An-Najah National University

Faculty of Graduate Studies

PROTOCOLIZED VERSUS NON-PROTOCOLIZED WEANING FOR REDUCING THE DURATION AND COMPLICATIONS OF INVASIVE MECHANICAL VENTILATION IN PREMATURE INFANTS

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Dedication

الى من علمني كيف أقف بكل ثبات فوق الارض ..... أبي

الى من علمتني الصبر وتحمل ضغوطات الحياة ..... أمي

الى من أمداني بالنصح و الإرشاد وسندي بالأفراح و الأحزان ..... إخوتي

الى جميع الذين وقفوا بجانبي خلال مسيرة حياتي الجامعية ..... أساتذتي

إن إنهائي عملي لم يكن ليتم لولا دعمكم أهديكم خلاصة جهدي العلمي

واتمنى أن ينال رضاكم

Acknowledgment

To the one who taught me how to stand firmly above the ground.....Dad

To the one who taught me patience and bearing the pressures of life..... Mom

To the one who provided me with advice and guidance and supported me in joys and sorrows... my brother and sister

To all those who stood by me during the course of my university life..... my professors

My job would not have been completed without your support I present to you the summary of my scientific effort, and I hope that it will satisfy you

Declaration

I, the undersigned, declare that I submitted the thesis entitled:

PROTOCOLIZED VERSUS NON-PROTOCOLIZED WEANING FOR REDUCING THE DURATION AND COMPLICATIONS OF INVASIVE MECHANICAL VENTILATION IN PREMATURE INFANTS

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: دسينا يوسف سيفوت شاهين

Signature: دسينا شاهين

Date: 1/2/2022

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PROTOCOLIZED VERSUS NON-PROTOCOLIZED WEANING FOR REDUCING THE DURATION AND COMPLICATIONS OF INVASIVE MECHANICAL VENTILATION IN PREMATURE INFANTS

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Abstract

Background: For critically unwell newborns with respiratory failure admitted to a neonatal intensive care unit, mechanical ventilation is a life-saving operation (NICU). Due to small tidal volumes, high breathing frequencies, and the use of un-cuffed endotracheal tubes, ventilating newborns can be difficult. Weaning off the ventilator is initiated as soon as feasible to avoid difficulties.

Aims: The aims of the study was to compare the effectiveness of protocolized versus non-protocolized ventilator weaning in reducing the duration of invasive mechanical ventilation, weaning time, and NICU and hospital length of stay for newborn infants. To see how effective, it is in specific subgroups, such as gestational age and birth weight.

Material and methods: A quasi-experimental study conducted in patients undergoing protocolized versus non-protocolized weaning from invasive mechanical ventilation in premature infants in neonatal intensive care unit. Experimental group (n=30) was infants undergoing a weaning protocol from mechanical ventilator at gestational age 26 week and above. Historical Control Group (n=30) includes patients who were on mechanical ventilation at gestational age 26 week and above, conducted between July 2019 and June 2020 at Holy Family Hospital. Bethlehem. Palestine. with the same, ICU staff.

Results: The results show that the mean of weaning duration till extubation, length of stay in NICU and Hospital length of stay in the Historical group is significantly higher than that in the Protocol group.

The results show that 7 cases of 30 had pulmonary interstitial emphysema in the Historical while no cases in the Protocol group. Also, there are 6 cases of 30 had ventilator-associated pneumonia (VAP) in the Historical group while no cases had ventilator-associated pneumonia (VAP) in the Protocol group.

Conclusion: Weaning protocol reduces the duration of mechanical ventilation, weaning duration till extubation, NICU and hospital length of stay (days), the risk of weaning failure and reintubation. There is evidence to support the superiority of protocol weaning over nonprotocol weaning on the duration of invasive mechanical ventilation in newborn infants, according to the findings of this study.

Key words: Neonatal intensive care unit; Newborn; Mechanical Ventilation; Respiratory Failure

Chapter One
Introduction

1.1 Introduction

The survival rate of preterm infants has risen steadily throughout time (Costeloe, et al., 2012; Younge et al., 2017). Because of breakthroughs in prenatal, perinatal, and neonatal care, extremely tiny and premature infants are now surviving (Walsh et al., 2011). Premature infants, on the other hand, are born with undeveloped organs. Nursing, medical, and parental care, as well as mechanical devices, are usually required to keep their organ systems functioning properly. Neonatal critical care units are the medical term for these facilities.

Preterm neonates may need days, weeks, or even months of neonatal intensive care to grow and develop to the point where they can survive without it. The respiratory system is one of the organ systems in premature infants. The upper and lower airways, lung tissue (parenchyma), and supporting muscles, bones and connective tissue are all part of this. All organ systems, including the heart and circulation, the gastrointestinal system, the immunological system, and the brain and neurological system, are intimately tied to the respiratory system (Rocha et al., 2018). (Rocha et al., 2018). The existence of a preterm baby is based on the normal and interdependent functioning of all of these organ systems. Mechanical ventilation using an endotracheal (breathing) tube may be necessary to support a premature infant's respiratory system. This requires placing an endotracheal tube (ETT) into the trachea (windpipe) and attaching the ETT to a ventilator (Ali et al., 2019).

Mechanical ventilation is one of the most prevalent therapies in the newborn intensive care unit and is associated with higher morbidity and death. The treatment of infants undergoing mechanical breathing remains primarily based on individual choices. Mechanical ventilation is a difficult and highly specialized field of neonatology, made more complicated by the availability of numerous different modes, procedures, and equipment (Larsson et al., 2018).

In the face of a lack of convincing scientific evidence for many elements of mechanical ventilation in preterm infants, attaining consensus may not be simple (Sant'Anna et al.,

2012). Serious physiological and psychological squeals are linked with extended intrusive mechanical ventilation, which demands effective techniques to safely reduce and eliminate ventilator support, dubbed weaning (Maheshwari et al., 2016).

Mechanical ventilation is a lifesaving treatment in the case of respiratory failure among very ill newborn infants who are admitted to a neonatal intensive care unit (NICU). The Neovent (2010) Study Group conducted a two-point cross-sectional short-term repercussions such as pneumonia, atelectasis and air leak syndrome as well as long-term consequences such as bronchopulmonary dysplasia (BPD) and neurodevelopmental impairments are associated with mechanical ventilation, according to Sant'Anna (2012).

Weaning processes and automated systems, for example, may aid in the systematic and early detection of spontaneous breathing ability and the possibility for ventilation discontinuation. By stressing timely and objective decision-making, these tools have the potential to reduce practice variation and increase efficiency (Newth et al., 2009).

A protocol, by definition, is a clear and complete plan with explicit inclusion and exclusion criteria that provides standardized methods for care for patients with specified illnesses (Prasad et al., 2011). Protocols have been extensively studied in both adult and pediatric populations, notably in neonates; however, only a small amount of retrospective research has been done to assess the impact of a ventilation method. Some of the most notable applications are the treatment of sepsis, diabetic control, and withdrawal from MV. Research has shown that they can enhance clinical results while also lowering overall medical costs. According to the evidence available, mechanical ventilation strategies have commonly resulted in faster weaning periods as compared to standard physician-driven treatment, while also imparting a reduced length of MV and ICU stay in both adult and pediatric patients (Blackwood et al., 2013). Evidence-based guidelines were published in 2001 by an international task force of pulmonary and critical care experts. As part of their standard of care, all ICUs were advised to expand and apply weaning procedures for non-physicians (such as nurses and respiratory therapists). (MacIntyre, 2011).

MV disconnection is a complicated and continuing operation following by the patient's extubation from MV, the patient's ventilatory settings are actively weaned, and appropriate monitoring and non-invasive care are provided (Shefali-Patel et al., 2012).

There are three major gaps in our understanding of this process in this vulnerable group, which we will discuss below. First and foremost, the strategies for weaning patients off the ventilator and progressing them toward extubation have been uneven and variable across neonatal institutions. For the second time, we have demonstrated a limited capacity to accurately predict which infants are ready for extubation. Finally, researchers are actively investigating the most effective method of delivering non-invasive support. These variables contribute to the high rates of extubation failure among extreme preterm newborns, with up to 50% of extreme low birth weight (ELBW) infants failing extubation in some settings (Shefali-Patel et al., 2012).

Weaning is the process of gradually decreasing ventilator support while simultaneously transferring respiratory control and the work of breathing back to the patient, with the goal of eventually eliminating artificial ventilation. The question of which ventilation strategy is most conducive to effective weaning is still up for debate. A protocol, according to the National Health Service Institute in the United Kingdom, is "descriptions of the actions required to care for and treat a patient..." that "...allows workers to put evidence into practice by addressing the important concerns of what should be done, when it should be done, where it should be done, and by whom at a local level" (NHS 2010). Protocolized weaning refers to a systematic strategy that is in accordance with a defined progressive reduction in the amount of invasive breathing that is used. When it comes to weaning protocols, three basic tactics are used: (1) a progressive reduction in invasive ventilator support (stepwise reduction procedures); (2) an abrupt cessation of ventilation assistance (a spontaneous breathing trial); or (3) a combination of the two strategies. These measures are intended to aid in the safe and quick transition from total mechanical ventilator support to spontaneous breathing activity, which will ultimately result in the cessation of mechanical ventilation support (Playfor, 2006).

A weaning protocol can be textual instruction supplied by healthcare personnel or can be assisted by a computer algorithm that comprises a partial or completely automated closed loop system managed by the ventilator itself (Blackwood 2013b).

In the neonatal intensive care unit, there are a variety of methods for determining extubation readiness. Extubation failure has been researched in terms of physiological variables such as rate and depth of breathing rate, respiratory muscle load and capacity,

fluids intake and output, and electrical diaphragmatic activity, among other things (Wolf et al., 2013). Additional tests, such as ETT leaks, spontaneous breathing trials (SBT) with or without continuous positive airway pressure (CPAP), and (or) the use of mechanical ventilation technologies, such as automated (computerized) weaning, are frequently performed in conjunction with these procedures. The heterogeneity of extubation failure definitions adds to the complexity of the situation even more. Depending on the clinical findings, such as the existence of apnea, oxygenation, effort of breathing, and/or arterial blood gases, the decision to re-intubate may be made. Extubation failure can be determined using a variety of time periods following extubation, ranging from 24 to 72 hours and up to 7 or 10 days after extubation (Al-Mandari et al., 2015).

A variety of respiratory measures, such as oxygen saturation, transcutaneous CO2, blood gas analyses, and chest radiography, are monitored as well as the patient's physical reaction to ventilation There are several different types of weaning protocols, and most of them specify criteria that indicate when a patient is ready to begin weaning, how much ventilator support should be gradually reduced, how to recognize difficulties (complications), and whether or not the patient needs to be extubated (Blackwood 2013b). There are usually three parts to a spontaneous breathing test protocol: (1) a set of readiness criteria to be followed, (2) a spontaneous breath test with continuous positive airway pressure or minimal pressure support for a predetermined period of time (between 30 and 120 minutes in adults), and (3) criteria for extubation. Medical practitioners may give textual weaning procedure instructions or computer algorithms may provide a completely automated closed-loop system operated by the ventilator itself may be used in weaning protocols (Blackwood 2013). By continually monitoring the patient's physiological changes and modifying breathing in response to these changes, automated closed-loop devices can optimize the titration of mechanical support to their demands. The ventilator's programmed software adjusts the fan's speed using a completely automated, loop-controlled system. Medical experts may give a documented procedure that stipulates that the ventilator settings must be manually adjusted when there is time. The weaning process is usually managed by doctors as an intervention. Mechanical breathing must be adjusted and stopped according to the patient's weaning process, which necessitates the presence of a physician. Because of differences in training, expertise, and weaning methods, there may be wide variations in

results among doctors. Clinical expert committees construct protocols based on the best available information and so help with the weaning process. This is better than a single clinician's judgment in most circumstances. It's possible that protocolized weaning can reduce or eliminate undesired clinical variance while also reducing or eliminating mistakes and increasing efficiency and efficacy. To make the weaning process go more smoothly, protocols allow additional healthcare experts (such as nurses and allied healthcare workers) to participate (Jubran 2012). Blackwood (2007) found that protocols for weaning have been shown to be useful in boosting confidence by offering valuable direction to healthcare providers (Blackwood, 2007). Inexperienced healthcare personnel may misuse this medication and cause harm to patients. While it's possible to blindly follow the protocol, there's also a danger of accelerating weaning too soon, which might lead to higher reintubation rates. According to theory, compliance with the weaning procedure should not be a problem because all mechanically ventilated patients must eventually leave ventilation, and protocols give advice for monitoring and changing support according to the patient's requirements. However, protocol stages might be slowed down if they are handled by someone who lacks confidence. As a result, the implementation of weaning protocols must be accompanied by education and training for all parties involved.

The aims of the study are to compare the effectiveness of protocolized versus non-protocolized ventilator weaning in reducing the duration of invasive mechanical ventilation, weaning time, and NICU and hospital length of stay for newborn infants. To see how effective, it is in specific subgroups, such as gestational age and birth weight, the aims of this study are also to investigate if protocolized weaning can reduce the duration of mechanical breathing without increasing the risk of adverse outcomes and to derive conclusions about the protocol's utility for weaning practice in neonatal care.

1.2 Statement of the problem

Despite the growth in the use of NIV, mechanical ventilation via an endotracheal tube (ETT) remains the basis of therapy for infants for whom NIV is not appropriate. Although some centers strive to employ NIV for all spontaneously breathing infants, regardless of their gestational age at delivery, many centers continue to use mechanical ventilation for infants born at the extremes of preterm (Sinha et al., 2011). Therefore,

mechanical ventilation remains a fundamental treatment strategy for the management of infants with respiratory failure.

Intubation is a typical treatment to support mechanical ventilation, airway protection, cardiac resuscitation, meconium aspiration, airway blockage, drug delivery, and perioperative support or management (Maheshwari et al., 2016). One of the most critical steps in the recovery of a patient is the removal of their endotracheal tube (ETT). Without prompt removal, mechanical ventilation duration can be prolonged when it is essential for the infant's well-being and harmful consequences such as cardiac and hemodynamic instability, ventilator-induced lung damage, and diaphragmatic muscle weakening may result. Removing the ETT in a timely manner reduces the length of mechanical ventilation, reduces the need for potentially hazardous sedatives, and lowers patient and parent anxiety. Extubation failure, on the other hand, is a common problem in the NICU, with 20% to 35% of preterm infants and 13% of term infants failing their initial extubation attempt (Hermeto, et al., 2009).

Survival rates in premature newborns have increased with the introduction of mechanical ventilation for the treatment of severe respiratory failure. However, prolonged mechanical ventilation might have unintended consequences. Preterm infants who are mechanically ventilated are at a greater risk of developing bronchopulmonary dysplasia, sepsis, brain damage, and retinopathy of prematurity, among other complications. In order to prevent these risks, doctors try to extubate preterm children as soon as possible after birth. Extubation is frequently ineffective in the most premature newborns due to lung illness or insufficient respiratory force, among other reasons (Klompas, et al., 2016).

Mechanical ventilation (MV) is widely acknowledged to increase the risk of death or BPD. Nonetheless, it remains a vital component of the initial respiratory management of most extremely preterm infants today. In an attempt to shorten the length of MV, physicians seek to convert these infants to some sort of non-invasive respiratory assistance as early as feasible. Unfortunately, this transition process (known as extubation) has proven challenging and surprisingly devoid of strong evidence to guide practice. Currently, the choice to extubate is generally based on an interpretation of the infant’s ventilatory needs, gas exchange, and overall clinical stability. But such clinical judgement is subjective, which often leads to variable practices and suboptimal

decisions. That is, some infants may be exposed to unnecessary harm from MV due to delayed recognition of their extubation potential, while many others require reintubation (and resumption of MV) if prematurely disconnected from the ventilator. Thus, it would be ideal to identify an accurate and objective predictor of extubation readiness that minimizes the duration of MV while maximizing the chances of a successful extubation, as a means of standardizing practices and improving outcomes. Although several predictors of extubation readiness have already been developed and adopted in clinical practice, their accuracies in predicting successful extubation have not been systematically evaluated. This is further complicated by the fact that no consensus exists in the literature as to what constitutes a clinically meaningful definition of extubation success or failure in this population. This study will be intended to assess the extent to which MV techniques have been implemented into current practice in NICUs.

1.3 Significant of study

There is evidence that clinical decision-making utilizing protocols minimizes practice variance amongst physicians, standardizes patient treatment, and improves patient outcomes (Schmolzer, et al., 2013). This is verified in adult critical care units with the use of written guidelines created to facilitate the weaning of respiratory assistance.

There is a compelling urgency to uncover economies in weaning resulting in reduced breathing time to avoid ventilator-associated morbidity and death, and also to find solutions to current limits in critical care services. The cost of care provided to these people is high. This growing demand is occurring alongside a lower availability of healthcare providers certified and experienced in mechanical ventilation management and its weaning (Zolnierek et al., 2010).

1.4 Aims of the study

The aims of the study are to compare the effectiveness of protocolized versus non-protocolized ventilator weaning in reducing the duration of invasive mechanical ventilation, weaning time, and NICU and hospital length of stay for newborn infants. To see how effective, it is in specific subgroups, such as gestational age and birth weight. The aims of this study are also to investigate if protocolized weaning can reduce the duration of mechanical breathing without increasing the risk of adverse outcomes and to derive conclusions about the protocol's utility for weaning practice in neonatal care.

1.5 Objectives

1. To assess the efficacy of weaning protocol from mechanical ventilator for premature infants in shorten the duration of mechanical ventilation and the duration of weaning

2. To assess whether weaning protocol from mechanical ventilator for premature infants is decreasing the NICU and hospital length of stay.

3. To determine whether weaning protocol from mechanical ventilator for premature infants is safe and clinically effective in decreasing the risk of adverse effect like pulmonary interstitial emphysema, air leak syndrome, Bronchopulmonary dysplasia (BPD), and ventilator-associated pneumonia.

1.6 Research question

1. What's the efficacy of weaning protocol from mechanical ventilator for premature infants in shorten the duration of mechanical ventilation and the duration of weaning?
2. Is weaning protocol from mechanical ventilator for premature infants decrease the NICU and hospital length of stay?
3. Is there a relationship between weaning protocol from mechanical ventilator for premature infants and decreasing the risk of adverse effect like pulmonary interstitial emphysema, air leak syndrome, Bronchopulmonary dysplasia (BPD), and ventilator-associated pneumonia?

1.7 Primary outcomes

Time duration of mechanical ventilation, defined in hours from the start of invasive mechanical ventilation to its termination, will be determined for each gestational age group as follows:

1. Infants born prematurely (subdivided into three groups)

- Infants born with exceptionally low birth weights (less than 1000 grams)
- Infants born with very low birth weights (less than 1500 grams)
- Preterm newborns (defined as those weighing less than 2500 grams or those born at a gestational age less than 36 weeks).

2. Term infants

- The total duration of mechanical ventilation, divided by the number of ventilation modes.
- The difference in the risk of death in children between the two groups.
- The time for weaning
- The amount of time spent on FIO2> 0.30

1.8 Secondary outcomes

1. The length of time until weaning from MV (hours, from initiation to discontinuation of invasive mechanical ventilation).
2. Mortality rate in the group
3. The duration of time spent in the NICU and the hospital (days).
4. The prevalence of mechanical ventilation-associated morbidity, such as bronchopulmonary dysplasia (BPD), pulmonary interstitial emphysema, air leak syndrome, and ventilator-associated pneumonia (VAP).
5. Incidence of adverse events: the number of infants who required re-initialization of mechanical ventilation within 24 hours following removal, who were extubated on their own, or who required prolonged mechanical ventilation
6. Noninvasive ventilation (nasal continuous positive airway pressure, high-flow nasal canula, oxygen delivery) is used after extubation in the following situations: (days).

1.9 Hypotheses

1. There is no significant difference at 0.05 level between the protocol group and historical group regarding duration of mechanical ventilation
2. There is no significant difference at 0.05 level between the protocol group and historical group regarding the time of weaning.
3. There is no significant difference at 0.05 level between the protocol group and historical group regarding NICU length of stay.
4. There is no significant difference at 0.05 level between the protocol group and historical group regarding hospital length of stay.
5. There is no significant difference at 0.05 level between the protocol group and historical group regarding adverse effect like pulmonary interstitial emphysema, air leak syndrome, Bronchopulmonary dysplasia (BPD), and ventilator-associated pneumonia.

Chapter Two

Background

2.1 Respiratory failure in newborn infants

2.1.1 Causes of respiratory failure

Respiratory failure can develop in infants of any gestation. It is substantially more prevalent in preterm infants. Some factors are comparable in preterm and term infants, but others tend to occur in one group rather than the other. Respiratory distress syndrome (RDS) is a major cause of respiratory failure in preterm infants (Hamvas, 2011). It occurs in roughly 80% of infants born at 24 weeks' gestation (very preterm) and even 5% of infants born at 36 weeks' gestation (late preterm) (Donn et al., 2017b).

The fundamental causes of RDS are multifaceted. Preterm infants are predisposed to RDS due to a combination of factors including immaturity of the lungs, pulmonary vasculature, respiratory muscles, and nervous system (Spitzer et al., 2011), surfactant immaturity and deficiency (Jobe, 2006), reduced pulmonary compliance and increased chest wall and airway compliance (Spitzer et al., 2011), and increased diffusion distance for gas exchange (Jobe, 2006).

2.1.2 Clinical features of RDS

RDS is defined by a combination of clinical, biochemical, and radiological characteristics (Donn et al., 2017b). It may also be found in other illnesses such as sepsis, congenital pneumonia, and hypothermia (Hamvas, 2011).

In practice, the tiniest and most premature infants may not display many of the traits. This may be because they have had mechanical ventilation and exogenous surfactant supplementation immediately after delivery, which may disguise the traditional signs of RDS. An essential aspect of RDS is the time of onset. It begins within the first few hours after birth and frequently peaks in severity at 48 to 72 hours of age (Hamvas, 2011). RDS can be deadly, yet most infants start to heal by 72 hours of age. Therefore, respiratory symptoms in a newborn that first arise beyond the first 48 hours of life are likely to be linked to other underlying illnesses.

2.2 Prevalence of Mechanical Ventilation Use

As a result of lung immaturity, limited respiratory drive and surfactant insufficiency, the majority of extremely preterm infants require endotracheal intubation and MV soon after birth. Based on the Canadian Neonatal Network annual report (2017), 76% of infants under 28 weeks of gestation required MV during hospitalization, and only 33% of infants had not received any MV in the first three days of life. According to a Norwegian cohort study, more than 95% of infants delivered in 2013–2014 with a gestational age of 25 weeks required MV (Guaman et al., 2015).

2.3 Complications Associated with Mechanical Ventilation Use

MV plays numerous roles in extremely preterm infants. Upon inflation it provides sufficient volume to allow for pulmonary gas exchange, and at the end of expiration it maintains a steady distending pressure to prevent the alveoli from entirely or partially collapsing (also known as atelectasis). It is also a vehicle for the transfer of surfactant to the young and insufficiently compliant lungs. Ultimately, it buys time for the preterm infant's lungs and brain to grow and mature before they are ready to breathe freely without the aid of the ventilator. Nevertheless, while MV can be a life-saving technique in most preterm infants, it is generally accompanied by many problems that increase the degree of pulmonary illness. These include ventilator-associated lung damage, air leak syndromes, airway trauma, ventilator associated pneumonia (VAP), ventilator-induced diaphragmatic dysfunction and other iatrogenic problems.

2.4 Weaning

In many NICUs nowadays, doctors have at their disposal a wide selection of modalities to choose from while administering MV. These include conventional modes such as assist control (AC) and synchronized intermittent mandatory ventilation (SIMV) with or without pressure support (PS), but also less conventional modes such as high frequency oscillatory ventilation (HFOV), high frequency jet ventilation (HFJV), and neurally adjusted ventilatory assist (NAVA) (NAVA). What's more, numerous MV modes offer the option of being either pressure-limited or volume-controlled, which adds an extra layer of complexity. All the foregoing modalities may conveniently be employed throughout the acute, chronic, or weaning periods of MV and are normally selected on the basis of the familiarity or preference of the NICU personnel. With regards to

weaning from MV, a Canadian survey found that doctors most typically selected SIMV as their preferred pre-extubation mode (74% of respondents), followed by AC and HFOV in 44% and 30% of respondents, respectively. This practice diverges from the current research demonstrating that assist control ventilation offers more homogenous tidal volume delivery, decreases labour of breathing and may be related to shorter weaning periods compared to SIMV. Additionally, it's noticed that only 44% of responders in the Canadian study employed volume-targeted ventilation throughout the weaning period of MV. Again, this contradicts data gained from randomized controlled studies demonstrating that volume-targeted ventilation is linked with quicker weaning and reduced risks of death/BPD, pneumothorax, and severe brain abnormalities compared to pressure-limited breathing (Klingenberg et al., 2018). The results paralleled those of prior surveys, whereby the acceptance of volume-guaranteed ventilation has likewise been apparently low (varying anywhere from 5 to 60% across centers) (ranging anywhere from 5 to 60% across centers) (Shalish, et al., 2016).

One means of unifying practices related to weaning from MV is through the establishment and implementation of weaning protocols. A protocol is a collection of instructions (or guidelines) to follow for a given patient group, ailment, or therapy. Weaning protocols are generally led by nurses and/or respiratory therapists, thereby allowing for more uniform and timely collection of blood gases and titration of ventilator settings. In adult critical care patients, weaning protocols have been found to enhance outcomes, reduce expenditures, and decrease MV duration and length of stay (Blackwood et al., 2014). In reality, they have been included as evidence-based recommendations by a joint task group led by the American College of Chest Physicians, the American Association of Respiratory Care, and the American College of Critical Care Medicine since 2001 (MacIntyre et al., 2001). In contrast to adults, the evidence for adopting MV weaning protocols in pediatrics and newborn patients is less convincing due to a scarcity of research on the issue. In the sole neonatal trial of its kind, the introduction of a weaning regimen in ventilated preterm infants with a birth weight of less than 1250g led to substantial decreases in weaning time, total MV duration, and extubation failure rates (Hermeto et al., 2009). As a result of the scant data, most NICUs have not yet adopted MV weaning protocols in their units. Only 36% of respondents in an international study reported having a guideline or documented procedure for ventilator weaning (Al-Mandari et al., 2015). Similarly, in a Canadian

study, only 7 out of 24 units (29%) had a procedure for weaning off MV (Shalish, et al., 2015). Interestingly, they observed in the Canadian survey that units with MV protocols were significantly more likely to use AC as a weaning mode of ventilation compared to units with no protocol (75% vs. 27%) and were more likely to use volume-targeted ventilation (63% vs. 33%), although this did not reach statistical significance (Shalish et al., 2015). These findings imply that institutions developing MV weaning protocols are more likely to embrace evidence-based practices.

Assessment of extubation readiness following weaning. An examination is often necessary to decide whether the newborn is ready for a trial of extubation. According to an international survey of NICU representatives from ten different neonatal networks, the majority relied on clinical judgment of the attending team to determine readiness for extubation, with less than 25% of units using a protocol or guideline for that process (Beltempo et al., 2018).Similarly, in a worldwide survey, most respondents also reported depending on clinical judgment, based on examination of the patient's ventilatory settings, blood gases, and general clinical/hemodynamic stability (Al-Mandari et al., 2015). Unfortunately, there is great heterogeneity across assessors as to what constitutes "clinical stability" and whether ventilator parameters or blood gases are judged low enough for extubation.

Another noteworthy trend has been the use of prediction tests or trials to identify readiness for extubation. Of all the predictor tests, the most commonly used in clinical practice is the spontaneous breathing trial (SBT), a brief challenge on endotracheal CPAP during which the infant is monitored for signs of clinical instability prior to extubation (apneas, bradycardias, desaturations, and/or increased O2 needs). SBTs were reportedly used by 10% of NICUs in one international survey encompassing ten distinct neonatal networks (Beltempo, et al., 2018). In another global study, they discovered that 16% of NICUs extubated extremely preterm infants based on SBT results (Al-Mandari et al., 2015). Furthermore, 38% of respondents said they used SBTs in their individual units at least occasionally to decide whether to extubate or not. Unfortunately, SBTs are done in extremely diverse ways, lasting anywhere from less than 3 minutes to more than 10 minutes in duration and utilizing various combinations of clinical criteria to determine pass/fail.

2.5 Impact of Practice Variability on Outcomes

Excessive variation in extubation practices has the potential to harm patients, their families, allied health care team members, and the general NICU workplace (Shalish, et al., 2016). Firstly, preterm infants are exposed to a range of clinical practice approaches due to the significant turnover of doctors, nurses, and respiratory therapists caring for them throughout hospitalization. Given the dearth of clinical evidence for many practices surrounding the extubation process, most decisions tend to be based on clinicians' own experiences and preferences. In circumstances where data is available, there is sometimes a delay in the acceptance of research recommendations, partly due to the increasing difficulty of remaining up-to-date with scientific discoveries in this information-saturated society. Besides, the existing data is typically inadequate or reveals inconsistent results across research, which makes its interpretation even more unpredictable from one provider to the next. Putting all these aspects together, it becomes unavoidable for the patient to experience some unfavorable repercussions from this practice heterogeneity. Indeed, a number of studies have indicated that center variations for several outcomes (including mortality and BPD) cannot be solely explained by indicators of disease severity, thereby implying that unmeasured practice variances have a significant role. Moreover, this fact is further enforced by the solid evidence in adults (Blackwood et al., 2014), and to a lesser extent in neonates, that standardization of weaning and extubation via protocols leads to improved patient outcomes by significantly reducing the total duration of MV and length of hospitalization. As such, simplifying the extubation procedure has the ability to sift out non-evidence-based practices and hence lower the risks of avoidable difficulties.

2.6 Extubation Failure

Considering that the assessment of extubation readiness remains highly subjective and imprecise, it is not unexpected that many extremely preterm infants fail their extubation attempts and require reintubation. According to some studies, approximately 70% of ELBW infants are reintubated during their NICU stay (Berger et al., 2014). That being stated, when determining whether a newborn is ready for extubation (or constructing a predictor of extubation readiness), it is crucial to first identify what exactly is deemed a clinically significant criterion of success or failure.

2.6.1 Definition of Extubation Failure

The definition of extubation failure is generally divided into two components: (1) a set of criteria that need to be fulfilled, and (2) a pre-set observation window.

2.6.2 Criteria to define extubation failure

In the literature, most studies define extubation failure as the requirement for reintubation (and continuation of MV) within a specified window of observation. However, there are inherent drawbacks to adopting reintubation as the result of interest. Typically, the choice to reintubate extremely preterm infants is determined by the medical team based on an examination of the frequency and severity of several symptoms (including apneas and bradycardias, increased work of breathing, respiratory acidosis, and increased oxygen demands) (Al-Mandari et al., 2015). But this choice is very subjective, as tolerance of respiratory episodes and thresholds for reintubation may vary amongst doctors and may depend on the contextual reality of the unit (e.g., staffing ratios, presence of in-house trained employees, and unit culture). Less than 10% of respondents reported having consistent criteria for reintubation in their respective units based on peri-extubation practices (Al-Mandari et al., 2015). Thus, whereas reintubation constitutes a clear and pragmatic definition of extubation failure, the results may not be repeatable or generalizable to other units. To sidestep the issues concerning diversity in reintubation practices, several clinical trials either suggest (or demand) criteria for reintubation, or characterize extubation failure as completion of these criteria (irrespective of reintubation). The latter studies were found using a recent systematic evaluation of the literature investigating strategies to enhance extubation success rates in preterm infants (Ferguson et al., 2017). Considerable discrepancies exist in the criteria proposed to identify failure, notably with regard to the frequency and severity of respiratory episodes (apneas, bradycardias, and/or desaturations). This is not unexpected, given relatively little is understood about how respiratory episodes of varied frequency, durations, and severities (e.g., the depth of bradycardias or desaturations) might negatively affect the preterm lung and brain in the long term. Besides, monitoring and recording of respiratory episodes in practice is highly challenging. As it stands, nurses and/or respiratory therapists are initially informed of respiratory episodes via integrated bedside alarms on the patient's monitor. As a result,

they frequently are unable to observe the triggers or the sequence of events in real time. As a result, their documentation often underestimates the real prevalence of respiratory episodes (Brockmann et al., 2013). In sum, defining extubation failure as either the requirement for reintubation or as a collection of clinical criteria is currently linked with major constraints. For that reason, additional work is needed to better understand the appropriate approach to describe extubation failure. Moreover, a more evidence-based and uniform strategy for reintubation is desirable.

2.7 Modern ventilator techniques

2.7.1 Synchronization

Synchronization is becoming a typical element of neonatal breathing. Ventilator algorithms strive to match delivery of the ventilator's positive pressure inflation with the infant's spontaneous breathing effort. This is referred to as patient-triggered ventilation (Sinha et al., 2011). Synchronization can be performed using a pneumotachograph or a hot wire anemometer to detect signals from the newborn signaling the commencement of spontaneous inspiration (Donn et al., 2015). These signals are generally variations in airway pressure or flow rate. They then 'trigger' the ventilator to provide an inflation (Donn, 2009). Synchronization is related with a reduction in the incidence of pneumothorax and a reduction in length of breathing. However, the effectiveness of synchronization is rarely documented in published research (Greenough et al., 2016).

2.8 Types of mechanical ventilation

There are several alternative techniques to give mechanical ventilation using an endotracheal tube. They are classified into two classes, tidal ventilation, and high frequency ventilation (Donn, 2009). Tidal ventilation involves numerous methods of ventilation. These modes try to emulate normal negative pressure respiration by producing positive inspired inflations and permitting passive expiration using the lung's elastic rebound. Rapid frequency ventilation distributes smaller gas quantities at extremely high rates utilizing very high continuous distending airway pressures.

2.8.1 Tidal ventilation

The many forms of tidal ventilation may be categorized according to the control variable that is addressed by the physician (Sinha et al., 2008). These variables consist of pressure, volume, and flow. In practice, volume is integral to flow (Sinha et al., 2008), and these two variables are managed simultaneously. Control of volume and flow forms the basis of volume-controlled ventilation (VCV). Therefore, traditional ventilation is given using either volume or pressure as the goal variable.

Tidal ventilation can later be sub-divided into modalities according to the variables that start, limit, or stop the inflation. These factors are known as phase variables (Donn et al., 2015). Pressure, volume, flow, and time can all be employed as phase variables (Sinha et al., 2008). Control and phase factors are utilized to give inflations, constituting the manner of ventilation. Intermittent mandatory ventilation (IMV), synchronized intermittent mandatory ventilation (SIMV), assist/control ventilation (A/C), and pressure support ventilation (PSV).

2.8.2 When it comes to weaning, ventilatory modalities are the best.

When it comes to weaning newborn infants off mechanical ventilation, a variety of different ventilatory modalities have been proposed, but the relative effects of these modalities on the outcome of weaning from respiratory support remain unclear. The most successful weaning modalities, according to the results of several randomized tests, are those that assist every spontaneous breath with breathing methods. When compared to conventional ventilation, Greenough et al. (2016) discovered that synchronized ventilation was related with a shorter period of ventilation in a recent comprehensive analysis. Preterm infants weighing less than 1,000 grams were studied in a randomized, controlled experiment by Reyes et al. (2016). They were divided into two groups: those who received synchronized intermittent mandatory ventilation (SIMV) and those who received synchronized intermittent mandatory ventilation plus pressure support (SIMV + PS) during their first 28 days of life. Compared to babies treated alone with synchronized intermittent mandated ventilation, those in the SIMV + PS support group achieved minimal ventilator settings and were extubated much sooner. Additionally, children in SIMV + PS had a shorter duration on supplemental oxygen and a lower oxygen need at 36 weeks' gestational age, albeit these differences were only

statistically significant in the subgroup of newborns weighing 700 to 1,000 g at birth. More recently, Shefali-Patel et al. (2012) conducted a randomized weaning trial in which they compared assist control ventilation with pressure support ventilation in 36 neonates delivered at a median gestational age of 29 weeks to see which was more effective. It was shown that, after changing the termination sensitivity of pressure support to maintain an inflating time of 0.25 to 0.3 seconds, there were no significant variations in effort of breathing, degree of respiratory muscle strength, time to successful extubation between the two groups. Wheeler and colleagues (2011) conducted a systematic Cochrane review in which they compared volume-targeted ventilation modes with usual pressure-restricted ventilator modes in newborns younger than 28 days of corrected age in neonates. Interestingly, when compared to infants supported using pressure-limited ventilation modes, those ventilated using volume-targeted modes had lower mortality and chronic lung disease, and they were less likely to develop pneumothorax. They also required ventilator assistance for a shorter period of time. High frequency ventilation (HFV) is another widely recognized ventilatory modality for assisting term and preterm newborns with respiratory insufficiency, particularly when adopting the open lung approach (De Jaegere et al., 2006). However, despite the fact that HFV is becoming more widely used, data on weaning and extubation from HFV are still lacking. In the past, some clinicians have preferred to switch from high-frequency ventilation to conventional modes once the acute lung sickness has recovered, with the goal of weaning and extubating patients from this breathing mode (Johnson et al., 2012). 214 preterm infants were studied in a comprehensive retrospective study by van Venzel and colleagues to determine whether weaning and prompt extubation from open lung HFV were feasible in this setting. The authors stated that they were able to reduce the continuous distending pressure to less than 8 cm H2O by using a FIO2 of 0.30 or lower. Furthermore, extubation was successful in the vast majority of patients in these situations, with a stunning 90% success rate. They were unable to demonstrate whether weaning and direct extubation from HFV was superior to switching to conventional mechanical ventilation and then weaning and extubating, owing to the retrospective nature of their study, and they called for future randomized controlled trials to be conducted to determine this (van Velzen et al., 2009).

2.9 Weaning protocols and reduction of MV duration

Many critical care units have protocols in place to help patients make the transition from assisted ventilation to spontaneous breathing and, ultimately, the cessation of mechanical ventilator support. Generally speaking, these protocols include at least the following issues in some form: There are three types of objective criteria to start the weaning process: 1) to determine whether a patient is ready to breathe while reducing ventilatory support; 2) structured guidelines for reducing ventilatory support (how to manipulate ventilatory parameters according to physiological or clinical response); and 3) well-defined criteria to determine whether a patient is ready to be extubated. Indeed, a number of studies have showed that the implementation of a systematic ventilator weaning regimen can reduce the amount of time that adult patients are required to be on mechanical ventilation without having negative implications (Marelich et al., 2010). In contrast, the results of pediatrics trials including ventilator weaning strategies have been less positive thus far, according to the literature. After participating in a large multicenter trial conducted in ten pediatric intensive care units (PICUs) across North America by the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network, researchers found that there was no difference between groups randomized to either an automated ventilator-adjusted volume support protocol, physician-directed pressure support weaning, or no protocol. Rather of being superior to no protocol, protocol-driven programs were equivalent to no protocol in terms of weaning time from randomization to successful extubation as well as the rate of extubation failure. Recent research has incorporated the same study as part of a systematic review, in which Blackwood et al. studied the effect of weaning by protocol on critically ill babies who were invasively ventilated (Blackwood et al., 2013). Only three studies with a low risk of bias were discovered, with a total sample size of 321 children participating. The available data did not allow us to decide whether obtaining shorter ventilation by protocolized weaning was beneficial or harmful to the children, despite the fact that there was a favorable tendency for a reduction in total time on ventilation and the length of weaning. Instead, Hermeto and colleagues (2009) reported more encouraging findings after doing research on a large cohort of extremely preterm neonates. The authors conducted a retrospective analysis to determine the impact of the implementation of a ventilation strategy on the respiratory outcomes of extremely premature newborns. Using data from 301 mechanically ventilated infants who were

born with birth weights less than 1,250 g, they discovered that the implementation of a ventilation protocol, driven by registered respiratory therapists, could significantly reduce the time required to wean the infant from mechanical ventilation and the length of time spent on mechanical ventilation. Although their remarkable observations have been confirmed, further research into the effects of protocol-based weaning approaches on important long-term outcomes, such as BPD or neurodevelopment, is still required to substantiate their findings (Hermeto et al., 2009).

2.10 Extubation readiness

Neonatologists should adopt a rapid technique for terminating mechanical ventilation, as well as an earlier evaluation of the infant's readiness for spontaneous breathing efforts, with the goal of reducing the duration of invasive respiratory support. Actually, both premature and delayed extubation can result in serious harm; therefore, finding the appropriate moment for extubation may prove to be quite difficult for some patients. A delayed extubation may increase the inherent risk of MV and ETT complications even further. The opposite is also true: an untimely termination of the MV may indicate a number of complications, including difficulty re-establishing artificial airways, decreased gas exchange, and hemodynamic instability. Because of this, a weaning technique that is both quick and safe is very desirable. After only a few minutes of MV, the majority of newborns are quickly extubated. In other circumstances, weaning may be significantly more difficult and time-consuming, and it may be made even more difficult and time-consuming by one or more bouts of extubation failure. Among other things, this might be caused by a variety of reasons such as iatrogenic airway injuries, congenital airway abnormalities, respiratory muscle weakness, underlying cardiac abnormalities, recurrent apneic episodes, or acquired infections. According to Sant'Anna (2012), the age of extubation failure in babies can vary significantly, ranging from 10 to 80%. Many factors contribute to this enormous variety, including1) significant shifts in the following aspects of human behavior: 2) local norms regarding pre- and post-extubation therapy; 3) failure definition and timing; 4) gestational age (very preterm neonates have the highest risk of reintubation); 5) failure definition and timing (e.g., use of CPAP, noninvasive ventilation, steroids, methylxanthines, and adrenaline). Among 162 ELBW babies who required mechanical ventilation, Stefanescu, et al. (2013) found an extubation failure rate of more than 40% in a study

published in 2009. Interestingly, the most common reasons for extubation failure in this group of patients were recurrent episodes of apnea and bradycardia (Stefanescu et al., 2013). The ability of a patient to be successfully extubated is often determined by both clinical and objective examinations of their condition. Despite this, not a single sign has been identified as being sufficiently sensitive and specific thus far (Newth, 2009). It would be wonderful if physicians had some basic metrics to assist them assess which newborns are suitable for spontaneous-breathing experiments (SBT) and in which situations these trials are most likely to succeed. An infant's ability to breathe on his or her own is tested through spontaneous breathing trials, which are conducted with minimum or no help from a trained professional. As a result, ventilatory modes such as pressure support, continuous positive airway pressure, and ventilation with a T-piece are used instead of comprehensive respiratory support modes such as volume assist control or pressure control. The latter is defined by the complete absence of positive end expiratory pressure, which makes it possible to provide the patient with the least amount of help that is reasonably possible. An integrated examination of numerous criteria is commonly performed during SBT, including the patient's breathing pattern and rate, gas exchange parameters, hemodynamic stability, mental status, comfort, and diaphoresis, among other things. SBT should be considered only when the patient is awake and not under substantial sedation, which is the case in the majority of cases. The use of a variety of tests to boost the ability to predict a successful extubation in preterm neonates has been researched over the last two decades. These tests include spontaneous minute ventilation, various spontaneous breathing tests, and pulmonary function testing. The truth is that no one of these predictions has been demonstrated to be consistently reliable in the long run (Kamlin, 2006). Gillespie et al. (2013) conducted small randomized clinical research in which they evaluated babies' readiness for extubation by using the minute ventilation test (MVT). In the MVT test, data collected using a very simple pulmonary monitoring device, which is now widely found in every ventilator, is processed to determine the effectiveness of spontaneous breathing and respiratory muscle endurance. When comparing the time from randomization to extubation in 42 preterm babies with respiratory distress syndrome who were reviewed by the MVT to those who were just evaluated clinically, it was shown that the MVT significantly reduced the time (mean time of 8 hours against 36 hours, respectively) (Gillespie et al., 2013). When Kamlin et al. conducted pilot research on 50 VLBW babies in Australia,

they found that a very brief SBT (three minutes of spontaneous breathing with ETT continuous positive airway pressure before extubation) could accurately predict the readiness for extubation in the group (Kamlin, 2006). Investigators simply observed fluctuations in heart rate and oxygen saturation for three minutes throughout this test, which yielded extremely promising results in terms of positive and negative predictive values, specificity, and sensitivity, according to the researchers' findings. Afterwards, SBT was established as the gold standard of care in their facility (Kamlin, 2006). Following that, in a large prospective study, Kamlin and colleagues discovered that, following the implementation of the 3-min SBT in their current practice, preterm infants were extubated earlier and at higher ventilatory settings than they were during the period prior to the implementation of the 3-min SBT.

Chapter Three

Literature Review

In this chapter previous studies related to protocolized weaning from MV among neonates presented.

Mandhari, et al., (2019) conducted review research to examine the effects of protocol weaning on critically ill infants who were invasively ventilated. Identify any changes in quality of life, ICU length of stay, mortality and adverse events between protocolized weaning and standard care. There was a significant reduction in total breathing duration (95% confidence interval (CI) 8 to 56; P = 0.01) following protocolized weaning in the biggest experiment (260 children). These trials found that mechanical ventilation before weaning, PICU and hospital length of stay, PICU mortality, and adverse events in the PICU were not affected by these interventions.

Prasad and Mishra (2019) conducted study aimed to purposefully reducing the rate of extubation failure by using protocol-driven ventilation and extubation strategies, From April 2017 to January 2018, a level II neonatal intensive care unit implemented a quality improvement plan. Efforts to improve patient care began on August 1, 2017. PDCA cycles I and II involved 16 ventilated infants and 17 unventilated infants. Initial failure of extubation after just 72 hours was the primary result. According to the authors, the pre-protocol failure rate reduced from 41.7% (OR 0.44, 95% CI 0.012 to 1.59, P = 0.21). Significant reduction for median time to first extubation attempt (71.5 hours to 38 hours, P=0.046). An improvement in successful extubation and a reduction in the median time to the first extubation attempt in ventilated infants were found in the research, which used a protocolized procedure through a quality improvement program.

Hiremath, et al. (2009) conducted a one-year prospective observational investigation at a level III neonatal unit. related clinical risk factors and extubation failure in ventilated infants were evaluated in all neonates ventilated for at least 12 hours. To check for extubation failure, eighty-two ventilated neonates were observed after 48 hours after extubation. Congenital pneumonia was far more prevalent (n=5, 22.7%) in the extubation failure group (n=5, 22.7%) than in the non- extubation failure group (n=2, 3.3%), with hyaline membrane disease (40.2%) being the second most common reason for ventilation in both groups. Recurrent apnea was more common in the no extubation

failure (n=14) group than in the extubation failure group, where it was absent. Vital signs and continuous saturation monitoring continued for 48 hours following extubation for all ventilated babies. Every 12 hours, biochemical and blood gas analysis was carried out. On the basis of unit policy, extubation was deemed appropriate based on a number of factors, including the patient's improvement in basic disease and complications (all hemodynamically significant PDAs had ECHOs and were treated) as well as acceptable blood gas, packed cell volume >30%, and normal blood sugars and electrolytes. Prior to extubation, aminophylline was given to infants under 34 weeks of gestation, and steroids were administered in situations of prolonged ventilation (more than 7 days). Suctioning of the stomach was performed just before extubation. CPR (4-5 cm H2O) was used for newborns under 1.5 kg; neonates weighing more than 1.5 kg were extubated to a head box O2 through the CPAP. According to the data, 22 babies (26.8%) were diagnosed with extubation failure. There was a strong correlation between extubation failure and the existence of a post-extubation lung collapse, patent ductus arteriosus, and acquired pneumonia. The extubation failure group's breathing duration, maximal oxygen gradient, and pre-extubation alveolar arterial oxygen gradient were all substantially greater (P0.05) than those of the control group (AaDO2). Anemia (P=0.004) and pneumonia (P=0.001) were substantially more common in the extubation failure group (P=0.034). Extubation failure in infants can be decreased if severe PDA is detected and sufficient post-extubation care is given following extubation.

Jurkevicz et al. (2021) conducted prospective observational research to evaluate ventilatory and gasometric parameters to identify potential variables that may impact the decision to extubate before extubation in preterm babies up to 32 weeks. The research included preterm newborns as young as 32 weeks gestation who had undergone at least 24 hours of invasive artificial breathing. Excluded from the study were newborns with anomalies, heart disease, and those who were transferred to other facilities before their first voluntary extubation. To ensure that the baby was able to breathe on his own, the NICU protocol for weaning and extubation was followed (Regular spontaneous breathing with a cough reflex, FiO2 40% to 90% saturation, inspiratory pressure 15-18 cmH2O, RR 15-20, pH 7.25 mmHg, PaCO2 50 mmHg). After being extubated, the baby was watched for seven days. There were four cases of extubation failure (50%), two cases of digestive issues or infections (25%) and one case of atelectasis (12.5%) in the study group (12, 5%). During the first 24 to 144 hours

following extubation, they occurred. An intubation was necessary in 75% of the cases where 20 preterm newborns were studied, which were all diagnosed with neonatal respiratory distress syndrome. 40% of the overall sample failed. Extubation was found to be significantly predicted by the inspired oxygen fraction ($p = 0.03$) and the mean airway pressure ($p = 0.03$). There was no statistical significance ($p = 0.06$) for the amount of time patients spent on invasive mechanical ventilation in the study's findings. For extubation to be successful, the team must know how much oxygen is being used and how much oxygen the patient is receiving in order to arrange a safe and meticulous extubation, while also being aware of the patient's clinical condition.

The Cochrane Central Register of Controlled Trials, CINAHL, Web of Science, EMBASE, MEDLINE, and the International Clinical Trial Registry Platform were used to conduct a systematic review of an investigation on how weaning protocols differ in severely ill infants and how they affect the length of time they are maintained on ventilators. Researchers investigated trials involving infants in which weaning procedures, both protocolized and non-protocolized, were examined or reported quantitatively and qualitatively. The primary outcome was a variation in the time required to wean. There were a total of 2099 articles that might be relevant to the topic. There were three studies that fulfilled the inclusion criteria. A separate neonatal dataset for two of them was not possible. There was just one retrospective study included in this review. In this study, the average weaning duration was lowered from 18 days to 5 and 6 days. No substantial evidence exists in the literature to support or deny the use of a weaning program for critically ill babies.

A systematic review was conducted by Wielenga, et al. (2016). According to previous protocolized weaning evaluations, all trials regardless of the randomization time point of entry are included. This led to a number of consequences: Infants born too soon (subdivided into three groups) Newborns weighing fewer than 1000 grams, those weighing less than 1500 grams, and those weighing less than 2500 grams are all considered extremely low birth weight infants. The entire amount of time spent on mechanical ventilation, measured in hours, from the onset of invasive mechanical ventilation until its removal. In addition to mortality and NICU and hospital length of stay (days), secondary outcomes included weaning duration, the incidence of mechanical ventilation-related morbidity such as pulmonary interstitial emphysema, air

leak systolic pressure, emphysema, and pulmonary hypertension, as well as the incidence of mechanical ventilation-related morbidity. When a baby needs mechanical ventilation reintroduced within 24 hours of being taken off of it, it is considered an adverse occurrence. Thereafter, noninvasive ventilation (nasal positive airway pressure, high-flow nasal canula, and oxygen delivery) is utilized (days), which incurs expenses (as reported by the study authors). It appears that protocol weaning is no better than nonprotocol weaning in terms of reducing invasive mechanical ventilation in newborns, according to this review.

Weaning by protocol on severely ill infants was thoroughly reviewed by Blackwood, et al. (2013), who conducted a comprehensive study. The purpose of this study was to investigate if critically ill infants who were weaned utilizing protocols had shorter invasive mechanical ventilation durations than those who were weaned using standard (non-protocolized) techniques. The researchers looked at three studies with little risk of bias, totaling 321 youngsters, for their findings. Prototyped weaning was shown to shorten total breathing time by 32 hours in a large study (260 babies) (95% confidence interval 8 to 56; P = 0.01). Non-significant reductions of -88 hours (95% CI -228 to 52; P = 0.02; 30 and 31 children, respectively) were seen in two further investigations (P = 0.06). More than 100 hours (95% confidence interval 28–184; P = 0.007) and 21 hours (95% confidence interval 9–32) were saved by protocolized weaning in these two small studies, respectively. For the duration of mechanical ventilation prior to weaning or length of stay in the PICU or general hospital, there were no significant impacts in these studies. Make sure that mortality, adverse events, ICU length of stay and patient satisfaction are not adversely affected by protocolized weaning vs. normal treatment. Weaning protocols may reduce the period of mechanical ventilation; however there is little data to determine if protocolized weaning is beneficial or harmful to children.

Chapter Four

Research Methodology and Results

4.1 Introduction

In this chapter addressed research method includes, population, study site, sample and sampling, instrument, ethical issues, data gathering procedure, and data analysis.

This portion outlines thoroughly the research approach employed for performing this investigation. Also clearly shows the manner of essential information and data address. Justifications and rationalization for using selected study design, population, data collecting instruments, sources of data, methodologies of data collection and procedure, presentation of data, analysis method and analytical techniques employed are described.

4.2 Design

A quasi-experimental study conducted in patients undergoing protocolized versus non-protocolized weaning from invasive mechanical ventilation in premature infants in neonatal intensive care unit.

Experimental group was infants undergoing a weaning protocol from mechanical ventilator at gestational age 26 week and above at neonatal intensive care unit at Holy Family hospital Bethlehem. Palestine. Protocolzed weaning is defined as having used a protocol, delivered by a healthcare professional with the intention of removing infants from invasive mechanical ventilation

4.3 Historical Control Group

This group includes patients who were on mechanical ventilation at gestational age 26 week and above at neonatal intensive care unit at Holy Family hospital Bethlehem. Palestine and Non-protocolized weaning were used as usual care, i.e., standard practice that incorporated any non-protocolized practice between July 2019 and June 2020 at the same hospital, with the same, ICU staff, during both periods. As part of the inclusion/exclusion criteria, this achieved by reviewing the hospital records of all patients admitted to the hospital and were on mechanical ventilation in the same ICU

during the same period one year earlier (July 2019 to June 2020) to minimize the impact of seasonal variations on two groups.

4.4 Setting

Neonatal intensive care unit, At Holy Family hospital. Bethlehem, Palestine.

The Holy Family hospital is a maternity hospital that provides a wide range of medical care that includes delivery services prenatal and antenatal care, well women clinics, diabetic clinics for pregnant women, gynaecology surgeries, intensive care unit for premature babies and outpatient clinics.

4.5 Participants

Premature infants included with a gestational age of 26 weeks or more. These infants cared for in a NICU. Neonates had to have initially been on mechanical ventilation via a nasal or oral endotracheal tube.

4.6 Sample size

Sample size is calculated based on Prasad and Mishra. (2019) study that conducted in the form of Quality improvement project aimed to reduce extubation failure rate by implementing protocol-driven ventilation and extubation strategies. Ventilation and extubation protocols implemented Primary outcome was extubation failure within the first 72 h of extubation. Results: Extubation failure rate reduced from 41.7% (pre-protocol period) to 23.8% Plan-do-check-act (PDCA)

Benchmark 6ix Sigma calculator.

Confidence Level: The minimum acceptable probability of preventing type I error is 95%.

Power of Test.

The minimum acceptable probability of preventing type II error.

Proportion 1:24%.

Proportion 2:42%.

Sample Size (2 - proportion test).

Minimum samples required is 52 patients.

Added 10% of the sample size to cover drop out, it will be 58 patients.

The authors decided to recruit 30 patients in each group.

4.6.1 Selection criteria

Inclusion criteria:

- Infant gestational age 26 Weeks and above.
- On mechanical ventilation

Exclusion criteria:

- Infants with significant birth defect or abnormalities (cyanotic congenital heart disease; primary pulmonary hypertension; neuromuscular disease; and tracheostomy)
- Infant weight less than 500 gm.
- All participants received ventilation exclusively via non-invasive techniques or tracheostomy.

4.7 Instrumentation

Structured data sheet including demographic factors and related factors according to previous relationship in other studies.

Data sheet in this study encompass of three parts:

1. Demographic variables.
2. Clinical variables.
3. Weaning Outcome.

4.7.1 Validity

The data collection tool was in English and then content validity applied and then it reviewed by expert's (one neonatology, three NICU nurses, two researchers with PhD and one statistician) to ensure the relevance of data sheet to subject under study.

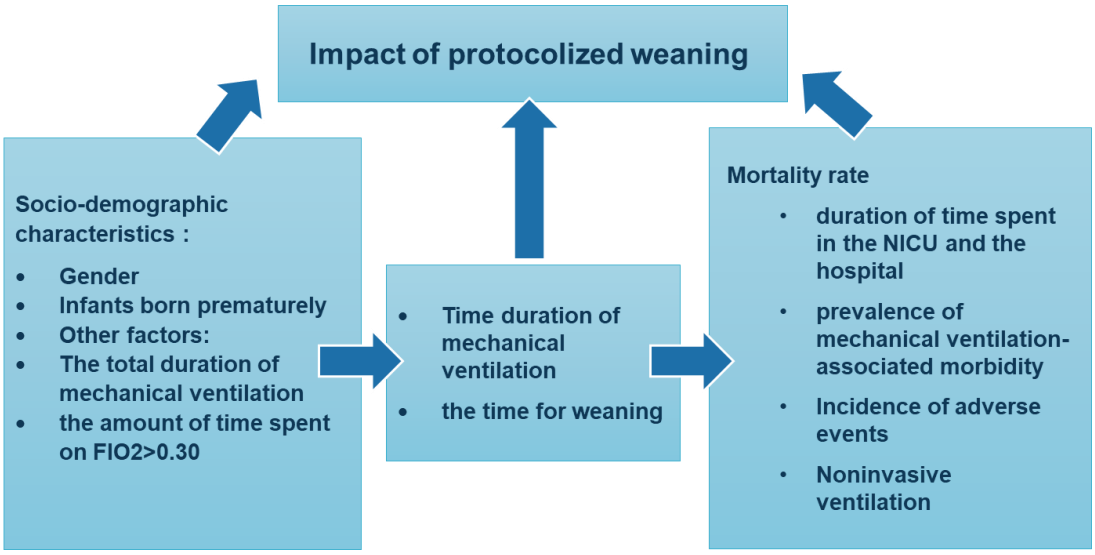
4.7.2 Readability (Pilot Study)

A pilot study conducted on 6 infants 3 for each group and it was excluded from sample size due to modification of data collection sheet variables. It conducted to determine the suitability of the data sheet, availability of data and to estimate the time required for the data collection.

4.8 Study variables

Figure 1

Impact of protocolized weaning.



4.9 Weaning Protocol

Weaning an endotracheal tube must be withdrawn and ventilatory aid stopped. Removing ventilator support is only possible if both the underlying cause of respiratory failure and concomitant complication are improved or resolved. In most cases, the patient is ready for ventilation to be removed and extubation to be performed when gas

exchange is adequate with a low positive end-expiratory pressure and low fraction of inspired oxygen, hemodynamics stabilizes, and the respiratory drive for initiating spontaneous breaths is maintained or re-established. A progressive reduction in ventilatory assistance and an evaluation of the patient's capacity to breathe on their own are necessary for MV weaning. By using objective indicators like as gas exchange and respiratory mechanics, as well as the ability of the infant to defend the airway (historical group), or by planned procedures with known treatment plans, weaning is typically directed by the neonatologist's individual opinion (experimental group). The present study's procedure included the following topics. To begin the weaning process, there must be objective criteria for assessing if a patient is ready to breathe without the assistance of a ventilator; 2) well-defined criteria for establishing the patient's extubation readiness; and 3) systematic instructions for lowering ventilation support (how to alter ventilatory parameters according to physiological or clinical response).

Pressure-Controlled SIMV is typically used to ventilate all newborns (conventional ventilation).

For babies on SIMV, suggested weaning protocol:

1. Baby must be stable (no desaturation episodes, no inotropes, no pulmonary hemorrhage) for the last 24 hours to start weaning.

2. Blood gases, are within normal or accepted range with low ventilators parameters.

3. Spontaneous respiratory effort above the set ventilator rate.

4. Accepted oxygen saturation with low FIo2 30% or less.

Weaning protocol: In the current study, weaning procedure refers to a standardized method that involves a gradual reduction in invasive breathing. The progressive lowering of invasive ventilation assistance was used in the weaning protocol (stepwise reduction protocol).

Table 1

Weaning protocol

CONDITION	Weaning Strategies
SPO2 > 95	Wean FiO2 by 5% steps till Fio2 <30%
SPO2>95% with normal PCO2 (35-45) and FIO2 <30%	1-Wean ventilation rate gradually by 5 bpm steps then evaluate blood gas in 1 hour and baby spontaneous breathing effort after weaning. 2-Wean PIP by 1-2 steps till PIP 18. 3-then state to wean PEEP gradually till4-5.
SPO2 91-95% - normal PACO2 With FIO2 >30%	Keep ventilation settings the same and keep follow up BG and baby spontaneous breathing effort.
SPO2 91-95% - Low PaCO2 with FIO2>30%	Only wean rate by 5 bpm steps don't intervene with pressures

Extubation Criteria

A. Good breathing effort – baby on caffeine if premature <34 weeks

B. Normal blood gas (PH >7.25, CO2 35-45)

C. SPO2 > 92% consistently within the last 12 hours

D. No sedation at least 6 hours.

AND

- PIP on MV <18
- FiO2 <30%
- PEEP 4-5
- MAP <8
- Rate <30 /minute

AND

Extubate to CPAP or NIV at A MAP equal to last MAP on MV of 5-8 CmH2O

During process:

1-Ensure thermoregulation.

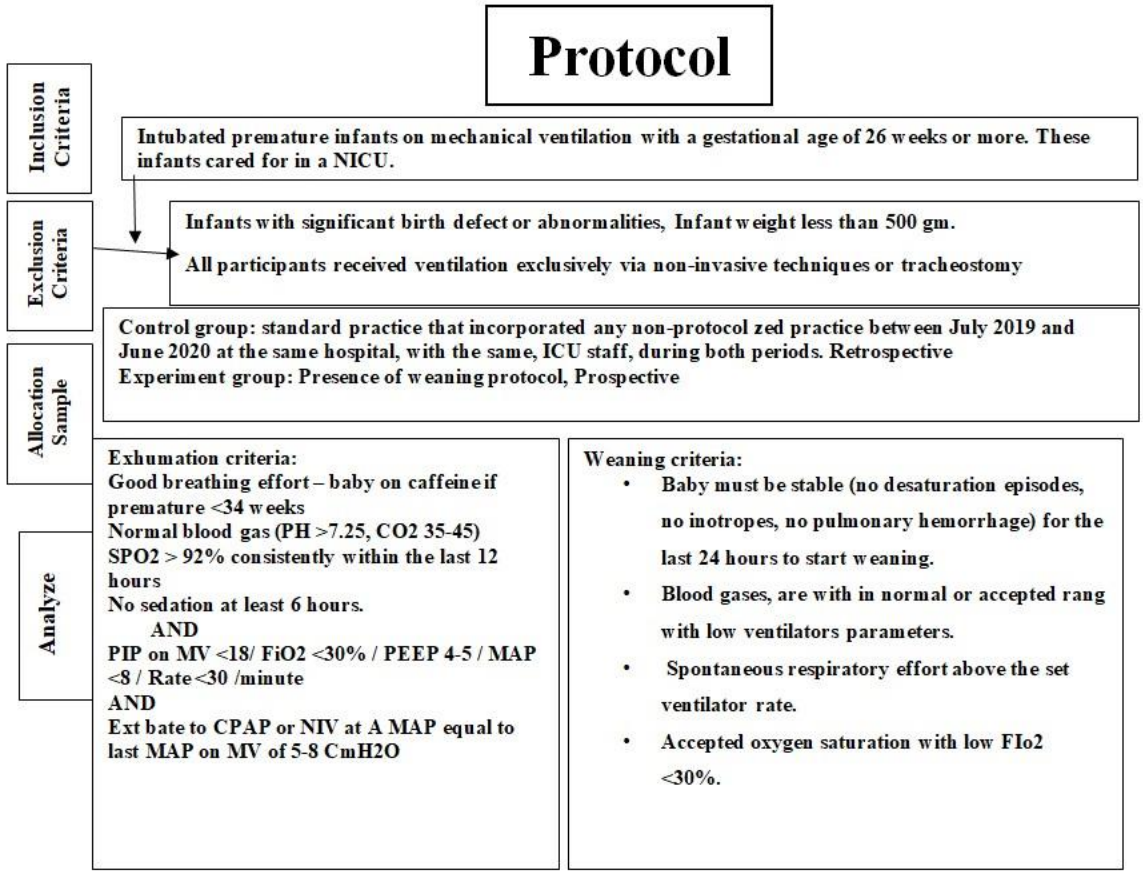
2- Pain management.

3- Hand hygiene.

Source of protocol (Rimensberger, 2015; USCF Benioff Children ‘s Hospital, 2004; Polin & Yoder, 2004; Donn & Sinha, 2017).

Figure 2

Protocol model



4.12 Data analysis

Data analysis conducted through Statistical package for social sciences (SPSS) V 25. Descriptive statistics (Means, Standard Deviations, frequency) are used. The following Tests and Methods were used to analyze the results assuming that the P-Value < 0.05 is considered significant:

1. Chi-Square test: tests the differences in ages between groups of patients for qualitative variables such as: If the baby received surfactant at first hours, If the mother takes steroids before delivery, If the mother had premature rupture of membrane (PROM), If the baby received caffeine before extubation, pulmonary interstitial emphysema, bronchopulmonary dysplasia (BPD), ventilator-associated pneumonia (VAP), Nasal continuous positive airway pressure following extubation, Nasal intermittent positive pressure (IPPV) following extubation, Oxygen delivery following extubation, If there was a need for reintubation (extubation failure within 5 days).

2. Two Independent Samples T test (Adjusted for Unequal variances) and Mann-Whitney test: tests the differences in means between groups of patients for quantitative variables such as: The Apgar score of the baby at 1 minute, The Apgar score of the baby at 5 minutes, Saturation, SBP, DBP, MAP (Vital Sign), Heart rate, Temperature, Spontaneous breathing effort (Respiratory Rate), PH, PCO2, PO2, Fio2(blood gas), FIO2(Ventilator parameter), PIP, PEEP, MAP(Ventilator parameter), Ventilator Rate, Weaning duration till extubation(days), Weaning duration till extubation(hours), NICU length of stay (days), Hospital length of stay (days), Duration of Nasal continuous positive airway pressure following extubation in days, Duration of Nasal intermittent positive pressure (IPPV) following extubation in days, Duration of Oxygen delivery following extubation in days.

Chapter Five

Results

5.1 Introduction

This chapter presents the results of analyzed data. SPSS software was used to manage and analyze these data. Data analyses included descriptive statistics and inferential statistics. Data arranged in tables as below.

5.2 Demographic Characteristics of the Study Sample

Table 2

Demographic Characteristics of the Study Sample.

	Historical N=30	Protocol N=30	Total N=60
Infant Type			
Preterm infants (ELBW)	12(40%)	3(10%)	15(25%)
Preterm infants (VLBW)	9(30%)	11(36.7%)	20(33.3%)
Preterm infants (LBW)	6(20%)	14(46.7%)	20(33.3%)
Term infants	3(10%)	2(6.7%)	5(8.3%)
Total	30(100%)	30(100%)	60(100%)
Gestational age (Weeks)	29.43±3.96	30.9±3.39	30.17±3.73
Chronological age (Days)	60.8±28.86	35.97±19.91	48.38±27.59
Infant's weight(gm)	1424.67±790.9	1768.83±654.23	1596.75±740.24
Sex			
Male	19(63.3%)	19(63.3%)	38(63.3%)
Female	11(36.7%)	11(36.7%)	22(36.7%)
Total	30(100%)	30(100%)	60(100%)
Mode of delivery			
C/S	24(80%)	18(60%)	42(70%)
NVD	6(20%)	12(40%)	18(30%)
Total	30(100%)	30(100%)	60(100%)
Illness			
Premature	28(93.3%)	27(90%)	55(91.7%)
Meconium aspiration	2(6.7%)	3(10%)	5(8.3%)
Total	30(100%)	30(100%)	60(100%)
Reason for intubation			
RDS	29(96.7%)	29(96.7%)	58(96.7%)
MAS	1(3.3%)	1(3.3%)	2(3.3%)
Total	30(100%)	30(100%)	60(100%)

Total duration of mechanical ventilation (days)	4.02±1.51	2.47±0.86	3.24±1.45
Total duration of mechanical ventilation per ventilation mode (days)	2.71±1.75	1.79±1.12	2.17±1.46
SIMV mode			
SIMV Rate	50.5±6.87	51.17±6.25	50.83±6.52
PIP	19.97±2.22	21±1.29	20.48±1.87
PEEP	5.03±0.32	5.15±0.35	5.09±0.34
FIO2	56.33±24.28	48.5±14.39	52.42±20.18
PCAC mode			
PCAC rate	41.25±2.5	35.71±7.32	37.73±6.47
PIP	16.33±2.08	18.29±2.14	17.7±2.21
PEEP	5±0	5±0	5±0
FIO2	28±9.06	28.29±7.61	28.18±7.7

The study sample consisted of 60 infants distributed on two groups, 30 for the Historical group and 30 for the protocol group. The sample consisted of 55 Preterm infants and 5 Term infants, and the Preterm infants contained three groups: 15 Extremely Low Birth Weight Infants (ELBW), 20 Very Low Birth Weight Infants (VLBW), and 20 Low Birth Weight Infants (LBW). The Historical group consisted of 12 Extremely Low Birth Weight Infants, 9 Very Low Birth Weight Infants, 6 Low Birth Weight Infants and 3 Term infants. The Protocol group consisted of 3 Extremely Low Birth Weight Infants, 11 Very Low Birth Weight Infants, 14 Low Birth Weight Infants and 2 Term infants. Both the Historical and the Protocol groups contained 19 Males and 11 Females. The total mean of Gestational age of the whole sample was 30.17 weeks; it was 29.43 in the Historical group and 30.9 in the protocol group. The total mean of Chronological age of the whole sample was 48.38 days; it was 60.8 in the Historical group and 35.97 in the protocol group. The mean of total duration of mechanical ventilation of the whole sample was 3.24 days, 4.02 in the Historical group and 2.47 in the protocol group, and the mean of total duration of mechanical ventilation per ventilation mode of the whole sample was 2.17 days, 2.71 in the Historical group and 1.79 in the protocol group.

Regarding Mode of delivery, the total number of (C/S) in the study sample was 42, 24 in the Historical group and 18 in the Protocol group, and the total number of (NVD) in the study sample was 18, 6 in the Historical group and 12 in the Protocol group. Regarding Illness, the total number of (Premature) in the study sample was 55, 28 in the Historical group and 27 in the Protocol group, and the total number of (Meconium

aspiration) in the study sample was 5, 2 in the Historical group and 3 in the Protocol group. Regarding reason for intubation, the total number of (RDS) in the study sample was 58, 29 in the Historical group and also 29 in the Protocol group, and the total number of (MAS) in the study sample was 2, 1 in the Historical group and also 1 in the Protocol group (Table 1).

All the infants in the study sample in this study were not on sedation before Extubation and all of them have not mortality rate.

In what follows, the results of comparisons between the Historical and the Protocol groups in each type of the four types of infants (ELBW, VLBW, LBW, and Term infants) for the following measurements and indicators:

1. Maternal data.
2. Vital Sign.
3. Blood Gas.
4. Ventilator parameters.
5. Weaning out comes.
6. Incidence of mechanical ventilation.
7. Use of noninvasive ventilation.

Table 3

Comparison between Historical and Protocol groups among all Infants in the study sample(N=60) in terms of receiving surfactant, maternal data, vital signs, blood gas, ventilator parameters, weaning out comes, incidence of mechanical ventilation

Outcome	Historical N=30	Protocol N=30	Total N=60	P-value
If the baby received surfactant at first hours	24(80%)	20(66.7%)	44(73.3%)	0.243
Maternal data				
If the mother takes steroids before delivery	11(36.7%)	20(66.7%)	31(51.7%)	0.020*
If the mother had premature rupture of membrane (PROM)	5(16.7%)	7(23.3%)	12(20%)	0.519
The Apgar score of the baby at 1 minute	6.27±1.87	7.43±1.3	6.85±1.71	0.007*
The Apgar score of the baby at 5 minutes	7.97±1.16	8.47±0.68	8.22±0.98	0.046*
If the baby received caffeine before extubation	23(76.7%)	21(70%)	44(73.3%)	0.559
Vital Sign				
Saturation	95.87±1.74	96.2±1.32	96.03±1.54	0.407
SBP	62.7±8.01	57.3±5.98	60±7.52	0.004*
DBP	33.93±7.91	33.13±6.21	33.53±7.06	0.665
MAP (Vital Sign)	44.53±8.06	42.73±6.1	43.63±7.14	0.333
Heart rate	148.77±12.9	143±9.26	145.88±11.5	0.027*
Temperature	36.86±0.22	36.92±0.13	36.89±0.18	0.265
Spontaneous breathing effort (Respiratory Rate)	50.5±6.45	49.5±4.84	50±5.68	0.500
Blood Gas				
PH	7.35±0.07	7.36±0.04	7.36±0.06	0.396
PCO2	36.16±5.95	35.17±5.57	35.66±5.73	0.508
PO2	55.63±14.17	57.07±17.15	56.35±15.61	0.725
Fio2(blood gas)	28.23±5.64	22.67±2.67	25.45±5.2	0.000*
Ventilator parameters				
FIO2(Ventilator parameter)	28.37±5.51	22.67±2.67	25.52±5.17	0.000*
PIP	15.8±2.7	15.63±1.97	15.72±2.34	0.786
PEEP	5.07±0.45	5±0	5.03±0.32	0.420
MAP (Ventilator parameter)	7.4±1.04	6.92±0.52	7.16±0.85	0.028*
Ventilator Rate	32.33±6.4	28.5±2.67	30.42±5.23	0.004*
Weaning out comes				

Outcome	Historical N=30	Protocol N=30	Total N=60	P-value
Weaning duration till extubation(days)	4.02±1.51	2.47±0.86	3.24±1.45	0.000*
Weaning duration till extubation(hours)	88.73±33.21	55.77±21.73	72.25±32.41	0.000*
NICU length of stay (days)	30.53±17.7	8.97±6.9	19.75±17.2	0.000*
Hospital length of stay (days)	60.8±28.86	35.97±19.91	48.38±27.59	0.000*
Incidence of mechanical Ventilation				
pulmonary interstitial emphysema	7(23.3%)	0(0%)	7(11.7%)	0.005*
bronchopulmonary dysplasia (BPD)	12(40%)	7(23.3%)	19(31.7%)	0.165
ventilator-associated pneumonia (VAP)	6(20%)	0(0%)	6(10%)	0.010*
Use of non-invasive ventilation				
Nasal continuous positive airway pressure following extubation	27(90%)	21(70%)	48(80%)	0.049*
Duration of Nasal continuous positive airway pressure following extubation in days	6.48±0	2.81±0	4.88±4.84	0.008*
Nasal intermittent positive pressure (IPPV) following extubation	26(86.7%)	18(60%)	44(73.3%)	0.020*
Duration of Nasal intermittent positive pressure (IPPV) following extubation in days	8.65±7.98	3.83±0	6.68±6.73	0.018*
Oxygen delivery following extubation	26(86.7%)	22(73.3%)	48(80%)	0.197
Duration of Oxygen delivery following extubation in days	19.08±20.24	4.32±2.57	12.31±16.61	0.001*
If there was a need for reintubation (extubation failure within 5 days)	20(66.7%)	1(3.3%)	21(35%)	0.000*

* The Numbers in the table represent: Mean ± Standard Deviation for Quantitative variables and frequencies with percentages N (%) for Qualitative variables.

** The P-values are related to the two independent samples T-test for Quantitative variables and the Chi-square test for Qualitative variables.

The results in the table (2) above show that there are significant differences at 0.05 level between Historical and Protocol groups among all infants in the study sample in the following indicators and measurements: If the mother takes steroids before delivery, the Apgar score of the baby at 1 minute, The Apgar score of the baby at 5 minutes, SBP, Heart rate, FiO2(blood gas), FIO2(Ventilator parameter), MAP(Ventilator parameter), Ventilator Rate, Weaning duration till extubation (days), Weaning duration till extubation (hours), NICU length of stay (days), hospital length of stay (days), pulmonary interstitial emphysema, ventilator-associated pneumonia (VAP), Nasal continuous positive airway pressure following extubation, Duration of nasal continuous positive airway pressure following extubation in days, nasal intermittent positive pressure (IPPV) following extubation, If there was a need for reintubation (extubation failure within 5 days), duration of oxygen delivery following extubation in days, duration of nasal intermittent positive pressure (IPPV) following extubation in days. The P-values corresponding to these indicators and measurements are less than 0.05.

The results show that 11 of 30 mothers in the Historical group took steroids before delivery (N=11/30 (36.7%) while 20 mothers in the Protocol group took steroids before delivery (N=20/30 (66.7%), p= 0.020.

The results show that the mean of the Apgar score of the baby at 1 minute in the Historical group (Mean=6.27) is significantly lower than that in the Protocol group (Mean=7.43), p= 0.007. The results also show that the mean of the Apgar score of the baby at 5 minutes in the Historical group (Mean=7.97) is significantly lower than that in the Protocol group (Mean=8.47), p= 0.046.

The results show that the mean of the SBP in the Historical group (Mean=62.7) is significantly higher than that in the Protocol group (Mean=57.3), p= 0.004, also the mean of the heart rate in the Historical group (Mean=148.77) is significantly higher than that in the Protocol group (Mean=143), p=0.027.

The results show that the mean of Fio2 (blood gas) in the Historical group (Mean=28.23) is significantly higher than that in the Protocol group (Mean=22.67), p= 0.000, and also the mean of FIO2 (Ventilator parameter) in the Historical group (Mean=28.37) is significantly higher than that in the Protocol group (Mean=22.67), p=0.000. The results also show that the mean of the MAP (ventilator parameter) in the

Historical group (Mean=7.4) is significantly higher than that in the Protocol group (Mean=6.92), p=0.028, also the mean of ventilator rate in the Historical group (Mean=32.33) is significantly higher than that in the Protocol group (Mean=28.5), p= 0.004.

The results show that the mean of Weaning duration till extubation (days) in the Historical group (Mean=4.02) is significantly higher than that in the Protocol group (Mean=2.47), p= 0.000. Also, the mean of weaning duration till extubation (hours) in the Historical group (Mean=88.73) is significantly higher than that in the Protocol group (Mean=55.77), p= 0.000.

The results show that the mean of NICU length of stay (days) in the Historical group (Mean=30.53) is significantly higher than that in the Protocol group (Mean=8.97), p= 0.000. Also, the mean of Hospital length of stay (days) in the Historical group (Mean=60.8) is significantly higher than that in the Protocol group (Mean=35.97), p=0.000.

The results in the table above show that 7 cases of 30 had pulmonary interstitial emphysema in the Historical group (N=7/30 (23.3%) while no cases had pulmonary interstitial emphysema in the Protocol group (N=0/30 (0%), p= 0.005. Also, there are 6 cases of 30 had ventilator-associated pneumonia (VAP) in the Historical group (N=6/30 (20%) while no cases had ventilator-associated pneumonia (VAP) in the Protocol group (N=0/30 (0%), p= 0.010.

The results show that the usage of Nasal continuous positive airway pressure following extubation was for 27 cases in the Historical group (N=27, P=90%) while the usage of Nasal continuous positive airway pressure following extubation was for 21 cases in the Protocol group (N=21/30(70%), p= 0.049, and the results exhibited that the mean of duration of nasal continuous positive airway pressure following extubation in days in the Historical group (Mean=6.48) which is significantly higher than that in the Protocol group (Mean=2.81), p= 0.008.

Also, the results show that the usage of Nasal intermittent positive pressure (IPPV) following extubation was for 26 cases in the Historical group (N=26 (86.7%) while the usage of it was for 18 cases in the Protocol group (N=18/30(60%), p= 0.020, and the mean of duration of nasal intermittent positive pressure (IPPV) following extubation in

days in the Historical group (Mean=8.65) is significantly higher than that in the Protocol group (Mean=3.83), p= 0.018.

The results show that the mean of duration of oxygen delivery following extubation in days in the Historical group (Mean=19.08) is significantly higher than that in the Protocol group (Mean=4.32), p= 0.001.

Finally, the results in the table show that there was a need for reintubation (extubation failure within 5 days) for 20 cases of 30 in the Historical group (N=20/30(66.7%) while there was only one case needed reintubation in the Protocol group (N=1/30(3.3%), p= 0.000.

From the other hand, the results in the table above show that there are no significant differences at 0.05 level between Historical and Protocol groups among all Infants in the study sample in the rest of indicators and measurements studied and appeared in the table, since their corresponding P-values are higher than 0.05.

Table 4

Comparison between Historical and Protocol groups among the Extremely Low Birth Weight Infants (N=15) in terms of receiving surfactant, maternal data, vital signs, blood gas, ventilator parameters, weaning out comes, incidence of mechanical ventilation

Outcome	Historical N=12	Protocol N=3	Total N=15	P-value
If the baby received surfactant at first hours	12(100%)	2(66.7%)	14(93.3%)	0.038*
Maternal data				
If the mother takes steroids before delivery	3(25%)	3(100%)	6(40%)	0.018*
If the mother had premature rupture of membrane (PROM)	2(16.7%)	2(66.7%)	4(26.7%)	0.08
The Apgar score of the baby at 1 minute	6.25±1.48	7.33±0.58	6.47±1.41	0.247
The Apgar score of the baby at 5 minutes	7.58±1.44	8.33±0.58	7.73±1.33	0.404
If the baby received caffeine before extubation	12(100%)	3(100%)	15(100%)	----
Vital Sign				
Saturation	95.33±1.07	95.67±0.58	95.4±0.99	0.619
SBP	61.58±8.45	57.33±2.52	60.73±7.75	0.416
DBP	32.33±6.14	32.33±4.62	32.33±5.72	1.000
MAP(Vital Sign)	43.5±7.12	41±2.65	43±6.47	0.569
Heart rate	149.42±13.01	141±11.53	147.73±12.81	0.327
Temperature	36.88±0.27	36.9±0.17	36.88±0.25	0.881
Spontaneous breathing effort (Respiratory Rate)	53.17±7.33	53±2.65	53.13±6.58	0.970
Blood Gas				
PH	7.33±0.07	7.35±0.05	7.33±0.07	0.688
PCO2	34.75±7.25	31.67±4.04	34.13±6.73	0.498
PO2	57.33±13.35	59.33±6.66	57.73±12.13	0.809
Fio2(blood gas)	26.83±4.17	21±0	25.67±4.42	0.035*
Ventilator parameters				
FIO2(Ventilator parameter)	26.83±4.17	21±0	25.67±4.42	0.035*
PIP	15.33±2.84	14±2	15.07±2.69	0.462
PEEP	4.96±0.33	5±0	4.97±0.3	0.837
MAP (Ventilator parameter)	7.19±1	6.63±0.67	7.08±0.95	0.384
Ventilator Rate	31.67±6.51	26.67±5.77	30.67±6.51	0.248
Weaning out comes				

Outcome	Historical N=12	Protocol N=3	Total N=15	P-value
Weaning duration till extubation(days)	5.08±1.08	3±1	4.67±1.35	0.010*
Weaning duration till extubation(hours)	112.33±21.55	74.33±27.3	104.73±26.82	0.021*
NICU length of stay (days)	47.08±8.86	18.33±10.41	41.33±14.79	0.000*
Hospital length of stay (days)	87.83±13.87	65.33±3.21	83.33±15.47	0.018*
Incidence of mechanical Ventilation				
pulmonary interstitial emphysema	2(16.7%)	0(0%)	2(13.3%)	0.448
bronchopulmonary dysplasia (BPD)	11(91.7%)	2(66.7%)	13(86.7%)	0.255
ventilator-associated pneumonia (VAP)	4(33.3%)	0(0%)	4(26.7%)	0.243
Use of non-invasive ventilation				
Nasal continuous positive airway pressure following extubation	12(100%)	2(66.7%)	14(93.3%)	0.038*
Duration of Nasal continuous positive airway pressure following extubation in days	9.08±5.65	4±0	8.36±5.51	0.010*
Nasal intermittent positive pressure (IPPV) following extubation	11(91.7%)	3(100%)	14(93.3%)	0.605
Duration of Nasal intermittent positive pressure (IPPV) following extubation in days	13.36±6.89	4.67±0.58	11.5±7.09	0.002*
Oxygen delivery following extubation	12(100%)	3(100%)	15(100%)	----
Duration of Oxygen delivery following extubation in days	32.08±23.34	5.33±4.16	26.73±23.52	0.003*
If there was a need for reintubation (extubation failure within 5 days)	10(83.3%)	0(0%)	10(66.7%)	0.006*

* The Numbers in the table represent: Mean ± Standard Deviation for Quantitative variables and frequencies with percentages N (%) for Qualitative variables.

** The P-values are related to the Two independent samples T-test for Quantitative variables and the Chi-square test for Qualitative variables.

The results in the table (2) above show that there are significant differences at 0.05 level between Historical and Protocol groups among the Extremely Low Birth Weight Infants in the following indicators and measurements: If the baby received surfactant at first hours, If the mother takes steroids before delivery, Fio2(blood gas), FIO2(Ventilator parameter), Weaning duration till extubation(days), Weaning duration till extubation(hours), Hospital length of stay (days), Nasal continuous positive airway pressure following extubation, Duration of Nasal continuous positive airway pressure following extubation in days, Duration of Nasal intermittent positive pressure (IPPV) following extubation in days, Duration of Oxygen delivery following extubation in days, and if there was a need for reintubation (extubation failure within 5 days). The P-values corresponding to these indicators and measurements are less than 0.05.

The results in the table above show that all infants in the Historical group received surfactant at first hours (N=12/12(100%) while only 2 of 3 infants in the Protocol group received surfactant at first hours (N=2/3(66.7%), p= 0.038.

The results also show that only 3 of 12 mothers in the Historical group took steroids before delivery (N=3/12(25%) while all mothers in the Protocol group took steroids before delivery (N=3/3(100%), the P-value of the test is 0.018.

The results show that the mean of Fio2 (blood gas) in the Historical group (Mean=26.83) is significantly higher than that in the Protocol group (Mean=21), p= 0.035. The same results and the same values were for FIO2(Ventilator parameter).

The results show that the mean of weaning duration till extubation (days) in the Historical group (Mean=5.08) is significantly higher than that in the Protocol group (Mean=3), p= 0.010. Also, the mean of weaning duration till extubation (hours) in the Historical group (Mean=112.33) is significantly higher than that in the Protocol group (Mean=74.33), p= 0.021.

The results show that the mean of NICU length of stay (days) in the Historical group (Mean=47.08) is significantly higher than that in the Protocol group (Mean=18.33), p= 0.000. Also, the mean of Hospital length of stay (days) in the Historical group (Mean=87.83) is significantly higher than that in the Protocol group (Mean=65.33), p=0.018.

The results show that the usage of nasal continuous positive airway pressure following extubation was for all cases in the Historical group (N=12/12 (100%) while the usage of Nasal continuous positive airway pressure following extubation was for 2 cases in the Protocol group (N=2/3 (66.7%), p=0.038, and the results exhibited that the mean of duration of nasal continuous positive airway pressure following extubation in days in the Historical group (Mean=9.08) which is significantly higher than that in the Protocol group (Mean=4), p= 0.010. Also, the results show that the mean of duration of nasal intermittent positive pressure (IPPV) following extubation in days in the Historical group (Mean=13.36) is significantly higher than that in the Protocol group (Mean=4.67), p= 0.002, and also, the mean of duration of oxygen delivery following extubation in days in the Historical group (Mean=32.08) is significantly higher than that in the Protocol group (Mean=5.33), p= 0.003.

Finally, the results in the table show that there was a need for reintubation (extubation failure within 5 days) for 10 cases of 12 in the Historical group (N=10/12 (83.3%) while there is no any case needed reintubation in the Protocol group (N=0/3 (0%), p= 0.006. There was no relation between the two groups in receiving caffeine because all ELBW infants received caffeine.

From the other hand, the results in the table above show that there are no significant differences at 0.05 level between Historical and Protocol groups among the Extremely Low Birth Weight Infants in the rest of indicators and measurements studied and appeared in the table 3, since their corresponding P-values are higher than 0.05. However there were no significant differences between the two groups in the incidence of VAP. BPD emphysema but the results show that the incidence more in the historical group.

Table 5

Comparison between Historical and Protocol groups among the Very Low Birth Weight Infants (N=20) in terms of receiving surfactant, maternal data, vital signs, blood gas, ventilator parameters, weaning out comes, incidence of mechanical ventilation.

Outcome	Historical N=9	Protocol N=11	Total N=20	P-value
If the baby received surfactant at first hours	7(77.8%)	6(54.5%)	13(65%)	0.279
Maternal data				
If the mother takes steroids before delivery	4(44.4%)	8(72.7%)	12(60%)	0.199
If the mother had premature rupture of membrane (PROM)	3(33.3%)	3(27.3%)	6(30%)	0.769
The Apgar score of the baby at 1 minute	5.33±1.66	7.73±1.19	6.65±1.84	0.001*
The Apgar score of the baby at 5 minutes	8.11±0.6	8.55±0.69	8.35±0.67	0.155
If the baby received caffeine before extubation	9(100%)	11(100%)	20(100%)	----
Vital Sign				
Saturation	96.44±2.01	96.18±1.47	96.3±1.69	0.739
SBP	59.11±8.55	58.18±7.22	58.6±7.65	0.795
DBP	28.33±4.58	36.45±7.62	32.8±7.52	0.012*
MAP (Vital Sign)	38.33±5	43.64±8.16	41.25±7.28	0.106
Heart rate	153.33±10.1	144.73±10.66	148.6±11.05	0.083
Temperature	36.83±0.18	36.91±0.16	36.88±0.17	0.330
Spontaneous breathing effort (Respiratory Rate)	50.22±4.32	49.91±6.19	50.05±5.3	0.899
Blood Gas				
PH	7.37±0.09	7.35±0.04	7.36±0.06	0.517
PCO2	35.52±4.26	33.09±5.94	34.19±5.27	0.317
PO2	53.67±9.14	61.27±20.05	57.85±16.18	0.308
Fio2(blood gas)	26.56±7	23.27±2.97	24.75±5.3	0.174
Ventilator parameters				
FIO2(Ventilator parameter)	26.56±7	23.27±2.97	24.75±5.3	0.174
PIP	14.89±2.52	14.73±2.24	14.8±2.31	0.881
PEEP	5.17±0.61	5±0	5.08±0.41	0.376
MAP(Ventilator parameter)	7.2±1.14	6.68±0.58	6.92±0.89	0.203
Ventilator Rate	31.11±7.82	27.73±2.61	29.25±5.68	0.193
Weaning out comes				

Outcome	Historical N=9	Protocol N=11	Total N=20	P-value
Weaning duration till extubation(days)	3.17±1.57	2.82±0.75	2.98±1.17	0.517
Weaning duration till extubation(hours)	70.44±35.71	63.18±20.38	66.45±27.73	0.574
NICU length of stay (days)	27.56±13.88	9.55±7.12	17.65±13.87	0.001*
Hospital length of stay (days)	56.33±20.89	47.55±12.61	51.5±16.96	0.260
Incidence of mechanical Ventilation				
pulmonary interstitial emphysema	1(11.1%)	0(0%)	1(5%)	0.257
bronchopulmonary dysplasia (BPD)	1(11.1%)	4(36.4%)	5(25%)	0.194
ventilator-associated pneumonia (VAP)	0(0%)	0(0%)	0(0%)	----
Use of non-invasive ventilation				
Nasal continuous positive airway pressure following extubation	8(88.9%)	8(72.7%)	16(80%)	0.369
Duration of Nasal continuous positive airway pressure following extubation in days	5.88±5.74	3.25±3.81	4.56±4.9	0.299
Nasal intermittent positive pressure (IPPV) following extubation	6(66.7%)	5(45.5%)	11(55%)	0.343
Duration of Nasal intermittent positive pressure (IPPV) following extubation in days	8.17±10.87	4.2±2.77	6.36±8.15	0.451
Oxygen delivery following extubation	9(100%)	9(81.8%)	18(90%)	0.178
Duration of Oxygen delivery following extubation in days	10±6.3	5.22±2.39	7.61±5.24	0.049
If there was a need for reintubation (extubation failure within 5 days)	6(66.7%)	1(9.1%)	7(35%)	0.007*

* The Numbers in the table represent: Mean ± Standard Deviation for Quantitative variables and frequencies with percentages N (%) for Qualitative variables.

** The P-values are related to the two independent samples T-test for Quantitative variables and the Chi-square test for Qualitative variables.

The results in the table (4) above show that there are significant differences at 0.05 level between Historical and Protocol groups among the very low birth weight infants in The following indicators and measurements: The Apgar score of the baby at 1 minute, DBP,

NICU length of stay (days), duration of oxygen delivery following extubation in days, and if there was a need for reintubation (extubation failure within 5 days). The P-values corresponding to these indicators and measurements are less than 0.05.

The results show that the mean of the Apgar score of the baby at 1 minute in the Historical group (Mean=5.33) is significantly lower than that in the Protocol group (Mean=7.73), p= 0.001. The results also show that the mean of the DBP in the Historical group (Mean=28.33) is significantly lower than that in the Protocol group (Mean=36.45), p= 0.012.

The results show that the mean of NICU length of stay (days) in the Historical group (Mean=27.56) is significantly higher than that in the Protocol group (Mean=9.55), p= 0.001.

The results show that the mean of duration of oxygen delivery following extubation in days in the Historical group (Mean=10) is significantly higher than that in the Protocol group (Mean=5.22), p= 0.049.

Finally, the results in the table (4) show that there was a need for reintubation (extubation failure within 5 days) for 6 cases of 9 in the Historical group (N=6/9, P=66.7%) while there was only one case of 11 needed reintubation in the Protocol group (N=1/11, P=9.1%), p= 0.007.

From the other hand, the results in the table (4) above show that there are no significant differences at 0.05 level between Historical and Protocol groups among the very low birth weight infants in the rest of indicators and measurements studied and appeared in the table, since their corresponding P-values are higher than 0.05.

Table 6

Comparison between Historical and Protocol groups among the Low-Birth-Weight Infants (N=20) in terms of receiving surfactant, maternal data, vital signs, blood gas, ventilator parameters, weaning out comes, incidence of mechanical ventilation.

Outcome	Historical N=6	Protocol N=14	Total N=20	P-value
If the baby received surfactant at first hours	4(66.7%)	11(78.6%)	15(75%)	0.573
Maternal data				
If the mother takes steroids before delivery	4(66.7%)	8(57.1%)	12(60%)	0.69
If the mother had premature rupture of membrance (PROM)	0(0%)	2(14.3%)	2(10%)	0.329
The Apgar score of the baby at 1 minute	7.83±1.94	7.21±1.48	7.4±1.6	0.444
The Apgar score of the baby at 5 minutes	8.5±1.22	8.43±0.76	8.45±0.89	0.874
If the baby received caffeine before extubation	2(33.3%)	7(50%)	9(45%)	0.492
Vital Sign				
Saturation	96.67±2.34	96.43±1.4	96.5±1.67	0.779
SBP	67.33±4.32	56.5±6.11	59.75±7.51	0.001*
DBP	40±5.48	31.64±4.38	34.15±6.04	0.002*
MAP (Vital Sign)	50.67±3.56	42.14±5.23	44.7±6.17	0.002*
Heart rate	144±16.63	141.64±8.61	142.35±11.17	0.677
Temperature	36.85±0.27	36.93±0.11	36.91±0.17	0.358
Spontaneous breathing effort (Respiratory Rate)	44.67±4.08	49.07±3.93	47.75±4.39	0.036
Blood Gas				
PH	7.35±0.04	7.37±0.04	7.37±0.04	0.232
PCO2	38±2.9	36.29±4.27	36.8±3.91	0.384
PO2	63±20.32	52±15.93	55.3±17.58	0.208
Fio2(blood gas)	30.17±5.12	22.5±2.74	24.8±5	0.000*
Ventilator parameters				
FIO2(Ventilator parameter)	30.83±3.76	22.5±2.74	25±4.92	0.000*
PIP	17.17±2.79	16.5±1.29	16.7±1.81	0.465
PEEP	5±0.32	5±0	5±0.16	1.000
MAP (Ventilator parameter)	7.73±1.12	7.11±0.38	7.3±0.72	0.072
Ventilator Rate	33.33±5.16	29.29±1.82	30.5±3.59	0.016*

Outcome	Historical N=6	Protocol N=14	Total N=20	P-value
Weaning out comes				
Weaning duration till extubation(days)	3.33±1.21	2.07±0.83	2.45±1.1	0.014
Weaning duration till extubation(hours)	71.17±28.57	46±19.13	53.55±24.6	0.032*
NICU length of stay (days)	12±2.45	7.14±4.83	8.6±4.77	0.033*
Hospital length of stay (days)	32.5±7.99	24.36±13.95	26.8±12.83	0.201
Incidence of mechanical Ventilation				
pulmonary interstitial emphysema	3(50%)	0(0%)	3(15%)	0.004*
bronchopulmonary dysplasia (BPD)	0(0%)	1(7.1%)	1(5%)	0.502
ventilator-associated pneumonia (VAP)	2(33.3%)	0(0%)	2(10%)	0.023*
Use of non-invasive ventilation				
Nasal continuous positive airway pressure following extubation	6(100%)	10(71.4%)	16(80%)	0.143
Duration of Nasal continuous positive airway pressure following extubation in days	2.83±1.33	2.4±2.46	2.56±2.06	0.699
Nasal intermittent positive pressure (IPPV) following extubation	6(100%)	9(64.3%)	15(75%)	0.039*
Duration of Nasal intermittent positive pressure (IPPV) following extubation in days	3.17±1.17	3.67±2.83	3.47±2.26	0.691
Oxygen delivery following extubation	2(33.3%)	8(57.1%)	10(50%)	0.329
Duration of Oxygen delivery following extubation in days	6±5.66	3.5±2.14	4±2.87	0.296
If there was a need for reintubation (extubation failure within 5 days)	3(50%)	0(0%)	3(15%)	0.004*

* The Numbers in the table represent: Mean ± Standard Deviation for Quantitative variables and frequencies with percentages N (%) for Qualitative variables.

** The P-values are related to the two independent samples T-test for Quantitative variables and the Chi-square test for Qualitative variables.

The results in the table (5) above show that there are significant differences at 0.05 level between Historical and Protocol groups among the low birth weight infants in the following indicators and measurements: SBP, DBP, MAP (Vital Sign), Spontaneous breathing effort (respiratory rate), Fio2(blood gas), FIO2 (ventilator parameter), ventilator rate, weaning duration till extubation (days), weaning duration till extubation (hours), NICU length of stay (days), pulmonary interstitial emphysema, ventilator-associated pneumonia (VAP), nasal intermittent positive pressure (IPPV) following extubation, If there was a need for reintubation (extubation failure within 5 days). The P-values corresponding to these indicators and measurements are less than 0.05.

The results in the table (5) above show that the mean of the SBP in the Historical group (Mean=67.33) is significantly higher than that in the Protocol group (Mean=56.5), p= 0.001, also the mean of the DBP in the Historical group (Mean=40) is significantly higher than that in the Protocol group (Mean=31.64), p=0.002. And, also the mean of the MAP (Vital Sign) in the Historical group (Mean=50.67) is significantly higher than that in the Protocol group (Mean=42.14), p= 0.002. From the other hand, the results exhibited that the mean of the Spontaneous breathing effort (respiratory rate) in the Historical group (Mean=44.67) is significantly lower than that in the Protocol group (Mean=49.07), p= 0.036.

The results show that the mean of FiO2 (blood gas) in the Historical group (Mean=30.17) is significantly higher than that in the Protocol group (Mean=22.5), the P-value of the test is 0.000, also the mean of FIO2 (Ventilator parameter) in the Historical group (Mean=30.83) is significantly higher than that in the Protocol group (Mean=22.5), p= 0.000. The results also show that the mean of ventilator rate in the Historical group (Mean=33.33) is significantly higher than that in the Protocol group (Mean=29.29), p= 0.016.

The results show that the mean of weaning duration till extubation (days) in the Historical group (Mean=3.33) is significantly higher than that in the Protocol group (Mean=2.07), p= 0.014. Also, the mean of Weaning duration till extubation (hours) in the Historical group (Mean=71.17) is significantly higher than that in the Protocol group (Mean=46), p= 0.032. The results also show that the mean of NICU length of stay (days) in the Historical group (Mean=12) is significantly higher than that in the Protocol group (Mean=7.14), p= 0.033.

The results in the table (5) above show that 3 cases of 6 had pulmonary interstitial emphysema in the Historical group (N=3/6, (50%) while no cases had pulmonary interstitial emphysema in the Protocol group (N=0/14, P=0%), p= 0.004. Also, we have 2 cases of 6 had ventilator-associated pneumonia (VAP) in the Historical group (N=2/6, P=33.3%) while no cases had ventilator-associated pneumonia (VAP) in the Protocol group (N=0/14 (0%), p=0.023.

The results show that the usage of nasal intermittent positive pressure (IPPV) following extubation was for all cases in the Historical group (N=6/6, (100%) while the usage of nasal intermittent positive pressure (IPPV) following extubation was for 9 of 14 cases in the Protocol group (N=9/14(64.3%), p= 0.039.

Finally, the results in the table show that there was a need for reintubation (extubation failure within 5 days) for 3 cases of 6 in the Historical group (N=3/6).

Table 7

Comparison between Historical and Protocol groups among the Term Infants (N=5).

Outcome	Historical N=3	Protocol N=2	Total N=5	P-value
If the baby received surfactant at first hours	1(33.3%)	1(50%)	2(40%)	0.709
Maternal data				
If the mother takes steroids before delivery	0(0%)	1(50%)	1(20%)	0.171
If the mother had premature rupture of membrance (PROM)	0(0%)	0(0%)	0(0%)	----
The Apgar score of the baby at 1 minute	6±2.65	7.5±2.12	6.6±2.3	0.555
The Apgar score of the baby at 5 minutes	8±1	8.5±0.71	8.2±0.84	0.591
If the baby received caffeine before extubation	0(0%)	0(0%)	0(0%)	----
Vital Sign				
Saturation	94.67±0.58	95.5±0.71	95±0.71	0.239
SBP	68.67±4.04	58±0	64.4±6.5	0.038 *
DBP	45±9.54	26.5±2.12	37.6±12.22	0.082
MAP(Vital Sign)	55±8.66	44.5±3.54	50.8±8.58	0.216
Heart rate	142±12.17	146±5.66	143.6±9.32	0.703
Temperature	36.93±0.12	36.9±0.14	36.92±0.11	0.789
Spontaneous breathing effort (Respiratory Rate)	52.33±6.43	45±0	49.4±6.07	0.223
Blood Gas				
PH	7.38±0.08	7.39±0.04	7.38±0.06	0.980
PCO2	40±9.17	44±4.24	41.6±7.16	0.617
PO2	40±1	66±19.8	50.4±17.36	0.089
Fio2(blood gas)	35±0	23±2.83	30.2±6.72	0.004 *
Ventilator parameters				
FIO2(Ventilator parameter)	35±0	23±2.83	30.2±6.72	0.004 *
PIP	17.67±0.58	17±1.41	17.4±0.89	0.495
PEEP	5.33±0.58	5±0	5.2±0.45	0.495
MAP(Ventilator parameter)	8.2±0.35	7.4±0.28	7.88±0.52	0.075

Outcome	Historical N=3	Protocol N=2	Total N=5	P-value
Ventilator Rate	36.67±2.89	30±0	34±4.18	0.053
Weaning out comes				
Weaning duration till extubation(days)	3.67±1.15	2.5±0.71	3.2±1.1	0.302
Weaning duration till extubation(hours)	84.33±22.28	55.5±17.68	72.8±23.99	0.227
NICU length of stay (days)	10.33±1.53	4.5±0.71	8±3.39	0.017*
Hospital length of stay (days)	22.67±7.57	9.5±0.71	17.4±8.99	0.102
Incidence of mechanical Ventilation				
pulmonary interstitial emphysema	1(33.3%)	0(0%)	1(20%)	0.361
bronchopulmonary dysplasia (BPD)	0(0%)	0(0%)	0(0%)	----
ventilator-associated pneumonia (VAP)	0(0%)	0(0%)	0(0%)	----
Use of non-invasive ventilation				
Nasal continuous positive airway pressure following extubation	1(33.3%)	1(50%)	2(40%)	0.709
Duration of Nasal continuous positive airway pressure following extubation in days	2±0	1±0	1.5±0.71	----
Nasal intermittent positive pressure (IPPV) following extubation	3(100%)	1(50%)	4(80%)	0.171
Duration of Nasal intermittent positive pressure (IPPV) following extubation in days	3.33±2.08	1±0	2.75±2.06	0.434
Oxygen delivery following extubation	3(100%)	2(100%)	5(100%)	----
Duration of Oxygen delivery following extubation in days	3±2	2±0	2.6±1.52	0.550
If there was a need for reintubation (extubation failure within 5 days)	1(33.3%)	0(0%)	1(20%)	0.361

* The Numbers in the table represent: Mean ± Standard Deviation for Quantitative variables and frequencies with percentages N (%) for Qualitative variables.

** The P-values are related to the Two independent samples T-test for Quantitative variables and the Chi-square test for Qualitative variables.

The results in the table (6) above show that there are significant differences at 0.05 level between Historical and Protocol groups among the Term Infants in the following indicators and measurements: SBP, Fio2(blood gas), FIO2(Ventilator parameter), and NICU length of stay (days). The P-values corresponding to these indicators and measurements are less than 0.05. The results in the table (6) above show that the mean of the SBP in the Historical group (Mean=68.67) is significantly higher than that in the Protocol group (Mean=58), p= 0.038. There was no relation between the two groups in the baby received caffeine before extubation because term baby did not take caffeine.

The results show that the mean of Fio2 (blood gas) and FIO2(Ventilator parameter) in the Historical group (Mean=35) is significantly higher than that in the Protocol group (Mean=23), the P-value of the test is 0.004.

Finally, the results show that the mean of NICU length of stay (days) in the Historical group (Mean=10.33) is significantly higher than that in the Protocol group (Mean=4.5), p= 0.017.

From the other hand, the results in the table above show that there are no significant differences at 0.05 level between Historical and Protocol groups among the Term Infants.

In the rest of indicators and measurements studied and appeared in the table, since their corresponding P-values are higher than 0.05.

Chapter Six

Discussion

6.1 Introduction

The study sample was comprised of 60 infants allocated across two groups: 30 for the historical group and 30 for the protocol group. The sample was comprised of 55 preterm infants and 5 term infants, and the preterm infants included three groups: 15 Extremely Low Birth Weight Infants (ELBW), 20 Very Low Birth Weight Infants (VLBW), and 20 Low Birth Weight Infants (LBW).

6.2 The weaning and safe extubation of premature newborns

Weaning and extubation of preterm neonates can be aided by objective criteria that can be defined and implemented utilizing readiness tests (Kaczmarek et al., 2013, Robles-Rubio, 2015) due to the unique characteristics of premature neonates. Although the majority of these tests have a high sensitivity for predicting extubation success (Shalish, et al. 2019) in the NICU, parameter reduction is a common practice (Bacci, et al. 2020). The current study's findings are consistent with what the international literature suggests: neonatal patients' weaning is still fraught with concerns and obstacles.

The weaning strategy used in neonates in the current study is gradual reduction of ventilatory support based on clinical judgment, with extubation performed once the minimum ventilation parameters have been reached. This finding is consistent with the findings of a study conducted by Newth, et al. (2009), who found that gradual withdrawal from ventilatory support, based on clinical judgment, is the weaning approach used most frequently in neonates, with extubation occurring after the patient has achieved minimal ventilation parameters or has undergone a successful SBT.

According to Al-Mandari et al. (2015), the most frequently examined criteria in NICUs are ventilation parameters, blood gas tests, and clinical stability/hemodynamics (Al-Mandari et al., 2015). On the other hand, they found that pre-extubation ventilatory parameters and arterial blood gas values were not linked to extubation success or failure (Laham et al., 2015; Johnston et al., 2010).

6.3 SIMV mode

SIMV mode has been used in the current study. SIMV is the preferred weaning or pre-extubation ventilation mode in NICUs in the United Kingdom (Sharma, et al 2007) and Canada, according to other surveys. (Shalish, et al 2015).

6.4 The mean airway pressure (MAP)

There is a significant difference in the MAP between historical 7.41.04 and protocol group 6.920.52 in the current investigation, p = 0.028. These findings are in line with the findings of Urkevicz et al. (2021), who found that the mean airway pressure (MAP) was a significant factor in extubation success, implying that the lower these parameters, the better the chance of success.

An extubation outcome that is positive is also connected to the variables mean airway pressure and time spent on mechanical ventilation. It's possible for the patient and the ventilator to be out of sync with each other when invasive mechanical ventilation is used for a lengthy period of time (Cabral et al. 2014; Vignaux et al. 2013). It has been shown that non-invasive ventilation, which keeps the airways open during spontaneous breathing in preterm neonates, improves the chances of extubation success (Weiss et al., 2016).

6.5 The noninvasive modality post extubation

For the service, NIPPV was the noninvasive mode of choice, and all extubated infants were put in this mode. Premature newborns that are unable to react to nasal CPAP might also benefit from this technique, as recommended Shalish, et al., (2016).

In preterm newborns, CPAP after extubation is preferable to extubation to a headbox or oxyhood (Davis et al., 2003). The immature rib cage of the ELBW infant's failure to maintain enough functional residual capacity due to its excessive compliance and insufficient stiffness is the physiologic basis for this observation. Furthermore, the infant's vocal cords were edematous after being intubated for a period of time, inhibiting effective grunting. Small, single-center clinical trials conducted about two decades ago demonstrated the benefits of sync nasal intermittent positive pressure ventilation (NIPPV) to sustain the extremely preterm newborn during the immediate post-extubation phase (Barrington et al. 2001; Friedlich et al. 1999; Khalaf et al. 2001).

Despite this, non-synchronized NIPPV has gained popularity (Owen et al. 2008; Kieran et al. 2011; Morcillo et al. 2009).

6.6 Duration of mechanical ventilation by days

The mean SD duration of MV in the current study fell from 4.021.51 days in the historical group to 2.470.86 days in the protocol group. Hermeto, et al. (2009) conducted a study that is similar to the current one. A retrospective analysis was carried out at a single-center tertiary NICU in Canada. There were three time periods: one year before a thorough ventilation protocol was implemented (control group), one year after the protocol was implemented, and two years after the protocol was implemented. Over 300 neonates were studied over the course of three years (n = 93/99/109, respectively). In all three cases, their gestational age was 27 2 weeks (mean SD). The median MV length had lowered from 18 days prior to the intervention to 5 days after one year and 6 days after two years. The changes in median MV duration between the time before the protocol was implemented and the time after 1 and 2 years were significant (P 05).

In a large group of critically preterm neonates, Miyosh et al. (2015) assessed the influence of implementing a ventilation protocol on respiratory outcomes in very preterm newborns in a retrospective study. They found that using a ventilation protocol could dramatically reduce the time and duration of mechanical ventilation in 301 mechanically ventilated newborns with a birth weight of less than 1,250 g.

According to the Canadian observational study. implementing a weaning protocol for the care of newborns with a BW of 1250 g or less. utilizing objective criteria for weaning, extubation, and reintubation, resulted in significant improvements in short-term respiratory outcomes. Infants were extubated earlier when the technique was applied, and there was an overall reduction in extubation failure and MV length (Hermeto et al., 2009). These results are congruent with the current study result, which showed that weaning duration till extubation (days) for very low birth weight in the historical group was reduced from 3.171.57 to 2.820.75 in the protocol group, p=0.517.

6.7 Weaning duration till extubation (hours)

Mean± SD of weaning duration till extubation (hours) in the current study was 88.73±33.21 in the historical group and 55.77±21.73 in the protocol group, p=0.000. In

the protocol group, there was a 33-hour reduction. These findings are consistent with those of Jouvet (2013) and Maloney (2007), who showed a statistically significant reduction in weaning duration of 106 and 21 hours, respectively, in protocolized groups versus non-protocolized groups.

6.8 Complications of mechanical ventilation

In the current study, there were 7 (23.3%) patients with pulmonary interstitial emphysema in the historical group compared to 0 (0%) in the protocol group, p = 0.005, and 12 (40%) patients with bronchopulmonary dysplasia (BPD) in the historical group compared to 7 (23.3%) in the protocol group, p = 0.165, as well as 6 (20%) patients with ventilator-associated pneumonia (VAP) in the historical group compared to 0 (0%) in the protocol group, p=0.010. The current study contradicts that of Hermeto et al. (2009), who found that neither the occurrences of bronchopulmonary dysplasia, air leak syndrome, nor pneumonia altered significantly across different study periods.

6.9 Extubation failure

Extubation failure is multifaceted, and a single intervention may not be enough to reduce the rate of extubation failure. The rate of extubation failure varies greatly between centers, depending on the patients' features and the style of support used after extubation. Extubation failure is defined differently in the literature, ranging from 24 hours to 7 days following extubation (Giaccone et al., 2014; Wang et al., 2017). In the current study, there was a significant difference in extubation failure between the historical group 20 (66.7%) and the protocol group 1 (3.3%), p = 0.00. The findings of the current study are consistent with those of Hermeto et al. (2009), who found that the extubation failure rate was 40%, 26%, and 20%, respectively, in three periods: one year before a thorough ventilation protocol was implemented (control group), one year after the protocol was implemented, and two years after the protocol was implemented. As has been previously described, apnea was the most common cause of extubation failure among newborns. (Chawla, et al., 2013, Giaccone, et al., 2013, Sant'Anna, 2012).

Hermato et al. (2009) found a significant reduction in the risk of extubation failure, the median age of the first extubation attempt, and the median duration of mechanical ventilation. These findings match those of the current investigation.

The current study's findings, on the other hand, do not agree with those of Foronda (2011), who found no significant differences in reintubation, self-extubation, or the use of non-invasive ventilation after extubation. According to Urkevicz et al. 2021, extubation failure in the investigated group of 20 premature newborns up to 32 weeks of gestational age was due to apnea (40.5%), gastrointestinal issues/infections (25%), atelectasis (12.5%), and surgical operations/examinations (12.5%). Failure of extubation happened within the first 24 hours of being extubated, and within the first 144 hours of being extubated, there was no significant difference between the success and failure rates in extubation groups. The current study's author believed that it could be due to the use of diverse weaning and extubation protocols.

Furthermore, a difference in extubation success and failure was not seen in this study in relation to birth weight and gestational age. This finding is in accordance with the findings of a study conducted by Urkevicz et al. in 2021, who found no difference in the success and failure of extubation groups in relation to birth weight and gestational age.

6.10 Gasometrical data

In terms of pH, PaCO2, positive inspiratory pressure, and positive expiratory pressure, the success and failure groups differed (Deguines, et al 2009). No statistically significant differences were found in the current investigation with regard to ventilatory and gasometrical parameters. The research implies that gas data such as pH, PaCO2, and HCO3 can be used as predictive factors, notwithstanding the lack of a significant difference between the success and failure groups.

6.11 The inspired percentage of oxygen (FIO2)

During invasive mechanical ventilation, one of the things that may be controlled is the amount of oxygen that the infant is exposed to. It is possible for hyperoxia to produce lung inflammation, alveolar damage, lung deterioration, and mortality (Carvalho, et al 2018). In the current study, researchers observed premature neonates that required a smaller proportion of inspired oxygen to maintain their peripheral oxygen saturation at a safe level. Urkevicz et al. 2021 found the same results, and these findings are compatible with their findings.

6.12 Conclusion

The weaning protocol reduces the duration of mechanical ventilation, weaning duration till extubation, NICU and hospital length of stay (days), the risk of weaning failure, and reintubation. According to the findings of this study, there is evidence to support the superiority of protocol weaning over nonprotocol weaning in the duration of invasive mechanical ventilation in newborn infants.

A weaning protocol for infants on mechanical ventilation was found to be necessary. For this reason, guidelines for reducing a child's reliance on mechanical ventilation have been developed to ensure consistency in the care provided.

The study's findings showed that collaborative guidelines in the form of a weaning protocol could be used safely to guide the weaning process for premature infants in the NICU. More research is needed to assess the clinical impact of the procedures and strategies used for MV weaning and extubation of neonatology patients. These investigations should be based on ICU-specific safety, quality, and productivity factors.

6.13 Strengths and limitations of the study

This study utilised a quasi-experimental design. Retrospective and prospective methods were utilised in this investigation to eliminate contamination between both groups.

During data collection, employees followed the weaning process to a tee. Weaning patterns were anecdotally compared to those recommended in the guidelines.

6.14 Implications for nursing practice

This study's greatest contribution is the creation of a practice program that will help doctors and nurses perform better in the clinical context. Inconsistent weaning decision-making can have negative consequences for the patient's physical and emotional health, as well as financial expenditures (Curley & Fackler, 1998). Premature weaning and/or extubation can occur as a result of quick or ineffective weaning. The frequency with which patients are re-intubated has been linked to negative outcomes, including an increase in mortality (Esteban et al., 1999).

This study's findings showed that using a procedure reduced the amount of volatility in the study's outcome variables. During the weaning process, the recommendations

offered a framework for making decisions and evaluating the patient. A common plan of action and aim for each patient was established, and standards were developed to keep the weaning process focused on patients rather than "doctors" or "nurses." This group of patients has particular requirements, and healthcare providers have a responsibility to evaluate and address those needs systematically. NICU personnel should explore a coordinated and collaborative approach to weaning in light of the findings of this study to enhance the consistency of weaning management and optimise patient outcomes. To be effective, guidelines must be customized to the needs of various patient populations. Short-to medium-term ventilated patients (up to eight days) must be distinguished from long-term ventilated patients (more than eight days).

Critical care nurses' roles and duties are expanding, and that means supportive education and training must also increase. To make NICU courses more readily available and/or accessible, further cooperation from clinical areas is required.

6.15 Implications for nursing research

There was just one NICU where this research was done, but it seemed to be reflective of the others (in relation to activity, admission criteria, staffing profiles). However, because this is one of the first and few studies to look at weaning in this area, more comprehensive research including many sites would be ideal.

Future weaning research should take into account the various patient demographics and analyse each one independently (e.g., short, medium, and long-term ventilation). In addition to evaluating different weaning methods, there is still a lack of conclusive information concerning the best ways to wean children and predictive indices in this age group. As a result, further study is required to determine the best ways to wean children who are on mechanical breathing.

Much previous research focused on predictive processes, modalities, and/or tactics aimed at specific staff groups (e.g., nurses, respiratory therapists, or doctors). Involving all members of the healthcare team in the weaning process will help every unit's most precious resource—its staff—performs better.

6.16 Recommendations

National recommendations for weaning baby patients from mechanical breathing should be created and distributed based on the findings of this study. Guidelines should be designed to meet the needs of certain patient groups, and they can then be altered to match local needs before being implemented and assessed in various locations.

Universities, nursing schools, and hospitals all need to help fund NICU patient care and staff development. Healthcare workers will be more interested in NICU courses if they are more readily available and easily accessible (via external or online modalities). There is a trade-off between the greater expense of providing this support and the possible improvement in outcomes and quality of care given in NICUs.

Weaning preterm new-borns from artificial ventilation requires more study. In general, SIMV was the preferred method of weaning patients from their SIMV use. More study comparing weaning methods in preterm babies' population is needed, since the available research and literature are equivocal at this time.

Abbreviation

AC: Assist Control

ALISI: Acute Lung Injury and Sepsis Investigators

BPD: Bronchopulmonary Dysplasia

CO2: Carbon dioxide

CPAP: Continuous Positive Airway Pressure

ELBW: Extreme Low Birth Weight

ETT: Endotracheal Tube

FiO2: Fraction of Inspired Oxygen

HFJV: High Frequency Jet Ventilation

HFOV: High Frequency Oscillatory Ventilation

HFV: High Frequency Ventilation

ICU: Intensive Care Unit

IMV: Intermittent Mandatory Ventilation

IPPV: Intermittent positive-pressure ventilation

IRB: Institutional Review Board

MmHg: Millimeter of mercury

MV: Mechanical Ventilation

MVT: Minute Ventilation Test

NAVA: Neurally Adjusted Ventilatory Assist

NICU: Neonatal Intensive Care Unit

PALISI: Pediatric Acute Lung Injury and Sepsis Investigators

PH: Power of Hydrogen

PS: Pressure Support

PSV: Pressure Support Ventilation

RDS: Respiratory Distress Syndrome

SBT: Spontaneous Breathing Trial

SIMV: Synchronized Intermittent Mandatory Ventilation

SpO2: Oxygen Saturation

VAP: Ventilator Associated Pneumonia

VLBW: very low birth weight

VCV: Volume-Controlled Ventilation

Definitions of term

Bronchopulmonary dysplasia (BPD) is a chronic lung disease most commonly seen in premature infants who required mechanical ventilation and oxygen therapy for acute respiratory distress" (Davidson & Berkelhamer, 2017).

Continuous positive airway pressure (**CPAP**) is a form of positive airway pressure ventilator, which applies mild air pressure on a continuous basis. It keeps the airways continuously open in people who are able to breathe spontaneously on their own, but need help keeping their airway unobstructed (Werman, et al., 2014).

Failure Extubation: is defined as inability to sustain spontaneous breathing after removal of the artificial airway; an endotracheal tube or tracheostomy tube; and need for re-intubation within a specified time period: within 24-72 h (Martinez, et al., 2003).

ET tube: An endotracheal tube is a flexible plastic tube that is placed through the mouth into the trachea (windpipe) to help a patient breathe. The endotracheal tube is then connected to a ventilator, which delivers oxygen to the lungs.

Extubation is the removal of an endotracheal tube (ETT), which is the last step in liberating a patient from the mechanical ventilator. To discuss the actual procedure of extubation, one also needs to understand how to assess readiness for weaning, and management before and after extubation (Boles, et al., 2007).

Extubation Readiness Test (ERT) is a formal trial of spontaneous breathing to evaluate readiness for discontinuation of the endotracheal tube and/or ventilatory support. This may be performed with variable pressure support assist but we propose spontaneous breathing be evaluated for 2 hours on CPAP ≤5 cmH2O or T-piece (ZEEP)

hours of extubation; and late extubation failure is defined as that which occurs from 24 to 48 hours of extubation (Martinez, et al., 2003).

Mechanical ventilation is a complex and highly specialized area of neonatology, made more complicated by the availability of many different modes, techniques and devices"(Sant'Anna & Keszler, 2012a), for this study is a life-saving intervention for critically ill newborn infants with respiratory failure admitted to a neonatal intensive care unit (NICU)"(Wielenga et al., 2016).

Protocols are a widely used tool to help implement evidence-based therapies and reduce unnecessary variations in practice“(Sant’Anna & Keszler, 2012a).

Sepsis is a complex condition characterized by the simultaneous activation of inflammation and coagulation in response to microbial insult. These events manifest as systemic inflammatory response syndrome or sepsis symptoms through the release of proinflammatory cytokines, procoagulants, and adhesion molecules from immune cells and/or damaged endothelium” (Polat, et al., 2017).

Spontaneous Breathing Test (SBT) is a subjective determination of whether the underlying disease process necessitating mechanical ventilation has improved sufficiently to allow the patient adequate gas exchange with spontaneous breathing.

Weaning is the transition from ventilatory support to completely spontaneous breathing, during which time the patient assumes the responsibility for effective gas exchange while positive pressure support is withdrawn. Note that spontaneous breathing is a prerequisite for weaning to begin and decreasing ventilator support is not the sole criterion of successful weaning (Sant’Anna & Keszler, 2012b).

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Appendices

Appendix 1 Data collection sheet

Data Collection Sheet

A- Demographic data:

1- Gestational age:
2- Chronological age:
3- Infant's weight:
4- Sex:
5- Mode of delivery:
6- Illness:
7- Reason for intubation:
8- Ventilation mode
9- Total duration of mechanical ventilation:
10- Total duration of mechanical ventilation per ventilation mode:

11- if the baby received surfactant at first hours (----------) ? Yes No

B- Maternal data:

1-If the mother takes steroids before delivery? Yes No

2-Did the mother have premature rupture of membrane (PROM)? Yes No

3. the Apgar score of the baby at 1 minute ……

4-the Apgar score of the baby at 5 minutes ……

C- Clinical variables during weaning:

1- weaning time and ventilator parameters:

Day (1):

Time	Ventilation Mode	F(IO) (2)	Rate	PEEP	PIP	MAP
7:30-8:30 (AM)						
8:30 – 9:30(AM)						
9:30- 10:30(Am)						
10:30- 11:30(Am)						
11:30- 12:30(Am)						
12:30- 1:30(PM)						
1:30-2:30(Pm)						
2:30-3:30(Pm)						
3:30-4:30(Pm)						
4:30-5:30(Pm)						
5:30-6:30(Pm)						
6:30-7:30(Pm)						
7:30-8:30(Pm)						
8:30-9:30(Pm)						
9:30- 10:30(Pm)						
10:30- 11:30(Pm)						
11:30- 12:30(Pm)						
12:30- 1:30(Am)						
1:30-2:30(Am)						
2:30_3:30(Am)						
3:30-4:30(Am)						
4:30-5:30(Am)						
5:30-6:30(Am)						
6:30-7:30(Am)						

--Blood gas changes:

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Day (2):

Time	Ventilation Mode	F(IO)(2)	Rate	PEEP	PIP	MAP
7:30-8:30 (AM)						
8:30 – 9:30(AM)						
9:30-10:30(Am)						
10:30-11:30(Am)						
11:30-12:30(Am)						
12:30-1:30(PM)						
1:30-2:30(Pm)						
2:30-3:30(Pm)						
3:30-4:30(Pm)						
4:30-5:30(Pm)						
5:30-6:30(Pm)						
6:30-7:30(Pm)						
7:30-8:30(Pm)						
8:30-9:30(Pm)						
9:30-10:30(Pm)						
10:30-11:30(Pm)						
11:30-12:30(Pm)						
12:30-1:30(Am)						
1:30-2:30(Am)						
2:30_3:30(Am)						
3:30-4:30(Am)						
4:30-5:30(Am)						
5:30-6:30(Am)						
6:30-7:30(Am)						

- -Blood gas changes:

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Day (3):

Time	Ventilation Mode	F(IO)(2)	Rate	PEEP	PIP	MAP
7:30-8:30 (AM)						
8:30 – 9:30(AM)						
9:30- 10:30(Am)						
10:30- 11:30(Am)						
11:30- 12:30(Am)						
12:30- 1:30(PM)						
1:30-2:30(Pm)						
2:30-3:30(Pm)						
3:30-4:30(Pm)						
4:30-5:30(Pm)						
5:30-6:30(Pm)						
6:30-7:30(Pm)						
7:30-8:30(Pm)						
8:30-9:30(Pm)						
9:30- 10:30(Pm)						
10:30- 11:30(Pm)						
11:30- 12:30(Pm)						
12:30- 1:30(Am)						
1:30-2:30(Am)						
2:30_3:30(Am)						
3:30-4:30(Am)						
4:30-5:30(Am)						
5:30-6:30(Am)						
6:30-7:30(Am)						

-Blood gas changes:

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Day (4):

Time	Ventilation Mode	F(IO)(2)	Rate	PEEP	PIP	MAP
7:30-8:30 (AM)						
8:30 – 9:30(AM)						
9:30- 10:30(Am)						
10:30- 11:30(Am)						
11:30- 12:30(Am)						
12:30- 1:30(PM)						
1:30-2:30(Pm)						
2:30-3:30(Pm)						
3:30-4:30(Pm)						
4:30-5:30(Pm)						
5:30-6:30(Pm)						
6:30-7:30(Pm)						
7:30-8:30(Pm)						
8:30-9:30(Pm)						
9:30- 10:30(Pm)						
10:30- 11:30(Pm)						
11:30- 12:30(Pm)						
12:30- 1:30(Am)						
1:30-2:30(Am)						
2:30_3:30(Am)						
3:30-4:30(Am)						
4:30-5:30(Am)						
5:30-6:30(Am)						
6:30-7:30(Am)						

-Blood gas changes:

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Day (5):

Time	Ventilation Mode	F(IO)(2)	Rate	PEEP	PIP	MAP
7:30-8:30 (AM)						
8:30 – 9:30(AM)						
9:30- 10:30(Am)						
10:30- 11:30(Am)						
11:30- 12:30(Am)						
12:30- 1:30(PM)						
1:30-2:30(Pm)						
2:30-3:30(Pm)						
3:30-4:30(Pm)						
4:30-5:30(Pm)						
5:30-6:30(Pm)						
6:30-7:30(Pm)						
7:30-8:30(Pm)						
8:30-9:30(Pm)						
9:30- 10:30(Pm)						
10:30- 11:30(Pm)						
11:30- 12:30(Pm)						
12:30- 1:30(Am)						
1:30-2:30(Am)						
2:30_3:30(Am)						
3:30-4:30(Am)						
4:30-5:30(Am)						
5:30-6:30(Am)						
6:30-7:30(Am)						

-Blood gas changes:

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Day (6):

Time	Ventilation Mode	F(IO)(2)	Rate	PEEP	PIP	MAP
7:30-8:30 (AM)						
8:30 – 9:30(AM)						
9:30- 10:30(Am)						
10:30- 11:30(Am)						
11:30- 12:30(Am)						
12:30- 1:30(PM)						
1:30-2:30(Pm)						
2:30-3:30(Pm)						
3:30-4:30(Pm)						
4:30-5:30(Pm)						
5:30-6:30(Pm)						
6:30-7:30(Pm)						
7:30-8:30(Pm)						
8:30-9:30(Pm)						
9:30- 10:30(Pm)						
10:30- 11:30(Pm)						
11:30- 12:30(Pm)						
12:30- 1:30(Am)						
1:30-2:30(Am)						
2:30_3:30(Am)						
3:30-4:30(Am)						
4:30-5:30(Am)						
5:30-6:30(Am)						
6:30-7:30(Am)						

-Blood gas changes:

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort (Respiratory Rate):

Day (7):

Time	Ventilation Mode	F(IO)(2)	Rate	PEEP	PIP	MAP
7:30-8:30 (AM)						
8:30 – 9:30(AM)						
9:30- 10:30(Am)						
10:30- 11:30(Am)						
11:30- 12:30(Am)						
12:30- 1:30(PM)						
1:30-2:30(Pm)						
2:30-3:30(Pm)						
3:30-4:30(Pm)						
4:30-5:30(Pm)						
5:30-6:30(Pm)						
6:30-7:30(Pm)						
7:30-8:30(Pm)						
8:30-9:30(Pm)						
9:30- 10:30(Pm)						
10:30- 11:30(Pm)						
11:30- 12:30(Pm)						
12:30- 1:30(Am)						
1:30-2:30(Am)						
2:30_3:30(Am)						
3:30-4:30(Am)						
4:30-5:30(Am)						
5:30-6:30(Am)						
6:30-7:30(Am)						

-Blood gas changes:

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Time:(_)

PH:

PCO2:

PO2:

Fio2

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

Vital Sign: time (_)

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

2- DID the baby receive caffeine before extubation? Yes No

3- Was the baby on sedation before extubation? Yes NO

D: ready to extubate:

1- Vital Sign:

Saturation:

Blood pressure:

Systole:

Diastole:

MAP:

Heart rate:

Temp:

Spontaneous breathing effort

(Respiratory Rate):

2- Blood Gas:

PH:

PCO2:

PO2:

Fio2

3- Ventilator parameters:

time on F(IO)(2) >0.30

PIP: <18

PEEP: 4-5

MAP: <8

Rate:<30/min

E_weaning out comes

1- Weaning duration till extubation

2-NICU length of stay (days):

3. Hospital length of stay (days):

4-Incidence of mechanical ventilation-correlated morbidity like:

4. 1. pulmonary interstitial emphysema

4. 2. bronchopulmonary dysplasia (BPD)

4. 3. ventilator-associated pneumonia (VAP).

5- Use of non-invasive ventilation:

5.1 Nasal continuous positive airway pressure following extubation (duration):

5.2 nasal intermittent positive pressure IPPV) following extubation (duration):

5.3 oxygen delivery following extubation (duration):

6- if there is a need for reintubation (extubation failure within 5 days)

7- Mortality Rate:

Appendix 2 (IRB approval)

An-Najah
National University
Health Faculty of medicine&
Sciences
IRB

جامعة النجاح
الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref :Mas July /2020/16

IRB Approval Letter

Study Title:

"Protocolized versus non-protocolized weaning for reducing the duration and complications of invasive mechanical ventilati."

Submitted by:
Despina Shaheen

Supervisor:
Aidah Alkaissi

Date Approved:
22nd July 2020

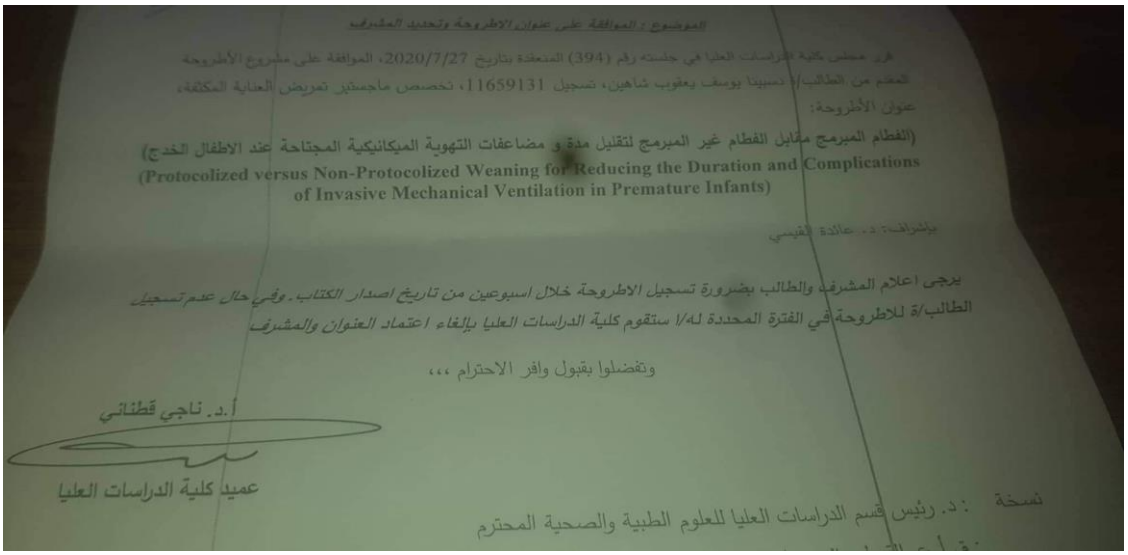
Your Study Title **"Protocolized versus non-protocolized weaning for reducing the duration and complications of invasive mechanical ventilati.."** was reviewed by An-Najah National University IRB committee and was approved on **22nd July 2020**

Hasan Fitian, MD

IRB Committee Chairman
An-Najah National University

IRB

Appendix 3 (Approval of the supervisor and the title)



الموضوع : الموافقة على عنوان الاطروحة وتحديد المشرف

قرر مجلس كلية الدراسات العليا في جلسته رقم (394) المنعقدة بتاريخ 2020/7/27، الموافقة على مشروع الأطروحة المقدم من الطالب/ة تسنيما يوسف يعقوب شاهين، تسجيل 11659131، تخصص ماجستير تمريض العناية المكثفة، عنوان الأطروحة:

(الفطام الميرمج مقابل الفطام غير الميرمج لتقليل مدة و مضاعفات التهوية الميكانيكية المجتاحة عند الاطفال الخدج)
(Protocolized versus Non-Protocolized Weaning for Reducing the Duration and Complications of Invasive Mechanical Ventilation in Premature Infants)

بإشراف: د. عائدة القيسي

يرجى اعلام المشرف والطالب بضرورة تسجيل الاطروحة خلال اسبوعين من تاريخ اصدار الكتاب. وفي حال عدم تسجيل الطالب/ة للاطروحة في الفترة المحددة له/ا ستقوم كلية الدراسات العليا بإلغاء اعتماد العنوان والمشرف

وتفضلوا بقبول وافر الاحترام ،،،

أ.د. ناجي قطناني

عميد كلية الدراسات العليا

نسخة : د. رئيس قسم الدراسات العليا للعلوم الطبية والصحية المحترم

جـامعـــة النجاح الوطنية
كليـــة الدراســـات العليـــا

الفطام المبرمج مقابل الفطام غير المبرمج لتقليل مدة ومضاعفات التهوية الميكانيكية المجتاحة عند الاطفال الخدج

إعداد
دسبينا يوسف يعقوب شاهين

إشراف
د. عائدة القيسي

قدمت هذه الرسالة استكمالاً لمتطلبات الحصول على درجة الماجستير في تمريض العناية المكثفة، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس–فلسطين.

2022

الفطام المبرمج مقابل الفطام غير المبرمج لتقليل مدة ومضاعفات التهوية الميكانيكية المجتاحة عند الاطفال الخدج

إعداد

دسبينا يوسف يعقوب شاهين

إشراف

د. عائدة القيسي

الملخص

الخلفية: بالنسبة لحديثي الولادة المصابين بأمراض خطيرة والذين يعانون من فشل تنفسي تم إدخالهم إلى وحدة العناية المركزة لحديثي الولادة، فإن استخدام عملية التنفس الصناعي تكون ضرورية لإنقاذ حياتهم. قد يكون من الصعب استخدام التنفس الصناعي للأطفال حديثي الولادة بسبب حجم الرئة الصغير، ومعدلات التنفس العالية، واستخدام أنابيب القصبة الهوائية غير المقيدة لذلك يجب ان يتم فصل الطفل عن جهاز التنفس الصناعي في أقرب وقت ممكن لتجنب هذه الصعوبات والاثار الجانبية

الأهداف: تتمثل أهداف الدراسة في مقارنة فصل الطفل عن جهاز التنفس الصناعي باستخدام الفطام المبرمج (باستخدام بروتوكول) مقابل الفطام الاعتيادي والمقارنة بينهم من حيث مدة الاستخدام، ووقت الفطام ، والمكوث في وحدة العناية المركزة لحديثي الولادة وطول الإقامة في المستشفى لحديثي الولادة. لمعرفة مدى فعاليته في مجموعات فرعية محددة ، مثل عمر الحمل ووزن الولادة. تهدف هذه الدراسة أيضًا إلى التحقق مما إذا كان الفطام المبرمج يمكن أن يقلل من مدة التنفس الميكانيكي دون زيادة مخاطر النتائج السلبية واستخلاص استنتاجات حول فائدة البروتوكول لممارسة الفطام في رعاية الأطفال حديثي الولادة.

منهجية البحث: دراسة شبه تجريبية أجريت على مرضى يخضعون لفطام مبرمج مقابل فطام غير مبرمج من جهاز التنفس الصناعي عند الاطفال الخدج في وحدة العناية المركزة لحديثي الولادة.

كانت المجموعة التجريبية (عدد = 30) طفلا يخضعون لبروتوكول فطام من جهاز التنفس الصناعي في عمر الحمل 26 أسبوعًا وما فوق. مقابل مجموعة التحكم (عدد = 30) تشمل الاطفال الذين كانوا يخضعون للتهوية الميكانيكية في عمر الحمل 26 أسبوعًا وما فوق في وحدة العناية المركزة لحديثي الولادة وتم استخدام الفطام غير المنظم كعناية عادية (بدون استخدام بروتوكول)، بين يوليو 2019 ويونيو 2020 في نفس المستشفى، مع نفس موظفي وحدة العناية المركزة.

النتائج: أظهرت النتائج أن متوسط مدة الفطام حتى نزع الأنبوب (أيام) في المجموعة التاريخية (المتوسط = 4.02) أعلى بكثير من متوسط فترة الفطام (المتوسط = 2.47)، ف = 0.000. كما أن متوسط مدة الفطام حتى نزع الأنبوب (بالساعات) في المجموعة التحكم (المتوسط = 88.73) أعلى بكثير من تلك في مجموعة البروتوكول (المتوسط = 55.77)، ف = 0.000.

أظهرت النتائج أن متوسط مدة الإقامة في العناية المركزة (أيام) في المجموعة التحكم (المتوسط = 30.53) أعلى بكثير من تلك الموجودة في مجموعة البروتوكول (المتوسط = 8.97)، ف= 0.000. أيضًا، متوسط مدة الإقامة في المستشفى (أيام) في المجموعة التحكم (المتوسط = 60.8) أعلى بكثير من تلك الموجودة في مجموعة البروتوكول (المتوسط = 35.97)، ف = 0.000.

الخلاصة: يقلل بروتوكول الفصل عن جهاز التنفس الصناعي من مدة التهوية الميكانيكية، ومدة الفطام حتى نزع الأنبوب، ووحدة العناية المركزة لحديثي الولادة ومدة الإقامة في المستشفى (أيام)، وخطر فشل الفطام وإعادة التنفس الصناعي. هناك دليل يدعم تفوق الفطام البروتوكول على الفطام العادي على مدة التهوية الميكانيكية الغازية عند الأطفال حديثي الولادة، وفقًا لنتائج هذه الدراسة.

الكلمات المفتاحية: وحدة العناية المركزة لحديثي الولادة؛ مولود جديد؛ التهوية الميكانيكية؛ توقف التنفس.