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TESI DI LAUREA

PENGUIN VERSUS CATHERTER FOR AIRWAY SUCTIONING AT BIRTH: A RANDOMIZED CONTROLLED TRIAL IN A LOW RESOURCE SETTING

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ABSTRACT

Background: evidence from literature showed that suctioning should be offered only to newborn infants who have obvious obstruction to spontaneous breathing or who require positive pressure ventilation. International guidelines recommend the use of a penguin suction device or a suction catheter in newborn infants needing suctioning at birth, but literature does not provide any information on clinical differences between the two procedures.

Objectives: this trial aims to compare two different methods of oropharyngeal suctioning (with penguin suction device or suction catheter) in newborn infants needing suctioning at birth. The primary outcome measure is oxygen saturation during the first 10 minutes of life.

Setting: the study was conducted at the St. Luke Catholic Hospital in Wolisso (Ethiopia), which is a level III hospital with around 3,600 deliveries per year. This is a referral, private, nonprofit hospital located in Wolisso town, which is the capital of the Southwest Shoa Zone in the Oromiya region.

Material and methods: this is a single center, prospective, randomized clinical trial comparing two different methods of oropharyngeal suctioning (with bulb syringe or suction catheter) in newborn infants needing suctioning at birth. 61 neonates, term and preterm, is enrolled in this study. Immediately after birth, all infants needing suctioning will be randomized to receive suctioning with bulb syringe or suction catheter. All resuscitative procedures will be performed following the Help Babies Breathe algorithm. An external observer, not involved in the care of the newborn, will be responsible of the positioning the probe of the pulse oximeter and the collection of the data.

Results: 61 participants were enrolled in the trial (31 in electrical arm and 30 manual arm). The oxygen saturation increases over time in both arms ($p < 0.0001$), with the same slope ($p = 0.7728$). The heart rate increases over time in both arms ($p < 0.0001$), with no different slope ($p = 0.9089$). Admission to special care unit is more frequent in electrical vs. manual arm (61% vs. 33%, $p = 0.0288$).

Conclusions: oxygen saturation and heart rate during the first ten minutes of life were the same when using a penguin suction device or a suction catheter. There were no differences between the two arms regarding the study secondary outcomes, except for the admission to the special care unit (NICU) which was significantly higher in the suction catheter group.

Trial Registration: the study has been registered in ClinicalTrials.gov with identifier: NCT05472155.

Chapter 1 – Introduction

1.1 Burden of Disease

According to the United Nations Inter-Agency Group for Child Mortality Estimation (UN IGME) 2021 Report, more than 5.0 million children under age 5 died in 2020, including 2.4 million newborns (0-28 days) (1). Many of these deaths are easily preventable with simple, cost-effective interventions, that address the needs of women and newborns across the continuum of care, with an emphasis on care around the time of birth (2).

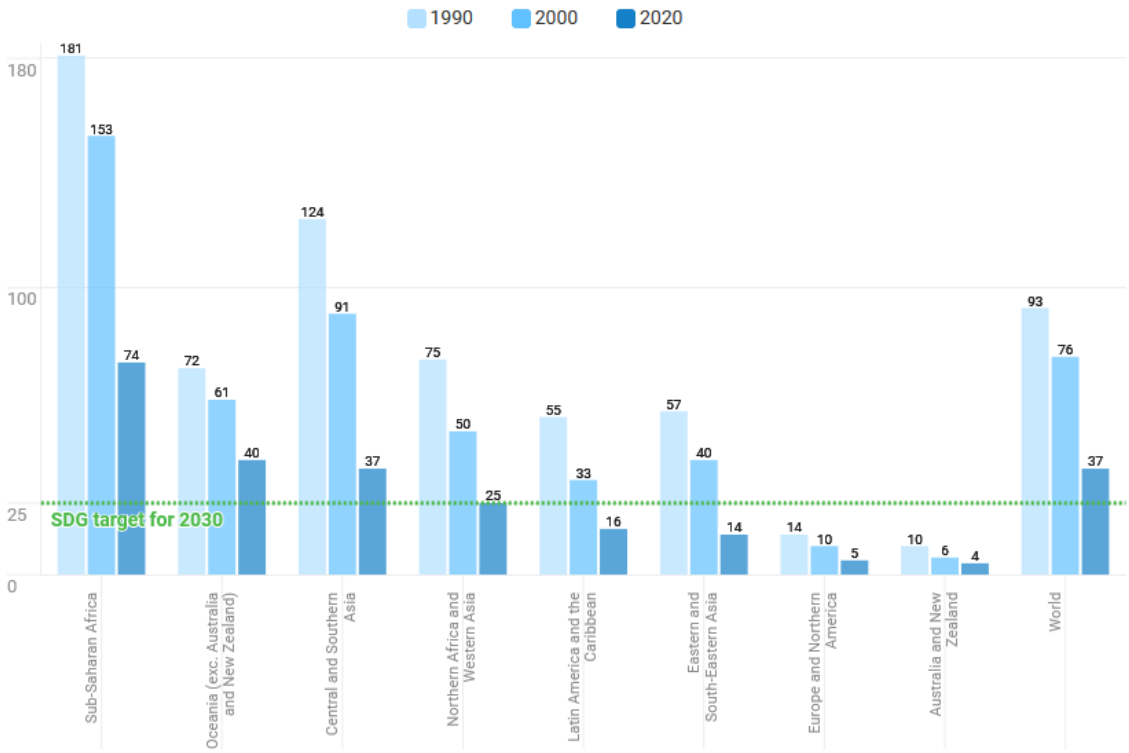


Figure 1 - Under-five mortality rate (deaths per 1,000 live births) by Sustainable Development Goals (SDG) region,1990, 2000 and 2020 (UN IGME: : Levels and trends in child mortality, Report 2021)

Geographic and economic disparities heighten the risk of death for children (Figure 2). Well over half of under-five deaths – 54 % – take place in sub-Saharan Africa (2.7 million), with another 25 % occurring in Southern Asia (1.2 million).

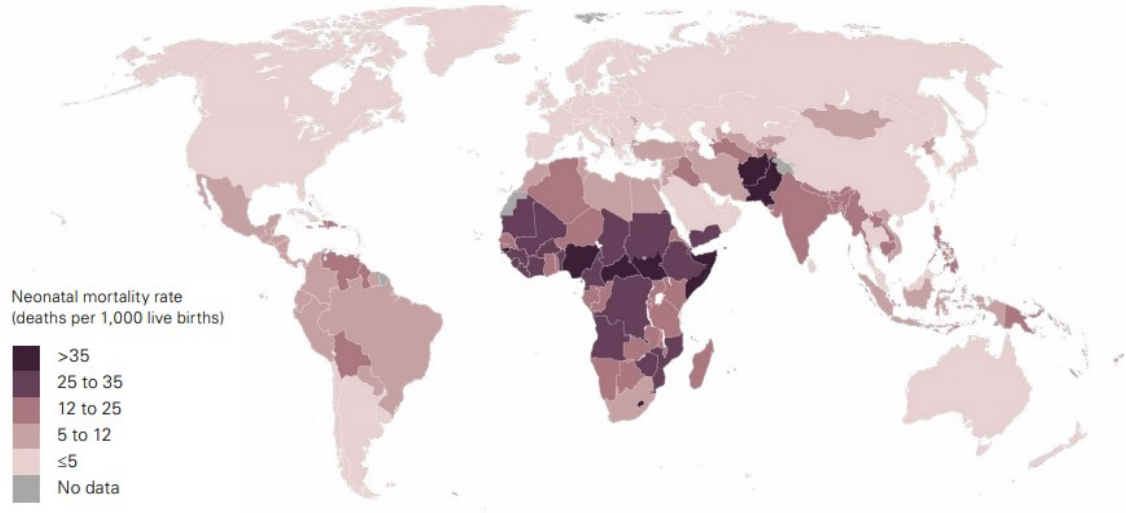


Figure 2 – Neonatal mortality rate (deaths per 1000 life births) by country in 2020 (UN IGME: Levels and trends in child mortality, Report 2021)

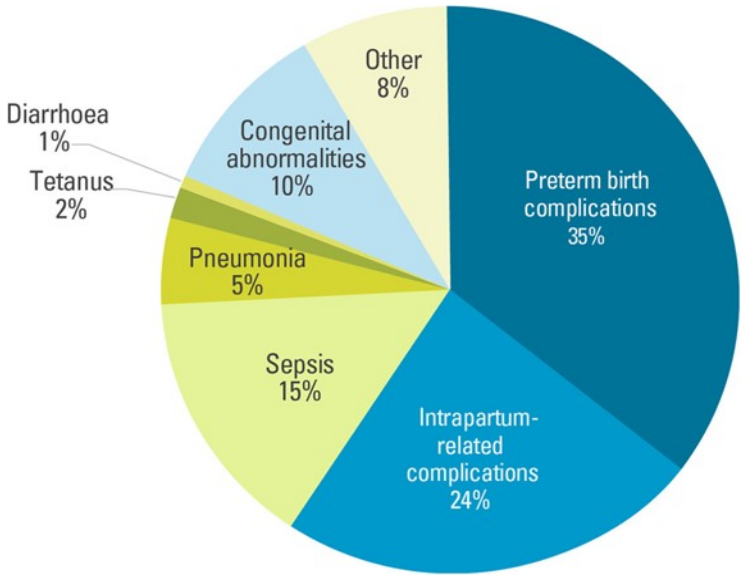


Figure 3 – Global distribution of neonatal deaths, by cause (UN IGME: Levels and trends in child mortality, Report 2021)

Globally, almost 3 in 4 neonatal deaths were caused by preterm birth complications (35%), complications during labour and delivery (intrapartum) (24%), and sepsis (15%) (2). Up to 24% of deaths depends on intrapartum-related complications because the transition from intrauterine to extrauterine life at birth involves many critical interdependent events that culminate in the conversion

from placental to pulmonary gas exchange. Most infants usually adapt well to extrauterine life but some require help with support or resuscitation. Data in the literature actually indicate that up to 85% of babies born at term start breathing within 10 to 30 seconds (3,4). A further 10% initiate breathing once accomplished some support actions: drying, stimulation, suctioning and airway opening maneuvers (5). However, a small percentage, around 5% of newborns, receive positive pressure ventilation to breathe autonomously (5,6). Only 0.4% to 2% of newborns needs to be intubated and less than 0.3% receives chest compressions. Finally 0.05 % of babies receives epinephrine (7,8). Neonatal resuscitation can be very critical especially in low-resource countries, where the lack of equipment and training of birth attendants cannot ensure safety and well-being of newborn infants. Implementation strategies to improve the practices of unskilled birth attendants can lead to better outcomes in preventing asphyxia (9).

1.2 Physiology of Birth

During the fetal life the respiratory function is performed by the placenta instead of the fetal lungs. The fetus lives in a relatively hypoxemic environment that allows the spread of the oxygen from the maternal blood through the free-following placental space. The oxygen is transferred into chorionic villi which are full of capillaries that merge forming the umbilical vein. Umbilical venous blood has an oxygen saturation of 70-80 %, it passes across the liver and enters into the ductus venosus. This well oxygenated blood is directed from the right atrium, across the foramen ovale, to the left side of the heart and after it goes to the carotids and coronary arteries.

The poorly oxygenated blood from inferior vena cava and superior vena cava also arrives into the right atrium, but it is directed preferably into right ventricle. A small portion of this blood goes to the lungs, instead most of it is shunted across ductus arteriosus to the descending aorta with an oxygen saturation of 60 % (10). Only a small amount of poorly oxygenated blood flows in to the lungs because the pulmonary vessels are tightly constricted. In fact, the fetal lungs are not functional for gas exchange because they are filled of alveolar fluids. During the development of alveolar ducts, distal pulmonary epithelial cells actively secrete a chloride-rich fluid into the bronchial tree. The hyper-expansion of fetal lungs, due to the accumulation of fluid, increases intrapulmonary vascular pressure. The

hypoxemia suppresses the production of nitric oxide (NO) and prostaglandin I_2 (PGI_2) and, together with high intrapulmonary pressure, contributes to increased pulmonary vascular resistance.

At birth, transition from fluid-filled environment of the womb to the air-filled environment of the birthing room, needs some physiological adaptations. Lung adaptation requires the coordinated clearance of fetal lung fluid, that plays a key role, surfactant secretion and the onset of consistent breathing (11).

In spontaneous labour, mechanical compression of the thorax during passage through the birth channel is responsible for ejection of a part of the pulmonary fluid. Furthermore, before and after birth, the increase of cortisol and thyroid hormone levels activates the basal Na^+, K^+ and ATPase of type II cells on the airway epithelium. Sodium is pumped into the interstitium with water and other electrolytes following passively, thus removing fluid from the airways. The increased oxygenation after birth helps to maintain the expression of sodium-mediated channels (11).

The respiratory activity plays the final and most important role in airway liquid clearance at birth. The inspiration, by expanding the chest wall, reduces intrapleural and interstitial tissue pressures, and produces a gradient between the interstitial tissue and airway lumen and also between the upper and lower airways.

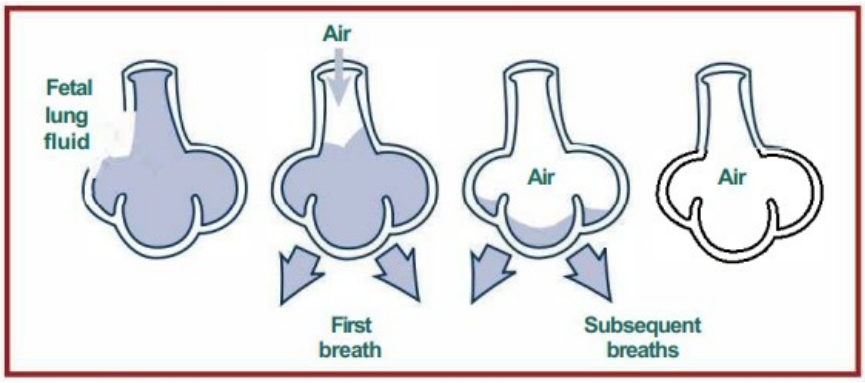


Figure 4 – The movement of fluid in the airways, from the proximal into the distal, until interstitial tissue space

As a result, the liquid is driven from the proximal into the distal airway from where it is cleared across the distal airway wall into the surrounding interstitial tissue space (12). From here fluids can be removed by the pulmonary microcirculation and lymphatic vessels.

Thankful to the increase in oxygen of air sacks, due to the ventilation of the lungs, the levels of NO and PGI_2 increase with a rapid fall in pulmonary vessel resistance. The blood from the right ventricle flows through pulmonary bloodstream, until the capillaries of the air sacks. Afterwards the oxygenated blood flows to the left side of the heart and then to the systemic bloodstream. The higher oxygen levels are the trigger of the ductus arteriosus' functional closure. After that the umbilical cord is clamped, the low-resistance vascular bed of the placenta is disconnected, leading to an increase in the systemic vascular resistance. The pressure of the left atrium becomes higher than that of the right atrium, thus the foramen ovale starts to closure. As pulmonary resistance decreases, systemic resistance increases and all the right-left shunts start to close, the circulation changes from 'parallel' to 'series, with an increase in the left ventricular output. It is established the newborn circulation (10).

At birth an effective ventilation of the lungs is the critical central event that is responsible for pulmonary gas exchange and also for initiating the cardiovascular changes, that enable the infant transition to independent life (12). For all these reasons the focus and the most important step of Neonatal Resuscitation is the effective ventilation of the baby's lungs.

1.3 Risk Factors

Approximately 10% of newborns requires assistance to breath after birth. Before every delivery, a standardized risk factors assessment toll should be used to evaluate perinatal risk and, in case, prepare the environment and personnel competent in the delivery room. Both antepartum and intrapartum risk factors have been identified, which can help to predict the need for advanced life support prior to delivery (Table 1). The most important antepartum factors are substantially a low gestational age (less than 37 weeks gestation), oligo/polyhydramnios, multiple pregnancies and the maternal factors like infections and hypertension. Each of these approximately double the risk of need positive pressure ventilation (PPV) after birth. Some significant intrapartum risk factors include meconium-stained amniotic fluid, breech presentation, emergency C-section and non-reassuring heart rate. On the other side elective C-section is protective against the need for PPV (13,14).

Antepartum Factors	
Fetal	**Maternal**
Intrauterine growth restriction (IUGR) < 37 weeks gestation Multiple pregnancies Serious congenital abnormalities Oligo and polyhydramnios	Infection Gestational diabetes Pregnancy-induced hypertension Pre-eclampsia High Body Mass Index Short stature Preterm lack of antenatal steroids
Intrapartum factors	
Evidence of fetal compromise (non-reassuring CTG etc.) Meconium-stained amniotic fluid (MSAF) Delivering vaginally by breech Forceps or vacuum delivery Significant bleeding C-section before 39 weeks Emergency C-section General anesthesia	

Table 1 – Common factors associated with an increased risk of need for stabilization or resuscitation at birth (ECR Guidelines 2021)

When anticipating a high-risk birth, a skilled and trained team is mobilized and present during the labor in order to perform in a proper way all the resuscitative procedures. Moreover, a standardized checklist is used to ensure the presence of the supplies and the equipment for a complete resuscitation in the delivery room. The equipment aimed to monitor the condition of the infant (like pulse-oximetry and stethoscope) and to support ventilation (like face mask, self-inflating bag, flow-inflating bag or T-piece resuscitator) should be available or should be prepared. At last it is important that resuscitation takes place in a warm and draught-free area with a flat surface and a radiant heater (15).

All these actions allow to reduce morbility and mortality at birth. In the absence of risk stratification up to half of babies requiring PPV may not be identified and the resuscitation may be delayed with an increase in the risk of mortality (5,6).

1.4 Neonatal Resuscitation Algorithms

Different neonatal resuscitation algorithms show how to make a proper initial assessment and all the sequence of life-saving actions for the newborn infants. The main three algorithms are:

- American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care – 2020;
- European Resuscitation Council Guidelines (ERC) – 2021;
- Helping Babies Breathe 2nd edition algorithm - 2016.

The AHA and ERC Guidelines are used in the high-resource settings and provide similar assessments and steps for neonatal resuscitation.

In the American Heart Association Guidelines the initial assessment requires the evaluation of gestational age (term/preterm), breathing or crying (present/apnea or gasping), and tone (good/floppy). Term babies that cry or breathe and have a good tone should be managed skin-to-skin with their mothers (16).

European Resuscitation Council Guidelines suggest to evaluate breathing or crying (adequate/inadequate/absent), heart rate (fast ≥ 100 bpm/slow = 60-100 bpm/very slow < 60 bpm) and tone (good/floppy). If the baby breathes or cries, has a fast heart rate and is not floppy should go to the mother (15).

In general if one of these first assessments is not good, the umbilical cord should be clamped immediately, the baby should be transferred under the radiant heater and the first steps of resuscitation should be started without delay (15,16). First, it is important to keep the baby warm, do tactile stimulation and oronasopharyngeal suction. If the baby still does not breathe, it necessary to start ventilation with PPV, and after it is possible to consider other measures of resuscitation like intubation, CPAP, chest compressions or drugs.

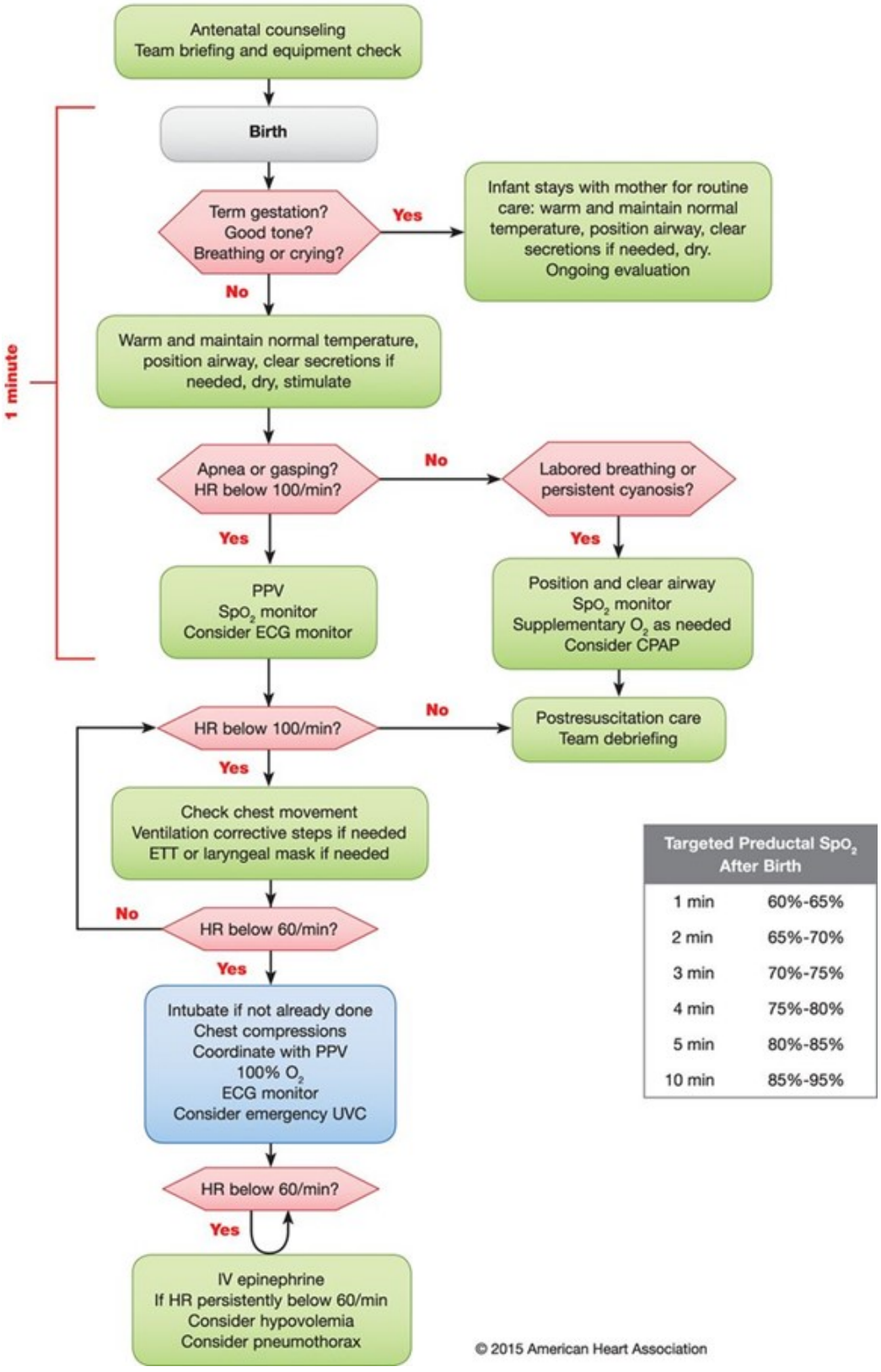


Figure 5 - Neonatal Resuscitation Algorithm according to American Heart Association Guidelines (2020)

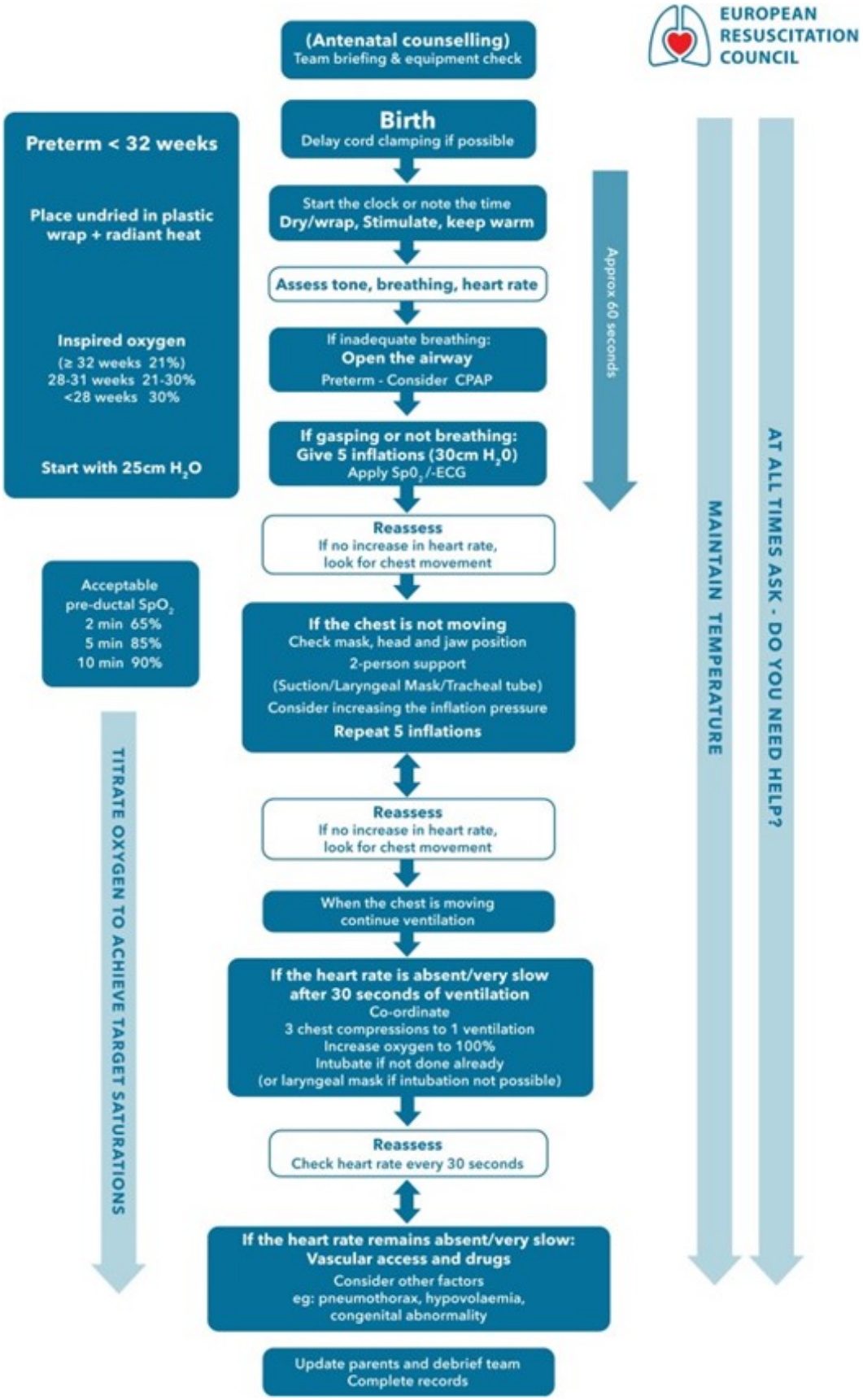


Figure 6 - Neonatal Resuscitation Algorithm according to European Resuscitation Guidelines (2021)

On the other side, the Helping Babies Breathe (HBB) was founded in 2010 with the aim of prevent and manage newborn asphyxia in low-resource settings. Between June 2010 and December 2014 HBB was introduced in 77 countries. Program reports from several countries indicate a high rate of successful resuscitation (79%-89%). 7 countries including Ethiopia have begun to implement HBB in over 40% of health facilities (17,18).

The first step of HBB algorithm is preparing a warm well-lighted and clean area for delivery and checking the equipment, before birth. The initial assessment is simplified than the AHA and ERC guidelines, based on the evaluation of crying over the mother abdomen after birth. If the baby is crying means that he is breathing well so he can go to the mother side after the cord clamping. If the baby is not crying, gasping or not breathing at all, he needs immediate help to breathe. The umbilical cord should be cut quickly, the airway should be cleared to remove secretions and the baby should be stimulated. If he is still not breathing, the ventilation should be started with a bag and a face-mask. The main difference is that the HBB, unlike the other guidelines for high-resource settings, does not include intubation, chest compressions or drugs on the following steps (19–21). However, in some hospitals adopting HBB protocol, for example, Saint Luke Catholic Hospital in Ethiopia, after ventilation, the chest compressions are done and the epinephrine is available for neonatal resuscitation.

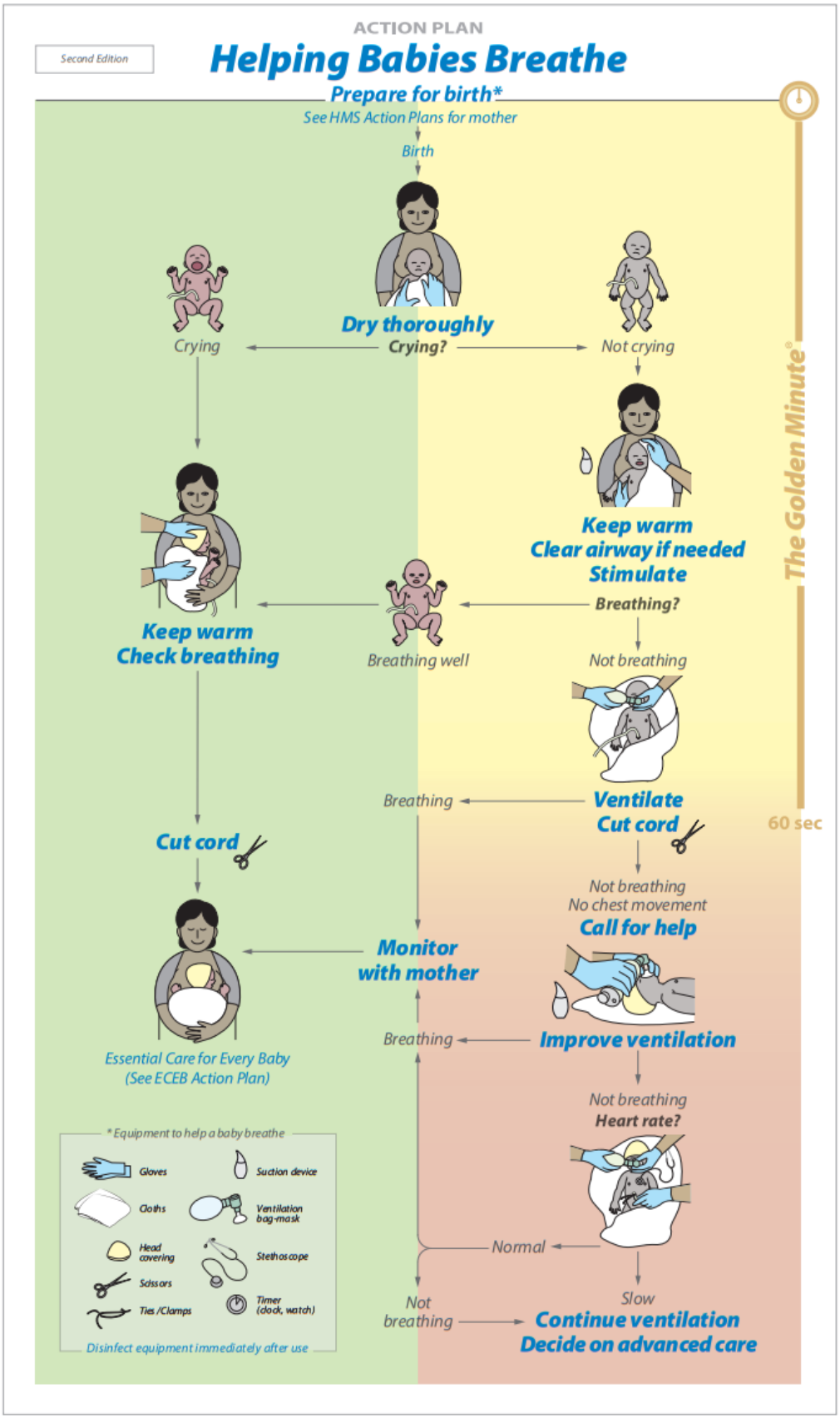


Figure 7 - Helping Babies Breathe Algorithm 2nd Edition

1.4.1 Initial Assessments

For every delivery it is essential to make a rapid assessment immediately after birth in order to establish if the newborn needs support and resuscitation maneuvers. When the transition to extrauterine life is altered or impair, an effective neonatal resuscitation can reduce the risk of mortality and morbidity. According to ERC Guidelines, evaluation of tone, respiratory rate and heart rate may help to identify infants likely to need resuscitation immediately after birth (15).

- Tone: can be good or absent, in this case a floppy infant needs ventilatory support. It is possible to evaluate also the color of the skin but it is a poor mean to judging oxygenation. Moreover, the healthy infants are cyanosed at birth and peripheral cyanosis is common and does not indicate hypoxia. Only a persistent pallor despite ventilation may be significant (22).
- Breathing (or crying): it is important to note the rate, depth and symmetry to establish if the breathing is adequate, inadequate (such gasping or grunting) or absent. Not crying may be due to apnea or to inadequate breathing, both needing support (23).
- Heart rate: is the most sensitive indicator of a successful response to interventions and guide the following steps of neonatal resuscitation (24). It can be fast and satisfactory (≥ 100 bpm), slow or intermediate (60-100 bpm), very slow or critical (< 60 bpm). The assessment of heart rate can be done by stethoscope, a saturation monitor or electrocardiogram (25).

When the baby has a good tone, vigorous breathing or crying and fast heart rate he does not require support. It is possible to delay cord clamping, cover the baby and consider skin-to-skin with the mother.

If the tone is reduced and the baby breathes inadequately with a slow heart rate, delaying the cord clamping should be considered only if it is possible to perform adequate support. In this case it is necessary to dry, stimulate, wrap the baby in a towel, clean the airway and start the ventilation without delay. While ventilating the newborn, changes in heart rate and breathing should be assessed continuously. If there is no improvement, ventilation should be continued and some other helps may be needed.

If the baby is floppy and pale, the breathing is inadequate and heart rate is very slow or undetectable, the cord should be immediately clamped, and the baby should be transferred to the resuscitation platform. Airway should be maintained for lung inflation and ventilation. Assessing continuously heart rate and breathing can help establishing if the ventilation is effective. If it is not, newborn life support should be continued with other more invasive actions, as for example intubation, chest compressions or epinephrine (15).

1.4.2 Initial Steps

Before every birth the personnel should ensure that the delivery room is warm at 23-25° C for term infants and > 25° C for infants < 28 weeks gestation (26). The normal body temperature of newborn babies is between 36.5 and 37.5° C. Hypothermia (less than 36° C) after birth is common worldwide, mostly in very preterm (less than 33 weeks) and very-low-birth-weight babies (less than 1500 g), and it is associated with increased peri-natal mortality and morbility (27,28). It should be prevented with the checking of the baby's body temperature and with a warm environment. Even if the baby does not need support or resuscitation, it is essential to dry him and cover the head and the body (not the face) with some warm towels to prevent heat loss. After he can go to the mother for skin-to-skin contact. For preterm and low-birth weight babies or babies requiring resuscitation, warming adjuncts should be considered, for example: radiant warmers, plastic wraps or bags (like a clean food-grade plastic bag in low-resource settings), hats, blankets and warmed humified inspired gas (29,30). It is important to remember that also hyperthermia (greater than 38 °C) is associated with increased risk of adverse outcomes (28).

During uncomplicated births, it may be reasonable to delay cord clamping longer than 30 seconds (until 1-3 minutes) because it is associated with higher hematocrit after birth, better iron levels in infancy and lower need for transfusion in preterm infants (31,32). Umbilical cord clamping has a major impact on infant's cardiovascular system if it takes place after onset of spontaneous respiration. Thankful to the ventilation of the lungs, pulmonary blood flow increases and then pulmonary venous return can immediately take over the supply of left ventricular preload upon cord clamping. As a result, there is no intervening period of reduced

preload and cardiac output and the large swings in arterial pressures and flows are reduced leading to a more stable circulatory transition (33,34).

The first assessments (tone, breathing, heart rate) are very important to decide if a baby needs initial steps of support like tactile stimulation and oronasopharyngeal suction or if he can go to the mother side. When one of the first assessments is not good, the cord should be immediately clamped, and the baby should be transferred to the resuscitation platform, under the radiant warmer. While drying the baby, it is possible to gently stimulate him by rubbing the soles of the feet or the back of the chest. Repetitive stimulation improves breathing effort and oxygen saturation (35).

After, the newborn infant has to be placed on his back with the head supported in a neutral position: the face must be horizontal, neither flexed or extended. This *sniffing position* helps to open airway and, if the baby needs ventilation, ensures to achieve an effective aeration of the lungs.

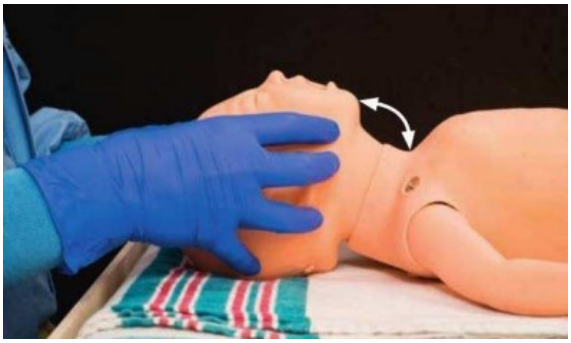


Figure 8 – Sniffing position (Textbook of Neonatal Resuscitation, 8th edition)

Oronasopharyngeal suction (ONPS) may help pulmonary fluid expulsion from the trachea, facilitate the entrance of air, prevent aspiration of mucus and blood. But it has possible harmful effects like vagal-induced bradycardia or apnea, irritation to mucus membranes and increased risk for iatrogenic infection (36). For all these reasons the suction may be considered only if there are secretions, an airway obstruction due to mucus, vernix, blood clots, meconium or if PPV is required and the airway appears obstructed.

The ONPS can be managed with a sterile soft rubber bulb syringe or with a silicon penguin suction device (manual suction), or with a sterile polyethene electric catheter (electrical suction). The bulb syringe and the penguin generate less suction pressure and are not inserted as deeply as the second, on the other side the second one could induce vagal bradycardia or apnea (37). But in the literature there is no evidence about the superiority of bulb syringe, penguin suction device or electric catheter, so they are considered equivalents. After the head is delivered it is possible to suction first the mouth and then the nares. It is really important

that mouth is suctioned first because stimulation of nares can cause reflex inspiration and possible inhalation of oropharyngeal fluids (37). Drying, stimulating, positioning and suctioning are the first steps of neonatal resuscitation, and they should be done during the first 30 seconds of life. Newborns who do not breathe within the first 60 seconds after birth or are persistently bradycardic, despite appropriate initial steps may receive PPV.

1.4.3 PPV and CPAP

After initial assessments at birth, if the baby is still apneic, gasping, not breathing or with a heart rate less than 100 bpm it is important to start PPV as soon as possible, ideally within 60 seconds of birth. For every 30 seconds delay in starting ventilation after birth there is an increase about 16% in morbility and mortality (6). To provide PPV is necessary to apply an appropriately fitting face-mask and start with five initial breaths with inflation pressures maintained for up to 2-3 seconds. This may help lung expansion (38–40).

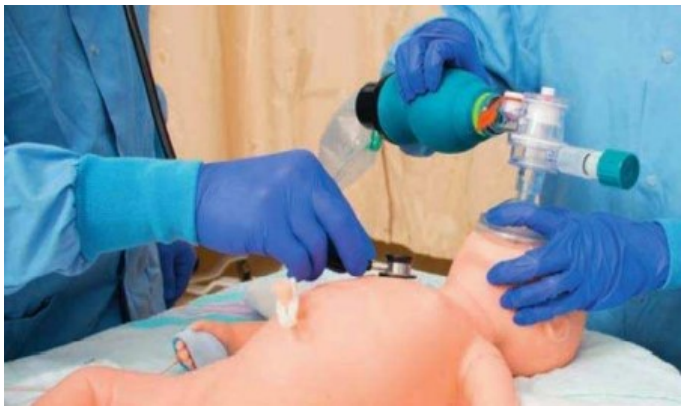


Figure 9 – Mask ventilation with self-inflating bag (Textbook of Neonatal Resuscitation, 8th edition)

To reduce mask leak a two-person approach to mask ventilation is used and a finger is applied around the infant's chin and hold firmly during the recording (41). For term infant is provided an initial inflation pressure of 30 cmH_2O commencing with air, instead for preterm infant (≤ 32 weeks) is provided a pressure of 25 cm H_2O using 21-30% inspired oxygen (42).

Observational studies on breathing newborn infants suggest that the aim of PPV is the respiratory rate between 30 and 40 breath per minute using an inspiratory time of 0.3-0.4 seconds (43,44).

Adequate ventilation is confirmed by a rapid improvement (in 30 seconds) in heart rate or a stable heart rate if initially high (24). It is also important to check for chest wall expansions, if they are visible indicate that there is no obstruction of the airway and the inflation pressure is sufficient to aerate the lungs (45).

If there is a heart rate response it is necessary to continue uninterrupted ventilation until the infant begins to breath adequately and the heart rate is above 100 beats per minutes. On the other side, failure of the heart rate response is most likely secondary to inadequate airway control or inadequate ventilation, so it is important to consider the ventilation corrective steps (MR. SOPA): face mask size and placement, head and airway position, suction of the mouth and the nose, opening of the mouth, inflation pressure (may need to be higher). After checking all these features, it is possible to consider via tracheal intubation or insertion of a laryngeal mask.

There are three different devices which can be used to assisted ventilation: self-inflating bag (SIB), flow-inflating bag (FIB) or T-piece resuscitator (TPR) (25). In the low resource setting it is usually employed the self-inflating balloon.

Figure 10 – Self inflating bag (left), flow-inflating bag (middle), T-piece resuscitator (rigth)

For spontaneously breathing preterm newborn infants with respiratory distress requiring respiratory support, it is suggested that Continuous Positive Airway Pressure (CPAP) should be used initially rather than intubation and PPV. It may reduce the risk of death and bronchopulmonary dysplasia (3). Instead in term infants caution is prompted in the use of CPAP because it may be associated with an increase incidence of pneumothorax. This different outcome may, due to some differences between the physiology of term and preterm infants, include higher surfactant load at the delivery, lower surface tension and higher compliance (46). Previous studies suggest to apply a Positive End Expiratory Pressure (PEEP) of approximately 5-6 cmH_2O immediately after birth for premature newborn infants

receiving PPV. That may improve lung aeration, functional residual capacity, compliance and gas exchange aim to prevent lung collapse at the end of expiration (47). TPR allows to provide either CPAP or PPV with PEEP, especially in the preterm infant (25).

1.4.4 Oxygen

During resuscitation in term and late preterm newborns (≥ 35 weeks of gestation) receiving respiratory support at birth, it is reasonable to start with room air (21% oxygen). It is associated with statistically significant benefit in short-term mortality compared with 100% oxygen (48). On the other side in preterm newborns (≤ 35 weeks of gestation) resuscitation should be initiated in a low inspired oxygen concentration based on gestational age: 21% of oxygen in preterm ≥ 32 weeks, 21 – 30% in 28 – 31 weeks, 30 % in < 28 weeks (49). Oxygen saturation of the newborn should be monitored with pulse-oximetry and should be titrated as necessary every 30 seconds. The supplemental oxygen may be provided to prevent harm from inadequate oxygen supply to peripheral tissues (hypoxemia), like hypoxic-ischemic encephalopathy or necrotizing enterocolitis (50). However, high exposure to oxygen (hyperoxia) may cause tissue injury through the formation of reactive oxygen intermediates and peroxidation of membrane lipids. Premature infants, who have severely reduced antioxidant defences, are particularly sensitive to the toxic effects of oxygen, for example many common morbidities such as retinopathy of prematurity, bronchopulmonary dysplasia and intraventricular hemorrhage (51). For these reasons and for an excess of mortality, 100% oxygen should not be used (48).

1.4.5 Chest Compressions

If the heart rate remains at less than 60 beats per minute or absent despite adequate ventilation for at least 30 seconds, initiating chest compressions is reasonable. It is important to remember that circulatory support with chest compressions is effective only when the lungs have been successfully inflated and oxygenated blood can be delivered to the heart (16). Ventilation should be optimized through endotracheal intubation if it is possible, because the face-mask ventilation can be compromised during synchronised chest compressions (52). According to expert opinion it may be reasonable to increase inspired oxygen to

100% during chest compressions; but once return of spontaneous circulation (ROSC) is achieved, the supplemental oxygen may be decreased to air to reduce risks associated with hyperoxia (53).

The optimal compression to ventilation ratio is 3:1 (3 compressions followed by one inflation) aiming to achieve a total of approximately 90 compressions and 30 ventilations per minute (54). The sternum is compressed to a depth of approximately one-third of the anterior-posterior diameter of the chest, allowing the chest wall to return to its relaxed position between compressions. The most effective method for providing chest compression is the two-thumb-encircling hands technique, with the hands encircle the chest and support the back, while two thumbs depress the lower third of the sternum. It is superior than two-fingers technique to improve blood pressure and coronary and cerebral perfusion, also it is better to achieve greater depth with less fatigue and less variability of each compression (55). Chest compressions may be discontinued when the heart rate is faster than 60 beats per minute, so it is recommended to check heart rate every 30 seconds using ECG.

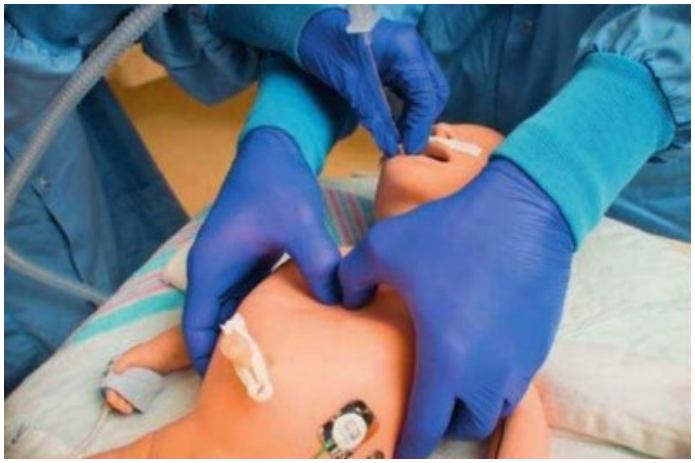


Figure 11 – Two-thumb-encircling hands technique (Textbook of Neonatal Resuscitation, 8th edition)

1.4.6 Drugs

Drugs are rarely required during newborn resuscitation and the evidence for their efficacy is limited. However, when the heart rate remains less than 60 beats per minute, despite effective ventilation and chest compressions, it is reasonable to consider use of drugs. Umbilical vein catheterisation (UVC) is suggested as the primary method of vascular access to drugs administration. If UVC is not available, the intraosseous (IO) access is a reasonable alternative (56).

- Epinephrine (adrenaline): with an initial dose of 0,1 – 0,3 mL/kg given intravenously, is the drug of choice during newborn resuscitation. It allows to increase the heart rate above 60 bpm. If the heart rate remains less than 60 bpm further doses every 3 – 5 minutes are suggested (57).

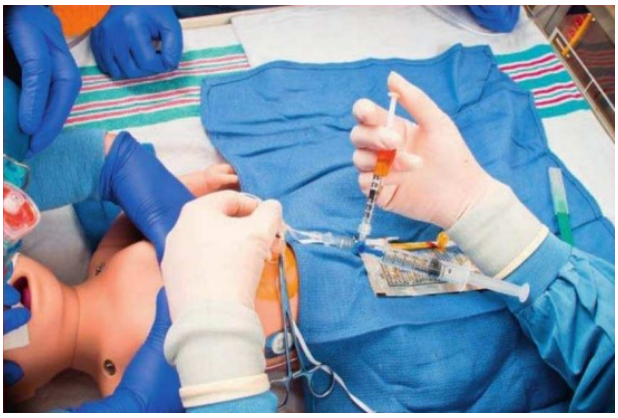


Figure 12 – Drug infusion in Umbilical Vein during Neonatal Resuscitation (Textbook of Neonatal Resuscitation, 8th edition)

- Glucose: in protracted resuscitation endogenous glycogen stores are rapidly depleted due to prolonged hypoxia, and this leads to blood glucose decrease. So it is reasonable to give a bolus of glucose (250 mg/kg) to prevent brain injury related to hypoglycaemia (58).
- Volume replacement: if the newborn infant has a blood loss or a hypovolemic shock early volume replacement, with crystalloid or red cells, is indicated.
- Sodium bicarbonate: may be helpful in prolonged unresponsive resuscitation to reverse intracardiac acidosis, but with no strong evidence in literature (59).
- Naloxone: can be reserved for infants whose cardiac output has been restored but who remain apneic despite resuscitation and where the mother has received opioid analgesia, with no strong evidence (60).

1.4.7 In the absence of adequate response

After 20 minutes of no response, with no heart rate and all the steps of resuscitation performed, the parents should be consulted in order to decide whether continue to resuscitate or to discontinue life support (61).

In situation where mortality is highly predictable, it is reasonable to withdraw resuscitation. Discontinuation of life support is considered to be ethical if prolonged resuscitation would no longer be in the best interests of the neonate (62,63).

In some other cases, after all the steps of resuscitation have been completed and if the clinical condition of the baby allows it, it is possible to consider other advanced care options as for example therapeutic hypothermia, if available. Palliative and supportive care plan should be always developed and ready throughout the process of neonatal resuscitation.

Chapter 2 - Oropharyngeal Suctioning

Suctioning is one of the previous steps of the neonatal resuscitation, but the guidelines do not recommended it as a routine in the normal newborn infants (16). Oronasopharyngeal suction (ONPS) may help pulmonary fluid expulsion from the trachea, may facilitate the entrance of air, may prevent aspiration of mucus and blood, and may provide tactile stimulation to assist the initiation of respiration. But it has possible harmful effects like vagal-induced bradycardia or apnea, irritation to mucus membranes and increased risk for iatrogenic infection (36). Multiple or prolonged suctioning can also delay initiation of resuscitation measures in a compromised infant at birth (37).

Previous studies have reported that the routine use of ONPS does not show any benefit in the oxygenation of normal vigorous newborn infants delivered vaginally or by cesarian section. Newborns receiving suction showed a statistically significant slightly lower SaO_2 value and a higher heart rate in the first minutes of life. They also take more time to reach the of $SaO_2 \geq 92\%$ (36,64,65).

For all these reasons the suction may be considered only if there are secretions, an airway obstruction due to mucus, vernix, blood clots, meconium, or if PPV is required and the airway appear obstructed. The obstruction has to be confirmed through a rapid inspection of the pharynx after failure to achieve aeration (15). Although, ONPS can be beneficial in the presence of meconium-stained which causes an obstruction of the airway, but it does not prevent meconium aspiration syndrome (66).

The ONPS can be managed with a sterile soft rubber bulb syringe or with a silicon penguin suction device (manual suction), or with a sterile polyethene electric catheter (electrical suction). The bulb syringe and the penguin device generate less suction pressure and are not inserted as deeply as the second, on the other side the electric catheter could induce vagal bradycardia or apnea (37). But in the literature there is no evidence about the superiority of manual suctioning, with bulb syringe and penguin device, or electrical suctioning, with electric catheter, so they are considered equivalents. Also wiping the mouth and the nose with a towel has equal efficacy to suction with regards to the respiratory rate and various other clinical outcomes at birth (67). After the head is delivered it is possible to suction first the mouth and then the nares. It is really important that mouth is suctioned

first because stimulation of nares can cause a reflex inspiration and a possible inhalation of oropharyngeal fluids (37).

Figure 13 – Bulb syringe (on the left) and Penguin suction device (on the right) for manual suction in the newborn infants

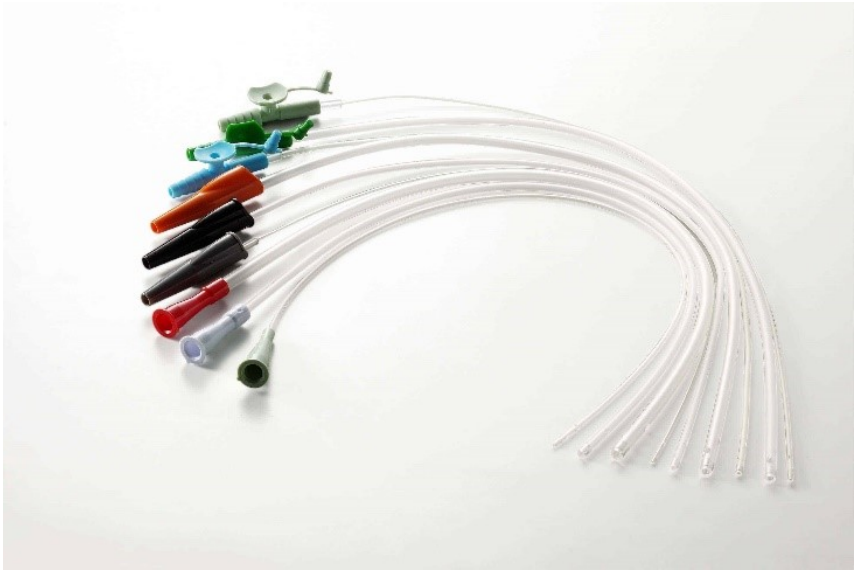


Figure 14 – Different type of suction catheters for electrical suction in the newborn infants

Pulse-oximetry with a saturation sensor on the right hand should be used during resuscitation in the delivery room. It aims to check the preductal oxygen saturation and the heart rate in the newborn, during the neonatal resuscitation. Normally the increase of SpO_2 levels occurs gradually in the first 10 minutes of life (Table 2) and the most of newborns is able to reach a $SpO_2 \geq 92\%$. Titrate of

oxygen saturation (every 30 seconds) is important to avoid both hypoxia and hyperoxia (15). On the other side newborn heart rate is used to assess the effectiveness of spontaneous respiratory effort, the need for interventions and the response to resuscitation.

It is important to remember that pulse-oximetry is slower in detecting heart rate and tends to be inaccurate during the first few minutes. So it may be better to check heart rate with ECG, or in the low resource settings with a stethoscope (68).

APGAR score (Appearance, Pulse, Grimace, Activity, Respiratory effort) is another commonly used procedure for assessing immediate neonatal well-being at birth. But it is considered as a subjective measurement and its diagnostic value in fetal asphyxia is not significant (36).

Targeted Preductal SpO_2 After Birth	
1 min	60%-65%
2 min	65%-70%
3 min	70%-75%
4 min	75%-80%
5 min	80%-85%
10 min	85%-95%

Table 2 – Targeted preductal SpO_2 in a normal newborn infant

Chapter 3 – Objectives

This study aims to explore potential clinical differences between two methods of oropharyngeal suctioning, with the penguin suction device or the suction catheter, in newborn infants needing suctioning at birth. The primary outcome of the study is the oxygen saturation during the first ten minute of life.

Chapter 4 – Methods

4.1 Study design

This is a single center, prospective, randomized clinical trial comparing two different methods of oropharyngeal suctioning with the penguin suction device or the suction catheter in newborn infants needing suctioning at birth. The Institutional Review Board of the St. Luke Catholic Hospital approved this study.

4.2 Setting

The study was conducted at the St. Luke Catholic Hospital in Wolisso (Ethiopia), which is a level III hospital with around 3,600 deliveries per year. This is a referral, private, nonprofit hospital located in Wolisso town, which is the capital of the Southwest Shoa Zone in the Oromiya region. The area has a population of about 1.1 million inhabitants and is served by 81 health facilities (including only one hospital). At St. Luke Wolisso Hospital, midwives are responsible for maternal and neonatal management at delivery. Midwives receive education on neonatal resuscitation (Helping Babies Breathe program) and courses on postnatal management. This study will be part of a collaborative project between the St. Luke Catholic Hospital in Wolisso and Doctors with Africa CUAMM, a non-governmental organization.

4.3 Inclusion and exclusion criteria

Infants satisfying the following inclusion criteria are eligible to participate in the study:

- inborn infants (and);
- need for suctioning at birth: is defined as difficult breathing due to the presence of abundant oronasopharyngeal secretions (mucus, vernix, blood clots, meconium) or need for positive pressure ventilation (and);
- parental consent: a written informed consent will be obtained by a member of the neonatal staff involved in the study from a parent or guardian at maternal admission to the obstetrical ward or prior to delivery.

The exclusion criteria are:

- the presence of major congenital malformations;
- the parental refusal to participate to the study.

4.4 Outcome measures

The primary outcome measure is the oxygen saturation of each minute, during the first 10 minutes of life, collected with pulse oximetry on the right hand.

The secondary outcome measures are:

- Heart rate of each minute during the first 10 minutes of life;
- The proportion of neonates with heart rate > 100 bpm at 5 minutes;
- Episodes of bradycardia (defined as heart rate < 100 bpm) in the first 10 minutes of life;
- The proportion of neonates with saturation > 80% at 5 minutes;
- The proportion of neonates with saturation0 > 90% at 10 minutes;
- Need for face-mask ventilation;
- Need for supplemental oxygen in delivery room;
- Admission to the special care unit (NICU);
- Length of hospitalization (days);
- Occurrence of local lesions (defined as bleeding from the mouth and/or the nose) due to suctioning procedure;
- Occurrence of respiratory distress defined as need for supplemental oxygen and/or nasal-CPAP during the first 48 hours of life.

4.5 General usability

The findings of this study will be important to understand if there may be some clinical differences between oropharyngeal suctioning using a penguin suction device or a suction catheter in newborn infants needing suctioning at birth. The results of the present study will be useful to assess the presence and the magnitude of such clinical differences, and will be the basis for the design of a future larger randomized controlled trial.

4.6 Sample size

The sample size could not be calculated a priori given the lack of information in the literature regarding the study question. Hence, an arbitrary sample size of 60 infants (30 in each arm) was chosen for this pilot study.

4.7 Recruitment

Neonates born in the St. Luke Catholic Hospital in Wolisso, Ethiopia, between June 2022 and September 2022, of any gestational age, needing suctioning, were eligible for study enrolment. Gestational age was based on best obstetric estimate. Written and oral information was offered to parents at maternal admission to the obstetrical ward or prior to delivery. A senior investigator was available at all times to discuss concerns raised by parents or clinicians during the course of the trial. Parents or guardians were asked to sign a written informed consent. After obtaining parental consent, the neonate was considered for inclusion in the study.

4.8 Randomization

Each eligible newborn was randomly assigned to either oropharyngeal suctioning with the penguin suction device or the suction catheter in a 1:1 ratio by using a small opaque plastic container concealing n/2 white and n/2 black toothpicks. The color of the randomly plucked toothpick determined if the penguin suction device or the suction catheter would be used. If the baby needed suctioning, the toothpick was broken and removed from the container. If the baby did not need suctioning, the toothpick was put back into the container. This randomization method is considered appropriate for a low-resource context with limited space and power availability. The assigned procedure (penguin suction device or suction catheter) was then performed. Contamination between arms was not allowed.

4.9 Blinding

Due to the characteristics of the intervention, neither caregivers nor outcome assessors were masked to treatment allocation. Caregivers were masked to oxygen saturation and heart rate values provided by the pulse-oximeter. The statistician was masked to the arm allocation during data analysis.

4.10 Guidelines for management

Before starting the study, all those involved in the study participated to a meeting where all the details of the study were presented. A one-day refresher course of neonatal resuscitation, following Help Babies Breathe version 2, was offered to the midwives and doctors responsible for neonatal management at birth, with particular focus on the use of penguin suction device and suction catheter (20).

Written and oral information was offered to parents or guardians by the research assistant at maternal admission to the obstetrical ward or before delivery. Parents or guardians were asked to sign a written informed consent. After obtaining parental consent, the neonate was considered for inclusion in the study. Immediately after birth, all infants needing suctioning were randomized to receive suctioning with penguin suction device or suction catheter. Suctioning with the penguin device was performed following the Help Babies Breathe algorithm and using a penguin suction device made by silicon (Laerdal Global Health, Laerdal, Norway). Suctioning with the suction catheter was performed following the Neonatal Resuscitation Program and using an 8-Fr flexible catheter made by polyethene (Covidien, Dublin, Ireland) connected to an electrical aspirator (Aesculap, Tuttlingen, German) with a maximum negative suctioning value of 100 mmHg.

Figure 15 – Devices for suction used in the trail: Penguin suction device (on the left) and Suction catheter (on the right)

As indicated by the guidelines, the mouth was suctioned before the nose, immediately after the umbilical cord was cut. All other resuscitative procedures were performed following the Help Babies Breathe algorithm version 2.

An external observer, not involved in the care of the newborn, was responsible of the positioning the probe of the pulse oximeter on the baby's right hand and the collection of the data. Oxygen saturation and heart rate were collected with the pulse oximeter, from the first minute of life, each minute, until the tenth minute. APGAR score was reported at the first, fifth and tenth minute following delivery. If the baby did not need others resuscitation's maneuvers he could go to the mother side, and started skin-to-skin contact. The newborn infants requiring other resuscitation maneuvers (like face-mask ventilation, oxygen supplementation, chest compressions, adrenaline) after birth were carried to Neonatal Intensive Care Unit (NICU) for observation or for recovery. They were followed during the first 48 hours of life to see the outcome, the presence of local lesions due to the suction or the need for supplemental oxygen and/or nasal CPAP.

In the end, a survey was administered to the midwives of St. Luke Hospital who took part of the study doing neonatal resuscitation. They had to answer some questions about suctioning and about which method of suctioning, manual or electrical, they preferred (Appendix 3).

4.11 Data collection

Data was recorded in a data sheet designed for this study, where all the data obtained during delivery room management were collected by an observer not involved in the care of the neonates (pediatric resident). Registered clinical information was: eligibility and randomization; maternal and neonatal characteristics; all data above listed in 'Primary outcome measure', 'Secondary outcome measures' sections; length of stay and in-hospital mortality. Further information was collected as notes.

4.12 Abbreviation

ONPS: oronasopharyngeal suction; CPAP: continuous positive airway pressure; PPV: positive pressure ventilation; NICU: neonatal intensive care unit; PEEP: positive end expiratory pressure; C/S: cesarean section; SVD: spontaneous vaginal delivery; ANC: ante-natal care; GA: gestational age; AHA: American

Heart Association; ERC: European Resuscitation Council, ECG: electrocardiogram; APGAR: Appearance, Pulse, Grimace, Activity, Respiration; MR. SOPA: Mask adjustment, Reposition head, Suction mouth and nose, Open mouth, Pressure increase, Alternative airway; HIV: Human Immuno-deficiency Virus; NO: Nitric Oxide; PGI_2: Prostaglandin I_2; IUGR: Intrauterine Growth Restriction; MSAF: Meconium stained amniotic fluid; MAS: Meconium Syndrome Aspiration; CTG: Cardiotocography; IQR: interquartile range.

4.13 Trial registration

The study has been registered in ClinicalTrials.gov NCT05472155.

Chapter 5 – Statistical Analysis

The statistical analysis was performed as intention-to-treat. Categorical data were summarized as frequency and percentage, while continuous data as median and interquartile range (IQR). Oxygen saturation and heart rate during the first 10 minutes of life were compared between the two arms using linear regression models (including the arm and time as fixed effects, and the neonate as random effect). The other secondary outcome measures were compared between the two arms using Chi Square test or Fisher's exact test (binary data), or Mann-Whitney test (numerical data). All tests were two-sided and a p-value less than 0.05 was considered statistically significant. Data were analyzed using GraphPad Prism version 9 (Dotmatics, San Diego, California).

Chapter 6 – Results

6.1 Participant characteristics

At the time of the analysis, a total of 61 participants were enrolled in the trial (31 in electrical arm and 30 manual arm). All participants received the allocated intervention. Baseline characteristics are displayed in Table 1.

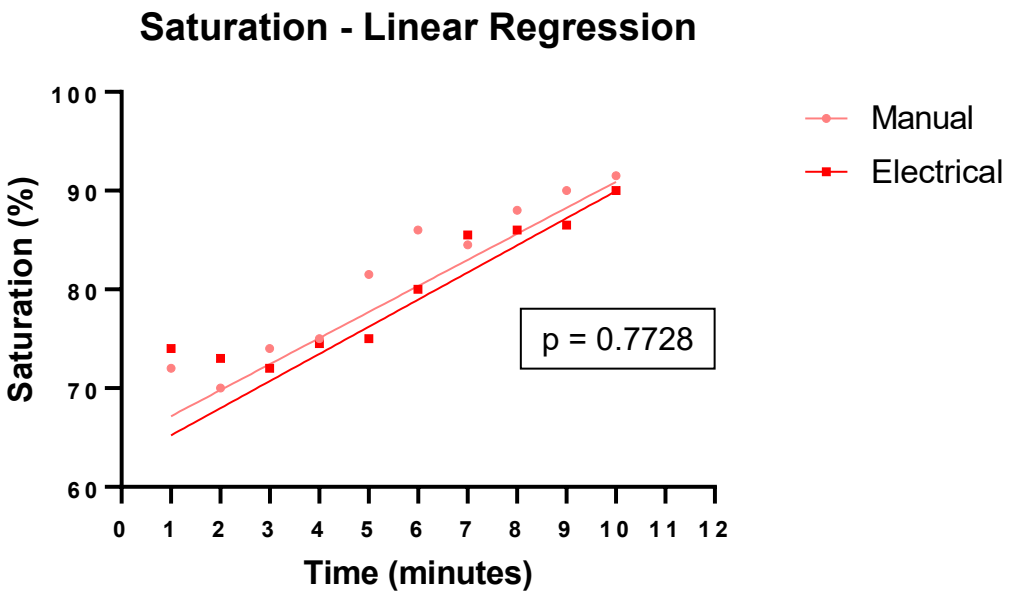
Table 1. Baseline characteristics

	Electrical arm (n=31)	Manual arm (n=30)
Maternal age, years: median (IQR)	25 (22-28)	25 (22-28)
ANC: n (%)	27/31 (87%)	24/30 (80%)
Steroids: n (%)	0/31 (0%)	1/30 (3%)
Meconium: n (%) No Grade 1 Grade 2 Grade 3	 22 (71%) 2 (6%) 0 (0%) 7 (23%)	 21 (70%) 4 (13%) 3 (10%) 2 (7%)
HIV negative: n (%)	31/31 (100%)	30/30 (100%)
Caesarean section: n (%)	10/31 (32%)	6/30 (20%)
Males: n (%)	15/31 (48%)	20/30 (67%)
Birthweight, g: median (IQR)	2980 (2650-3325)	3035 (2709-3408)
GA, weeks: median (IQR)	40 (38-40)	40 (37-40)
Apgar 1 minute: median (IQR)	7 (5-8)	7 (5-8)
Apgar 5 minutes: median (IQR)	9 (7-9)	8 (7-9)
Apgar 10 minutes: median (IQR)	9 (8-9)	9 (8-9)

6.2 Primary outcome measure

The primary outcome measure is the oxygen saturation during the first 10 minutes of life. The oxygen saturation increases over time in both arms ($p < 0.0001$), with similar slope between the two arms ($p = 0.7728$) (Figure 1).

Figure 1. Oxygen saturation during the first 10 minutes of life



6.3 Secondary outcome measures

The heart rate increases over time in both arms ($p < 0.0001$), with no different slope between the two arms ($p = 0.9089$) (Figure 2). Admission to special care unit is more frequent in electrical vs. manual arm (61% vs. 33%, $p = 0.0288$; Table 2). There is no evidence that the other secondary outcome measures differed between the two arms (Table 2). No local lesions occur during the study.

Figure 2. Heart rate during the first 10 minutes of life

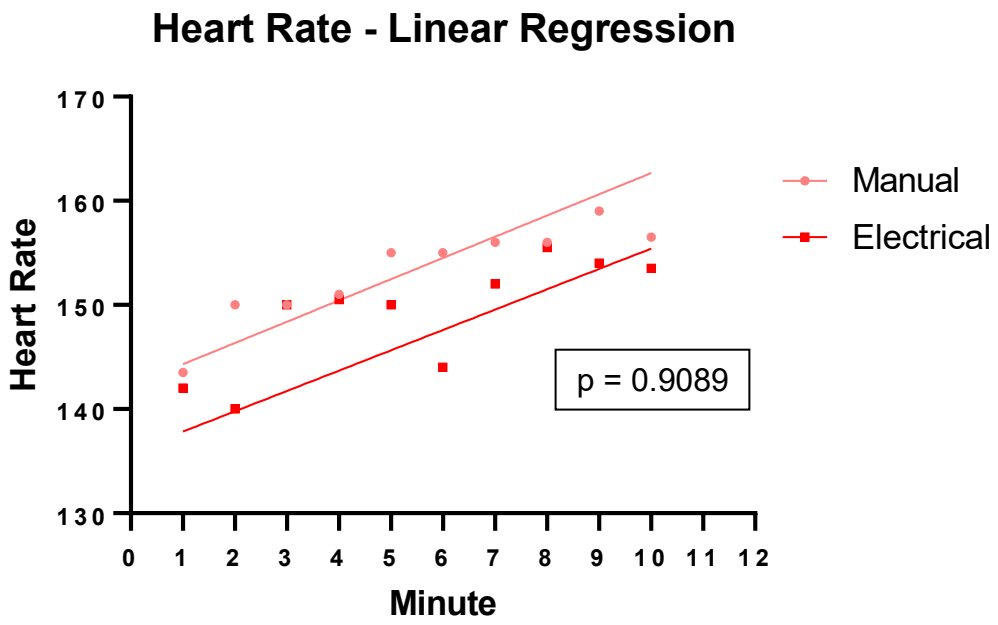
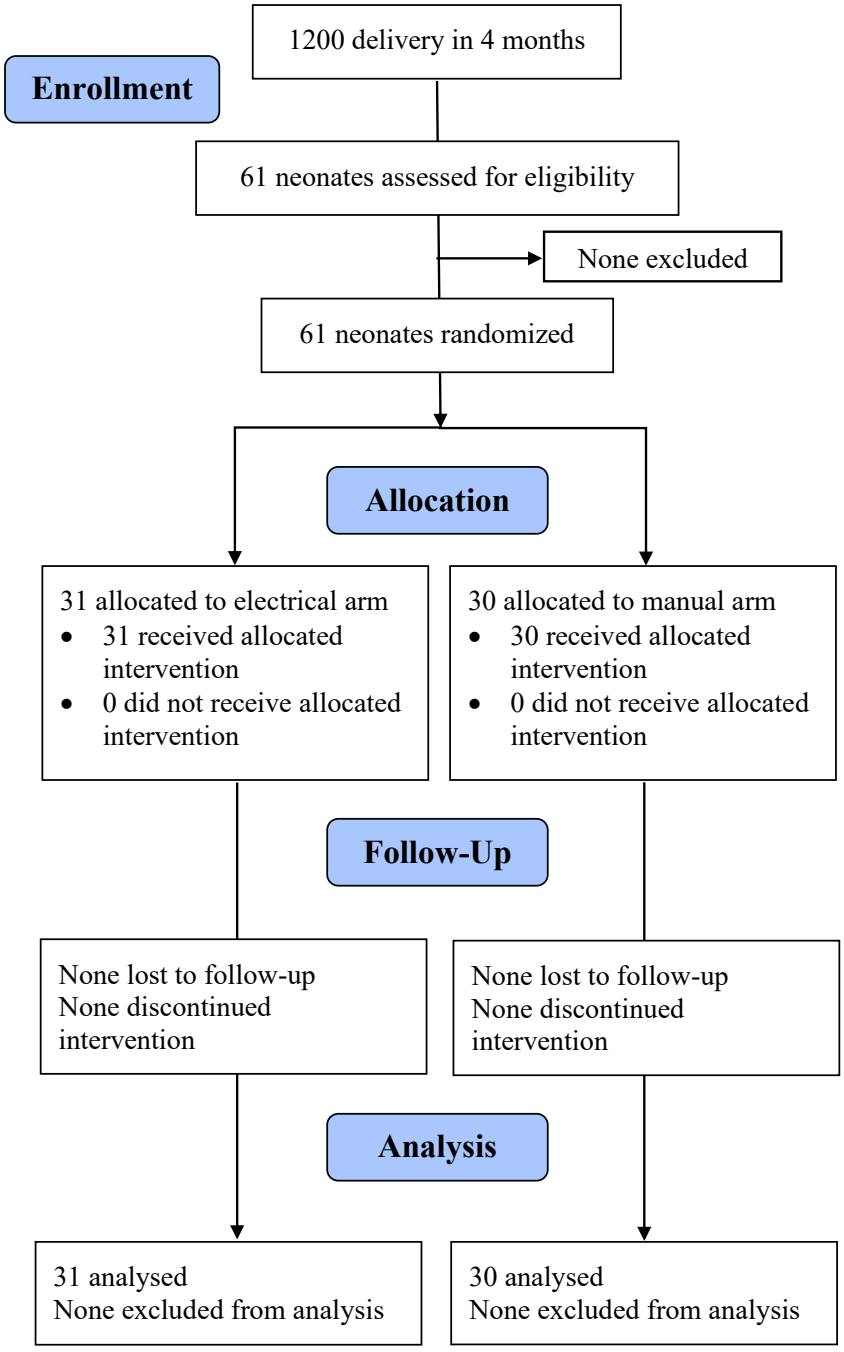


Table 3. Secondary outcome measures

	Electrical arm (n = 31)	Manual arm (n = 30)	p-value
The proportion of neonates with heart rate > 100 bpm at 5 minutes: n (%)	27/30 (90%)	25/27 (93%)	> 0.9999
Episodes of bradycardia (defined as heart rate <100 bpm) in the first 10 minutes of life: n (%)	6/31 (19%)	3/31 (10%)	0.4729
The proportion of neonates with saturation > 80% at 5 minutes: n (%)	11/30 (83%)	14/29 (48%)	0.4348
The proportion of neonates with saturation > 90% at 10 minutes: n (%)	25/30 (83%)	20/31 (65%)	0.1455
Need for face-mask ventilation: n (%)	13/31 (42%)	10/30 (33%)	0.5996
Need for supplemental oxygen in delivery room: n (%)	11/31 (35%)	5/30 (17%)	0.1455
Admission to the special care unit: n (%)	19/31 (61%)	10/30 (33%)	**0.0288**
Length of hospitalization: median (IQR)	4 (1 – 7)	4 (1 - 7)	0.4236
Occurrence of local lesions (defined as bleeding from the mouth and/or the nose) due to suctioning procedure: n (%)	0 (0%)	0 (0%)	-
Occurrence of respiratory distress (defined as need for supplemental oxygen and/or nasal-CPAP during the first 48 hours of life): n (%)	10/19 (53%)	6/10 (22%)	> 0.9999

6.4 Consort Diagram



Chapter 7 – Discussion

7.1 Discussion

This pilot study showed that oxygen saturation and heart rate during the first ten minutes of life where comparable when using a penguin suction device or a suction catheter for suctioning a neonate at birth. There were no differences between the two arms regarding the secondary outcomes of the study, except for the admission to the special care unit (NICU). More newborn infants in the electrical arm were admitted to the NICU than those in the manual arm (19 [61%] vs 10 [33%], p = 0.0288). Of note 33 % of neonates in the manual suction device arm were admitted to NICU suggesting that suctioning was provided to a moderately ill population. Although most patients showed a physiological postnatal improvement of oxygen saturation and heart rate, a consistent part of them were admitted to the NICU immediately after birth. It is reasonable to believe that the neonates who received postnatal airway suctioning really needed maneuvers aimed to helping the breath at birth, despite their acceptable levels of oxygen saturation. Despite the differences regard admission to NICU, the length of the hospitalization was similar in the electrical and in the manual arm (4 [1 - 7] vs [1 -7]; p = 0.4236). The modal value also is the same for both arms (1 vs 1). Even if the neonates in the electrical arm were most frequently admitted in NICU, their recovery had the same length of the manual arm's recovery. Most of neonates staid in NICU for only one day, that usually is the time for observation. However, these results should be interpreted with caution, because the study was not powered to assess this outcome. The result of the present trial should be confirmed by a larger randomized controlled trial focused on the impact of suctioning at birth on the NICU admission.

The use of suction in the delivery room is part of the initial management of neonatal resuscitation, which helps airway fluid removal. Current guidelines recommend to use suction in neonates after delivery only if there are secretions, an airway obstruction or if PPV is required (15,16).

Evidence from previous animal studies shows that rapid removal of fluid from airspaces develop gradually during the latter part of third trimester of pregnancy, together with an acceleration of clearance during the labour (69,70). If a rapid clearance of liquid from the airway is a key step in establishing the timely

transition from placental to lungs respiration in the first minutes of life it might be expected that ONPS would have a positive effect on oxygen saturation after delivery. However previous studies showed that the routine use of post-partum ONPS has to be avoided (3,8,71). Previous randomised controlled trials compared no suction versus ONPS at birth with a sterile polyethylene tube (72), or with soft rubber bulb syringe (37). The results indicated that the suction group had lower oxygen saturation after birth and it needed a longer time to reach 92 % of saturation. Two randomized, controlled trials – one in 140 vaginally born term neonates (64) and the other in 140 neonates delivered by elective cesarean section (36) – assessed ONPS with a catheter versus no suction. Both trials concluded that routine use of suctioning was associated with a significant reduction in oxygen saturation and 5 min APGAR score and a higher heart rate. Others studies compared the effects ONPS versus no suction in term infants delivered vaginally (65) or in term infants delivered by elective caesarean section (73). Another randomised equivalency trial showed that wiping the nose and the mouth with a towel has equivalent efficacy to routine use of ONPS (67). The results obtained in all these studies provide basis to no recommend routine airway suctioning at birth in healthy, term infants.

ONPS is also used in clinical situations such as the presence of meconium. In a randomised controlled trial Vain showed that routine intra-partum ONPS in term neonates born through meconium-stained amniotic fluid did not prevent from Meconium Aspiration Syndrome (MAS) (66).

In all these studies it is compared the suction, with bulb syringe or with catheter, versus no suction in newborn with or without airway obstruction or secretions. However, the literature does not provide any information on clinical differences between the use of a penguin suction device and the use of a suction electric catheter in newborn infants who need suctioning. The guidelines also consider equally the two procedures, but evidence is lacking. This is the first study, which compares penguin and catheter for suctioning newborn infants who need postnatal suctioning, according to the current guidelines (15,16).

7.2 Strength points

This study has several strengths. First, the study design was appropriate for the purpose and to assess the primary and secondary outcomes. The protocol of the

study, was written and registered in an international register before the beginning of patients' collection, was followed and complied in all the aspect and procedures.

To our knowledge, this is the first study which compares the penguin suction device with the suction catheter. The trial took place in a low-resource setting where high quality early steps of neonatal resuscitation, like suctioning, should decrease the need of PPV, supplemental oxygen or admission to the NICU (6). During the trial, all the resuscitation maneuvers, including suctioning, were provided by the local midwifes after participation a re-fresher course on neonatal resuscitation based on the HHB algorithm version 2. The local health caregivers were involved in this study with the purpose of increasing their independence. Finally, at the end of the study a survey was given to the midwives to assess their opinion among the two methods of suction (Appendix 3).

The cost of the penguin is lower than those of the catheter; in addition, the penguin can be washed and reused many times. If it will be possible to demonstrate that the penguin and the catheter have equivalent efficacy for airway cleaning, this should save money and resources, which are very low and restricted in some countries like Ethiopia.

According to this pilot study the two different methods of suctioning were clinically equivalent in terms of oxygen saturation and heart rate during the first 10 minutes of life. However, the suctioning performed with a catheter was associated with a higher rate of NICU admission. If these findings are confirmed, a penguin suction device instead of catheter should be preferable for suctioning the newborns immediately after birth in low resource settings. The penguin device is easier to use, like it was reported by the participants' opinion (Appendix 3). Among the 16 midwifes, 14 reported that the manual suction with penguin device was easier compared to the catheter. The penguin device is moreover cheaper than the catheter. It can be washed, disinfected and ready to be reused. On the contrary, the catheter is more expensive and single use. In conclusion, in the low resource countries the penguin device could represent the more appropriate choice for ONPS.

7.3 Limitations

The study also has some limitations. First of all, the delivery room staff could not be masked to the study interventions because of the intrinsic characteristics of the trial. Nevertheless, the caregivers were blinded about the levels of oxygen saturation and heart rate, and an external observer, not involved in the care of the neonates, collected the data during delivery room procedures. According to the answers of the survey (Appendix 3) the delivery staff preferred the use of penguin device for suctioning so they were more experienced and confident in the use of it. However, before the beginning of the trial, a re-fresher course about neonatal resuscitation, focused on the suction with both study suction devices, was offered to all the midwifes of the St. Luke Hospital.

Chapter 8 – Conclusions

Oxygen saturation and heart rate during the first ten minutes of life were the same when using a penguin suction device or a suction catheter for suctioning neonates at birth. There were no differences between the two arms regarding the study secondary outcomes, except for the admission to the special care unit (NICU) which was significantly higher in the suction catheter group. Although our findings support the use of a penguin suction catheter immediately after birth, further research is needed to confirm our data.

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Appendix 1 – STUDY PROTOCOL

TITLE: Penguin versus catheter for airway suctioning at birth: a randomized controlled trial in a low resource setting.

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Abstract

Background: Evidence from literature showed that suctioning should be offered only to newborn infants who have obvious obstruction to spontaneous breathing or who require positive pressure ventilation. International guidelines recommend the use of a penguin suction device or a suction catheter in newborn infants needing suctioning at birth, but literature does not provide any information on clinical differences between the two procedures.

Objective of the study: This trial aims to compare two different methods of oropharyngeal suctioning (with penguin suction device or suction catheter) in newborn infants needing suctioning at birth.

Primary outcome measure: Oxygen saturation during the first 10 minutes of life.

Study design: This is a single center, prospective, randomized clinical trial comparing two different methods of oropharyngeal suctioning (with penguin suction device or suction catheter) in newborn infants needing suctioning at birth.

Setting: The study is conducted at the St. Luke Catholic Hospital in Wolisso (Ethiopia), which is a level III hospital with around 3,600 deliveries per year.

Study procedures: Before starting the study, all those involved in the study will participate to a meeting (where all the details of the study will be presented). A one-day refresher course of neonatal resuscitation (Help Babies Breathe version 2) will be offered to the midwives responsible for neonatal management at birth, with particular focus on the use of penguin suction device and suction catheter.
Written and oral information will be offered to parents or guardians by the research assistant at maternal admission to the obstetrical ward or before delivery. Parents or guardians were asked to sign a written informed consent.
Immediately after birth, all infants needing suctioning will be randomized to receive suctioning with penguin suction device or suction catheter. All resuscitative procedures will be performed following the Help Babies Breathe algorithm. An external observer, not involved in the care of the newborn, will be

responsible of the positioning the probe of the pulse oximeter and the collection of the data. We aim to enroll 60 neonates.

Introduction

A quarter of neonatal deaths are due to intrapartum-related events, with around 99% occurring in low-resource settings [1]. Education on neonatal resuscitation is most urgent in settings with poor access to intrapartum obstetric care, where immediate postnatal mortality can be reduced by 30% with basic training in neonatal resuscitation [2-4].

Management of newborns at birth includes different interventions based on progressive steps (initial steps, ventilation, chest compressions, and medications) [5,6]. Initial steps include oropharyngeal suctioning (with penguin suction device or suction catheter), which is recommended in infants who have obvious obstruction to spontaneous breathing or who require positive pressure ventilation [7]. Such restriction has been recommended since 2010 because of concerns related to adverse events associated with routine suctioning [8].

International guidelines recommend the use of a penguin suction device (Helping Baby Breathe) or a suction catheter (Manual of Neonatal Resuscitation) in newborn infants needing suctioning at birth [9,10], but literature does not provide any information on clinical differences between the two procedures.

This study is designed to compare two different methods of oropharyngeal suctioning (with penguin suction or suction catheter) in newborn infants at birth.

Literature review

Previous studies assessed the effect of routine oropharyngeal/nasopharyngeal suction compared to no suction in newborn infants [11]. Evidence from literature showed that suctioning should be offered only to newborn infants who have obvious obstruction to spontaneous breathing or who require positive pressure ventilation [7]. International guidelines recommend the use of a penguin suction device or a suction catheter in newborn infants needing suctioning at birth [9,10], but literature does not provide any information on clinical differences between the two procedures. The use of a suction catheter implies a suction system which is often unavailable in low resource settings, hence penguin suction device is actually the most used method in such settings. This study is designed to compare

two different methods of oropharyngeal suctioning (with bulb syringe or suction catheter) in newborn infants needing suctioning at birth.

Methods/Design

Aim

This pilot study aims to explore potential clinical differences between two methods of oropharyngeal suctioning (with penguin suction device or suction catheter) in newborn infants needing suctioning at birth.

Study design

This is a single center, prospective, randomized clinical trial comparing two different methods of oropharyngeal suctioning (with penguin suction device or suction catheter) in newborn infants needing suctioning at birth.

Setting

The study was conducted at the St. Luke Catholic Hospital in Wolisso (Ethiopia), which is a level III hospital with around 3,600 deliveries per year. This is a referral, private, nonprofit hospital located in Wolisso town, which is the capital of the Southwest Shoa Zone in the Oromiya region. The area has a population of about 1.1 million inhabitants and is served by 81 health facilities (including only one hospital). At St. Luke Wolisso Hospital, midwives are responsible for maternal and neonatal management at delivery. Midwives receive education on neonatal resuscitation (Helping Babies Breathe program) and courses on postnatal management. This study will be part of a collaborative project between the St. Luke Catholic Hospital in Wolisso and Doctors with Africa CUAMM, a non-governmental organization. [12]

Inclusion criteria

Infants satisfying the following inclusion criteria will be eligible to participate in the study:

- inborn infants (and)
- need for suctioning at birth (and)

- parental consent; a written informed consent will be obtained by a member of the neonatal staff involved in the study from a parent or guardian at maternal admission to the obstetrical ward or prior to delivery.

The need for suctioning at birth is defined as difficult breathing due to the presence of abundant oronasopharyngeal secretions or need for positive pressure ventilation.

Exclusion criteria

- major congenital malformations;
- parental refusal to participate to the study.

Primary outcome measure

The primary outcome measure will be the oxygen saturation during the first 10 minutes of life.

Secondary outcome measures

1. Heart rate during the first 10 minutes of life;
2. The proportion of neonates with heart rate >100 bpm at 5 minutes;
3. Episodes of bradycardia (defined as heart rate <100 bpm) in the first 10 minutes of life;
4. The proportion of neonates with saturation >80% at 5 minutes;
5. Time to achieve transcutaneous saturations >90%;
6. Need for face-mask ventilation;
7. Need for supplemental oxygen in delivery room;
8. Admission to the special care unit;
9. Occurrence of local lesions (defined as bleeding from the mouth and/or the nose) due to suctioning procedure;
10. Occurrence of respiratory distress defined as need for supplemental oxygen and/or nasal-CPAP during the first 48 hours of life.

General usability

The findings of this study will be important to understand if there may be some clinical differences between oropharyngeal suctioning using a penguin suction device or a suction catheter in newborn infants needing suctioning at birth. The

results of the present study will be useful to assess the presence and the magnitude of such clinical differences, and will be the basis for the design of a future larger randomized controlled trial.

Sample size

The sample size could not be calculated a priori given the lack of information in the literature regarding the study question. Hence, an arbitrary sample size of 60 infants (30 in each arm) was chosen for this pilot study.

Recruitment

Written and oral information will be offered to parents at maternal admission to the obstetrical ward or prior to delivery. A senior investigator will be available at all times to discuss concerns raised by parents or clinicians during the course of the trial.

Randomization

Each eligible newborn will be randomly assigned to either oropharyngeal suctioning with penguin suction device or suction catheter in a 1:1 ratio by using a small opaque plastic container concealing n/2 white and n/2 black toothpicks. The color of the randomly plucked toothpick will determine if penguin device or suction catheter would be used. If the baby will need suctioning, the toothpick will be broken and removed from the container. If the baby will not need suctioning, the toothpick will be put back into the container. This randomization method is considered appropriate for a low-resource context with limited space and power availability [13]. The assigned procedure (penguin suction device or suction catheter) will then be performed. Contamination between arms will not be allowed.

Blinding

Due to the characteristics of the intervention, neither caregivers nor outcome assessors will be masked to treatment allocation. Caregivers will be masked to oxygen saturation and heart rate values provided by the pulse-oximeter. The statistician will be masked to the arm allocation during data analysis.

Guidelines for Management

Before starting the study, all those involved in the study will participate to a meeting where all the details of the study will be presented. A one-day refresher course of neonatal resuscitation (Help Babies Breathe version 2) [9] will be offered to the midwives responsible for neonatal management at birth, with particular focus on the use of bulb syringe and suction catheter.

Written and oral information will be offered to parents or guardians by the research assistant at maternal admission to the obstetrical ward or before delivery. Parents or guardians were asked to sign a written informed consent. After obtaining parental consent, the neonate was considered for inclusion in the study.

Immediately after birth, all infants needing suctioning will be randomized to receive suctioning with bulb syringe or suction catheter. Suctioning with bulb syringe will be performed following the Help Babies Breathe algorithm and using penguin suction device (Laerdal Global Health, Laerdal, Norway) [9]. Suctioning with suction catheter will be performed following the Neonatal Resuscitation Program [10] and using an 8-Fr catheter (Covidien, Dublin, Ireland) connected to an electrical aspirator (Aesculap, Tuttlingen, German) with a maximum negative suctioning value of 100 mmHg. As indicated by the guidelines, the mouth will be suctioned before the nose [10]. All other resuscitative procedures will be performed following the Help Babies Breathe algorithm [9]. An external observer, not involved in the care of the newborn, will be responsible of the positioning the probe of the pulse oximeter and the collection of the data.

Data collection

Data will be recorded in a data sheet designed for this study, where all the data obtained during delivery room management will be collected by an observer not involved in the care of the neonates (pediatric resident). Registered clinical information will be: eligibility and randomization; maternal and neonatal characteristics; all data above listed in ‘Primary outcome measure’, ‘Secondary outcome measures’ sections; length of stay and in-hospital mortality. Further information will be collected as notes.

Statistical analysis

Categorical data will be summarized as number and percentage, and continuous data will be summarized as mean and standard deviation or median and interquartile range. Categorical data will be compared between arms using Fisher test or Chi Square test, and effect size will be reported as risk ratio with 95% confidence interval. Continuous data will be compared between arms using Student t test or Mann-Whitney test, and effect size will be reported as mean difference or median difference with 95% confidence interval. The trend of oxygen saturation, heart rate and respiratory rate over time will be assessed in the two arms using linear regression models. All tests will be 2-sided and a p-value less than 0.05 will be considered statistically significant. Statistical analysis will be performed using GraphPad Prism version 9 (Dotmatics, San Diego, California).

Duration of study

The trial will terminate when the last recruited infant is discharged from hospital, or dies. Based on preliminary observations, we consider the following duration of the study (10 months):

- 1 month: ethics committee approval;
- 3 months: data collection
- 1 month: analysis of the data;
- 2 months: preparation of the manuscript.

Ethical considerations

Written parental consent is necessary before enrollment of the patients in the study. We consider that there will be not risks for both study groups. Clinical conditions will be strictly monitored in both groups during the study.

Ethics Committee approval

The study needs to be approved by the Institutional Review Board of the St. Luke Catholic Hospital.

Compliance to protocol

Compliance will be defined as full adherence to protocol. Compliance with the protocol will be ensured by some members of the project (FC, EF, DM) responsible for local data collection, who will weekly monitor the adherence to the study protocol.

Data Safety and Monitoring Board

Safety measures will include incidence, severity and causality of reported severe adverse events, represented by changes in occurrence of the expected common neonatal complications and the development of unexpected severe adverse events. All severe adverse events will be followed until complete resolution or until the clinician responsible for the care of the recruited patient considers the event to be chronic or the infant to be stable.

A monitoring board including an independent assessor (not involved in the study) from the University of Padova and an assessor from St. Luke Wolisso Hospital will review all the deaths and adverse effects. If there is a reasonable suspected causal relationship with the intervention, severe adverse events will be reported to the Institutional Review Board to guarantee the safety of the participants.

Discussion

Neonatal resuscitation guidelines recommend naso-oropharyngeal suctioning a birth in newborn infants who have obvious obstruction to spontaneous breathing or who require positive pressure ventilation. The suctioning device can be a penguin suction device or a suction catheter, but literature does not provide any information on clinical differences between the two procedures. This study aims to provide more information on this topic and will provide the baseline findings for designing further confirmative trials.

Trial status

The trial is complete for submission to the Institutional Review Board of the St. Luke Catholic Hospital.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors have made substantial contributions to the conception and design of the study protocol, and have given final approval of the actual version.

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Appendix 2 – STUDY CASE REPORT FORM

1. **Inclusion Criteria**

Infant **MUST** present with all of the following (please tick the items below as appropriate):

☐ Inborn infant AND

☐ Absence of major congenital malformations AND

☐ Parental consent AND

☐ Need for suctioning at birth (defined as difficult breathing due to the presence of abundant oronasopharyngeal secretions or need for PPV).

Please indicate if the suctioning was needed due to:

☐ difficult breathing due to the presence of abundant oronasopharyngeal secretions

☐ need for positive pressure ventilation

☐ both of them

2. **Randomization**

RANDOMIZED TO:

- Suctioning with bulb syringe ☐
- Suctioning with suction catheter ☐

THE PATIENT WAS NOT RANDOMIZED DUE TO:

- Major congenital malformations ☐
- Parental refusal to participate to the study ☐
- Other reasons (specify)…… ☐

3. Baseline Information

IDENTIFICATION	
ID number	
Name of the patient	
Date of birth	
Hour of birth	
ANTENATAL RECORDS	
Mother's name	
Mother's age	
Did the mother attend antenatal clinic?	
Did the mother receive antenatal steroids?	
Pregnancy complications	
HIV serology (positive/negative)	
Other	
NEONATAL HISTORY	
Mode of delivery (vaginal/cesarean section)	
Indication to cesarean section	
NEONATAL INFORMATION	
Sex of the neonate	
Birth Weight	
Gestational Age	
Apgar score 1 min	
Apgar score 5 min	
Apgar score 10 min	
Resuscitation interventions:	- Stimulation - Face-mask ventilation - Chest compressions
Time of the first breath (sec.)	
Time of regular breathing (sec.)	
Episodes of bradycardia (defined as heart rate <100 bpm) in the first 10 minutes	
Time to achieve transcutaneous saturations >90%;	

4. Outcome Measures

Date and hour of birth: ……

Name of the midwife attending the birth: ……

Year of experience in delivery room: …….

Postnatal time (minutes)	**1 min**	**2 min**	**3 min**	**4 min**	**5 min**	**6 min**	**7 min**	**8 min**	**9 min**	**10 min**
OXYGEN SATURATION										
HEART RATE (bpm)										

Did the baby need face-mask ventilation? ☐ YES ☐ NO

Did the baby need supplemental oxygen in delivery room? ☐ YES ☐ NO

Was the baby admitted to the special care unit? ☐ YES ☐ NO

Occurrence of local lesions (defined as bleeding from the mouth and/or the nose). ☐ YES ☐ NO

Occurrence of respiratory distress defined as need for supplemental oxygen and/or nasal-CPAP during the first 48 hours of life. ☐ YES ☐ NO

Postnatal time (hour)	**1 hour**	**2 hour**	**3 hour**	**4 hour**	**5 hour**	**6 hour**
RESPIRATORY RATE						

5. Discharged Data

Dead

- Date of death: ……...

- Diagnosis: ☐Prematurity ☐Asphyxia ☐ Infection/sepsis ☐ Other (specify)

Alive

- Admitted to the NICU: …….

- Date at discharge: ……... Weight at discharge (kg) …….

- Diagnosis: ☐ Prematurity ☐Asphyxia ☐ Infection/sepsis ☐ Other (specify)

Local lesions due to sucioning (i.e. blodd from the mouth/nose) ☐

Need for supplemental oxygen and/or nasal-CPAP during the first 48 hours of life ☐

Appendix 3 – SURVEY FOR MIDWIVES

1. How old are you?

.....……

2. How long have you been working in Delivery Unit?

……

3. Can you tell me the average number of newborns requiring suctioning?

……

4. In your opinion which way of suctioning (electrical vs manual) leads to better neonatal outcomes? And why?

……

……

5. In your opinion which way of suctioning (electrical vs manual) is easier to employ?

……

……

Age	**Years of work**	**Average number of newborns requiring suctioning**	**Which way of suctioning for better neonatal outcomes?**	**Why?**	**Which one is easy to use?**
21	1 year	50 per month	**Electrical**	It helps more in case of critical condition	**Manual**
25	4 years	50%	**Manual**	It protects the newborn preventing from vagal reflex	**Manual**
26	4 years	40%	**Manual**	It protects the newborn preventing	**Manual**

				from vagal reflex	
28	6 years	40%	**Manual**	Easier and faster to use	**Manual**
21	2 years	50%	**Electrical**	It can remove a large amount of secretions	**Manual**
24	2 years	30%	**Manual**	The Delivery Unit staff know how to use it properly	**Manual**
27	6 years	25%	**Manual**	Electrical suctioning can cause damages in respiratory trait	**Manual**
25	6 years	20%	No difference between the two	/	**Manual**
20	2 years	30%	**Electrical**	1.It removes a large amount of secretions 2.You can reach the stomach	**Manual**
25	4 years	30%	**Electrical**	It prevents from meconium swallowing	**Manual**
24	4 years	40%	**Manual**	It is more available	**Manual**
28	1 year	2/day	**Electrical**	It is faster and easier to use	**Electrical**
24	3 years	20%	**Manual**	It protects the	**Manual**

				newborn preventing the vagal reflex and bradycardia.	
23	3 years	20%	**Manual**	Electrical suctioning could cause bradycardia and damage the respiratory trait	**Manual**
20	2 years	10%	**Electrical**	It is more effective in neonatal resuscitation	**Electrical**
27	1 year	15%	**Electrical**	It is more effective in distressed babies	**Manual**

1. 16 midwives filled the form for this survey
2. 50% of them consider manual suctioning more effective. The other half prefers electrical.
3. The reason why 50% prefers electrical suctioning is the effectiveness of this method. In critical conditions or in case of a large amount of secretions, it is possible to clean the airways better.
4. It seems that experienced midwives prefer manual suctioning.
5. 14 over 16 considers manual suctioning easier to use.