A STUDY REGARDING MECHANICAL VENTILATION AMONG 153 PREMATURE NEWBORN BORN AT A GESTATIONAL AGE LESS THAN 32 WEEKS

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Abstract

The hyaline membrane disease is a typical disease of prematurity and it is caused by surfactant deficiency. The incidence of hyaline membrane disease is inversely related to gestational age, but it is not influenced by the birth weight. The therapy involves: prophylactic therapy, supportive therapy, mechanical ventilation, surfactant replacement. *Objective.* To set up a guideline for the respiratory therapy of premature newborns with respiratory distress syndrome, in order to rise survival, decreasing complications and sequaelae, lower hospitalization's duration. *Method*. There were 153 premature newborns included in study, all born before 32 weeks of gestational age, born in Oradea Maternity Hospital or transferred here from level II units, between 01.01.2010- 31.08.2011. *Results and conclusions:* These times, the neonatal intensive care is improving day after day, the respiratory care is a necessity for premature newborns' survival. For the prematures under 29 weeks of gestation, exogenous surfactant instillation immediately after birth and CPAP respiratory support improves lung ventilation, lower oxygen requirements, lowers the incidence of immediate complications (air leak, infection, intraventricular hemorrhage) and of long term complications (bronchopulmonary dysplasia). INSURE therapy and CPAP were effective in promoting an adequate ventilation and had low complication rate in newborns > 29 weeks of gestation with severe/medium RDS. In the future, it will be a necessity to use other ventilation mode, currently unavailable for our clinical practice (NO, liquid ventilation, ECMO)

Key words: premature newborn, ventilation, survival

Introduction

The hyaline membrane disease is a typical disease of prematurity and it is caused by surfactant deficiency.

The incidence of hyaline membrane disease is inversely related to gestational age, but it is not influenced by the birth weight. The clinical course of the disease starts in the first 10 hours of life with symptoms of respiratory distress of various severity and it worsens for the next 24-72 hours of life. After that, the disease may have a favorable course or it may worsen and may result in complications, sequelae or death.

The therapy involves: prophylactic therapy, supportive therapy, mechanical ventilation, surfactant replacement.

The ventilation modes and strategies used in clinical practice are

1.1 *Continuous Positive Airway Pressure (noninvasive respiratory care).* The continuous positive airway pressure may be achieved by mask, by nasal prongs or by endotracheal intubation or nasopharyngeal intubation. Nasal CPAP is considered the most gentle kind of respiratory support, having less adverse outcomes. The many forms of CPAP ventilation include bubble CPAP and variable flow CPAP[1].

1.2 *Positive pressure ventilation, time-control, limited pressure, conventional rate* (Intermitent Positive Pressure Ventilation- IPPV) is conventional ventilation and it is the most used mode of ventilation in the neonate. In IPPV mode are used ventilator rates between 30-120/min (with a lower rate the ventilation mode is called IMV- Intermittent Mandatory Ventilation) the inspire/expire fraction is inversed (there is an inversion when the inspire is longer than the expire), positive end expiratory pressure of 0-12 cm H_2O (the most used are the pressures between 3-6 cm H_2O).[2]

1.3 *Volume-control mechanical ventilation (VCV).* In this ventilation mode a preset volume of air is delivered to the neonate. The efficiency of this mode of ventilation was compared to IPPV in many trials and meta-analyses which showed that VCV was linked to lower ventilation time and air leak rate, but there weren't differences in chronic lung disease and mortality rates.[3]

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Increasing regular physical activity is accompanied by slowing the pulmonary function decline and constant participation in various physical activities may increase the compliance in the long term (12, 23). Short-term studies have shown an improvement in *lung function* and wellbeing of these children as a result of sustained physical activity programs in outpatient (20).

This study provides evidence for the earliest possible implementation of a sustained program of usual physical activity at home, as part of therapy in patients with CF. The study presents spirometry indices: *vital capacity* (VC), *forced expiratory volume in one second* (FEV1), *forced expiratory flow between 25 and 75% of forced vital capacity* (FEF25-75) and *airway permeability index* (FEV1/VC report), in a group of patients with CF, after implementing an outpatient program to increase the level of physical activity for one year.

Material and method

The study design was prospective, multicenter, and included a group of 52 children (older than 6 years), adolescents and young adults diagnosed with CF, which are found in the records of the 2nd Pediatric Clinic of Emergency Hospital from Craiova, Children's Emergency Hospital "Maria Sklodowska Curie" and the Institute for Maternal and Child, "Alfred Rusescu" (IOMC), both from Bucharest. We included patients with definite diagnosis of CF, based on characteristic anamnestic - clinical criteria and confirmed by two positive sweat tests and in some patients by the genetic test (1, 9, 13, 27), without acute respiratory failure, chronic pulmonary heart (CPC) or the coexistence of decompensated heart disease, independent of respiratory disease but exacerbated by it. Any patient in the study had no contraindications to perform airway clearance techniques (ACTs). Were included only patients who did regular treatment and were able to perform spirometry tests. General characteristics of patients, weight (W), size (S) and body mass index (BMI) were recorded in case report forms and those values (expressed in kg, m and kg / m²) were converted into number of standard deviations (SD) compared with mean values correlated with the age and gender (Z score).

Spirometry tests were conducted in laboratories functional exploration of the three medical units who studied for the treatment of CF. Has been recorded vital capacity (VC), forced expiratory volume in one second (FEV1) and forced expiratory flow between 25 and 75% of forced vital capacity (FEF25-75) and the report FEV1/VC (airway permeability index). During spirometry test was performed three forced expiration maneuvers were recorded the best results. All values were expressed in liters and percentage of predicted for age, height and sex. Spirometry records were analyzed in two different moments of time: before (the beginning of 2009) and one year after implementation of an outpatient program to increase physical activity level (end 2009). We considered the lower limit of normal the 80% of predicted for VC, FEV1 and FEF25-75 and 0.75 for the ratio FEV1/VC (6, 26).

All enrolled patients received a comprehensive treatment, according to management guidelines in CF (1, 9, 13, 27): dietary and hygiene measures, drug treatment (by systemic antibiotic, anti-inflammatory and antifungal therapy) and aerosol therapy (antibiotics , mucolytics, corticosteroids and bronchodilators), depending on the specifics of each case. In terms of respiratory physiotherapy, airway clearance techniques (ACTs) were given daily, two sessions per day, morning, before a meal and evening, two hours after eating, before going to bed, each session lasting 30 minutes. All patients performed *active cycle of breathing techniques* (ACBT): *controlled breathing* (CB), *thoracic expansion exercises* (TEE) and *forced expiratory technique* (FET), performed in different *postural drainage positions* (depending on the lobe or lung segment drained), which alternated with *percussion*, *vibration* and *assisted cough*. Number of postural drainage positions was limited to three for the each session. Once a patient with CF was placed in a *postural drainage positions*, the person assisting him performed chest wall percussion, for a period of 3-5 minutes for each position, followed by vibration on the same segment, for approximately 15 seconds (or during the five exhales). Then, the patient was encouraged *to cough* or perform *huff* for elimination of excess mucus. *Modified postural drainage positions* were indicated in patients with gastroesophageal reflux (GOR).

Since 2009, all the 52 patients have been included in an outpatient exercise program to increase the usual physical activity level. Although a correct prescription for such a program would have to start from the results of the *exercise testing* (17), this test could not be performed due to lack of adequate equipment, including blood gas analysis, lack of compliance for patients or carers in some cases, the absence of a full medical team to allow safe testing conditions.

According to the literature, practice has shown that the vast majority of patients with respiratory disease do not need an exercise testing to be prescribed them a program of physical activity (18, 19). Medical history of the different types (respectively degree) of physical effort that these patients are made daily in the normal activity, and on aspects of how the patient supports this efforts, provided us sufficient data to recommend complete safety an outpatient exercise program for patients from this study. Thus, depending of the intensity of exercise supported by the patient and of the patient age, we recommended the following types of physical activity, according to specialized studies (22, 28):

- moderate physical activities: walking briskly - about 3 ½ miles (5.6 km) per hour, hiking, gardening/yard work, dancing, golf (walking and carrying clubs), bicycling - less than 10 miles (16 km) per hour, weight training (general light workout);
- vigorous physical activities: running/jogging - 5 miles (8 km) per hour, bicycling - more than 10 miles (16 km) per hour, swimming (freestyle laps), aerobics, walking very fast - 4 ½ miles (7.2 km) per hour, heavy yard work, such as chopping wood (for teens and adults), weight lifting (vigorous effort), basketball (competitive).

1.4 *Patient-triggered ventilation.* Through the last 2 decades this mode of ventilation was used in neonatal respiratory care as control-assisted ventilation (ventilation is triggered by spontaneous breaths which exceed the trigger's threshold) and as synchronized intermittent mechanical ventilation (SIMV)(the rate is preset and it isn't related to spontaneous breaths' rate but inflation is synchronized to spontaneous breaths).[4] The trigger modes- PSV- Pressure Support ventilation, VG- Volume Guarantee ventilation, PAV- Proportionally Assisted ventilation, are not usually available.

1.5 *High frequency ventilation* is a mode of ventilation that uses respiratory rates which are much higher than normal respiratory rates. There are 3 modes of HFV:
1.5.1. High Frequency Positive Pressure Ventilation (HPPV, rates 60-150/min)
1.5.2. High Frequency Jet Ventilation (HFJV, rates 100-600/min)
1.5.3. High Frequency Oscillator Ventilation (HFOV, rates 300-3000/min)[5]

High Frequency Ventilation indications: conventional ventilation failure, prevention of pulmonary injury, neonatal chronic pulmonary disease, air leak syndromes, diaphragmatic hernia, meconium aspiration syndrome.[6]

1.6 *Liquid Ventilation* (LV) is a technique of mechanical ventilation in which the lungs are insufflated with an oxygenated perfluorocarbon (PFC) liquid. The perflourocarbon is comparable to water and it has low superficial tensions and a high solubility for respiratory gases.
1.7 *Extracorporeal membrane oxygenation (ECMO)* is the use of an artificial lung (membrane) located outside the body (extracorporeal), that puts oxygen into the blood and then carries this blood to the body tissues (oxygenation). The CO_2 and the water are eliminated and the blood is rewarmed before reintroducing it into the body.[7] Ecmo is generally used in those neonates with intractable but reversible respiratory disease which failed other therapies.[8]
1.8 *Nitric oxide therapy.* Nitric Oxide is inhaled into the lungs and acts as a pulmonary selective vasodilator used for hypoxemic respiratory distress linked to pulmonary hypertension. The trials showed that NO ventilation lowers the necessity for ECMO and mortality in premature and term newborns.[9]

Objective

To set up a guideline for the respiratory therapy of premature newborns with respiratory distress syndrome, in order to rise survival, decreasing complications and sequaelae, lower hospitalization's duration.

Method

There were 153 premature newborns included in study, all born before 32 weeks of gestational age, born in Oradea Maternity Hospital or transferred here from level II units, between 01.01.2010- 31.08.2011.

Results

1.The incidence of Prematurity in Maternity Hospital of Oradea between 01.01.2010- 31.08.2011: from a total 7277 newborns, 153 where premature newborns (GA under 32 weks) with prematurity rate (GA under 32 weeks): 2,1%

2.Totality of premature newborns treated in Neonatal Intensive Care Unit between 01.01.2010- 31.08.2011
- Neonates born in Maternity Hospital of Oradea - 131 cases (86%)
- Neonates transferred from other hospitals - 19 cases (12%)
- Neonates born at home - 3 cases (2%)

3.Gender distribution: 87 cases where female and 66 cases where male.

4.Birth weight distribution:
<799g - 18 Newborns, 800-999 g - 24 Newborns, 1000-1249g - 38 Newborns, 1250-1499g - 43 Newborns, >1500g - 30 Newborns

5.Apgar Score Distribution:
Apgar Score 1-3 / 56 Newborns; Apgar Score 4-5 / 49 Newborns; Apgar Score 6-7 / 38 Newborns; Apgar Score 8-10 / 7 Newborns

6.Neonatal deaths - 21 cases
Cause of death: Intra-ventricular haemorrhage 10 cases, hydrocephaly 1case, infection 4 cases, pneumothorax 2 bronchopulmonary dysplasia 1 case, congenital malformations 2 cases.

7.Strategies of neonatal ventilation
- Neonates with severe respiratory distress syndrome (radiological ground-glass image) - 32 cases,
- Surfactant (prophylaxis or curative) treated newborns - 52 cases,
- Neonates treated with CPAP without surfactant therapy - 23 cases,
- Surfactant and CPAP treated newborns - 49 cases,
- Neonates treated only by oxygen flow - 49 cases,
- SIMV ventilated newborns - 12 cases,
- HFOV ventilated newborns - 3 cases,
- IPPV ventilated newborns - 3 cases,
- INSURE therapy - 14 cases.

8.The respiratory care groups were compared regarding:
- Blood gases in the first 10 days of life
- FiO2 used
- radiologic al findings
- oxgen therapy total duration
- enteral feeding tolerance
- hospitalisation time
- complications
- sequellae

3.9.Newborns treated with CPAP without surfactant therapy-23

Neonates GA>29 weeks- 20 • Fi O_2 used- 25-45% • Radiological image improved in 4-5 days • CPAP treated for 7-8 days and oxygen therapy until 2 weeks of age • Enteral feedings well tolerated within 14 days • Complication- gastric air distention, bronchopulmonary dysplasia- 3 cases • Hospital staying- for 2 months (average)	*Neonates GA< 29 weeks-4* • FiO_2 used: 40-70% • PEEP>5cm H_2O • Radiological image improved after 10 days in one case • CPAP treated for 20 days and oxygen therapy beyond 25 days of age • Enteral feedings well tolerated within 21 days • Complication gastric air distention, bronchopulmonary dysplasia, pneumothorax- 2 cases, infection • Hospital staying for 3 month (average)

10. Surfactant+CPAP treated newborns- 49

Neonates <29 weeks of GA and neonates >29 weeks of GA with severe respiratory distress syndrome

- FiO_2 used of 21-35% after surfactant treatment
- PEEP of 2 to 4 cm H_2O
- Radiological improvement within 2 days
- CPAP treated for 7-10 days and oxygen therapy for 12-15 days
- Enteral feedings tolerated within 14 days
- Complication- gastric air distension
- Hospital staying for 6-8 weeks (average)

11.SIMV ventilated newborns - 12 cases.

Neonates <32 weeks of GA with severe respiratory distress syndrome or no spontaneous breathing or CPAP therapy failure:

- FiO_2 of 40-70% before surfactant treatment and 30-40% after surfactant instillation
- Radiologic improvement in 4-5 days
- SIMV ventilated for 6 days (maximum), CPAP treated after extubation for 7-10 days and oxygen therapy within 15-25 days of life
- Enteral feedings tolerated within 14 days (maximum)
- Complications: bronchopulmonary dysplasia, infections, intraventricular hemorrhage
- Hospital staying for 8 weeks (average)

12.HFOV ventilated Newborns -3 cases.

Neonates <32 weeks of GA with severe respiratory distress syndrome or no spontaneous breathing or conventional ventilation failure:

- HFOV was not effective in two cases of severe RDS and they were switched on IPPV
- HFOV was used with outstanding results in a case of severe RDS and pneumothorax

13.IPPV ventilated newborns - 3 cases.

Newborns <32 weeks of GA which failed other ventilation strategies

14.INSURE therapy -14 cases.

Neonates <32 weeks of GA with medium or severe respiratory distress syndrome which could not be CPAP treated for technical reasons

- FiO_2 used after surfactant instillation: 21-35%
- Radiological improvement within 2 days
- Oxygen therapy for 15-20 days
- Enteral feedings tolerated within 14 days
- Complications- infection
- Hospital staying- an average of 6-8 weeks

Conclusions

- These times, the neonatal intensive care is improving day after day, the respiratory care is a necessity for premature newborns' survival.
- For the prematures under 29 weeks of gestation, exogenous surfactant instillation immediately after birth and CPAP respiratory support improves lung ventilation, lower oxygen requirements, lowers the incidence of immediate complications (air leak, infection, intraventricular hemorrhage) and of long term complications (bronchopulmonary dysplasia).
- Bronchopulmonary dysplasia occured in very premature newborns which also had early-onset sepsis.
- Pneumothorax occured in prematures under 29 weeks of gestation with severe RDS, not surfactant treated and a PEEP > 4 cm H_2O. PEEP>4 cm H_2O set up immediately after birth in lung pathology neonates was linked to increased incidence of pneumothorax.
- Intraventricular hemorrhage occured in severely asphyxiated newborns, in twins (second twin) and in newborns born by vaginal delivery rather than cesarian section.
- INSURE therapy and CPAP were effective in promoting an adequate ventilation and had low complication rate in newborns > 29 weeks of gestation with severe/medium RDS.
- HFOV did not have superior results compared to conventional ventilation in RDS but it was highly effective in air leak treatment.
- In the future, it will be a necessity to use other ventilation mode, currently unavailable for our clinical practice (NO, liquid ventilation, ECMO).
- This study has to continue with comparisons of different ventilator settings and oxygenation effect in order to achieve an effective and less invasive respiratory care and the maximal benefit for the patient.

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