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TESI DI LAUREA

Applied forces with partially vs. fully inflated face masks during neonatal ventilation: a randomized crossover manikin study

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1. ABSTRACT

Background

More than 5% of newborns don't initiate an adequate autonomous respiratory effort, requiring positive pressure ventilation with a face mask or more invasive procedures.

Face mask ventilation is the most important and effective procedure in newborn' resuscitation but, even though the presence of a cushion rim reduces air leaks and the pressure exercised on the face independently of the type of face mask, there isn't any guideline about the best filling level for the cushion rim.

Using the right amount of air to fill the mask's cuff can be effective not only for the procedure's effectiveness, as it can reduce air leak, but also to reduce the forces exerted on the newborn's face and prevent pressure injuries.

Face mask ventilation can trigger the trigeminal-cardiac reflex (TCR), a vagally mediated brainstem reflex that leads to apnoea and bradycardia. As the intensity of the TCR depends on the type and intensity of trigeminal stimuli, but the threshold to trigger it is still unknown and varies between neonates, applying the lowest force possible to the infant's face during resuscitation procedures is desirable.

Purpose

This trial compared the applied forces on key points of a newborn manikin's face during positive pressure ventilation, cuff pressure, and air leak with a partially (25 mL) vs a fully (35 mL) inflated face mask.

Materials and Methods

We conducted a randomized, controlled crossover trial of mask ventilation on a modified neonatal manikin with a partially (25 mL) and a fully (35 mL) inflated face mask. Twenty-eight neonatal/pediatrics/anesthesiology consultants and residents trained in neonatal resuscitation participated in the study.

The primary outcome measure was the forces applied to key regions of the manikin's face. Secondary outcome measures included the pressure generated within the mask cuff during ventilation, the percentage of inflations with a mask leak < 25%, and subjective workload.

Results

The pressure generated within the mask's cuff and the forces exerted on the manikin's face sensors were higher with the partially cuffed mask. There were no significant differences in acceptable leak and subjective workload impression with the two levels of cuff filling.

Conclusion

Using a partially inflated face mask was associated to higher applied forces and higher cuff pressures compared to a fully inflated face mask. Using a partially or fully inflated face mask does not result in a significant difference in mask leak and neither in the participants' subjective impression to prefer one mask over the other.

This finding holds potential benefits in the prevention of pressure injuries, although further research is needed to assess its implications on the likelihood of eliciting the trigeminal-cardiac reflex.

Clinical implications require assessment in future studies.

2. RIASSUNTO

Presupposti dello studio

Più del 5% dei neonati non inizia autonomamente una respirazione adeguata, rendendo necessaria la ventilazione a pressione positiva con maschera facciale o procedure più invasive.

La ventilazione con maschera facciale è la procedura più efficace nella rianimazione neonatale ma, nonostante la presenza di un cuscinetto gonfiabile riduca le perdite d'aria attorno alla maschera e la pressione esercitata sul volto indipendentemente dal tipo maschera, non ci sono linee guida che indichino il miglior livello di riempimento del cuscinetto.

L'uso della corretta quantità di aria per riempire il cuscinetto della maschera può essere efficace non solo per l'efficacia della tecnica, dato che riduce le perdite d'aria attorno alla maschera, ma anche per ridurre le forze applicate sulla faccia del neonato e prevenire lesioni da pressione.

La ventilazione con maschera facciale può causare l'attivazione del riflesso trigemino-cardiaco (RTC), un riflesso del tronco encefalico mediato dal nervo vago che causa apnea e bradicardia. Dato che l'intensità del RTC dipende dal tipo e dall'intensità dello stimolo trigeminale, ma la soglia per attivarlo non è nota e varia tra i neonati, è auspicabile applicare la minor forza possibile sulla faccia del bambino durante la rianimazione.

Scopo dello studio

Questo studio ha confrontato le forze applicate sui punti chiave della faccia di un manichino neonatale durante la ventilazione a pressione positiva, la pressione nella cuffia e le perdite d'aria attorno alla maschera con maschera facciale parzialmente (25mL) contro completamente (35mL) gonfiata.

Materiali e Metodi

Abbiamo condotto uno studio randomizzato, controllato e con crossover su manichino neonatale modificato, usando maschere facciali parzialmente (25mL) e completamente (35mL) gonfiate. Hanno partecipato ventotto persone tra

neonatologi/pediatri/anestesisti strutturati o specializzandi formati sulle tecniche di ventilazione neonatale.

L'outcome primario era la misura delle forze applicate sui punti chiave della faccia del manichino. Gli outcome secondari includevano la pressione generate all'interno della cuffia della maschera durante la ventilazione, la percentuale di ventilazioni con fuga di aria dalla maschera <25% e le impressioni dei partecipanti.

Risultati

La pressione generata all'interno della maschera e le forze esercitate sui sensori della faccia del manichino sono maggiori con la maschera parzialmente gonfia. Non ci sono state differenze significative riguardo le perdite d'aria attorno alla maschera né riguardo le impressioni dei professionisti tra i due livelli di cuffiaggio.

Conclusioni

L'uso di una maschera facciale parzialmente gonfia è associato all'applicazione di forze maggiori sulla faccia e a pressioni maggiori nella cuffia rispetto alla maschera completamente gonfia. L'uso di una maschera facciale parzialmente o totalmente gonfia non comporta differenze significative nelle perdite d'aria attorno alla maschera, né nell'impressione soggettiva dei partecipanti a preferire una maschera rispetto all'altra.

Questo risultato potrebbe essere utile nella prevenzione di lesioni da pressione, anche se servono ulteriori studi riguardo le implicazioni sulla probabilità di stimolare il riflesso trigemino-cardiaco.

Le implicazioni cliniche richiedono verifiche in studi futuri.

3. BACKGROUNDS

3.1. INTRODUCTION

Over 130 million babies are born annually worldwide and more than 10% (nearly 15 million) of these babies are preterm births, which is the main risk factor for death in newborns and which number has slowly but constantly grown in almost all countries during the last 30 years (1,2).

Over 1 million children die each year due to complications of preterm birth. For those who survive, preterm birth significantly increases the likelihood of serious illnesses, disabilities and developmental delays, as well as chronic adult diseases such as diabetes and heart disease.

The first month of life is the most vulnerable period for child survival, with nearly half (47%) of all deaths in children under 5 years of age occurring in the newborn period (the first 28 days of life). Prematurity is the leading cause of newborn deaths (followed by birth complications (birth asphyxia/trauma), neonatal infections and congenital anomalies), and the second leading cause of death, after pneumonia, in children under the age of 5 (2,3).

Inequalities in survival rates around the world are huge: half of the babies born at 24 weeks survive in high-income countries, but in low-income settings half of the babies born at 32 weeks continue to die due to lack of care or training, even though recent studies showed that, with the right behaviors, deaths from preterm birth complications can be reduced by over three-quarters even without the availability of neonatal intensive care (2).

This means that we need to improve healthcare procedures and frontline workers' education to reduce the incidence of neonatal death.

3.2. WORLD INCIDENCE OF RESUSCITATION PROCEDURES IN NEWBORNS

The transition from intrauterine to extrauterine life requires several critical interdependent physiological events occurring rapidly to allow successful conversion from placental to pulmonary gas exchange. Air breathing leads to significant reductions in pulmonary vascular resistances, which increase pulmonary blood flow and thereby maintain left ventricular filling and output (vital for coronary and cerebral perfusion) when the umbilical cord is clamped. When the low-resistance placental circulation is removed, systemic vascular resistance and blood pressure increase, and right-to-left shunting across the ductus arteriosus decreases leading to its closure (2).

The majority (approximately 85%) of babies born at term initiate breathing within 10-30 seconds after birth without assistance and an additional 10% will do so with drying, tactile, or warming stimulation. If they have good tone and adequate heart rate, these newborns may be dried and placed skin-to-skin with their mother to prevent hypothermia. However, this does not preclude the need for clinical assessment as secondary apnoea, persistent cyanosis, or breathing difficulties can still occur (4).

For the remaining 5% of newborns who do not initiate adequate respiratory effort after adequate stimulation, caregivers must deliver effective ventilation with a face mask within 1 minute after birth, which is effective in most cases.

If it isn't effective, it is mandatory to consider and start more invasive approaches such as endotracheal intubation (2%), chest compressions (0,1%) or intravenous epinephrine (0,05%) (4).

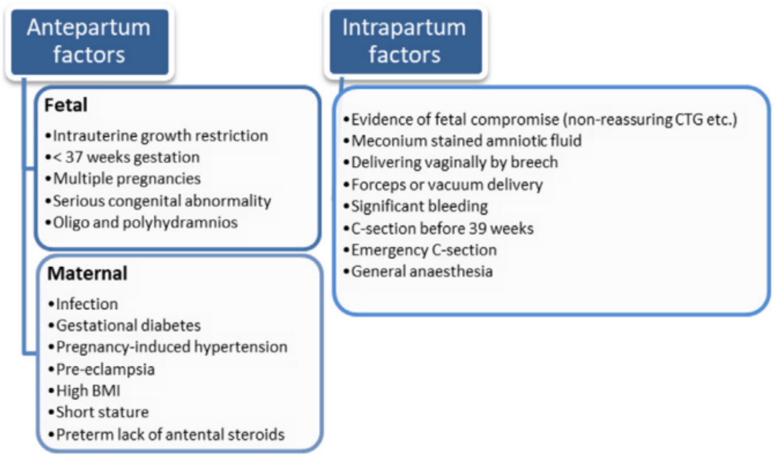
3.3. RISK FACTORS ASSOCIATED WITH AN INCREASED RISK OF A NEED FOR STABILIZATION OR RESUSCITATION AT BIRTH

There are many risk factors associated with an increased risk for stabilization and/or resuscitation at birth and they can be divided into three main groups depending on the timing and the origins (5).

The most common causes can be classified (as shown in *Fig. 1*) in:

- **Fetal antepartum factors**:
  - Intrauterine growth restrictions.
  - < 37 weeks gestation.
  - Multiple pregnancies.
  - Serious congenital abnormality.
  - Oligo and polyhydramnios.
- **Maternal antepartum factors**:
  - Infections.
  - Gestational diabetes.
  - Pregnancy-induced hypertension.
  - Pre-eclampsia and eclampsia.
  - High BMI.
  - Short stature.
  - Preterm lack of antenatal steroids.
- **Intrapartum factors**:
  - Evidence of fetal compromise (non-reassuring CTG, ecc).
  - Meconium-stained amniotic fluid.
  - Delivering vaginally by breech.
  - Forceps or vacuum delivery.
  - Significant bleeding.
  - Caesarean section before 39 weeks.
  - Emergency caesarean section.
  - General anesthesia.

Figure 1: Common factors associated with an increased risk of a need for stabilization, or resuscitation at birth. From: Madar J et al., Resuscitation (2021).



3.4. CURRENT AMERICAN HEALTH ASSOCIATION (AHA) NEWBORN RESUSCITATION GUIDELINES

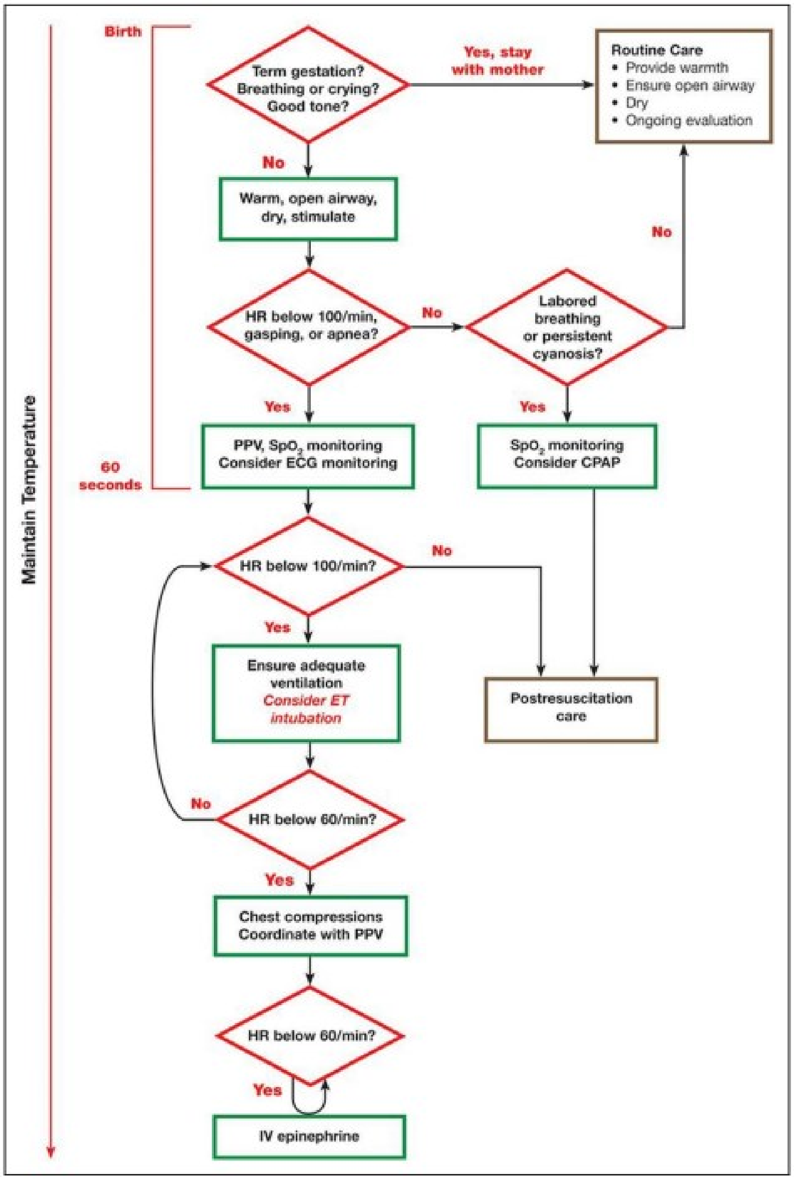
Newborn infants who are breathing or crying and have good tone and an adequate heart rate may undergo delayed cord clamping and should be dried and placed skin-to-skin with their mothers to prevent hypothermia. This does not preclude the need for clinical assessment of the newborn as secondary apnea, persistent cyanosis, or breathing difficulties can still occur. For the approximately 5% of newborn infants who do not initiate adequate respiratory effort after stimulation, providers must deliver effective ventilation with a face mask. This is effective in most cases and healthcare providers must optimize it because it is the most important step for successful transition.

If it is not effective, providers should adopt interventions to eliminate mask leaks, check for airway patency, and ensure that adequate inflation pressures are used; if ventilation is still not effective, an alternative airway (endotracheal tube or supraglottic airway device) must be considered.

If, despite efforts to optimize ventilation, the newborn has a persistent heart rate of less than 60/min or asystole, then chest compressions are needed. Epinephrine and administration of fluids for circulatory volume expansion may also be required (2).

The AHA neonatal resuscitation algorithm is shown in *Fig. 2*.

Figure 2: AHA neonatal resuscitation algorithm. From: Aziz K et al., Circulation (2020).



3.5. EUROPEAN RESUSCITATION COUNCIL (ERC) CLASSIFICATION AND GUIDELINES ACCORDING TO INITIAL ASSESSMENT

For an adequate initial assessment the caregiver should consider, while keeping the baby worm, the following parameters:

- Tone and color: an uncompromised newly born infant will be able to maintain a pink color of the mucous membranes without supplemental oxygen. Central cyanosis is determined by examining the face, trunk, and mucous membranes. Acrocyanosis is usually a normal finding at birth and is not a reliable indicator of hypoxemia, but it may indicate other conditions, such as cold stress. Pallor may be a sign of decreased cardiac output, severe anemia, hypovolemia, hypothermia, or acidosis.

- Breathing quality and rate: after initial respiratory efforts, the newly born infant should be able to establish regular respirations sufficient to improve color and maintain a heart rate >100 bpm. Gasping and apnoea are signs that indicate the need for assisted ventilation.
- Heart rate: it is determined by listening to the precordium with a stethoscope or feeling pulsations at the base of the umbilical cord (central and peripheral pulses in the neck and extremities are often difficult to feel in infants, but the umbilical pulse is readily accessible in the newly born and permits assessment of heart rate without interruption of ventilation for auscultation). Heart rate should be consistently >100 bpm in an uncompromised newly born infant. An increasing or decreasing heart rate also can provide evidence of improvement or deterioration (4,6).

Frequent re-assessment is necessary to identify whether the infant is adequately transitioning or whether further interventions are needed.

Initial handling is an opportunity to stimulate the infant during assessment by drying the infant and gently stimulate it by rubbing the soles of the feet or the back of the chest (more aggressive methods of stimulation should be avoided).

ERC guidelines also suggest clamping the umbilical cord after at least 60 seconds to give time for the lungs to get aerated or, if it is not possible, to consider cord milking in infants >28 weeks gestation (5).

Based on the initial assessment, an infant can usually be placed into one of three transition groups, as shown in *Table I*:

Table I: Transition groups. From: Madar J et al., Resuscitation (2021).

Parameters	**Satisfactory transition**	**Incomplete transition**	**Poor/Failed transition**
Tone and color	Good tone	Reduced tone	Floppy ± Pale
Breathing	Vigorous breathing or crying	Breathing inadequately (or apnoeic)	Breathing inadequately or apnoeic
Heart rate	Fast (≥100/min)	Slow (<100/min)	Very slow (<60/min) or undetectable

Depending on the group, the caregiver's further actions should be:

- **In case of a satisfactory transition**:
    - Delay cord clamping of at least 60sec.
    - Dry and wrap in a warm towel.
    - Keep with mother or carer and ensure maintenance of temperature.
    - Consider early skin-to-skin care if stable.
- **In case of an incomplete transition**:
    - Delay cord clamping only if you are able to appropriately support the newborn.
    - Dry, stimulate, and wrap in a warm towel.
    - Maintain the airways, lung inflation and ventilation.
    - Continuously assess changes in heart rate and breathing.
    - If there is no improvement in heart rate, continue with ventilation.
    - Help may be required.
- **In case of poor/failed transition**:
    - Clamp the cord immediately and transfer to the resuscitation platform.
    - Dry, stimulate, and wrap in a warm towel.
    - Maintain the airway – lung inflation and ventilation.
    - Continuously assess heart rate, breathing, and effective ventilation.
    - Continue newborn life support according to response.
    - Help is likely to be required.
- **In the case of preterm infants**:
    - Apply the same principles as above.
    - Consider alternative/additional methods for thermal care (e.g. polyethylene wrap).
    - Gently support, initially with CPAP if breathing.
    - Consider continuous rather than intermittent monitoring (pulse oximetry ± ECG).

3.6. EQUIPMENT AND PERSONNEL NECESSARY IN NEONATAL RESUSCITATION

Although the need for resuscitation at birth often can be predicted by risk factors, for many infants resuscitation cannot be anticipated. Therefore, a clean and warm environment with a complete inventory of resuscitation equipment and drugs should be immediately available and in a fully operational condition wherever deliveries occur. An appropriate area for resuscitation of the newborn should also contain: infant resuscitaire with an inbuilt heater and light, or a firm, padder resuscitation surface and an overhead warmer; clock with time in seconds; good light in the area (6).

All the equipment must be regularly checked and ready for use and, where possible, it should be prepared in advance of the delivery of the infant or easily accessible (checklists and an adequate evaluation of the risk factors facilitate these tasks) (4). *Table II* presents a list of suggested neonatal supplies, medications, and equipment that should be present in the resuscitation area.

Standard precautions should be followed carefully in delivery areas, where exposure to blood and body fluids is likely. All fluids from patients should be treated as potentially infectious. Personnel should wear gloves and other appropriate protective barriers when handling newly born infants or contaminated equipment. Techniques involving mouth suction by the healthcare provider should not be used (6).

Personnel capable of initiating resuscitation should attend every delivery. At least 1 such person should be responsible solely for the care of the infant. A person capable of carrying out a complete resuscitation should be immediately available for normal low-risk deliveries and in attendance for all deliveries considered high-risk. More than 1 experienced person should attend an anticipated high-risk delivery. Resuscitation of a severely depressed newly born infant requires at least 2 persons, 1 to ventilate and intubate if necessary and another to monitor heart rate and perform chest compressions if required. A team of 3 or more persons with designated roles is highly desirable during an extensive resuscitation including medication administration. A separate team should be present for each infant born from multiple gestations. Each resuscitation team should have an identified leader, and all team members should have specifically defined roles (4–6).

Table II: Equipment available at every delivery. From: Sweet DG et al., Neonatology (2023).

Material classification	Equipment
Temperature maintenance	- Warmed towels or warm wraps - Woollen hats - Polyethylene bag or sheet for infants <1500 g birth weight
Medical gases	- A source of medical oxygen - A source of medical air - Oxygen and air flow meters allowing a flow rate of up to 10L/min - Oxygen and air tubing - Air/oxygen blender
Monitoring equipment	- Stethoscope - Pulse oximeter and neonatal probe - Psy to secure the oximeter sensor
Suction equipment	- Suction catheters: Fg from 6 up to 12 - Suction tubing - Access to a suction unit set at a negative pressure of 100mmHg
PPV equipment	- T-piece device or Flow inflating bag with a pressure safety valve and a manometer - Self-inflating bag with a removable oxygen reservoir - Face masks in an adequate range of sizes - Laryngeal mask airway - Oropharyngeal airways
Intubation equipment	- Laryngoscope - Endotracheal tubes - Endotracheal stylet or introducer - End tidal CO_2 detector - Meconium aspirator to apply suction directly to the endotracheal tube
Equipment for gastric decompression	- Feeding tubes - 10mL syringe for aspirating the gastric contents
Equipment for umbilical venous catheterization	- Umbilical catheters of different sizes
Equipment for peripheral intravenous cannulation or intra-osseus cannulation	- Intravenous cannula - Intra-osseus needle - Skin preparation solution - Three way tap and extension tubing

	- Arm board - Non-latex adhesive tape - Cotton or silk ties - Thin duoderm to protect the skin on the face - Scissors
Drugs and fluids	- Adrenaline 0,1 mg/mL - Volume expanders (0,9% sodium chloride and O Rh- blood) - Sterile water for injections

3.7. MOST COMMONLY USED VENTILATION INTERFACES AND INDICATIONS FOR THEIR USE

Most newborn infants who require positive-pressure ventilation (PPV) can be adequately ventilated with a facemask. Indications for PPV include apnoea or gasping, heart rate <100 bpm, and persistent central cyanosis despite 100% oxygen.

Although the pressure required for the establishment of air-breathing is variable and unpredictable, higher inflation pressures (30 to 40 cm H2O or higher) and longer inflation times may be required for the first breath (7). The assisted ventilation rate should be 40 to 60 breaths per minute (30 breaths per minute in case of chest compressions).

Signs of adequate ventilation include bilateral expansion of the lungs, as assessed by chest wall movement and breath sounds, and improvement in heart rate and color. Visible chest expansion is a more reliable sign of appropriate inflation pressures than any specific manometer reading.

In this context, the equipment of choice to ventilate the preterm consists mainly of two devices: the T-piece resuscitator and the ventilation bags (8).

If the ventilation is inadequate, it is mandatory to check the seal between mask and face, clear any airway obstruction (adjust head position, clear secretions, open the infant's mouth), and, finally, increase inflation pressure. If such maneuvers do not result in adequate ventilation, endotracheal intubation should follow.

After 30 seconds of adequate ventilation, spontaneous breathing and heart rate should be checked.

If spontaneous respirations are present and the heart rate is ≥100 bpm, PPV may be gradually reduced and discontinued.

If spontaneous respirations are inadequate or if the heart rate remains below 100 bpm, assisted ventilation must continue with a bag and mask, a laryngeal mask or a tracheal tube.

If the heart rate is <60 bpm, healthcare providers must continue assisted ventilation, begin chest compressions, and consider endotracheal intubation (6).

The key to successful neonatal resuscitation is the establishment of adequate ventilation. Reversal of hypoxia, acidosis, and bradycardia depends on adequate inflation of fluid-filled lungs with air or oxygen. Although 100% oxygen has been used traditionally for rapid reversal of hypoxia, there is biochemical evidence to argue for resuscitation with lower oxygen concentrations to prevent oxidative stress damage; so a lower percentage of O2 is preferable (9).

3.7.1. FACE MASKS

Face mask ventilation is the most important technique for initial resuscitation and stabilization of newly born infants because, even though most very preterm infants breathe at birth, this is often insufficient for adequate respiratory gas exchange, requiring infants to initially receive non-invasive ventilation (NIV). By applying positive pressure to the airway, NIV increases the surface area for gas exchange by promoting alveolar liquid absorption and preventing alveolar collapse at end-expiration (10).

Face mask ventilation aims are:

- To provide PPV for newborns who are apnoeic or have inadequate breathing.
- To facilitate the clearance of lung fluids, aerate the lungs, establish and maintain a functional residual capacity (FRC), and thereby ensure oxygenation as soon as possible after birth.

There are many shapes of masks: most are round with a cushioned rim; some are triangular, called ‘anatomically’ shaped masks; older designs have a flat, uncushioned rim (11). Round face masks are the most used (in 85% of the centres), anatomically shaped masks are used exclusively at 15% centres, and a mixture of types is used at 28%. Anyway, currently, there are no recommendations on which mask should be preferred for neonatal resuscitation (12,13).

For sure masks should have an appropriate size to seal around the mouth and nose but not cover the eyes or overlap the chin, so a range of sizes should be available.

Masks should be designed to have low dead space (<5 mL). A round mask can seal effectively on the face of a small infant; anatomically shaped masks better fit the contours of a large-term infant’s face; in any case, a mask with a cushioned rim is preferable to one without because the cushioned rim facilitates the creation of a tight seal without exerting excessive pressure on the face (7).

During mask ventilation of infants, obstruction can be caused by several factors including: liquid in the oropharynx, positioning of the head, neck and tongue or by pressing down on the mask too hard, leading to obstruction of the nose and mouth. Resuscitation staff should be aware of these causes and do their best to avoid them (14).

3.7.2. AIR CUSHION RIMS IN FACE MASKS

An airtight seal between the mask and the face is important for successful ventilation. Achieving an airtight seal can be difficult and most clinicians do not recognize leaks between the mask and the face (15,16).

Both round and anatomically shaped face masks have an air-filled rubber cushion rim to fit the face of a newborn infant properly and it can be filled or emptied by a valve on the upper rim of the mask. Although the anatomical shape mask provides a better seal leading to decreased pressure on the eyes, O'Donnell et al. found no difference in mask leak between the round and the anatomical mask with an air cushion rim in first-time users (17).

Noteworthy, the presence of a cushion rim is effective in reducing air leaks and pressure exercised on the face independently of the type of face mask (18).

There are several potential pitfalls when using anatomical masks:

- there is only one correct method to position the mask onto a newborn's face (false orientation may increase mask leak during PPV);
- the air-filled cushion rim can be filled with various amounts of air, which could potentially decrease the effectiveness of the mask seal;
- it is possible that the air-filled cushion rim could be perforated, resulting in an airless rim and altering the seal of the face mask (13).

3.7.3. VENTILATION BAGS

Ventilation bags for neonatal resuscitation are hand-driven pressure devices and they can be either:

- Self-inflating bags: refills independently of gas flow because of the recoil of the bag.
- Flow-inflating bags: inflates only when compressed gas is flowing into it and the patient outlet is at least partially occluded. For the correct use of a flow-inflating bag the adjustment of the flow of gas into the gas inlet, adjustment of the flow of gas out through the flow-control valve, and the creation of a tight seal between the mask and face are required. Even though a longer training is required for its proper use, it can provide a greater range of PIP and a more reliable control of O2 concentration.

The self-inflating bag is the most commonly used manual ventilation device while flow-inflating bags are less used (12).

Resuscitators must be aware that the manual squeezes of the bags lead to variable insufflation pressures and that prolonged bag-mask ventilation may produce gastric inflation; this should be relieved by insertion of an 8F orogastric tube that is aspirated with a syringe and left open to air. However, the use of ventilation bags increased awareness of changes in lung compliance during the dynamic resuscitation process and allowed for faster pressure adjustments (6,19).

Anyway, resuscitation bags used for neonates should be no larger than 750 mL; larger bag volumes make it difficult to judge the delivery of the small tidal volumes (5 to 8 mL/kg) required by newly born infants (6).

3.7.4. T-PIECE RESUSCITATOR

The T-piece resuscitator (TPR) is a mechanical device capable of automatically providing ventilation and its use as a primary resuscitation device with newborns is constantly increasing. Traditional TPR design uses a high-resistance expiratory valve to produce positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) at resuscitation, while most recent TPR devices use a dual flow ratio valve (fluidic flip) to produce PEEP/ CPAP (rPAP) (20).

TPR can have an incorporated spiral heater wire throughout the circuit tubing, designed to deliver warm, humidified gas, and its use is associated with a higher rate of normothermia (rectal temperature between 36.5 °C and 37.5 °C) on admission to the neonatal intensive care unit (21).

Compared to self-inflating bags (SIB), the TPRs provide more consistent inflation pressures and tidal volumes. However, the comparison with SIBs resulted in comparable SpO_2 at 5 min along with similar minute-specific SpO_2, HR, and FiO_2 trends and the use of a T-piece resuscitator did not show a statistically significant effect in pre-term or very-low birth weight infant short-term complications and mortality rates except for the incidence of bronchopulmonary dysplasia (19,22,23).

3.7.5. LARYNGEAL MASK AIRWAY VENTILATION

Even though the endotracheal tube is the most common alternative airway used during neonatal resuscitation when the face mask ventilation is not effective, in infants with birth weight over 1500 g and more than 34 weeks gestation, laryngeal mask airway (LMA), if used by appropriately trained providers, is more effective compared to bag and face mask for providing PPV (24).

LMA ventilation is even more effective than facemask ventilation in delivering PPV with lower failure rates and reduced need for intubation during neonatal resuscitation in term infants without any difference in the incidence of encephalopathy or death (25).

In studies that allowed LMA rescue of infants failing facemask ventilation, it was possible to avoid intubation in the majority, so it is important to use LMA more proactively to provide effective ventilation when a newborn is not responding to facemask ventilation before attempting endotracheal intubation or initiating chest compressions (5,26).

Furthermore, it is possible to perform a surfactant administration via LMA in preterm newborns with respiratory distress syndrome (RDS). As showed by Gallaup JA et al., surfactant therapy via LMA is non-inferior to surfactant administration via endotracheal tube and it is associated with a decrease in early failures, possibly by avoiding adverse effects of premedication, laryngoscopy, and intubation. These characteristics make the LMA a desirable conduit for surfactant administration (27).

3.7.6. ENDOTRACHEAL INTUBATION

Endotracheal intubation may be indicated at several points during neonatal resuscitation:

- When tracheal suctioning for meconium is required.
- If bag-mask ventilation is ineffective or prolonged.
- When chest compressions are performed.
- When tracheal administration of medications is desired.
- Special resuscitation circumstances, such as congenital diaphragmatic hernia or extremely low birth weight (6).

To perform endotracheal intubation it is preferred to use a videolaryngoscopy instead of a direct laryngoscopy; in fact, if used by medical staff with experience, there are no differences in terms of success, time to intubation, or perceived workload but it reduces the applied forces on the epiglottis (median force of 6.8N with direct laryngoscopy vs 2.1N with videolaryngoscopy) and possibly reduces local trauma, upper airway injuries and sympathetic activation (28,29). However, these results, demonstrated in neonatal manikins, need to be confirmed in neonates.

Preferred tracheal tubes should have a uniform diameter (without a shoulder) and have a natural curve, a radiopaque indicator line, and markings to indicate the appropriate depth of insertion. If a stylet is used, it must not protrude beyond the tip of the tube. The timing of endotracheal intubation also depends on the skill and experience of the resuscitator (6).

After endotracheal tube positioning, it is mandatory to confirm the correct position with the following interventions:

- Observing symmetrical chest-wall motion.
- Listening for equal breath sounds, especially in the axillae, and for the absence of breath sounds over the stomach.
- Confirming the absence of gastric inflation.
- Watching for a fog of moisture in the tube during exhalation.
- Noting improvement in heart rate, color, and activity of the infant.

An exhaled-CO_2 monitor may be used to verify tracheal tube placement. Monitoring of exhaled CO_2 can be useful in the secondary confirmation of tracheal intubation in the newly born, particularly when clinical assessment is equivocal (6).

3.8. COMPARISON OF AHA VS. ERC GUIDELINES FOR INITIAL VENTILATION PARAMETERS

Both AHA and ERC guidelines are valid, and they are the most widely adopted all around the world; the main differences in initial ventilation parameters are shown in *Table III*:

Table III: AHA vs ERC guidelines initial ventilation parameters. From: Aziz K et al., Circulation (2020) and Madar L et al, Resuscitation (2021).

Parameters	AHA	ERC
Initial Peak Inspiratory Pressure (PIP)	Term newborns: 25cmH_2O Preterm newborns: 20cmH_2O	Term newborns: 30cmH_2O Preterm newborns: 25cmH_2O
Initial sustained inflations	Not recommended	Begin ventilation with 5 sustained inflations (maintaining inflation pressure for 2-3 sec)
Positive End Expiratory Pressure (PEEP)	5cmH_2O	Minimum of 5-6cmH_2O
Respiratory Rate (RR)	40-60 breaths per minute	30 breaths per second

3.9. AIR LEAK IN FACE MASK VENTILATION AND TIPS TO REDUCE IT

Several things need to be known before using face masks:

- The mask must be the right size. It must extend from the chin tip and not encroach on the eyes. Therefore, one size will not fit all babies.
- There is little evidence that different-shaped masks are better than others at forming a seal on the face. However, a soft and flexible edge does help to form a seal. A firm top that does not indent when held on the face is preferable.
- More important than the shape is how it is used (11).

Mask ventilation is a difficult technique to master and ensure appropriate tidal volume delivery. The main problems are:

- Mask leak is very common and varies a lot during resuscitation.
- Masks are difficult to hold on the face in a way that ensures a leak-free seal.
- With a very large leak the tidal volume delivered may be too small.
- If there is little or no leak the tidal volumes may be dangerously large.
- Pushing the mask too hard with poor technique may obstruct gas flow.

Mask leaks are common and can lead to inadequate ventilation and failure of resuscitation. Manikin and observational delivery room studies, done with different masks and between professional categories, have shown that mask leaks vary widely during PPV, with mask leaks often exceeding 50% (11,16,30).

There are many different types of face masks and of mask holds; it has been proved that holding the mask stem between the index finger and thumb is least effective, as it is difficult to achieve a balanced downward pressure and jaw lift.

While with a Laerdal round mask, the ‘two-point top hold’, with good jaw lift, is most effective, the ‘OK rim hold’ is most effective with the Fisher and Paykel anatomical mask because this stabilized the pliable top (*Figs. 4 and 5*).

Of the mask techniques it has been found that the two-point top-hold is the single resuscitator technique that most reliably reduces mask leak and is the one that should be used as the force applied on newborns’ head is predominantly determined by the way the mask is held and not by the device used to administrate the inflations (14,30).

Figure 4: photographs of the three one-hand mask hold. From: Schmolzer GM et al., Arch Dis Child Fetal Neonatal (2011).

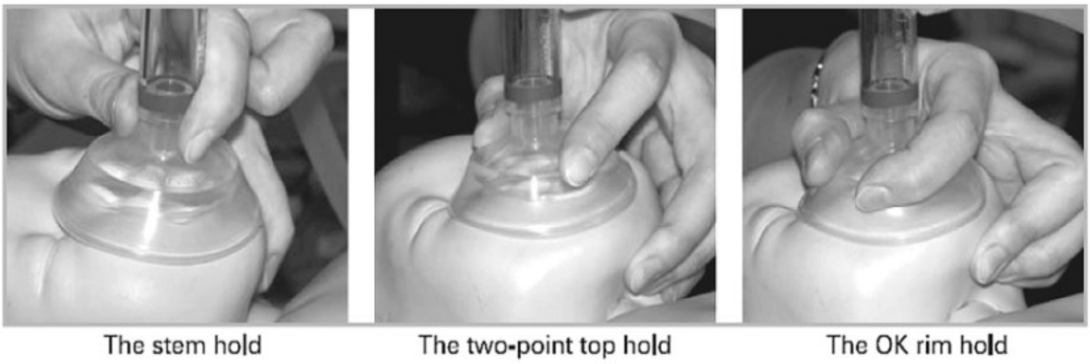
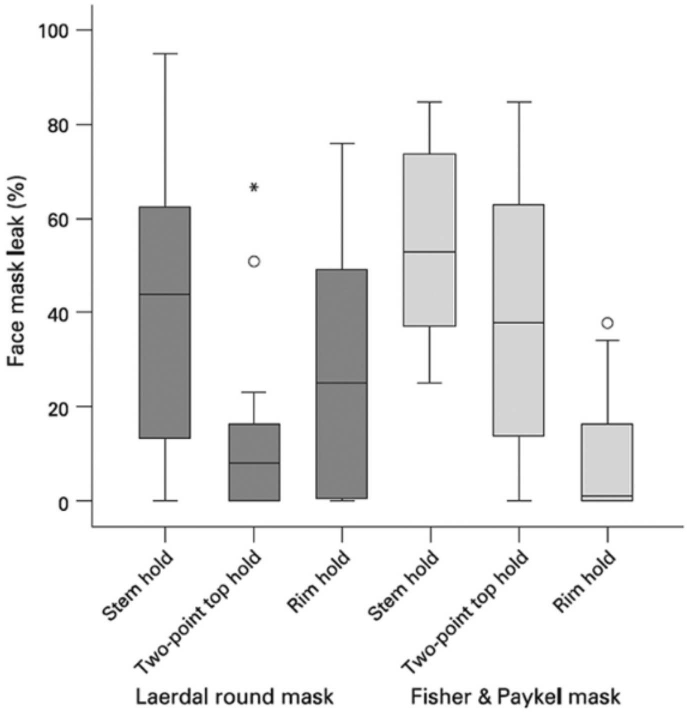


Figure 5: Percentage leak at the face mask for two face masks with three hold types. From: Schmolzer GM et al., Arch Dis Child Fetal Neonatal (2011).



Some tips to improve the mask seal and reduce air leaks are:

- Roll the mask onto the face rather than placing it straight down. This is done by positioning a finger on the baby's chin tip to align the mask edge ensuring that it is not extended beyond the chin, then gently rolling it upwards onto the face ensuring it is not encroaching on the eyes. A mask over the orbits will not seal well and may damage the eyes.

- Check that the mask is positioned evenly on the face when viewed from above and side, being upright and not tilted.
- For masks with a solid top, downward pressure must be applied evenly using an index finger and thumb, not touching the stem and not encroaching on the side of the mask. The index finger should be on the chin side. This is the ‘two-point top-hold’. The finger and thumb should apply a firm pressure on the mask to ensure that it is sealed on the face.
- If the mask has a flexible top, then holding this with the index finger and thumb encircling the top outside edge of the mask helps stabilize the top and apply even downward pressure. This is the ‘OK rim hold’.
- Fingers should not push on the skirt of the mask because this distorts it.
- The other fingers of the hand holding the mask should be placed under the jaw on that side to apply jaw lift; drawing the face upwards into the mask with a pressure equal to the downward force being applied.

There are several other techniques to apply a mask. However, the only one that reliably minimizes leaks is the two-handed technique. This is similar to the two-point top-hold, with equal downward pressure on the top of the mask from the index fingers and thumbs with good jaw lift, but two hands are used, so it needs a person responsible only for the ventilation (30).

3.10. TRIGEMINAL-CARDIAC REFLEX (TCR)

The trigeminal-cardiac reflex (TCR) is a brainstem reflex that has been demonstrated both experimentally and clinically. This reflex has been defined from a clinical point of view as hypotension with a 20% drop in mean arterial blood pressure and bradycardia lower than 60 beats/min in response to surgical manipulation of the trigeminal nerve trunk or disturbances in the territory of one of its branches, including autonomic symptoms such as a decrease in cardiovascular function lower than 20%. In severe instances, this response can sometimes lead to asystole.

It can be classified into two subtypes, depending on which sensory territory is stimulated: the central TCR (ganglion to nucleus) and the peripheral TCR (peripheral divisions to ganglion) (10,31).

This trigeminal response is often referred to as the diving reflex, which is one of the three peripheral subtypes of the TCR. The diving reflex covers the first branch of the trigeminal nerve and can be stimulated mainly by cold air or water to the infant's face. Two other TCR subtypes are the oculocardiac reflex, which can be stimulated by pressure on the eye globe, and the maxilla-mandibular/nasopharyngeal reflex induced by pressure on the second and third branches (32,33).

The peripheral TCR is an oxygen-preserving brainstem reflex, which can be activated by stimulating at least one of the three branches of the trigeminal nerve. The intensity of the TCR depends on the type (pressure, thermic or nociceptive, duration, intensity and localization) of the trigeminal stimuli. During activation of the peripheral TCR there is a strong synergistic co-activation of the parasympathetic and sympathetic system resulting in closure of the larynx which will tend to avoid aspiration, a reduction of heart rate thereby lessening oxygen consumption, and peripheral vasoconstriction which should preserve cerebral blood flow and delay the progression of asphyxia, and gastric hypermobility (32,34,35).

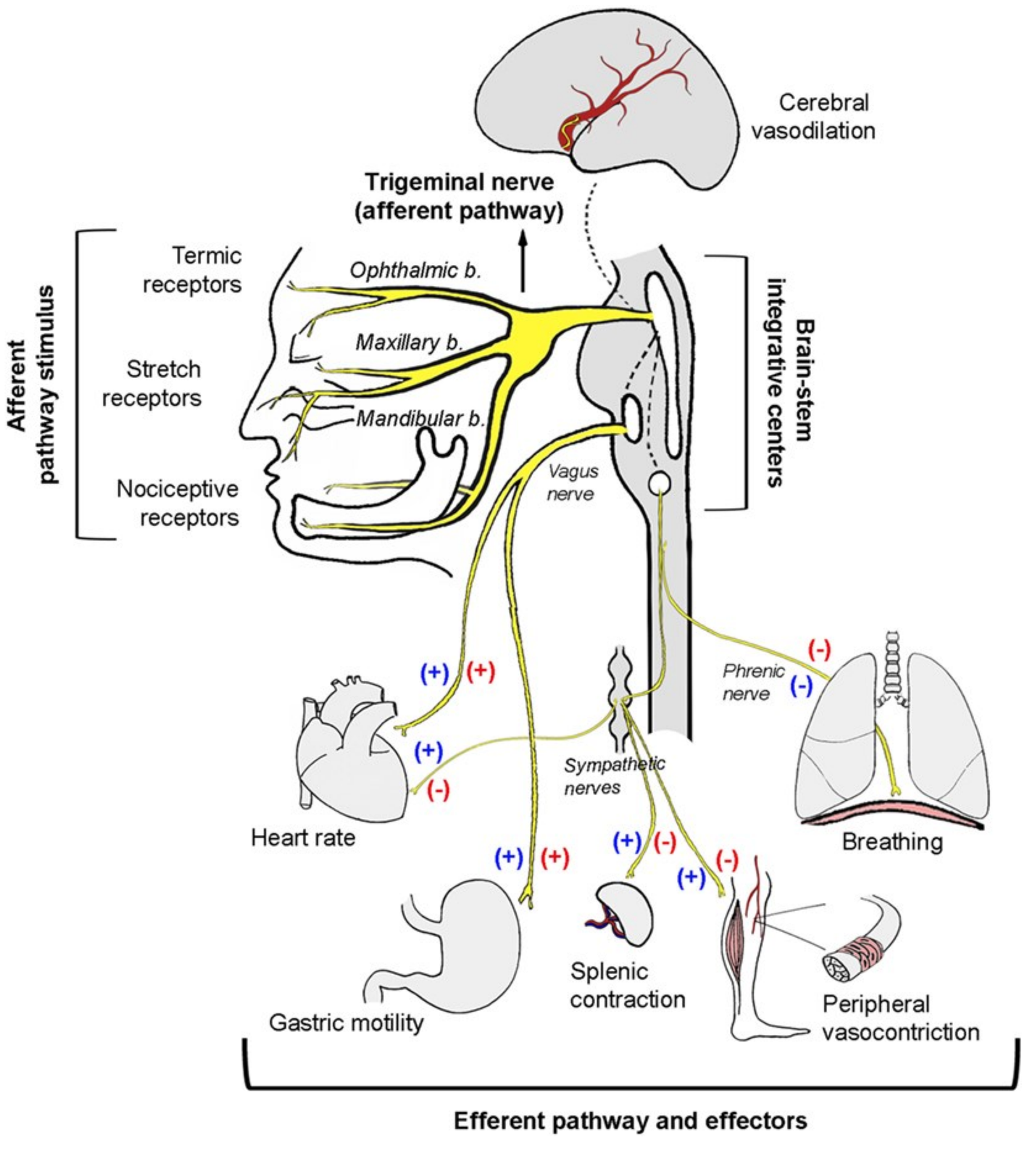
It has also been demonstrated that, in TCR, hypotension is independent of heart rate reduction and occurs as a result of vasodilation induced by the sustained decrease in peripheral vascular sympathetic tone. In contrast, heart rate reduction occurs via a combination of parasympathetic activation and sympathetic inhibition (31).

You can see the effects of the trigeminal reflex subtypes in *Table IV* and a scheme of the neural pathways is shown in *Figure 6*.

Table IV: Summary of the characteristics of the trigeminal reflex subtypes. From: Buchholz B et al., Neurol (2017).

Trigeminal reflex	Triggered by	Efferent pathway	Arterial pressure	Heart rate	Gastric motility	Splenic contraction	Peripheral vascular tone	Breathing
Trigeminocardiac reflex	Direct stimulation of the trigeminal nerve	Parasympathetic ↑ Sympathetic ↓	↓	↓	↑	?	↓	Apnea
Diving reflex	Thermoreceptors in the facial skin	Parasympathetic ↑ Sympathetic ↑	↑	↓	–	↑	↑	Apnea
Nasopharyngeal reflex	Nasal mucosa irritation	Parasympathetic ↑ Sympathetic ↑	=	↓	–	↑	↑	Apnea
Oculocardiac reflex	Physical stimulation of the eye or adnexa	Parasympathetic ↑ Sympathetic ↑	↓	↓	↑	?	↓	Apnea

Figure 6: Schematic illustration of the autonomic neural pathways and effectors activated as a consequence of trigeminal nerve stimulation. Protection reflexes like the diving, the nasopharyngeal, or the oculocardiac reflex involve simultaneous co-activation of both autonomic limbs (blue symbols). The trigeminocardiac reflex induces a strong depressor response by a reciprocal activation of the parasympathetic system and an inhibition of the sympathetic system (red symbols). From: Buchholz B et al., Neurol (2017).



Heart rate (HR) is regarded as the most important marker of infant well-being after birth and it is a major determinant of cardiac output; as newborn resuscitation algorithms recommend maintaining HR >100-120 bpm in newborns, bradycardia induced by the activation of the TCR could change the behavior of the resuscitation personnel (36,37).

3.11. FACE MASK VENTILATION AS A TRIGGER FOR TRIGEMINAL-CARDIAC REFLEX

As we already said, depending on which branch of the trigeminal nerve is stimulated, we can identify three peripheral subtypes of TCR: the diving reflex (depending on stimulation on the first branch), the oculocardiac reflex (stimulated by pressure on the eye globe) and the maxilla-mandibular/nasopharyngeal reflex (covered by second and third branches). As the face mask is placed over the mouth and nose covering all three branches of the trigeminal nerve, we will refer to the effect of the facemask as the peripheral TCR in general.

NIV strategies are universally adopted as the first choice for respiratory support at birth, but their effect on breathing is unclear.

The application of NIV may have a variable response: by improving oxygenation, it could stimulate breathing, but it could also induce vagally mediated reflexes, such as TCR, that inhibit spontaneous breathing at birth.

PPV requires a careful balance of applied force on the face mask to provide enough pressure to form a tight seal for air flow without delivering too much pressure that could activate the cutaneous stretch receptors of the trigeminal nerve, triggering the TCR and leading to apnoea and a decrease in heart rate or even injure the infant (12,31,32).

3.11.1. FACE MASK VENTILATION AS A TRIGGER FOR TRIGEMINAL-CARDIAC REFLEX IN PRETERM INFANTS

As neural circuits are more immature in preterm infants, the breathing responses to different types of stimuli are unclear. The effects of applying a face mask in newborns have been studied in several studies and their results suggest that the face mask could trigger the TCR thereby compromising the capacity of infants to breathe and contribute to their own pulmonary ventilation, increasing the necessity of applying PPV (10,32,33).

In these studies, it has been proved that facemask respiratory support is temporally associated with a clinically important decrease in HR in newborns the decrease in HR occurs rapidly (within 15 s), but in some cases, it occurs up to 120 s after the initiation of respiratory support. This highlights the high degree of variation between individuals in response to facemask application, which likely indicates that the underpinning physiology is multifactorial and may depend on the physiological state of the infant when the facemask is applied (36,38).

In fact, even though only 24% of term infants had a reduction in breathing rate, (studies reported a change in breathing pattern with an increased tidal volume and decreased breathing rate after application of just the face mask rim, which persisted for at least 5min and returned to control values after removing the rim (32)), a larger proportion of preterm infants (54%) were affected as they stopped breathing after applying the face mask and they had a lower heart rate as well; this confirms that the occurrence of apnoea after face mask application is inversely associated with gestational age (10,36,39).

Recent studies also discovered that apnoea and bradycardia occurred more often after initial compared with subsequent mask applications in preterm infants, which may result from sensory adaptation of the trigeminal receptors (39,40).

Because of its propensity to stimulate this reflex, a face mask might not be the best interface for applying respiratory support in preterm infants at birth. It is currently unknown whether other interfaces, such as prongs, might be a good alternative for avoiding the TCR (10).

3.12. CORRELATION BETWEEN FORCES APPLIED ON NEWBORN'S FACE AND THE TRIGEMINAL-CARDIAC REFLEX

There might be a threshold to exceed for provoking the peripheral TCR as applying a lightweight cardboard ring does not have similar effects as compared with a face mask rim in terms of association with apnoea and bradycardia (32).

However, as infants with lower gestational age, lower heart rates, and lower oxygen saturations have an higher risk of apnoea, this reflex is clearly modified by other factors as well. Caregivers should be vigilant in applying a face mask and be aware that the amount of force exerted on it may compromise the breathing they intend to support (10).

While investigating mask ventilation techniques it turned out that the resuscitator applied high forces on the mask as a corrective action to reduce mask leak.

As it has been proved there is no correlation between mask leak and the force used to correct it (even with different types of devices), personnel should use the minimum force able to seal the mask and, in case of the presence of any leak, they should correct the position of the mask rather than apply more force on the infant's face (14).

To prevent the excess of force applied on the newborn face during PPV with a facemask, a live feedback interface showing the pressure applied on the face mask during training and real-life resuscitation could be useful (41).

4. OBJECTIVE

PPV using a facemask is recommended as the first and most effective approach for neonatal resuscitation in newborns with respiratory disease or bradycardia and it is necessary for the 5-10% of all deliveries. If this technique isn't effective, we must use more invasive techniques such as the laryngeal mask or the endotracheal intubation (4,5).

All the face masks used nowadays for resuscitation, although their form can change depending on the model, have an inbuilt cushion rim that can be filled with different amounts of air to seal air leaks better and permit ventilation properly. Still, there isn't any guideline indicating the best level of inflation to use; we only know, as Deindl et al. proved, that an empty cushion rim causes excessive leaks and should not be used, while other volumes don't have significant differences in terms of leaks (13).

It has been demonstrated that the forces applied on the newborn's face during mask ventilation have a wide heterogeneity among different health caregivers and that an excessive force can trigger the trigeminal-cardiac reflex (TCR), a vagally-mediated reflex that can lead to bradycardia and apnoea. With its activation the assessment of the infant's transition could drastically change, leading to the necessity to start more invasive procedures to stabilize the newborn and the risk of causing complications (12,14).

Knowing these notions, we hypothesized that healthcare providers could exert different forces on the newborn's TCR trigger points (nasal bridge, mentum, and left and right zygomatic arch) to improve mask seal if they use different air cushion volumes. This trial may give us some indication about the best cuff inflation level to reduce the incidence of the activation of the TCR and give newborns a safer reanimation process.

In this study, twenty-eight trained residents and consultants from the neonatal intensive care unit of the Hospital of Padua were asked to perform one minute of face mask PPV on a modified manikin with a medium-filled mask (filled with 25mL of air) and a fully inflated mask (35mL). Participants could verify the correctness of the maneuver solely through visual confirmation of the manikin's chest movements and by monitoring the parameters visible on the manometer on the Neopuff T-piece, replicating the same conditions of a real-life resuscitation.

The objective of the study is to verify the amount of force applied on newborns' face during PPV using different cuff volumes in order to discover if there is an ideal cuff volume that permits obtaining an adequate PPV with an anatomical facemask while concurrently minimizing the force applied on the TCR key points of the manikin’s face to reduce the risk of its stimulation.

The Primary outcome of this trial is to measure the forces applied by the participants to the manikin face trigger points during PPV.

Secondary outcomes are the overall cuff pressure, the percentage of ventilation time with leak lower than 25% around the mask, and the participant’s subjective opinion about the difficulty in providing effective ventilation, the fatigue in obtaining a good mask seal and the overall satisfaction about the mask seal during the ventilation.

5. METHODS

5.1. ABBREVIATIONS

- AHA: American Heart Association.
- ERC: European Resuscitation Council.
- NRP: Neonatal Resuscitation Program.
- NIV: Non-invasive ventilation.
- PPV: Positive pressure ventilation.
- RFM: Respiratory function monitor.
- PIP: Peak inspiratory pressure.
- PEEP: Peak expiratory pressure.
- RR: Respiratory rate.
- VTi: Inspired tidal volume.
- VTe: Expired tidal volume.
- IW: Infant warmer.
- HR: Heart rate.

5.2. SETTING AND PARTICIPANTS

The current research was carried out in the Neonatal Intensive Care Unit of the Woman and Child Health department of Padova University Hospital. Padova University Hospital is a tertiary perinatal center, overseeing approximately 3000 deliveries and admits nearly 100 preterm infants weighing less than 1500 g annually.

Paediatrics Residents during their Neonatology rotation and Neonatology Consultants were invited to participate in the study. All participants had received prior training in neonatal resuscitation and mask ventilation techniques.

5.3. STUDY DESIGN

The study was a randomized controlled crossover (AB/BA) trial of mask ventilation with two different levels of mask cuffing performed by trained pediatrics residents, consultants, and anesthetists on a modified air leak-free newborn Anne manikin.

5.4. INCLUSION AND EXCLUSION CRITERIA

Eligible participants for this study were level III neonatal intensive care unit consultants and residents. There were no exclusion criteria for this study, besides their refusal to participate.

5.5. RANDOMIZATION

Participants were randomly assigned to AB or BA arms in a 1:1 ratio. Randomization was performed using a computer-generated random assignment list. Arm assignments were included in sealed opaque envelopes sequentially numbered.

5.6. VENTILATION DEVICE

Positive pressure ventilation was provided with a T-piece resuscitator (Neopuff; Fisher & Paykel Healthcare, Auckland, New-Zealand) and the following parameters were set:

- Gas flow of 10 L/min;
- Peak Inspiratory Pressure (PIP) 25 cmH2O;
- Positive End Expiratory Pressure (PEEP) 5 cmH2O.

PIP and PEEP were set in accordance with the AHA NRP guidelines (4).

5.7. INFANT WARMER

For this study, we used an ATOM Infa Warmer infant warmer (Atom Medical Corporation, Stoke on Trent, Cheshire, UK) with its height set to have the infant's head at the level of the participant's superior anterior iliac spines as it is the most common height used in neonatal reanimation procedures.

5.8. MODIFIED MANIKIN

A Laerdal Newborn Anne manikin (Laerdal, Stavanger, Norway) was modified to be able to objectively detect chest motion and to measure the forces applied to the manikin face during PPV.

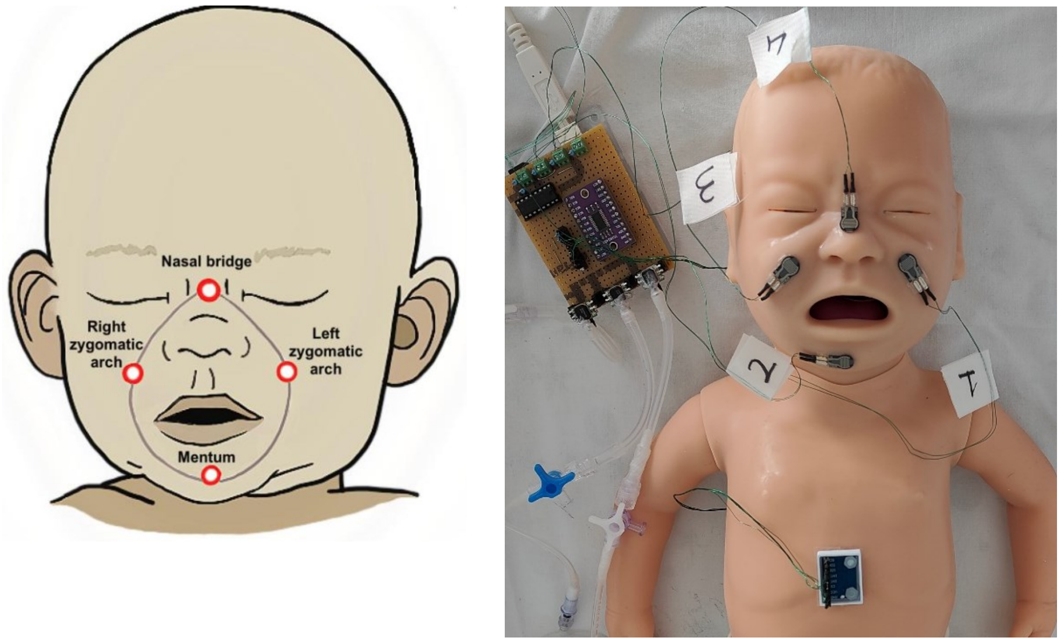
Chest motion was objectively assessed using an accelerometer (ADXL345, JinZhiKu Electronic Co., China), and the forces exerted by the mask on the manikin face were measured using four force sensors (FSR 400 short, Interlink Electronics, USA).

The accelerometer was placed in the lower region of the manikin sternum, where the maximum chest excursion was visible.

The force sensors were placed in correspondence with the nose bridge, chin, and the left and right cheekbones of the manikin as shown in *Figure 7*. These regions were selected as the points where the mask was more likely to stimulate the trigeminal nerve during ventilation.

All sensor data were collected by the Arduino Uno board (Arduino, Italy) and displayed and saved through an ad hoc user interface programmed using LabView software (NI, USA).

Figure 7: Position of the force sensors. From: Hannan J et al., Proc Hum Factors Ergon Soc Annu Meet (2022).



5.9. FACE MASK

Two cuffed resuscitation masks size 1 (GIMA, Gessate, Italy) were modified to continuously measure the pressure inside the mask cushion. The valve of the cushion was kept open by an ad hoc connector and interfaced with a three-way stopcock (Delta Med, Italy). The second outlet of the stopcock was left unconnected, and the third outlet was connected to a differential pressure sensor (ABP2MRRT005PD2A3XX, Honeywell, USA). Through the unconnected outlet of the stopcock, one of the two cuffed masks was inflated with 25 ml and the other with 35 ml of air. The 35 ml of air corresponds to the cushion inflation grade at which the mask is sold.

From now, the first mask will be called the medium mask and the second will be called the filled mask.

5.10. RESPIRATORY FUNCTION MONITORING (RFM)

The RFM was the ALD resuscitation monitor (Advanced Life Diagnostics, Weener, Germany). This monitor contained Polybench software (Advanced Life Diagnostics, Weener, Germany) which digitized and recorded at 200 Hz all signals from the New Life Box (NLB) physiological recording system (Advanced Life Diagnostics, Weener, Germany). The NLB utilizes a dead space (1 mL) variable orifice anemometer (AveaVarflex Flow Transducer, Carefusion, Yorba Linda, CA, USA) to measure circuit pressure and gas flow in and out of a T-piece.

The monitor displays the following parameters: PIP, PEEP, flow, VTi, VTe, and mask leak ([VTi-VTE]/VTi).

5.11. TASK

Participants were asked to provide 2 sessions of 1 minute each of positive pressure ventilation to a newborn manikin with the medium and the full masks; participants in AB arm were assigned to perform ventilation with the medium mask, followed by ventilation with the filled mask. Participants in the BA arm were assigned to the reverse sequence.

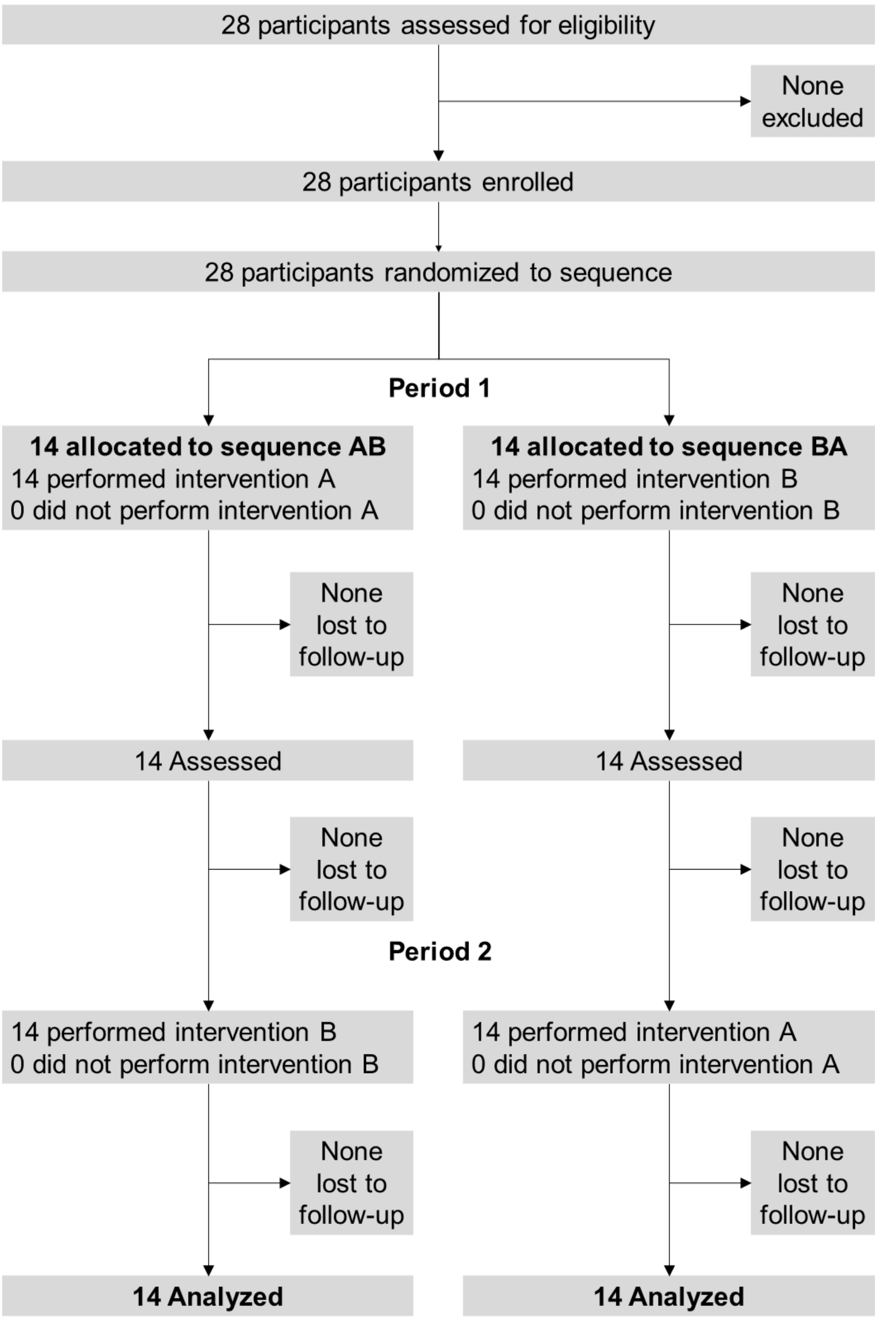
The infant warmer height was set to position the infant's head at the level of the participant's superior anterior iliac spines.

Participants were asked to perform ventilation with parameters in accordance with AHA NRP guidelines for term newborns (PIP 25 cmH2O, PEEP 5 cmH2O, RR 40-60 bpm), administrating PPV by placing the manikin head in a neutral position and providing face mask ventilation using the "two-point top hold" method. Ventilatory performance was assessed and recorded using the ALD resuscitation monitor. Cuff pressure and the forces applied on the manikin's face were also displayed and recorded.

Participants were blinded to both the RFM and force data and were asked to assess ventilation efficacy through visual confirmation of chest movement and by looking at the manometer on the Neopuff T-piece; they were allowed to perform corrective maneuvers if ventilation was ineffective.

Before the simulation started, all participants were given time to familiarize themselves with the equipment. Between each minute of mask PPV, participants were allowed to rest for two minutes to reduce the possibility of fatigue. After each ventilation session, participants were asked to grade three specific aspects of the procedure on a Likert scale: difficulty in providing effective ventilation, difficulty in providing a good mask seal, and satisfaction for the mask seal.

Figure 8: Diagram of the study design.



5.12. SAMPLE SIZE

As we were unable to predict the magnitude of the difference in forces applied with the devices, a formal sample size calculation could not be performed during study planning and a convenience sample size of 28 participants was chosen for the trial.

5.13. RECRUITMENT

A proficient professional trained in neonatal resuscitation provided the participants with written and oral information, and all participants gave consent for the use of the data.

5.14. BLINDING

Due to the characteristics of the interventions, neither caregivers nor outcome assessors were blinded to treatment allocation. However, the statistician performing data analysis was masked to treatment allocation.

5.15. DATA COLLECTION

Information on participants (age, level of experience), randomization sequence and outcome measures were collected by an observer who was not involved in the simulation.

Data were recorded in a data sheet designed for this study and maintained in order to protect confidentiality before, during and after the trial by the principal investigator in a personal computer protected by password. All data were collected by an observer not involved in the simulation.

The following information were registered in a Case Report Form:

- participant age
- years of NICU experience
- number of mask PPV/year and PPV/life.

6. STATISTICAL ANALYSIS

A formal sample size calculation could not be performed a priori because we could not predict the magnitude of the difference in applied forces, therefore a convenience sample size of 28 participants was chosen for the trial.

In the analysis of cuff pressure and applied forces, 50th percentile (median) and top 10th percentile were calculated as relevant indicators of peak pressure/force, average pressure/force, and standard deviation of pressure/force, while median and top 10th percentile of the paired differences between two groups were used for comparisons. The top 10th percentile difference in forces was chosen to assess the maximum difference in pressure/forces.

In the analysis of the percentage of leak <25%, the 50th percentile (median) was calculated as a relevant indicator, while the median of the paired differences between the two groups was used for comparisons. The analysis of participant's opinions was performed similarly.

Bootstrap confidence intervals (CI) were calculated for percentiles and differences, and any CI for the difference not including zero suggested a statistically significant difference.

Because of the coverage error of bootstrap CIs for percentiles in small-sized samples, empirical bootstrap 99% CIs were calculated using re-sampling with replacement to create 1,000 samples of the same size as the original. (29)

Statistical analysis was performed using R 4.3 (R Foundation for Statistical Computing, Vienna, Austria) (42).

7. RESULTS

The study included 28 participants (13 NICU consultants and 15 pediatric residents) with a median age of 32 years (IQR 30-37).

In the previous 12 months, 12 participants had performed more than 20 face mask ventilations, 10 participants had performed 5-20 face mask ventilations and six participants had performed less than five face mask ventilations.

Complete data were obtained for all participants using the partially and the fully inflated masks. All participants performed the allocated procedure and there was no loss to follow-up.

Tables V, VI, VII, and *VIII* summarize the forces applied by the participants during the procedures.

No one of the four face sensors registered a median significant difference in terms of peak, average, or standard deviation.

The left cheekbone sensor recorded a higher top 10th percentile of average applied forces with the partially inflated mask compared to the fully inflated mask (*Tab. V*).

The chin sensor recorded a higher top 10th percentile of applied forces in all the parameters studied (peak, average and standard deviation) with the partially vs. the fully inflated mask (*Tab. VI*).

The right cheekbone sensor recorded a higher top 10th percentile of applied forces in the average and standard deviation parameters with the partially vs. the fully inflated mask (*Tab. VII*).

No statistically significant differences were recorded by the nose bridge sensor (*Tab. VIII*).

Table IX shows the cuff pressures during the procedures. Median and top 10th percentile of all the cuff pressure indicators (peak, average and standard deviation) were significantly higher with the partially inflated mask.

Chest raise was obtained by 28/28 participants (100%) using the partially inflated mask and 25/28 participants (89%) using the fully inflated mask ($p=0.25$). The median difference in the percentage of ventilation time with a leak of less than

25% around the mask was not statistically different between partially and fully inflated masks (*Tab. X*).

Participants' subjective opinions about the difficulty in providing effective ventilation, fatigue in obtaining a good mask seal, and satisfaction about the mask seal were not statistically different between the partially and the fully inflated masks (*Tab. XI*).

Table V: Primary outcome measures: forces applied by the participants to the left cheekbone sensor during PPV.

Area	Outcome	Percentile	Partially inflated mask (A)	Fully inflated mask (B)	Paired difference (A-B)
Left cheekbone sensor	Peak	Median (bootstrap 99% CI)	0.67 (0.51 to 0.84)	0.61 (0.35 to 0.78)	0.03 (-0.15 to 0.18)
		Top 10th percentile (bootstrap 99% CI)	1.05 (0.81 to 2.35)	1.03 (0.80 to 2.28)	0.46 (-0.31 to 0.74)
	Average	Median (bootstrap 99% CI)	0.31 (0.20 to 0.48)	0.23 (0.01 to 0.34)	0.03 (-0.05 to 0.15)
		Top 10th percentile (bootstrap 99% CI)	0.53 (0.38 to 0.67)	0.58 (0.26 to 0.79)	**0.34 (0.14 to 0.57)**
	Standard deviation	Median (bootstrap 99% CI)	0.19 (0.14 to 0.24)	0.16 (0.07 to 0.20)	0.01 (-0.02 to 0.09)
		Top 10th percentile (bootstrap 99% CI)	0.29 (0.07 to 0.41)	0.29 (0.18 to 0.37)	0.13 (-0.03 to 0.21)

Any confidence interval (CI) for the difference between forces not including zero indicated a statistically significant difference.

Table VI: Primary outcome measures: forces applied by the participants to the chin sensor during PPV.

Area	Outcome	Percentile	Partially inflated mask (A)	Fully inflated mask (B)	Paired difference (A-B)
Chin sensor	Peak	Median (bootstrap 99% CI)	0.58 (0.31 to 0.80)	0.56 (0.37 to 0.73)	-0.01 (-0.39 to 0.28)
		Top 10th percentile (bootstrap 99% CI)	1.04 (0.59 to 1.39)	1.56 (0.88 to 2.50)	**0.53 (0.03 to 1.02)**
	Average	Median (bootstrap 99% CI)	0.17 (0.05 to 0.25)	0.10 (-0.17 to 0.19)	0.03 (-0.11 to 0.22)
		Top 10th percentile (bootstrap 99% CI)	0.35 (0.09 to 0.49)	0.56 (0.35 to 0.85)	**0.18 (0.07 to 0.30)**
	Standard deviation	Median (bootstrap 99% CI)	0.14 (0.11 to 0.22)	0.11 (0.00 to 0.15)	0.01 (-0.07 to 0.09)
		Top 10th percentile (bootstrap 99% CI)	0.26 (0.20 to 0.36)	0.28 (0.18 to 0.39)	**0.12 (0.04 to 0.20)**

Any confidence interval (CI) for the difference between forces not including zero indicated a statistically significant difference.

Table VII: Primary outcome measures: forces applied by the participants to the right cheekbone sensor during PPV.

Area	Outcome	Percentile	Partially inflated mask (A)	Fully inflated mask (B)	Paired difference (A-B)
Right cheekbone sensor	Peak	Median (bootstrap 99% CI)	0.59 (0.39 to 0.77)	0.68 (0.55 to 0.95)	-0.11 (-0.23 to 0.00)
		Top 10th percentile (bootstrap 99% CI)	0.97 (0.31 to 1.23)	1.02 (0.00 to 1.24)	0.18 (-0.02 to 0.39)
	Average	Median (bootstrap 99% CI)	0.28 (0.20 to 0.33)	0.35 (0.25 to 0.62)	-0.03 (-0.16 to 0.14)
		Top 10th percentile (bootstrap 99% CI)	0.45 (0.32 to 0.57)	0.62 (0.42 to 0.80)	**0.17 (0.07 to 0.34)**
	Standard deviation	Median (bootstrap 99% CI)	0.14 (0.05 to 0.19)	0.19 (0.15 to 0.230)	-0.03 (-0.04 to 0.03)
		Top 10th percentile (bootstrap 99% CI)	0.31 (0.28 to 0.42)	0.27 (0.16 to 0.32)	**0.08 (0.04 to 0.16)**

Any confidence interval (CI) for the difference between forces not including zero indicated a statistically significant difference.

Table VIII: Primary outcome measures: forces applied by the participants to the nose bridge sensor during PPV.

Area	Outcome	Percentile	Partially inflated mask (A)	Fully inflated mask (B)	Paired difference (A-B)
Nose bridge sensor	Peak	Median (bootstrap 99% CI)	0.39 (0.13 to 0.58)	0.46 (0.28 to 0.64)	-0.07 (-0.24 to 0.11)
		Top 10th percentile (bootstrap 99% CI)	0.79 (0.68 to 1.09)	0.71 (0.61 to 0.86)	0.35 (-0.09 to 0.67)
	Average	Median (bootstrap 99% CI)	0.12 (0.00 to 0.20)	0.20 (0.05 to 0.37)	-0.06 (-0.18 to 0.12)
		Top 10th percentile (bootstrap 99% CI)	0.32 (0.14 to 0.51)	0.40 (0.23 to 0.57)	0.12 (-0.03 to 0.26)
	Standard deviation	Median (bootstrap 99% CI)	0.10 (0.02 to 0.15)	0.15 (0.09 to 0.23)	-0.04 (-0.11 to 0.01)
		Top 10th percentile (bootstrap 99% CI)	0.23 (0.15 to 0.32)	0.21 (0.20 to 0.26)	0.08 (-0.03 to 0.25)

Any confidence interval (CI) for the difference between forces not including zero indicated a statistically significant difference.

Table IX: Secondary outcome measure: cuff pressure (cmH_2O).

Outcome	Percentile	Partially inflated mask (A)	Fully inflated mask (B)	Paired difference (A-B)
Peak	Median (bootstrap 99% CI)	171 (125 to 193)	110 (82 to 121)	**50 (28 to 60)**
	Top 10th percentile (bootstrap 99% CI)	257 (221 to 309)	187 (168 to 237)	**89 (23 to 112)**
Average	Median (bootstrap 99% CI)	101 (88 to 121)	62 (50 to 75)	**38 (32 to 44)**
	Top 10th percentile (bootstrap 99% CI)	133 (118 to 156)	94 (66 to 117)	**55 (50 to 66)**
Standard deviation	Median (bootstrap 99% CI)	43 (28 to 52)	29 (21 to 36)	**13 (8 to 17)**
	Top 10th percentile (bootstrap 99% CI)	71 (41 to 87)	49 (34 to 64)	**35 (24 to 53)**

Any confidence interval (CI) for the difference between forces not including zero indicated a statistically significant difference.

Table X: Secondary outcome measure: percentage of ventilation time with leak less than 25% around the mask.

Outcome	Percentile	Partially inflated mask (A)	Fully inflated mask (B)	Paired difference (A-B)
Percentage of ventilation time with leak less than 25% around the mask	Median (bootstrap 99% CI)	85 (26 to 100)	44 (18 to 99)	0.5 (-5 to 22)

Any confidence interval (CI) for the difference between forces not including zero indicated a statistically significant difference.

Table XI: Secondary outcome measure: participants' opinions (Likert scale from 1 lowest grade to 5 highest grade).

Outcome	Percentile	Partially inflated mask (A)	Fully inflated mask (B)	Paired difference (A-B)
Difficulty in providing effective ventilation	Median (bootstrap 99% CI)	2 (1 to 3)	2 (2 to 3)	0 (0 to 1)
Fatigue in obtaining a good mask seal	Median (bootstrap 99% CI)	2 (1 to 3)	2 (2 to 3)	0 (-1 to 0)
Satisfaction about the mask seal	Median (bootstrap 99% CI)	3 (2 to 3)	3.5 (3 to 4)	0 (0 to 1)

Any confidence interval (CI) for the difference between forces not including zero indicated a statistically significant difference.

8. DISCUSSION

Our trial compared the use of partially inflated (25 ml) and fully inflated (35 ml) face masks during PPV in a neonatal manikin. The underlying hypothesis was that healthcare providers could exert different forces on a newborn's face to improve mask seal when using different air cushion volumes.

There is increasing interest in understanding the forces applied to the newborn's face during mask ventilation because higher forces have been associated with an increased likelihood of apnoea and bradycardia via the stimulation of the TCR (38). In 2012, van Vonderen et al. highlighted that large forces are exerted on a neonatal manikin head during mask ventilation, with a wide heterogeneity among different health caregivers (14). Recently, Hanna et al. found that applied forces in key locations (nasal bridge, mentum, and left and right zygomatic arch) on a neonatal manikin face during facemask PPV are different, probably depending on the facemask holding technique (12).

In our trial, we measured the applied forces in those key locations but added the comparison of different air cushion volumes of the mask. Our findings showed that using a partially inflated face mask led to higher maximum applied forces to the manikin face compared to a fully inflated face mask. Interestingly, this difference was noted in the chin and cheekbones sensors, but not in the nose bridge sensor. We can speculate that this variation may be attributed to the mask holding technique or because, as the nasal bridge is a less pronounced feature on the manikin face and the cushion is deformable, a lower portion of the forces are applied to this area.

It is important to note that the magnitude of unsafe applied forces during PPV is still unknown, despite a previous study proposing a maximum of 4N of overall force applied on the manikin's face as a target to obtain to perform a low leak-low forces ventilation. The problem with this porpoise is that in this study the overall pressure was evaluated with a small sensor under the manikin's head, but it is important to note that the forces vary depending on the sensor's position and area and currently there isn't a standard way to measure these forces (12).

Applying different forces on the face mask can result in varying pressures in the mask cuff. In our trial cuff pressure was higher when the participants used the partially inflated face mask, in agreement with the higher applied forces on the manikin face when using that mask. This finding was in contrast to our expected result of observing lower force values at each location on the face with the partially inflated mask. In fact the applied forces generate an increased pressure within the bladder, which increases tension in the bladder material and expands the contact surface area, leading to the forces being distributed over a greater surface (see *Fig. 9*). This effect can explain why the pressure differences in the face sensors are smaller than the ones in the cuff pressure. As it is still unclear whether the likelihood of eliciting the TCR is higher with the application of a more intense, localized pressure or with a less intense, and more widely distributed one, this should be assessed in future studies. However, our study showed that the forces were higher with the partially inflated mask.

Figure 9: Fully vs. partially inflated mask contact surface.

The success of face mask ventilation relies on the resuscitator's ability to provide sufficient pressure to ensure a tight seal (12). Deindl et al. investigated mask leak with decreasing inflation of the air cushion (fully inflated, 2/3 inflated, 1/3 inflated, emptied) in a neonatal manikin, and reported a significant increase of the leak with the emptied air cushion rim, while in the other cases there wasn't a significant difference (13).

Our study found that the ventilation time with mask leak <25% was not statistically different when using the partially and the fully inflated masks. However, the confidence interval does not rule out that using the partially inflated mask may offer some advantages in terms of mask seal, which agrees with the higher applied forces and the cuff pressures. This finding may suggest that an adequate mask seal can be achieved with a sub-inflated face mask at the cost of applying more force on newborn's face.

It is important to point out that participants did not have a significant preference for either air cushion inflation in terms of difficulty in providing an effective ventilation, fatigue in obtaining a good mask seal, and satisfaction about the mask seal. We can speculate that the participants judged the procedures in terms of their assessment of chest rise and their perception of mask leak, despite exerting more force with the partially inflated face mask.

To our knowledge, this is the first trial comparing the applied forces on a newborn manikin face during PPV with a partially vs. fully inflated face mask.

The development of a quantitative tool assessing the applied forces may provide useful feedback during PPV training (12,36). In addition, healthcare providers may optimize the ventilation by combining information from such tool (applied forces) and the respiratory function monitor (mask leak) in real-life situations where the magnitude of unsafe applied forces is unclear.

8.1. STRENGTHS AND LIMITATIONS OF THE STUDY

The strengths of our trial include:

- the crossover design,
- the objective and reliable force measurement,
- the participation of healthcare givers with heterogeneous experience in face mask ventilation.

However, some limitations should be acknowledged:

- we used only one model of manikin and face mask,
- the manikin eliminates the anatomical heterogeneity among patients and the rubber surface of the manikin is much firmer compared to human skin, which potentially reduces the mask seal (13,28),
- the applied forces may be different during real-life ventilation,
- the sensors exclusively detected forces within restricted areas, but we don’t know their distribution across the entire contact surface between the mask and the face,
- the generalizability of the findings should be limited to healthcare givers with similar experience.

9. CONCLUSIONS

In a neonatal manikin model, comparing PPV with a partially (25mL) versus a fully (35mL) inflated mask did not reveal a significant difference in mask leak or in other objective parameters of ventilation effectiveness, and neither on the participants' subjective impression to prefer one mask over the other.

Using a partially inflated face mask during PPV was associated to higher applied forces and higher cuff pressures compared to a fully inflated face mask. While the differences between the partially and the fully inflated mask in pressure in the cuff was greater, the difference in force exerted on the manikin's face was lower, likely due to the higher deformability of the cuff when not full, allowing for the distribution of force on a wider area.

Applying lower forces on the newborn's face is the desirable goal and from our study emerged that using a fully inflated face mask could be better, although further research is needed to assess its implications on the likelihood of eliciting the trigeminal-cardiac reflex (TCR).

Clinical implications should be evaluated in future studies.

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