The Egyptian Journal of Hospital Medicine (January 2018) Vol. 70 (11), Page 2025-2028

Respiratory Aspects of Approach to Neonatal Resuscitation

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ABSTRACT

Introduction: Around 10% of live births globally require immediate intervention, and 4 million neonatal deaths happen in a year, where one fourth of them are due to asphyxia. Regular respiration may fail to achieve spontaneously in about ten percent of live births, with one percent of cases needing resuscitation with chest compressions, and about 0.06% needing epinephrine. The target in neonatal resuscitation is to achieve sufficient functional residual capacity, while avoiding pulmonary damage, and to optimize the tissue delivery of oxygen without causing toxicity

Methodology: We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through February 2017. The following search terms were used: neonatal asphyxia, neonatal resuscitation, neonatal intensive care, respiratory distress syndrome, complications of prematurity, oxygen therapy, neonatal ventilation

Aim: In this review, we aim to study the various approach taken to provide immediate resuscitation to neonates with respect to respiratory distress.

Conclusion: With advancing research, physicians should have more devices to decrease the mortality rates among infants. We also need more research to establish best recommendations and guidelines on the use of best interventions especially in clinical setting with limited resources.

Keywords: neonatal resuscitation, neonatal intensive care, respiratory distress syndrome, complications of prematurity, oxygen therapy, neonatal ventilation, neonatal asphyxia.

INTRODUCTION

It is estimated that about 10% of live births worldwide will need an immediate intervention following birth. Four million neonatal deaths occur annually, with about a quarter of them as a result of asphyxia [1]. Infants' adaptation to extrauterine life normally occurs through physical transition, but needs external help in most cases to be achieved without complications. This adaptation happens through respiratory and circulatory changes. Regular respiration may fail to achieve spontaneously in about ten percent of live births, with one percent of cases needing resuscitation with chest compressions, and about 0.06% needing epinephrine [2].

To understand the physiology of neonatal resuscitation, there has been significant research in this field, with multiple attempts to establish new guidelines and recommendations that will lead to better outcomes at birth. The target in neonatal resuscitation is to achieve sufficient functional residual capacity (FRC), while avoiding pulmonary damage, and to optimize the tissue delivery of oxygen without causing toxicity.

METHODOLOGY

- **Data Sources and Search terms**

We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1986, through February 2017. The following search terms were used: neonatal asphyxia, neonatal resuscitation, neonatal intensive care, respiratory distress syndrome, complications of prematurity, oxygen therapy, neonatal ventilation

- **Data Extraction**

Two reviewers have independently reviewed the studies, abstracted data, and disagreements were resolved by consensus. Studies were evaluated for quality and a review protocol was followed throughout.

The study was done after approval of ethical board of King Abdulaziz university.

Ventilation

Fetal lung fluid and first breaths

To reach proper in-utero lung development, it is critical to maintain the active secretion of chloride. Late in pregnancy, mechanisms responsible for the

Received: 20/12/2017
Accepted: 30/12/2017
DOI: 10.12816/0044863

absorption of sodium are stimulated by thyroid hormones and glucocorticoids. Then, uterine contractions cause significant stress that will increase epinephrine levels [3]. This will be later followed by high inhaled oxygen levels that will help the physiological transition into the extrauterine environment. To empty the lung from fluids that are present before birth, all the previous steps are essential, and they begin shortly before birth to complete soon after birth. Respiratory muscles movements are decreased during delivery. This can in some cases be associated with meconium aspiration causing severe asphyxia. Immediately after delivery, the cooling, increase in carbon dioxide, the epinephrine high levels, the stimulation of substance P genes and other substances, and the cessation of placental inhibition, all lead to the initiation of breathing [4].

To reach a volume of 40 mL, the first breaths need to create relatively high pressures; inspiratory pressure can range from -28 to -105 cm H_2O, with a mean of -52 cm H_2O, and expiratory pressure can range from 18 to 115 cm H_2O with a mean of 71 cm H_2O [5]. They also need to be relatively long and deep, with a deep short inspiration that is followed by a long expiration while the larynx is partially closed (a phase called the expiratory braking). A similar physiology is applied when using continuous positive airway pressure (CPAP) for treatment [6]. To facilitate the movement of lungs with sufficient volume, infants (preterm and term) cry immediately at birth. All the previously mentioned mechanisms have encouraged researchers to study apneic infants and the effects of sustained inflation (SI) [7].

Sustained Inflation (SI)

Until now, no established ideal protocol has been established to manage term and preterm infants with respiratory failure who fail to achieve spontaneous respiration or who still have fluid in their lungs. Recently, it has been suggested that applying SI with the initiation of resuscitation will help maintain better aeration of lungs. However, the pressure and duration of SI are still controversial [8]. A previous research on preterm rabbits showed that positive end-expiratory pressure (PEEP) with positive pressure ventilation (PPV) applied after twenty seconds of SI led to significant improvement in lungs aeration and FRC [9]. Another study found higher stability of pulmonary and cerebral blood flow when applying SI in preterm lambs [10]. Lindner et al. conducted an randomized controlled trial (RCT) on sixty-one preterm infants and reported no significant difference in outcomes and adverse events following either nasal-intermittent mandatory ventilation or SI for fifteen seconds [11]. On the other hand, it was found by Lista et al. that SI for fifteen seconds with subsequently applying nasal CPAP caused a significant decline in mechanical ventilation rates, the use of surfactant and steroids, the need of long-duration ventilation, and dysplasia in preterms [12]. Many RCTs are still ongoing to study and evaluate the use of SI in preterms, and its potential effects. However, these results provided by trials must be carefully studied as significant bias and confounding may have been present during conduction.

Assisted ventilation and ventilation devices in the delivery room

Soon after birth, many infants need to get ventilatory support. This support is usually divided into two subtypes according to the cause: insufficient respiratory effort/inspiratory depression, and respiratory distress. The first case results in apnea or hypopnea associated with central nervous system (CNS) abnormalities, sepsis, and/or asphyxia. The other case (respiratory distress) will cause relatively high breathing workload, and is associated usually with retained lung fluid, respiratory distress syndrome, air-leak syndromes, congenital anomalies, and pleural effusions. Assisted ventilations aims at the creation and maintenance of a sufficient FRC and tidal volume (VT), to achieve breathing with gas exchange and minimal pulmonary damage. Commonly used methods include SI, CPAP, and PPV with the use of these three devices: a self-inflating bag, a T-piece resuscitator, or a flow-inflating bag.

In some cases, where infants breathe spontaneously, but there is a narrow glottis, PEEP application can help get sufficient FRC by increasing the intrathoracic pressure. In cases of severe respiratory distress or apnea, infants can get initial SI but they will also need PPV. Unfortunately, the ideal VT and FRC need to have accurate inspiratory pressures during PPV, which represents difficult challenge to physicians. This is due to the face that VT depends on many factors including the resistance and compliance of pulmonary tissue, the inflation-time used, the breathing activity of the infant, and the volume of liquid present in the lungs [13]. In addition, the use of masks can be associated with leaks that will cause significant compromise to VT and FRC. When there is insufficient ventilation, Neonatal Resuscitation Program guidelines have introduced the 'MR SOPA' acronym that will keep resuscitators reminded of the steps that need to be applied. These steps are: Mask adjustment, Reposition airways, Suction of nose and mouth, Opened mouth, Pressure elevation, Alternative airway establishment.

Each device of ventilation is associated with both advantages and disadvantages, making the recommendation of a single choice challenging, and depends on the physician [14]. A large international crossover RCT on infants found a significant decrease in intubation need following using the T-piece resuscitator when compared to the use of the self-inflating bag (17% vs 26%) [15]. Post hoc analysis of the results of this study showed that infants with very low birth weight who used the T-piece resuscitator have a significantly less risk of needing intubation and developing broncho-pulmonary dysplasia BDP [16]. Despite all drawbacks of self-inflating bags, the choice at the real setting will mainly depend on the available devices and the experience of physicians who are providing the service. Therefore, it is essential to emphasize on the importance of proper training and education on the use of all available devices [17].

Oxygen

Organisms get the energy needed for life from mitochondria through aerobic metabolism. This process includes the production of reactive oxygen species by mitochondria. This will subsequently lead to formation of reactive free radicals that will cause structural and functional damage to cells. Newborns (especially premature infants) have an immature antioxidants defense system that will predispose them to higher oxidative damage. The use of 100% oxygen in asphyxiated infants was found to cause oxygen toxicity with cellular damage, along with a delay in the first cry and spontaneous respiration [18; 19]. This suggests that oxygen can decrease the activity of respiration in infants. A decline in pulmonary resistance has been effectively achieved in asphyxiated newborn lambs when applying 21% oxygen for ventilation [20]. This was also observed in the presence of arterial remodeling or pulmonary hypertension [21].

Since 1980s, physicians have realized the significant damage that resulted from oxidative stress. This led to recommendations to control levels of oxygen used among infants. In 2010, the International Liaison Committee on Resuscitation (ILCOR) published their new guidelines that recommended the use of air ventilation instead of pure oxygen. However, no sufficient evidence is present to support the use of oxygen supplementation following resuscitation. On the other hand, solid evidence is present to support the serious complications that occurs following hypoxemia [22].

Asphyxia and hyperoxemia

Recently, a retrospective study was conducted on infants with severe academia found that hyperoxemia was associated with the later development of hypoxic-ischemic encephalopathy (HIE) [22]. In fact, 30% of included infants who were diagnosed with HIE were found to have had hyperoxemic with a PaO_2 that is more than 100 mm Hg during the first hour of life. Researchers concluded that a 4-fold higher risk of HIE was present in infants with hyperoxemia, and the risk of HIE increases with higher levels of hyperoxemia. Moreover, researchers found that 79% of infants with hyperoxemia had MRI changes suggesting HIE [23].

All these findings are similar to previous findings that reported poorer outcomes following early hyperoxemia ($PaO2 > 200$ mmHg) [24]. A significant correlation is also present between the long-term complications in HIE, and the fraction of inspired O_2 (FiO_2) during the first 6 hours. It was proven in a recent meta-analysis on preterm infants that low FiO_2 (0.21-0.30) was associated with used with significantly decreased mortality rates when comparing with the use of high FiO_2 (0.60-1.0) [25]. The serious long-term complications of hyperoxemia should be well-known to physicians, so they target normoximec status.

CONCLUSIONS

The field of neonatal resuscitation have improved significantly recently. Moreover, many gaps in our knowledge have been identified allowing for the recommendations of better approaches and protocols to treat infants who need aggressive resuscitation. Optimal ventilation is essential to prevent hyperoxemia and pulmonary damage. SI is a beneficial method that has been found to provide positive outcomes. However, it is not established how to best provide PPV and how to reduce the rate of mask leak. Chest compressions and medical therapy are rarely needed to achieve spontaneous circulation and respiration, but more studies on these interventions are still needed. With advancing research, physicians should have more devices to decrease the mortality rates among infants. We also need more research to establish best recommendations and guidelines on the use of best interventions especially in clinical setting with limited resources. In some cases, interventions as simple as delayed cord clamping can have a significant effect and cause a great reduction in morbidities and mortality following asphyxia.

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