Original Research Article

Study on effect of duration of mechanical ventilation on retinopathy of prematurity in low birth weight neonates admitted to neonatal intensive care unit

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ABSTRACT

Background: There has been an increase in morbidity in low birth weight infants, since the advancement in field of neonatology. Various resuscitation methods and life saving interventions are associated with adverse effects. One such intervention is mechanical ventilation and if prolonged, it is known to cause various morbidities like bronchopulmonary dysplasia, retinopathy of prematurity, vocal cord injury. In this study we are considering the effect of duration of ventilation on retinopathy of prematurity.

Methods: This study is a prospective study, an observational study. The study was conducted in Kempegowda Institute of Medical Sciences, Bangalore. Total of 60 low birth weight infants (<2500gm) who were admitted to the Neonatal Intensive Care Unit (NICU) and were on mechanical ventilator support were included in the study. The study was conducted for a duration of 18 months, between January 2019 to June 2020.

Results: Retinopathy of prematurity (ROP) was seen in 19 cases and was the most common complication associated with increasing duration of mechanical ventilation, which accounted for 48% of total complications, followed by abnormal otoacoustic emission (OAE) 17.95%, pneumothorax 10.26%, apnea 7.69%, pneumonia and bronchopulmonary dysplasia 5.13% and Hypoxic ischaemic encephalopathy (HIE) and seizures 2.46%.

Conclusions: In this study, we were able to know the common complications involved in prolonged mechanical ventilation. This provides us to think about needs for measures to reduce the duration of mechanical ventilation and thereby reducing morbidities associated with it.

Keywords: Low birth weight neonates, Mechanical ventilation, Retinopathy of prematurity

INTRODUCTION

Recently the field of neonatology and newborn care have advanced and as a result there is decrease in the mortality with respect to low birth weight infants.1,3

According to the recent survey out of all deliveries 1/4th of newborn are low birth weight.4 However these resuscitation methods leads to various morbidities and consequences.5 In this study we are going to see the outcome of one such resuscitation method which is of utmost importance for survival of a newborn, which is mechanical ventilation.6-7

If ventilation gets prolonged they can be associated with complications and sequelae like BPD, subglottic stenosis, ROP, bronchial hyper-reactivity, abnormal hearing and also atelectasis, barotrauma and volutrauma.8-10
In this study we try to know the impact of prolonged ventilation on development of retinopathy of prematurity and also about various complications associated with prolonged ventilation.

**Retinopathy of prematurity**

Retinopathy of prematurity is a multifactorial vasoproliferative retinal disorder that increases in incidence with decreasing gestational age. Around 65% of neonates with birth weight of <1.250gm and around 80% of neonates with <1,000gm birth weight are likely to develop ROP at some stage.

**Risk factors**

Low birth weight, low gestational age, high ambient light, prolonged ventilation, vitamin E deficiency, shock, sepsis, apneic attacks, acidosis, anaemia and blood transfusions.\(^{11}\)

**Severity of retinopathy of prematurity**

- **Stage 1** A thin white line appears as a demarcation between vascular retina and underdeveloped avascular retina.
- **Stage 2** A fibrovascular ridge develops from the demarcation line and it extends inwards from retina.
- **Stage 3** There is extraretinal proliferation of fibrovascular ridge. Abnormal development of fibrous tissue and vascular system into the vitreous is seen.
- **Stage 4** Fibrovascular tissue pulls on retina and there may be resultant partial detachment of retina.
- **Stage 4A** is partial detachment where macula is not involved, and chance of good vision is still possible.
- **Stage 4B** is partial detachment where macula is involved and possibility of good vision is less.
- **Stage 5** There is complete detachment of retina and it assumes funnel shape.\(^{12}\)

**Prognosis**

Stage 1 and 2 ROP usually regress but need close follow-up. These stages are associated with complications such as refractive errors, amblyopia, cataract and strabismus.

Stage 3 ROP is associated with higher incidence of refractive errors and strabismus. Stage 4B and Stage 5 ROP are associated with risk of acute glaucoma, retinal detachment and blindness.\(^{13}\)

Cicatricial disease is the residual scarring in the retina, post treatment, and may lead to retinal detachment later.\(^{14}\)

In this study we try to know the impact of prolonged ventilation on development of retinopathy of prematurity and also about various complications associated with prolonged ventilation.

**METHODS**

This study is a prospective study, an observational study. The study was conducted in Kempegowda Institute of Medical Sciences, Bangalore. Total of 60 low birth weight infants (<2500gm) who were admitted to the Neonatal Intensive Care Unit (NICU) and were on mechanical ventilator support were included in the study.

**Sample size calculation**

Sample size calculated using open epi software, considering 95% confidence interval and 10% precision.

**Formula**

\[ 4PQ/D^2 \ldots \cdot 4 \times 0.15 \times 0.85]/0.1 \times 0.1 = 50 \]

The study was conducted for a duration of 18 months, between January 2019 to June 2020. The outline of the study was presented to the institutional ethical committee and approval and clearance was obtained from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study.

**Inclusion criteria**

All low birth weight infants (<2500gm) who were intubated and on ventilator support. Previously extubated cases who were reintubated.

**Exclusion criteria**

Major congenital anomalies. Extubated as a part of withdrawal of care.

We included all LBW infants (<2500gm) who were intubated and who were on mechanical ventilation. Infants demographics (including birth weight (BW), gestational age (GA), gender, race and Apgar scores at 1 and 5min) and prenatal characteristics (including prenatal steroids, maternal diabetes, chorio-amnionitis and use of magnesium sulfate) were reviewed using case records.

Then these infants were followed up for complications like retinopathy of prematurity, bronchopulmonary dysplasia, pneumothorax, seizures and abnormal hearing.

**Statistical analysis**

Descriptive statistics was used was statistical analysis. It included mean and inferential statistics (which include use of student t test and chi square test). Differences between the mean values of two continuous variables were tested using student t test and for categorical
variables, chi square test was used to test significance of differences in proportion of two or more groups. Fischer exact test was used in place of chi square test wherever necessary. The p value of <0.05 was considered as significant. Med Calc statistical software tool was used to calculate various statistics in the study.

**RESULTS**

Out of 60 neonates enrolled in this study, Retinopathy of prematurity (ROP) was seen in 19 cases and was the most common complication which accounted for 48% of total complications, followed by abnormal otocoustic emission (OAE) 17.95%, pneumothorax 10.26%, apnea 7.69%, pneumonia and bronchopulmonary dysplasia 5.13% and Hypoxic ischaemic encephalopathy (HIE) and seizures 2.46% (Table 1).

It can be seen from Table 2 that ROP is noticed in 17 cases who were on ventilator for >7 days to only 2 cases which were on ventilator for fewer than 7 days. Abnormal OAE is seen only in cases who were ventilated for more than 7 days.

**Table 1: Important complications noticed in our study population.**

| Complications               | Frequency | Percentage |
|-----------------------------|-----------|------------|
| Pneumonia                   | 2         | 5.13       |
| Pneumothorax                | 4         | 10.26      |
| Bronchopulmonary dysplasia  | 2         | 5.13       |
| ROP                         | 19        | 48.72      |
| HIE                         | 1         | 2.56       |
| APNEA                       | 3         | 7.69       |
| Seizures                    | 1         | 2.56       |
| Abnormal OAE                | 7         | 17.95      |

**Table 2: Comparing various complications with duration of mechanical ventilation.**

| Complications        | Mechanical ventilation for 7 days or less | Mechanical ventilation for more than 7 days | P value |
|----------------------|------------------------------------------|-------------------------------------------|---------|
| ROP                  | Yes 2                                    | 17                                        | <0.00001|
|                      | No 37                                    | 4                                         |         |
| BPD                  | Yes 0                                    | 2                                         | 0.1186  |
|                      | No 39                                    | 19                                        |         |
| Pneumothorax         | Yes 2                                    | 2                                         | 0.6064  |
|                      | No 37                                    | 19                                        |         |
| Abnormal OAE         | Yes 0                                    | 7                                         | 0.0003  |
|                      | No 39                                    | 14                                        |         |
| Reintubation         | Yes 3                                    | 8                                         | 0.011   |
|                      | No 36                                    | 13                                        |         |

Reintubations were more common in neonates who were on ventilator for >7 days and these findings were statistically significant. BPD was seen in 2 neonates both of them were on ventilator for more than 7 days.

**Table 3: ROP stages in cases based on duration of ventilation.**

| ROP staging | <7days | >7days | P value |
|-------------|--------|--------|---------|
| Stage 1     | 0      | 3      |         |
| Stage 2     | 2      | 11     | 1       |
| Stage 3     | 0      | 3      |         |

Table 3 shows comparison between stages of ROP and their correlation with duration of ventilation. ROP was found in 2 cases who were on ventilator for <7 days and in 11 cases who were ventilated for >7 days. However, there was no statistical difference in stage of ROP in these two groups. 2 cases out of 3 in stage 3 group received laser photoacoagulation.

**DISCUSSION**

Through this study the effort was made to study various complications related to prolonged ventilation. In our study retinopathy of prematurity (ROP) was seen in 19 cases and was the most common complication which accounted for 48% of total complications, it was followed by abnormal otocoustic emission (OAE) in 7 cases, pneumothorax in 4 cases, apnea in 3 cases, pneumonia and bronchopulmonary dysplasia in 2 cases and hypoxic ischaemic encephalopathy (HIE) and seizures were found in one case each.

It can be appreciated from our study that ROP is noticed in cases who were on ventilator for >7 days and in only 2 cases who were on ventilator for fewer than 7 days. Abnormal OAE is seen only in cases who were ventilated for more than 7 days.

Reintubations were more common in neonates who were on ventilator for >7 days and these findings were statistically significant. BPD was seen in 2 neonates both
of them were on ventilator for more than 7 days. A meta analysis which was done recently showed a significant change in incidence of BPD by avoiding prolonged mechanical ventilation.15

**Limitations**

In this study we included all low birth weight neonates, since ROP is more commonly seen in very low birth weight neonates, we were unable to include more sample. size from this group of neonates. And, also study was done in our institute, the treatment protocol followed may vary from institute to institute, so multicenter studies are required. This study prompts requirement of more such studies with more cases and also inclusion of other hospital setup, referral hospitals and tertiary centres.

To provide additional data about various adverse effects. This study also emphasises the fact that efforts are required to reduce the duration of mechanical ventilation and also on follow up of these cases to diagnose the complication and render treatment at the earliest.

**CONCLUSION**

In this study, we were able to know the common complications involved in prolonged mechanical ventilation. This provides us to think about needs for measures to reduce the duration of mechanical ventilation and thereby reducing morbidities associated with it.

Through this study we were able to understand the requirement of follow up in these situations to know the complete extent of morbidity and also to intervene early to prevent further complications.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India

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