SJGH) and compare this data to retrospective data from the same unit.

Method: A descriptive observational, longitudinal hospital based prospective study was conducted on ventilated babies in NICU, SJGH from1st July 2009 to 1st July 2010. Data were obtained using a pre-tested recording form. NICU records were used to gather data of infants ventilated from 1st July 2000 to 1st July 2001. Data obtained from the current study were compared to data in 2000/2001. Data were analysed using SPSS version 16 for Windows.

Results: During the study period 135 babies were ventilated. Four were excluded due to severe congenital defects. Seventy two percent were male and 53% had gestational periods of 32 weeks or less. There were 46% very low birth weight (VLBW) babies. In 72% the indication for ventilation was respiratory distress syndrome (RDS). Duration of ventilation was over one week in 34%. Continuous positive airway pressure (CPAP) was the sole mode of ventilation in 33%. Surfactant was used in 53% babies, 96% for RDS. Oxygen for over 2 weeks was required in 17% and 22% received theophylline as respiratory stimulants. Midazolam infusion was used for sedation in 56%. Total parenteral nutrition was started in 56%, 29% received blood transfusions and 65% received volume support or inotropes for hypotension. Complications included seizures (16%), persistent pulmonary hypertension of the newborn (9%), patent ductus arteriosus (8%), pulmonary haemorrhage (7%), retinopathy of prematurity (6%), nosocomial sepsis (6%), ventilator-associated pneumonia (5%), bronchopulmonary dysplasia (5%), necrotising enterocolitis (3%), intraventricular haemorrhage (2%) and pneumothorax (2%). Eighty eight percent babies were followed up till 2 years of age. Mortality in 2009/2010 was 18% compared to 39% in 2000/2001 (P<0.0001).

Conclusions: Babies with 32 weeks or less gestation and VLBW babies were significantly more in 2009/2010 (P<0.05). Complications such as VAP, nosocomial sepsis and pneumothorax were significantly more common in babies ventilated in 2000/2001 but ROP was significantly more common in babies ventilated in 2009/ 2010 (P<0.05). HIE caused significantly more deaths in 2000/ 2001 whilst significantly more deaths occurred in ex-utero babies and babies with pulmonary haemorrhage in 2009/2010 (P<0.05). Overall mortality, mortality in babies with 32 weeks or less gestation and mortality in VLBW babies were significantly lower in 2009/2010 (P<0.0001). In 2009/2010, the outcome in babies receiving CPAP only was significantly better than those receiving IMV only (P<0.0001). There was no morbidity at 2 years of age in significantly more babies over 32 weeks gestation in 2009/2010 compared to babies with gestation 32 weeks or less (P<0.0001).

(Key words: Ventilated neonate; prospective study; Sri Lanka)

Introduction

NICU of SJGH admits sick and premature neonates from SJGH and accepts ex-utero transfers. It is the training centre in neonatal intensive care. It has 7 ventilators (3 SLE 2000, 2 Infant star 200, 1 Bear cub 750 VS and 1 Bear cub 750 PSV), all having continuous positive airway pressure (CPAP) and intermittent mandatory ventilation (IMV) modes, some also with synchronized intermittent mandatory ventilation (SIMV). Neither volume cycled ventilation nor high frequency ventilation are available.

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An extensive online literary search using the key words 'ventilated neonate', did not reveal any prospective studies on ventilated neonates anywhere in the world. However, there were retrospective studies[1,2]. In Sri Lanka, 2 such studies were presented at the 12th Asia Pacific Congress of Paediatrics[3] and the 6th Annual Scientific Sessions of the Perinatal Society of Sri Lanka[4]. There are no other Sri Lankan studies on ventilated neonates and the present study was designed to address this deficiency.

Objectives

1. To prospectively study several aspects of ventilated neonates at the NICU, SJGH, such as gender difference, indications for ventilation, type and duration of ventilation, surfactant use, duration of oxygen therapy, use of muscle relaxants and sedation, complications of CPAP and IMV, incidences of ventilator associated pneumonia and colonization of the respiratory tract, other ventilation-related complications, weaning strategy, use of respiratory stimulants, need for re-intubation, use of parenteral nutrition, need for blood transfusion, incidence and treatment of hypotension, mortality, causes of death and short-term morbidity

2. To compare data from the current study with retrospective data from the same unit from 1st July 2000 to 1st July 2001.

Method

A descriptive observational, longitudinal, hospital based prospective study was conducted in NICU, SJGH from 1st July 2009 to 1st July 2010 on all ventilated babies, including ex-utero babies, but excluding babies with severe congenital anomalies. Data were obtained by the first author using a pre-tested recording form.

Several infection control policies are practised at NICU to minimise nosocomial infections. Hand washing was strictly enforced, a 2 minute hand washing before entering, followed by 20 second hand washing in between patients. Hand washing was done even if an inanimate object was touched before seeing a patient and also before any procedure. No hand accessories were worn by the staff. Clothes were folded above the elbow and a sterile gown and shoes worn prior to entry. Only mothers of admitted babies were allowed inside the NICU. Bacterial filters were used for both inspiratory and expiratory limbs, sterile water was used for the humidification systems, condensed water in the circuits was drained and circuits changed weekly. Disposable sterile suction catheters were used. Sterile needles were used for punctures. Orotracheal rather than nasotracheal tubes were used for intubation. Probes were disinfected. One to one nursing with barrier precautions was used whenever possible.

Period of gestation (POG) was estimated according to mother's obstetric record when supported by an obstetric ultrasound at 15-19 weeks. Otherwise, maturity assessment by the first author according to the new Ballard score was taken as the POG.

Respiratory distress syndrome (RDS) was diagnosed when the following were present within 4 hours of birth: respiratory rate over 60/minute, intercostal/ subcostal/sternal retractions, expiratory grunt and chest x-ray (CXR) having a ground glass appearance with air bronchogram / hazy appearance or white out appearance[5]. *Hypoxic ischaemic encephalopathy* (HIE) was diagnosed if the following were present: acidaemia, Apgar score 0-3 for over 5 minutes, neurological manifestations and multisystemic organ dysfunction[6]. *Persistent pulmonary hypertension of the newborn* (PPHN) was diagnosed when an infant with an echocardiographically confirmed structurally normal heart had the following: severe hypoxaemia (PaO_2 <45mmHg), hypoxaemia disproportionate to clinical and CXR findings, acid base abnormalities and a right to left shunt *via* ductus or foramen ovale[5]. *Meconium aspiration syndrome* (MAS) was defined as respiratory distress in an infant born through meconium stained amniotic fluid whose symptoms could not be otherwise explained[7]. *Sepsis* was diagnosed if blood cultures were positive in a baby with suggestive clinical features.

Ventilator associated pneumonia (VAP) was defined as follows: patients mechanically ventilated for 48 or more hours having an abnormal CXR with at least one of the following: new or progressive and persistent infiltrate, consolidation, cavitation and/or pneumatoceles in addition to: worsening gas exchange and at least 3 of the following: temperature instability with no other recognized cause, increased respiratory secretions, increased suctioning requirements, apnoea, tachypnoea, nasal flaring with chest wall retraction or grunting, wheezing, cough and bradycardia (<100 beats/min) or tachycardia (>170 beats/min)[8].

Colonisation of trachea without sepsis implied organisms isolated in endotracheal tube (ETT) secretions without systemic evidence of sepsis and negative blood cultures. *Colonisation of trachea with sepsis* implied organisms isolated on ETT secretions

with systemic evidence of sepsis with or without positive blood cultures. *Patent ductus arteriosus* (PDA) was diagnosed clinically supported by echocardiography. *Retinopathy of prematurity* (ROP) was diagnosed by one of the 2 consultant eye surgeons at SJGH when babies 34 weeks or less in gestation or birth weight less than 1500g were screened. *Intraventricular haemorrhage* (IVH) was diagnosed according to brain ultrasound scan performed by neonatologist or consultant radiologist. *Bronchopulmonary dysplasia* (BPD) was defined as babies needing over 21% oxygen at 28 days of age[9].

NICU records were used to gather data regarding infants ventilated from 1st July 2000 to 1st July 2001. All babies were seen by the first author during the study period. They were followed up in the clinic for 2 years.

Data obtained from the current study were compared to data of babies ventilated in 2000/2001.

Data were analysed using SPSS version 16 for Windows. Pearson's Chi Square Test was the statistical test used.

Ethical clearance for the study was obtained from the Ethics Review Committee of the Sri Lanka College of Paediatricians. Permission was obtained from the Director, SJGH prior to commencement of study. Informed consent was obtained from parents for the study.

Results

One hundred and thirty five babies were ventilated. Two babies with antenatally diagnosed hydrocephalus, a baby with complex cyanotic heart disease and a baby with meningocele and hydrocephalus were excluded. Ninety four (72%) were male. Distributions of ventilated babies in 2009/2010 and 2000/2001 according to their POG are shown in Table 1.

Table 1: ***Distribution of ventilated babies***

POG (weeks)	**2009/2010** *n =131* **No. (%)**	**2000/2001** *n =122* **No. (%)**
Less than 28	19 (14.5)	25 (20.5)
28-32	51 (39)	25 (20.5)
33-36	25 (19)	22 (18)
More than 36	36 (27.5)	50 (41)

There were significantly more babies with POG of 32 weeks or less in 2009/2010 compared to 2000/2001 (P=0.047). Thirty eight (29%) babies were small for gestational age in 2009/2010 compared to 33 (27%) in 2000/2001 (P=0.729). Twenty (15%) babies had birth weights <1000g in 2009/2010 compared to 15 (12%) in 2000/2001 (P=0.494). There were significantly more (60, 46%) very low birth weight (VLBW) babies (<1500g) in 2009/2010 compared to (40, 33%) VLBW babies in 2000/2001(P=0.034). Indications for ventilation in 2009/2010 and 2000/2001 are shown in Table 2.

Table 2: ***Indications for ventilation in 2009/2010 and 2000/2001***

	2009/2010 *n=131* **No. (%)**	**2000/2001** *n=122* **No. (%)**	**P value**
Respiratory distress syndrome	95 (72)	79 (65)	0.183
Hypoxic ischaemic encephalopathy	08 (06)	09 (07)	0.687
Meconium aspiration syndrome	04 (03)	12 (10)	0.027
Congenital pneumonia	14 (11)	08 (07)	0.244
Persistent pulmonary hypertension of the newborn	05 (04)	01 (01)	0.117
Sepsis	01(01)	0	0.334
Apnoea	02 (02)	04 (03)	0.360
Transient tachypnoea of the newborn	02 (02)	01 (01)	0.604
Pulmonary haemorrhage	0	01 (01)	0.299
Myopathy	0	01 (01)	0.299
Postmeningocele surgery	0	01 (01)	0.299
Congenital infection	0	01 (01)	0.299
Unknown	0	02 (02)	0.141
Congenital diaphragmatic hernia	0	01 (01)	0.299
Intracranial haemorrhage	0	01 (01)	0.299

MAS was seen in significantly more babies in 2000/2001 than in 2009/2010 (P=0.027). Group B streptococcus was isolated in all 14 babies with congenital pneumonia in the 2009/2010 group and 6 of 8 babies in the 2000/2001 group.

Durations of ventilation in 2009/10 and 2000/2001 are shown in Table 3.

Table 3: ***Duration of ventilation in 2009/2010 and 2000/2001***

Duration of ventilation	**2009/2010** *n=131* **No. (%)**	**2000/2001** *n=122* **No. (%)**	**P value**
<24 hours	12 (09)	06 (05)	0.190
24-48 hours	14 (11)	10 (08)	0.499
3-7 days	60 (46)	53 (43)	0.706
>7 days	45 (34)	53 (43)	0.138

There were no statistically significant differences between the 2 groups with regard to duration of ventilation.

Surfactant was unavailable for use in 2000/2001. In 2009/2010 surfactant was used in 69 babies, RDS being the commonest indication (66/69), other indications being MAS (1/4), congenital pneumonia (1/14) and pulmonary haemorrhage (1/2). Of the 94 babies ventilated for RDS, 65 received surfactant. Significantly more babies (54, 77%) in the 32 week or less age group received surfactant compared to babies (17, 26%) in the over 32 week age group (P=0.002).

Surfactant was used only as rescue therapy for babies with RDS. Fifty three were given surfactant for persistent or worsening respiratory distress or oxygen requirement exceeding 30% while on CPAP. Eight babies, 32 weeks of gestation or less, who required intubation at birth, were given surfactant as soon as it was available. Eight babies were given surfactant after developing persistent or worsening respiratory distress while on head box oxygen. Mean age of surfactant administration was 9 ± 9.9 hours. Of 66 babies admitted on day one of age, 65 received surfactant within the first 24 hours. The 2 babies receiving surfactant after 24 hours of age were both ex-utero transfers.

All babies were ventilated invasively *via* ETT in 2000/2001. Types of ventilation used in the 2009/10 along with the outcomes are shown in Table 4.

Table 4: ***Types of ventilation used in 2009/2010 with outcome***

Type of ventilation	**No. (%)** *n=131*	**Died (%)** *n=24*	**Survived (%)** *n=107*
Continuous positive airway pressure (CPAP) only	43 (33)	0 (0)	43 (100)
Intermittent mandatory ventilation (IMV) only	18 (14)	15 (83)	03 (17)
CPAP followed by IMV	50 (38)	09 (18)	41 (82)
IMV followed by CPAP	20 (15)	02 (10)	18 (90)

Outcome in babies receiving CPAP only was significantly better than those receiving IMV only (P<0.0001), CPAP followed by IMV (P=0.003) or IMV followed by CPAP (P=0.035). There was no statistically significant difference whether CPAP was followed by IMV or IMV was followed by CPAP (P=0.406).

Sedation was given to babies seen to breathe against the ventilator and to those who were uncomfortable. Whilst 57 babies did not receive sedation, 54 were given midazolam infusion, 19 also receiving morphine and one also receiving phenobarbitone Muscle relaxants were not used. Only 2 complications were noted during CPAP application. One baby developed nasal irritation and 12 developed feed intolerance.

In 2009/2010, 62 babies required oxygen for less than a week and 8 for over 4 weeks but no baby required oxygen for over 8 weeks. Babies with POG 32 weeks or less required significantly longer periods of oxygen therapy compared to babies with POG over 32 weeks (P=0.048). Two ventilated babies developed pneumothorax. Maximum peak inspiratory pressure (PIP) used in them was 20-22mmHg. There was no association between the occurrence of pneumothorax and the PIP used, in this study population.

Of 88 babies needing invasive ventilation, 24 (27%) needed re-intubation. Re-intubation was required in 6/44 babies ventilated for 0-7 days compared to 18/44 babies ventilated for over one week (P=0.004). *In the 0-7 day group*, 5 babies required one re-intubation and one required 2. *In the over one week group,* 11 babies needed one re-intubation and 13

needed 2-6. Significantly more babies in the over one week age group required 2 or more re-intubations compared to the 0-7 day group (P=0.026).

Fifty one babies receiving invasive ventilation were weaned off to nasal CPAP after extubation. Reduction of the pressure was the method used for CPAP weaning. Thirteen babies were extubated and connected to head box oxygen without connecting to CPAP. No baby received endotracheal CPAP. Weaning off to CPAP was the strategy used in a significantly higher number of babies 32 weeks or less POG compared to babies with POG over 32 weeks (P=0.019).

Respiratory stimulants, either oral theophylline or intravenous aminophylline, were given to 29 (22%) babies, 97% of whom had a POG of 32 weeks or less.

Total parenteral nutrition (TPN) was commenced in 74 (56%) babies. TPN was started in 55 (74%) babies with a POG of 32 weeks or less compared to 19 (26%) babies with a POG over 32 weeks (P<0.0001). TPN was used for a mean of 4 ± 5 days. No complications were encountered due to TPN.

The haemoglobin (Hb) level was maintained above 14g/dl in all ventilated babies. Blood was transfused if the Hb level fell below 14g/dl. Blood transfusions were given to 38 (29%) ventilated babies, 71% of them having a POG of 32 weeks or less.

Blood pressure was maintained at more than the mean for gestational age by volume expansion and inotrope infusions. Eighty five (65%) babies received either volume support or inotropes for hypotension. Of them, 54 had a POG of 32 weeks or less compared to 31 with a POG more than 32 weeks (P=0.006).

Complications noted prior to discharge in babies who were ventilated are shown in Table 5.

Table 5: ***Complications noted prior to discharge in ventilated babies***

Complication	**2009/2010** *n=131* **No. (%)**	**2000/2001** *n=122* **No. (%)**	**Statistical significance**	**Survivals in 2009/2010 No. (%)**	**Survivals in 2000/2001 No. (%)**	**Statistical significance**
VAP	07 (05)	22 (22)	P<0.001	07 (100)	17 (77)	P=0.000
Nosocomial sepsis	08 (06)	19 (16)	P<0.05	08 (100)	13 (68)	P=0.197
PDA	11 (08)	11 (09)	P=0.861	11 (100)	11 (100)	P=0.861
Seizures	21 (16)	13 (11)	P=0.210	14 (66)	06 (46)	P=0.274
IVH	02 (02)	04 (03)	P=0.120	01 (50)	01 (25)	P=0.419
NEC	04 (03)	04 (03)	P=0.919	04 (100)	01 (25)	P=0.326
PPHN	12 (09)	05 (04)	P=0.108	08 (66)	02 (40)	P=0.328
Pulmonary haemorrhage	09 (07)	02 (02)	P<0.05	03 (33)	01 (50)	P=0.776
Pneumothorax	02 (02)	21 (17)	P<0.001	0	16 (76)	P=0.000
BPD	07 (05)	03 (03)	P=0.310	06 (86)	01(33)	P=0.138
ROP	12 (09)	02 (02)	P=0.009	12 (100)	01 (50)	P=0.011

VAP = Ventilator associated pneumonia; PDA = Patent ductus arteriosus; IVH = *Intraventricular haemorrhage; NEC = Necrotising enterocolitis; PPHN = Persistent pulmonary hypertension of the newborn;* BPD = *Bronchopulmonary dysplasia; ROP=Retinopathy of prematurity*

VAP was seen in significantly more babies ventilated in 2000/2001 compared to 2009/2010 (P<0.0001). In 2009/2010, VAP was not seen in babies receiving CPAP. In babies ventilated invasively, incidence of VAP was 1/44 in babies ventilated from 0-7 days compared to 6/44 in babies ventilated for more than one week (P=0.049). In 2009/2010 VAP was due to coliforms in 5 babies and acenetobacter in one baby.

The incidence of nosocomial sepsis was significantly more in babies ventilated in 2000/2001 (P<0.05). In 2009/2010, 8 (7.5%) survivors developed nosocomial sepsis with positive blood cultures along with tracheal colonisation. Causative organisms were: coliforms (4), acenetobacter (2), staphylococcus (1) and candida (1). Sixteen (15%) survivors developed tracheal colonisation without sepsis. ETT secretions were positive for acenetobacter (9), coliforms (5), pseudomonas (3) and candida (1). None of the 12 babies ventilated for less than 24 hours developed nosocomial sepsis.

In 2009/2010, one PDA required ligation. One baby with IVH had a grade 4 haemorrhage requiring

evacuation due to midline shift. One baby with NEC required surgical intervention. One baby with BPD could not be weaned off and died on the ventilator. The other 6 babies had mild BPD and did not need oxygen on discharge.

Incidence of pneumothorax was significantly higher in 2000/2001 compared to 2009/2010 (P<0.001). Incidence of ROP was significantly higher in 2009/2010 compared to 2000/2001 (P=0.009). Survival in babies with ROP was significantly higher in 2009/2010 compared to 2000/2001 (P=0.011)

The outcomes in 2009/2010 and 2000/2001 are shown in Table 6

Mortality in 2009/2010 was significantly lower than in 2000/2001 (P<0.0001). There were 18 (26%) deaths in 70 babies with a POG 32 weeks or less in 2009/2010 compared to 32 (64%) deaths in 50 babies with a POG 32 weeks or less in 2000/2001 (P<0.0001). There were 19 (32%) deaths in 60 VLBW babies in 2009/2010 compared to 30 (75%) deaths in 40 VLBW babies in 2000/2001 (P<0.0001).

Table 6: ***Outcome in 2009/2010 and 2000/2001***

Outcome	**2009/2010** *n=131* **Number (%)**	**2000/2001** *n=122* **Number (%)**
Deaths	24 (18)	48 (39)
Survivors	107 (82)	74 (61)

Ten babies were transferred ex-utero in 2009/2010 with 7 (70%) deaths compared to 18 babies transferred ex-utero in 2000/2001 with 9 (50%) deaths (P=0.047). Causes of death in 2009/2010 and 2000/2001 are shown in Table 7.

Table 7: ***Causes of death in 2009/2010 and 2000/2001***

Causes of death	**2009/2010** *n= 24* **No. (%)**	**2000/2001** *n= 48* **No. (%)**	**P value**
Respiratory distress syndrome	11 (46)	14 (29)	0.161
Hypoxic ischaemic encephalopathy	01 (04)	09 (19)	0.092
Meconium aspiration syndrome	0 (0)	03 (06)	0.211
Congenital pneumonia	0 (0)	01 (02)	0.476
Pneumothorax	02 (08)	05 (10)	0.778
Other air leaks	0 (0)	01 (02)	0.476
Sepsis	0 (0)	06 (13)	0.070
Intraventricular haemorrhage	01 (04)	03 (06)	0.716
Persistent pulmonary hypertension of the newborn	04 (17)	03 (06)	0.160
Pulmonary haemorrhage	06 (25)	01 (02)	0.002
Necrotising enterocolitis	0 (0)	03 (06)	0.193
Bronchopulmonary dysplasia	01 (04)	03 (06)	0.716
Myopathy	0 (0)	01 (02)	0.476
Disseminated intravascular coagulation	01 (04)	01 (02)	0.612
Hydrops	0 (0)	01 (02)	0.476
Adrenal haemorrhage	0 (0)	02 (04)	0.310
Congenital diaphragmatic hernia	0 (0)	01 (02)	0.476

RDS was the highest contributor to deaths in both groups. Deaths due to pulmonary haemorrhage were significantly more common in babies who died in 2009/2010 compared to those who died in 2000/2001 (P=0.002). All 7 babies who died due to pulmonary haemorrhage were VLBW babies with underlying RDS, 3 of them receiving surfactant and one having PDA.

Cause specific mortality is shown in Table 8.

Table 8: ***Cause specific mortality***

	2009/2010 *n=131* No. (%)	2009/2010 Deaths No. (%)	2000/2001 *n= 122* No. (%)	2000/2001 Deaths No. (%)	P value
Respiratory distress syndrome	95 (72)	11 (12%)	79 (65)	14 (18%)	0.301
Hypoxic ischaemic encephalopathy	08 (06)	01 (13%)	09 (07)	09 (100%)	0.000
Meconium aspiration syndrome	04 (03)	0	12 (10)	03 (25%)	0.285
Congenital pneumonia	14 (11)	0	08 (07)	01 (13%)	0.302
Persistent pulmonary hypertension of newborn	05 (04)	04 (80%)	01 (01)	01 (100%)	0.292
Sepsis	01(01)	0	0	0	

HIE caused significantly more deaths in 2000/2001 compared to 2009/2010 (P<0.0001)

Of the 107 survivors, 2 babies died after discharge from the NICU. Both were VLBW babies with less than 32 weeks gestation; one died of milk aspiration within a week of discharge and the other died at 2 months of age due to a severe episode of bronchiolitis. They were not included in the outcome figures in Table 6 as corresponding figures were not available for the 2000/2001.

Eight babies (3 with POG <32 weeks, including the 2 deaths) did not attend clinic after discharge. Six were followed up for less than 3 months, one for 3 to 6 months and 92 (86%) till 2 years of age. The 92 included 46 (92%) of 50 babies with POG 32 weeks or less and 46 (78%) of 59 babies with POG over 32 weeks.

Morbidity at the end of 2 years follow up is shown in Table 9.

Table 9: ***Morbidity at 2 years of age***

Morbidity at 2 years of age	POG 32 weeks or less Number (%) *Total=46*	POG more than 32 weeks Number (%) *Total = 46*
No morbidity	24 (52.0)	43 (93.5)
ROP self-resolved	06 (13.0)	01 (02.2)
ROP needing laser treatment	06 (13.0)	0 (0)
Reduced visual acuity following laser treatment	03 (06.5)	0 (0)
Squint	01 (02.2)	03 (06.5)
Cerebral palsy	03 (06.5)	02(04.3)
Infantile spasms	02 (04.3)	0 (0)
Isolated speech delay	02 (04.3)	0 (0)
Poor weight gain	02 (04.3)	0 (0)
Hospital admission for respiratory infection	07 (15.2)	03 (06.5)
Gall stones	01 (02.2)	01(02.2)

Eight babies had 2 co-morbidities and 4 had 3 co-morbidities. There was no morbidity at 2 years of age in significantly more babies with a POG over 32 weeks compared to babies with POG 32 weeks or less (P<0.0001).

Discussion

A dramatic fall in neonatal mortality occurred in developed countries with the advent of mechanical ventilation and neonatal intensive care[10]. This has been greater for VLBW infants[11]. This is attributed to increased availability of mechanical ventilation, surfactant and TPN[12] and the level of intensive care received[13]. Noninvasive methods provide ventilation without insertion of an ETT. CPAP, the commonest noninvasive mode, applies continuous distending pressure to alveoli throughout the respiratory cycle, maintaining a degree of alveolar inflation during expiration and preventing complete collapse, thus following Laplace law, since a partially inflated alveolus is easier to expand than a fully collapsed one[14]. CPAP may also produce a more regular pattern of breathing in preterm infants by reducing thoracic distortion and stabilizing chest wall, splinting airway and diaphragm, decreasing obstructive apnoea and enhancing surfactant release[14]. In our study CPAP, alone or combined with IMV, was used in 86% ventilated neonates. CPAP can cause abdominal distension and feeding disturbances because of gas flow to the stomach. Nasal prongs or tubes can cause nasal irritation and excoriation. At high pressures, thoracic air leaks can occur and venous return and cardiac output can be impaired[15]. In our study the

only complications attributable to CPAP were nasal irritation and feed intolerance.

In IMV breaths are delivered at the rate set by the clinician, irrespective of the baby's breathing efforts. Asynchrony results in inefficiency of gas exchange, gas trapping and air leaks, irregularities in arterial blood pressure, cerebral blood flow velocity and IVH[16]. In SIMV the onset of inspiration of a mechanical breath is timed to the onset of a spontaneous breath if it occurs within a "timing window"[16]. In our study, CPAP was the sole mode of ventilation in 33% and IMV the sole mode in 14%. The outcome in babies receiving CPAP only was significantly better than in those receiving IMV only or in those who received IMV followed by CPAP or CPAP followed by IMV ($P<0.05$). Of 88 babies needing invasive ventilation, 27% needed re-intubation. Longer duration of ventilation and higher number of re-intubations were significantly associated ($P<0.05$).

Muscle relaxants and sedatives improve synchronization. Use of pancuromium in babies of 26-34 weeks gestation showed that adverse sequelae in the low birth weight ventilated baby was reduced by minimizing periods of non-optimal oxygenation and reducing intracranial pressure[17]. In our study muscle relaxants were not used. Opiates and benzodiazepines are used in ventilated neonates but midazolam has been associated with adverse effects in one study[18]. In our study 54 babies were given midazolam infusion, 19 also receiving morphine and one also receiving phenobarbitone.

Both prophylactic and early surfactant therapy reduce mortality and pulmonary complications in ventilated infants with RDS compared to later selective surfactant administration[19]. A lower threshold ($FIO2<0.45$) to administer surfactant minimizes air leaks and BPD as well as PDA[19]. In our study surfactant was used as rescue therapy in 69 babies, RDS being the indication in 96%. Therapy was initiated when the baby became distressed while on head box oxygen or on CPAP or had increasing oxygen requirement ($FiO2>0.30$) while on nasal CPAP. Significantly more babies with POG 32 weeks or less received surfactant compared to babies with POG over 32 weeks ($P<0.01$).

Of the 107 survivors, 92 (86%) babies, were followed up until 2 years of age. There was no morbidity at 2 years of age in significantly more babies with POG over 32 weeks compared to babies with POG of 32 weeks or less ($P<0.0001$).

Let us now compare ventilated babies in 2009/2010 and 2000/2001. There were significantly more babies with POG of 32 weeks or less in 2009/2010 ($P<0.05$). VLBW babies were significantly more in 2009/2010 ($P<0.05$). RDS was the commonest indication for ventilation in both groups. MAS was seen in significantly more babies in 2000/2001 compared to 2009/2010 ($P<0.05$). There were no statistically significant differences between the 2 groups regarding duration of ventilation. In 2000/2001, all babies were ventilated invasively whilst in 2009/2010 33% were ventilated non-invasively. VAP, nosocomial infection and pneumothorax were significantly more in 2000/2001 ($P<0.05$) but ROP was significantly higher in 2009/2010 ($P<0.01$). The greater percentage of VLBW babies and their increased survival in 2009/2010 probably accounts for the increased incidence of ROP.

The overall mortality in 2009/2010 was significantly less compared to 2000/2001 ($P<0.0001$). Mortality in babies with a POG of 32 weeks or less and mortality in VLBW in 2009/2010 were also significantly less than the corresponding mortalities in 2000/2001 ($P<0.0001$). RDS was the highest contributor to deaths in both groups. HIE caused significantly more deaths in 2000/2001 ($P<0.0001$) but pulmonary haemorrhage caused significantly more deaths in 2009/2010 ($P<0.01$). Incidence of pulmonary haemorrhage in VLBW babies is 2-12%[20] and the mortality 50-80%[21]. Risk factors for pulmonary haemorrhage include male sex, prematurity, VLBW, RDS, surfactant use and PDA[22]. Risk factors contributing to the 6 deaths in our study included VLBW (6/6), RDS (6/6) surfactant use (3/6) and PDA (1/6). Mortality of babies transferred ex-utero in 2009/2010 was significantly more compared to babies transferred ex-utero in 2000/2001 ($P<0.05$). This may be due to the higher percentage of babies of 32 weeks gestation or less in 2009/2010 compared to 2000/2001.

In the 2004 study[3] at General Hospital Matara, common indications for ventilation were: RDS (48%), MAS (33%), asphyxia (21%) and sepsis (15%) and the overall mortality rate 52%. In the 2006 study[4] at Teaching Hospital Peradeniya, common indications for ventilation were: RDS (44%), birth asphyxia (13%), MAS (5%) and sepsis (5%). Overall mortality rate was 42% and the mortality rate for RDS was 34%. In our study common indications for ventilation were: RDS (71%), congenital pneumonia (11%), asphyxia (6%), PPHN (4%), MAS (3%) and sepsis (1%). Overall mortality rate was 20% and mortality rate for RDS 12%.

Availability of surfactant, CPAP, parenteral nutrition and improved infection control policies probably contributed greatly to the lesser mortality in 2009/2010.

Conclusions

- Babies with 32 weeks or less gestation and VLBW babies were significantly more common in 2009/2010 compared to 2001/2002 ($P<0.05$).
- Complications such as VAP, nosocomial sepsis and pneumothorax were significantly more common in babies ventilated in 2000/2001 but ROP was significantly more common in babies ventilated in 2009/ 2010 ($P<0.05$).
- HIE caused significantly more deaths in 2000/ 2001 whilst significantly more deaths occurred in ex-utero babies and babies with pulmonary haemorrhage in 2009/2010 ($P<0.05$).
- Overall mortality, mortality in babies with a 32 weeks or less gestation and mortality in VLBW babies were significantly lower in 2009/2010 ($P<0.0001$).
- In 2009/2010, the outcome in babies receiving CPAP only was significantly better than those receiving IMV only and there was no morbidity at 2 years of age in significantly more babies over 32 weeks gestation compared to babies with gestation 32 weeks or less ($P<0.0001$).

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