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TESI DI LAUREA

USE OF LARYNGEAL MASK AIRWAY IN TRANSFERRED INFANTS: A RETROSPECTIVE STUDY

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Contents

Abstract

Background: The 2015 ERC guidelines suggest laryngeal mask airway (LMA) as an alternative to endo-tracheal intubation in term and late preterm newborns weighing over 1500 g when face mask (FM) ventilation is unsuccessful, and recommend it when ventilation with endo-tracheal tube (ETT) is not possible. LMA could bypass the problems of insufficient FM ventilation and ETT placement, providing an effective positive pressure ventilation (PPV). In particular, its use is lifesaving in patients with malformations of the upper airway. Because of its easy and safe insertion, LMA may be crucial in settings where operators' skills and experience on neonatal resuscitation procedures (such as intubation) may be suboptimal. LMA could be considered by health care givers of level I-II hospitals for neonatal resuscitation, but literature provides little information on this aspect. LMA use in interhospital transport context proved to play an important role in airway management both during stabilization at the referring hospital (before the arrival of the transport team), and during the transfer.

Aim: This study aims to review the use of LMA in a large series of neonates who underwent postnatal transfer by an Italian regional service.

Methods: This is a retrospective study evaluating the use of LMA in infants who underwent emergency transport by the Eastern Veneto Neonatal Emergency Transport Service between January 2003 and December 2021. All data were obtained from transport registry, transport forms and hospital charts.

Results: 64/3,252 transferred neonates (2%) received ventilation with a LMA, with increasing trend over time (p=0.001). Most neonates were transferred after birth (97%) due to a respiratory or neurologic disease (95%). LMA was used before the transport (n=60), during the transport (n=1) or both (n=3). No device-related adverse effects were recorded. Sixty-one neonates (95%) survived and were discharged/transferred from the referral center.

Conclusions: This study adds new data on LMA use in neonates born in level I-II

hospitals and undergoing postnatal transfer. In a large series of transferred neonates, LMA use was rare but increasing over time, and showed some heterogeneity among referring centers. However, LMA was safe and useful in “cannot intubate, cannot oxygenate” situations. Future prospective, multicenter research may provide more detailed insights on LMA use in neonates requiring postnatal transport.

Sommario

Presupposti dello studio: Le linee guida ERC del 2015 suggeriscono la maschera laringea (LMA) come alternativa all'intubazione endotracheale nei neonati a termine che pesano più di 1500 g quando la ventilazione con maschera facciale non ha successo, e la raccomandano quando l'intubazione endotracheale non è possibile. La LMA può superare i problemi legati all'insufficiente ventilazione con maschera facciale e al posizionamento del tubo endotracheale, fornendo un'efficace ventilazione a pressione positiva. Il suo utilizzo è salvavita in particolare nei pazienti con malformazioni delle vie aeree superiori. A causa del suo inserimento facile e sicuro, la LMA può essere fondamentale in contesti in cui le competenze e l'esperienza degli operatori nelle procedure di rianimazione neonatale (come l'intubazione) potrebbero essere subottimali. La LMA potrebbe essere presa in considerazione dagli operatori sanitari degli ospedali di I-II livello per la rianimazione neonatale, ma la letteratura fornisce poche informazioni su questo aspetto. L'uso della LMA nel trasporto interospedaliero ha dimostrato di giocare un ruolo importante nella gestione delle vie aeree sia durante la stabilizzazione nell'ospedale di riferimento (prima dell'arrivo dell'équipe di trasporto), sia durante il trasporto.

Obiettivo: Questo studio si propone di esaminare l'uso della LMA in un'ampia serie di neonati sottoposti a trasferimento postnatale da parte di un servizio regionale italiano.

Metodi: Si tratta di uno studio retrospettivo che valuta l'uso della LMA nei neonati sottoposti a trasporto d'emergenza dal Servizio di Trasporto d'Emergenza Neonatale del Veneto Orientale tra gennaio 2003 e dicembre 2021. Tutti i dati sono stati ottenuti dal registro dei trasporti, dalle schede di trasporto e dalle cartelle cliniche.

Risultati: 64/3.252 neonati trasferiti (2%) hanno ricevuto una ventilazione con LMA, con un trend crescente nel tempo (p=0,001). La maggior parte dei neonati è stata trasferita dopo la nascita (97%) a causa di una malattia respiratoria o neurologica (95%). La LMA è stata utilizzata prima del trasporto (n=60), durante il

trasporto (n=1) o entrambi (n=3). Non sono stati registrati effetti avversi legati al dispositivo. Sessantuno neonati (95%) sono sopravvissuti e sono stati dimessi/trasferiti dal centro di riferimento.

Conclusioni: Questo studio aggiunge nuovi dati sull'uso della LMA nei bambini nati in ospedali di I-II livello e sottoposti a trasferimento postnatale. In un'ampia serie di neonati trasferiti, l'uso della LMA è stato raro ma è aumentato nel tempo con una certa eterogeneità tra i centri di riferimento. La LMA è risultata sicura e utile nelle situazioni di "impossibilità di intubazione e ossigenazione". Future ricerche prospettiche e multicentriche potranno fornire informazioni più dettagliate sull'uso della LMA nei neonati che necessitano di trasporto postnatale.

Chapter 1

Introduction

One of the priorities of the regional perinatal care programs is the centralization of high-risk deliveries in level III hospitals to prevent neonatal morbidity and mortality (1), so maternal transfer remains the best choice.

Nonetheless, some infants born at level I-II hospitals and require urgent transport to a tertiary neonatal care facility, for unpredictable problems after birth or because maternal transfer was not possible (2).

1.1 NETS: Newborn Emergency Transport Service

1.1.1 NETS organization in Italy

Neonatal inter-facility transport is important to allow the best possible care with appropriate level of expertise for preterm or severely ill neonates, and to return convalescing infants to their referring facilities (back-transfer) (3).

Regarding the transport of the critical newborn in Italy, organized NETS activity became available during the eighties (4), but it was during the nineties that NETS coverage mainly spread throughout Italy, with 10 of the 20 Italian regions achieving regional coverage > 50% in 1999 (5). The agreement of the State-Regions Conference in December 2010 (also known as “birth path” or “percorso nascita”) approved the 'hub and spoke' model to guarantee the presence of Maternal and Neonatal Emergency Transport Services (NETS) (6). The implementation of NETS, together with programs of regionalization of perinatal care have played a major role in reducing the neonatal mortality rate that has been observed in Italy in the last two decades (from 5.2‰ in 1998 to 3.4‰ in 2014) (7). However, in 2014 Gente and collaborators published a nationwide survey on neonatal transport practices in Italy,

with an overall response rate of 100% among Italian regions, and the study group found regional differences that reflect the presence of different regional perinatal systems of organizations related to the autonomy of regional governments to legislate in matter of healthcare: only 12 of the 20 Italian regions (60%) were fully covered by NETS; 3 (15%) were only partially covered (Emilia-Romagna, Puglia, Sicily), while 5 (25%) had no NETS available in an organized form (Val d'Aosta, Umbria, Abruzzo, Calabria, Sardinia).

Moreover, half of the level III perinatal centers did not have a specially equipped ambulance for neonatal transport: non-dedicated ambulances are usually not equipped with dedicated infant incubators (8), and a lack of adequate equipment and low skill levels of the personnel involved in the transport increases the risk of serious adverse events in the transport of severely ill newborns (9,10).

1.1.2 NETS organization in Veneto

The Eastern Veneto Neonatal Emergency Transport Service was established in 1999, when the Hospital of Padova and the Integrated University Hospital of Verona were designated as reference centers for NETS. It became fully operative in August 2000.

The service covers a population of over 2 million people in Eastern Veneto Region over a radius of approximately 150 km, with approximately 20,000 births/year in 20 units stratified in three levels of care (11): level I includes postnatal wards for healthy neonates, level II includes neonatal units (equipped with noninvasive respiratory support) offering care to moderately ill neonates, and level III includes neonatal intensive care units (NICU). The service provides around 180–200 emergency transports and 70 back-transports every year. Ground ambulance is the main transport vehicle, while helicopter and boat can be used in special situations.

The transport team consists of a NICU neonatologist, a NICU nurse, a driver, and an assistant, who are on-call for 24 h (12). EV-NETS has the capacities and the equipment to provide care of high- risk patients during the transport including high-frequency oscillatory ventilation, inhaled nitric oxide, therapeutic hypothermia, and

ECMO. Since 2003, the LMA has been included in the equipment available to the transport team. Median response time is 37 min, with median overall duration of the mission for emergency transport of 182 min (11).

1.1.3 NETS activation criteria

The NETS activation criteria, according to DL 22/03/2017 no. 33 (13), are:

- Infant in oxygen therapy with increasing respiratory insufficiency;
- Infants with severe or life-threatening congenital malformations (e.g. pulmonary hypoplasia, diaphragmatic hernia, duct dependent heart disease, esophageal atresia, myelomeningocele, gastroschisis, etc.);
- Infant with severe impairment of vital signs (e.g. shock, neonatal sepsis, convulsions);
- Infant with possible therapeutic hypothermia due to suspected hypos-ischemic encephalopathy (EII), defined by the presence of both criteria a and b:
  a) Intrapartum asphyxia defined by at least one of the following parameters:
     - Apgar score <5 at 5 minutes;
     - Need to continue resuscitation with endotracheal tube or mask and balloon at 10 minutes of life;
     - Fetal or neonatal acidosis defined as pH <7.0 or base excess >12 mmol/l;
  b) Impaired neurological examination with moderate or severe EII (according to Sarnat & Sarnat score) between 30 and 60 min.

1.1.4 NETS functioning and changes over the years

The transport process begins with telephone communication between the referring physicians and the transport team personnel. The receiving center is responsible for providing referring physicians with any information that may enhance

understanding of the patient's needs before the arrival of the transport team (14).

In Italy the main neonatal diseases requiring NETS activation are respiratory (76.2%), followed by cardiac (9.5%), surgical (9.5%) and congenital malformative (4.8%) diseases (11,15). The most frequent respiratory diseases are: RDS (Respiratory Distress Syndrome), PPHN (Persistent Pulmonary Hypertension of the Newborn), Pneumothorax, PIE (Pulmonary Interstitial Emphysema) (16).

The article 'Baby on the move: issues in neonatal transport' published in 2008 in the Journal of Pediatric Nursing reports interesting data on neonatal transport in the UK that are of general relevance (17): research has shown that neonates are subjected to significant environmental stressors during transport (18) which may manifest as cardiovascular and respiratory instability. The first stress factor is temperature changes, so the aim on the journey is to intervene as little as possible (19), since every time the incubator doors are opened the infant is at risk of losing heat. This is also because, unlike most standard incubators which are double-walled and provide warm humidified gases to assist thermoregulation, transport incubators are single-walled with no humidification ability, so are poor insulators of heat. Other stress factors are vibrations and noise, so reduction in levels of noise and vibration continue to be a topic for research. First, the transport should proceed at a steady pace without increases or decreases in acceleration, sirens are rarely required, and aids such as rubber dampers, special tyres and gel mattresses may reduce the effects for the infant. However, the impact is reduced with decreasing weight (20).

Trevisanuto et al. (11) underlined the changes in patient characteristics and respiratory management of neonatal emergency transfers during the last two decades. These changes included:

- Gestational age: transfers of preterm (< 34 weeks' gestation) and low-birth weight (< 2.5 kg) infants increased during the first decade, while the trend reversed in the second decade. These findings may mirror the centralization of high-risk pregnancies (for infants with < 31 weeks' gestation and/or < 1.5 kg), as well as some enhancements of skills and equipment (i.e., nCPAP machine) at lower-level hospitals (for 32–37 weeks' gestation) (7,21);

- Age at transport: neonates transferred immediately after birth had an increasing trend which inverted in the last years; this finding underlines the centralization of high-risk pregnancies and enhancements of skills and equipment in delivery room management. One out of five transfers every year involved infants aged 2–30 days, thus indicating non-response to treatment at the referring hospital or onset of new clinical conditions;
- Diseases requiring NETS: there was a decrease of transfers for cardiac or surgical diseases during the two last decades, probably due to improvements in antenatal diagnosis. Respiratory disease remained the main reason for neonatal transport, in agreement with the past (4,22);
- The balance of transfers among hospitals of different levels: there was decreasing transfers from level I hospitals and increasing transfers from level III hospitals, mirroring the centralization of high-risk deliveries.

1.2 Neonatal Resuscitation

1.2.1 Neonatal resuscitation techniques

At birth, infants must quickly adapt from living in the fluid-filled intrauterine environment, where gas exchange is facilitated by the placenta, to the air-filled extrauterine environment, where gas exchange requires the functioning of the lungs (23). Although this is a normal physiological process, up to 10% of newborns require some kind of respiratory support at birth (24–26) involving the administration of positive pressure ventilation (PPV). This is central in newborns affected by perinatal asphyxia, because respiratory failure precedes cardiac failure (27), unlike in adults, where circulatory and respiratory failure co-exist (28).

Prolonged ineffective PPV could lead to use advanced resuscitation such as intubation, chest compression, and epinephrine (29). An observational study conducted in a rural hospital in Tanzania shows that every 30s delay in initiation of PPV increased the risk of death or morbidity by 16% (28) . Consequently, skillful airway management and rapid effective positive pressure ventilation is the most important aspect of successful neonatal stabilization and resuscitation (30,31).The

most performing interface for providing PPV in the early phases of resuscitation is still unclear (32,33).

Ventilation is frequently started manually with bag and face mask (FM) followed by endotracheal intubation (ETT) if respiratory depression continues. These techniques may be difficult to perform successfully, and the consequence is prolonged resuscitation or neonatal asphyxia.

Face mask (FM) is close-fitting held over the infant's nose and mouth and air is forced in through a manually pumped oxygen bag. It’s the most commonly used interface for delivering PPV in the delivery room (34). The problems associated with FM are mask leak (26,35), airway obstruction related to variable operator skills, and trigeminocardiac reflex (TCR). All the listed problems are more prevalent in preterm than term infants (36,37). In the absence of a respiratory function monitor during resuscitation, airway obstruction and mask leak are often unrecognized, and this could lead to a delay in the effective delivery of PPV (38) with negative consequences mentioned above. Effective FM ventilation is a skill that must be learned and practiced. Videotape recordings of neonatal resuscitations demonstrate that resuscitators are frequently unable to achieve adequate chest expansion using FM (39). TCR, more specifically the peripheral TCR, can occur due to the stimulation of maxillary (V2) and mandibular (V3) divisions of the trigeminal nerve activated by the application of an FM, which leads to stimulation of brainstem nuclei which in turn can cause apnea, bradycardia, and hypotension through reflex vagal action (40). This physiological response is more pronounced with the first application of the FM (41).

The interfaces studied as alternatives to FM for delivering PPV in the initial stages of resuscitation are nasal prong and nasopharyngeal tube (42). The nasal or nasopharyngeal interface seemed to have the advantage of reducing the effect of peripheral TCR, but recent studies did not find difference in the rate of occurrence of apnea and bradycardia with nasal prong compared to FM, probably because binasal prongs could still trigger the TCR by stimulating the trigeminal receptors inside the nose or over the maxillary region (V2) (43). Additionally, there was an increased risk of severe grade intraventricular hemorrhage (IVH) with the nasal interface than FM (44).

The most invasive resuscitation approach is endotracheal intubation, which consists of a tube placed directly into the infant's trachea. Endotracheal intubation may be indicated when bag-mask ventilation is ineffective or prolonged, when chest compressions are performed, or for special circumstances such as congenital diaphragmatic hernia. This procedure requires considerable training, experience, and skill: it has been reported that doctors completing pediatric training frequently fail to intubate the trachea despite multiple attempts (45). Even experienced resuscitators may sometimes require prolonged attempts to successfully intubate the neonate. The infant weight and gestational age can provide an estimate of correct endotracheal tube (ETT) insertion depth, allowing the number of malpositioned ETT to be significantly reduced (46). The best indicator of successful endotracheal intubation with successful inflation and aeration of the lungs is a prompt increase in heart rate (25). Although last reviewed in 2010 (47), exhaled CO_2 detection remains the most reliable method of confirmation of endotracheal tube placement (48). Failure to detect exhaled CO_2 in neonates with adequate cardiac output strongly suggests esophageal intubation. Clinical assessment such as chest movement, presence of equal breath sounds bilaterally, and condensation in the endotracheal tube are additional indicators of correct ETT placement (49).

Three randomized controlled trials enrolling 2358 preterm infants born at less than 30 weeks of gestation demonstrated that starting newborns on CPAP may be beneficial when compared with ETT (50,51). Starting CPAP resulted in decreased rate of intubation in the delivery room, decreased duration of mechanical ventilation with potential benefit of reduction of death and/or bronchopulmonary dysplasia, and no significant increase in air leak or severe IVH. Based on this evidence, spontaneously breathing preterm infants with respiratory distress may be supported with CPAP initially rather than routine intubation for administering PPV (evidence class IIb).

The laryngeal mask airway (LMA) is a supraglottic device consisting of a small mask attached to a silicone tube fitted into the throat up to the laryngeal inlet. Its use as an interface to deliver PPV for initial stabilization of the newborn has been studied for the last three decades, and studies suggest that could provide an alternative to either FM or ETT for newborns requiring assisted ventilation in the

delivery room (52). Data are limited for its use in preterm infants delivered at less than 34 weeks of gestation or who weigh less than 2000 g. Nowadays, the LMA may be considered as an alternative to ETT if face mask ventilation is unsuccessful in achieving effective ventilation (53) (evidence class IIb). A laryngeal mask is recommended during resuscitation of term and preterm newborns at 34 weeks or more of gestation when ET intubation is unsuccessful or is not feasible (evidence class I).

1.2.2 Guidelines for neonatal resuscitation

In 2015, the Neonatal Resuscitation Program (NRP) published updated guidelines for neonatal resuscitation (25,54) (*Figure 1*) that recommend a specific way of proceeding in the assessment of newborns: first, at birth operators rapidly assess the answers to the following 3 questions*: Term gestation? Good tone? Breathing or crying?*. If the answer to all 3 questions is "yes," the newborn may stay with the mother for routine care, that means the infant is dried, placed skin to skin with the mother, and covered with dry linen to maintain a normal temperature. Observation of breathing, activity, and color must be ongoing. If the answer to any of these assessment questions is "no," the infant should be moved to a radiant warmer to receive 1 or more of the following 4 actions in sequence:

A. Initial steps in stabilization (warm and maintain normal temperature, position, clear secretions only if copious and/or obstructing the airway, dry, stimulate);
B. Ventilate and oxygenate;
C. Initiate chest compressions;
D. Administer epinephrine and/or volume.

Approximately 60 seconds ("the Golden Minute") are allotted for completing the initial steps, reevaluating, and beginning ventilation if required. It is important to avoid unnecessary delay in initiation of ventilation, because this is the most important step for successful resuscitation. The decision to progress beyond the initial steps is determined by simultaneous assessment of two vital characteristics:

respirations (apnea, gasping, or labored or unlabored breathing) and heart rate (less than 100/min). Once positive-pressure ventilation (PPV) is started, assessment should consist of simultaneous evaluation of three vital characteristics: heart rate monitored by 3-lead electrocardiography (ECG), respirations, and oxygen saturation.

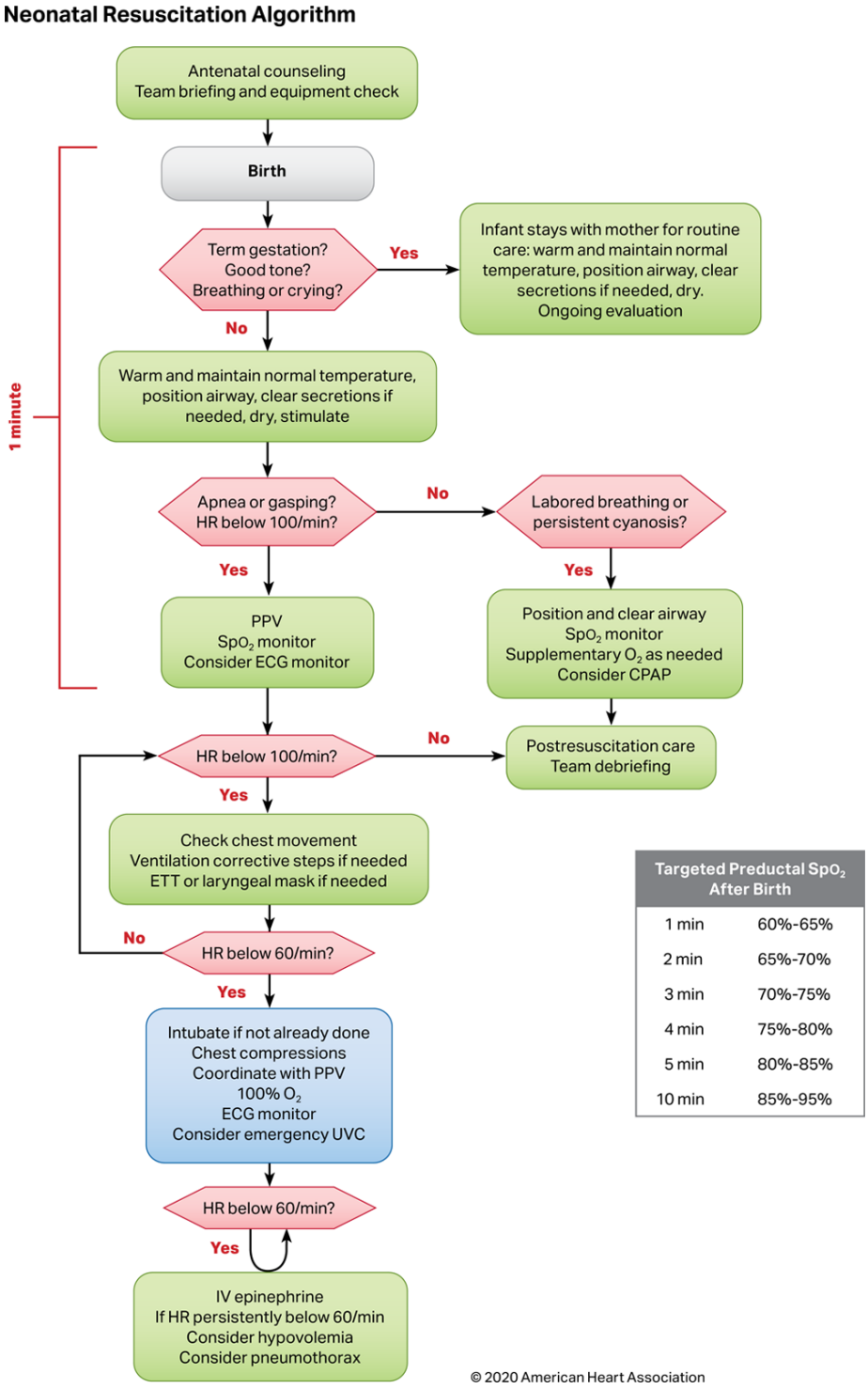

Figure 1. Neonatal Resuscitation Algorithm—2015 Update.

The most sensitive indicator of a successful response to each step is an increase in heart rate (47). For newborns at least 35 weeks' gestation, PPV should be started at 21% oxygen. For newborns less than 35 weeks' gestation, PPV should be initiated with 21% to 30% oxygen. Most infants respond to oxygen at 30% or less, and even brief exposure to 100% oxygen can be toxic to an infant. However, if chest compressions are necessary, oxygen should be increased to 100% (46).

A note must be made about very premature babies in which exposure to mechanical ventilation and oxygen after birth may cause the injury resulting in BPD (Broncho Pulmonary Dysplasia) (55). Therefore, application of noninvasive respiratory support and low oxygen concentration are appropriate strategies to reduce ventilator-associated injury (56).

Thermoregulation remains a key element of the NRP: hypothermia at the time of NICU admission is associated with a higher mortality rate (57) and increased risk of respiratory distress syndrome, hypoglycemia, and late-onset sepsis (58). Simple interventions can decrease these risks: all neonates without a concern for asphyxia should be maintained at a temperature between 36.5°C and 37.5°C. Newborns less than 32 weeks' gestation should be covered with plastic wrap or a bag and covered with a hat. If available, a thermal mattress should be used (33,59).

Recommendations regarding the management of infants born with meconium-stained fluid were updated in the 2015 guidelines (25). The recommendation that vigorous infants with meconium-stained fluid stay with their mother and receive the routine initial steps of newborn care is unchanged. However, infants born with meconium-stained fluids who are not vigorous at birth with poor tone and respiratory effort should no longer receive routine intubation for tracheal suctioning (60). Recent studies have found no difference in the frequency of meconium aspiration syndrome, pulmonary hypertension, asphyxia, or mortality in nonvigorous neonates who are not intubated for tracheal suction (61). Initial steps in the resuscitation of nonvigorous infants with meconium-stained fluids should be performed under the radiant warmer and include starting PPV if the HR is less than 100 beats/min or the infant is not breathing (46,62).

Because a newborn without apparent risk factors may unexpectedly require

resuscitation, each institution should have a procedure for rapidly mobilizing a team with complete newborn resuscitation skills for any birth. When perinatal risk factors are identified, a team should be mobilized, and a team leader identified. For example, preterm birth is a known perinatal risk factor that requires preparation of supplies specific to thermoregulation and respiratory support. As time permits, the leader should conduct a pre-resuscitation briefing, identify interventions that may be required, and assign roles and responsibilities to the team members (48,63). During resuscitation, it is vital that the team demonstrates effective communication and teamwork skills to help ensure quality and patient safety.

The 2010 Guidelines suggested that simulation should become a standard component in neonatal resuscitation training (64). Studies that explored how frequently healthcare providers or healthcare students should train showed that psychomotor performance, knowledge, and confidence were higher when focused training took place every 6 months or more frequently (65,66), even if there were no differences in patient outcomes. It is therefore suggested that training in neonatal resuscitation occur more frequently than the current 2-year interval.

1.3 Laryngeal Mask Airway (LMA)

1.3.1 Story of LMA and types

The laryngeal mask airway (LMA) is a supraglottic airway device used for airway management under anesthesia or during resuscitation maneuvers, with intermediate usability between FM and ETT.

It was invented in 1981 by a British anesthetist, Dr Archie Brain, and it seemed a safe and effective alternative to EET in selected cases (67). Since it was first marketed in the UK in 1988 and in the US in 1991, when it was approved by the Food and Drug Administration, emergency doctors worldwide have used the LMA in more than 150 million patients. Over 2500 publications and hundreds of clinical studies have tested and proven the effectiveness of the device in numerous varieties of use. The American Heart Association (AHA) and the American Academy of Pediatrics (AAP) have included the LMA in its algorithm

for difficult airway management since 2000 (68).

Initially developed for adult use only, then the laryngeal mask has gained widespread popularity and its design was modified for the pediatric and neonatal population (69,70). An observational study of LMA in infants during elective minor surgery for anesthesia established the feasibility and safety of its use in 1992 (71).

The classic LMA (*Figure 2*) is a small elliptical mask with the edge covered by an inflatable silicone cuff that occludes the hypopharyngeal space (72). The two aperture bars in the middle of the mask lumen are intended to prevent obstruction of the tube by the epiglottis. The anterior surface of the mask presents an opening facing the laryngeal aditus, while the back surface is attached to a wide bore airway tube which exits through the mouth with an internal diameter of 5.3 mm (73). The proximal end of the airway tube presents a 15 mm standard connector allowing connection to an ambu bag or ventilator circuit. The black line running along the tube helps to detect any rotation of the mask (52).

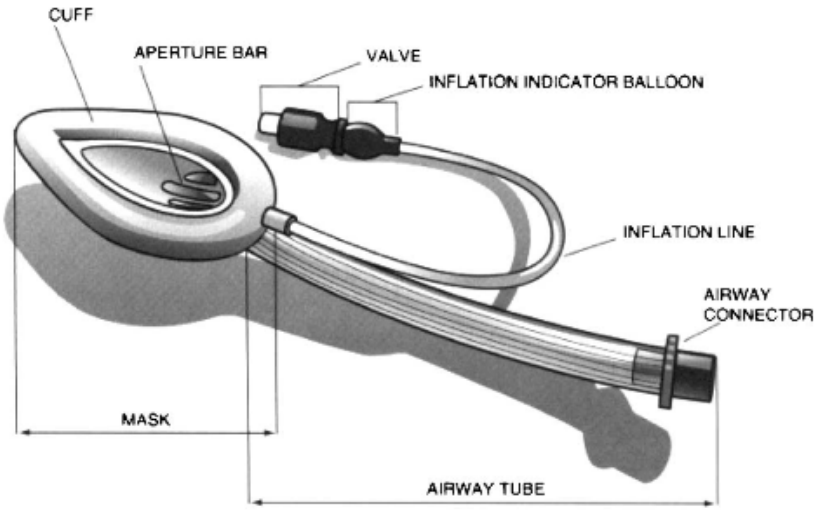

Figure 2. Basic laryngeal mask design. Reproduced from Dr. A.I.J. Brain. Laryngeal mask instructor manual, 2000.

Over the last 10 years several modifications have been made to the original model of the LMA Classic in order to improve its effectiveness and ease of use. Currently, there are various LMAs available for use in newborns (72) (*Figure 3*):

- LMA Classic,
- LMA ProSeal,
- LMA Supreme,
- Ambu AuraOnce,
- LMA Air-Q,
- LMA I-gel,
- LMA Shiley.

The Classic LMA is the first silicone ventilation tube and is a reusable device.

The ProSeal LMA has modified features to achieve greater adhesion to the periglottic tissues, making it possible to obtain higher holding pressures (up to 40 cmH20) while remaining safe with the same ease of insertion as the classic one (74). It also has a gastric drainage which aims to reduce the risk of gastric insufflation and the risk of aspiration of gastric contents (75,76). Another advantage of this type of device is that gastric drainage can help in verifying its correct positioning: an incorrect positioning (nasopharyngeal, endotracheal) causes air leakage from the gastric lumen, which can be verified by filling the initial part of the tube with a water-soluble lubricant and observing the appearance of bubbles or oscillation of the meniscus (77).

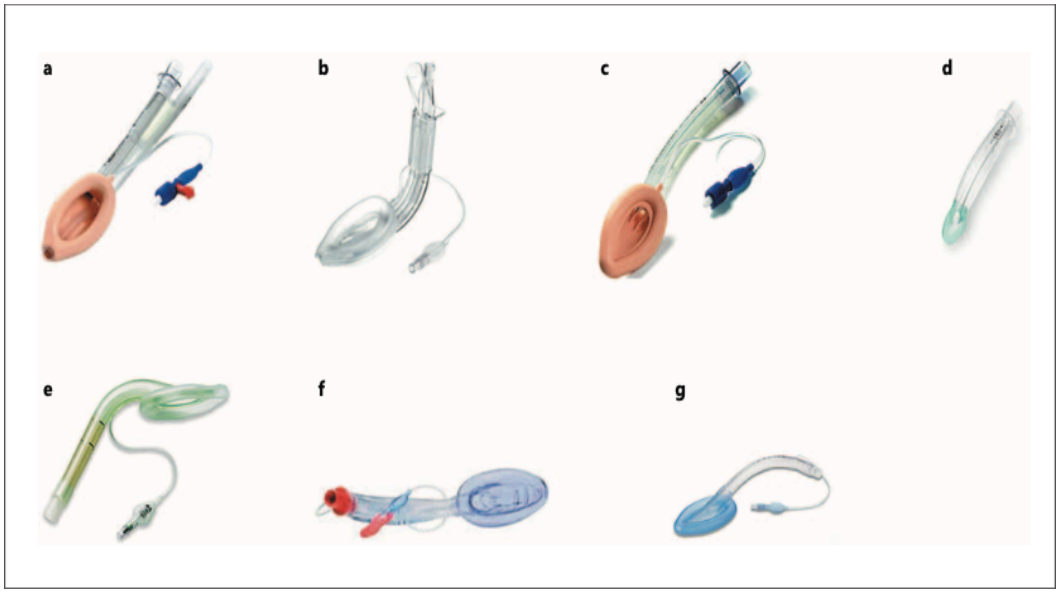

Figure 3. Various laryngeal mask airway (LMA) devices. a LMA Classic. b LMA Supreme. c LMA ProSeal. d i-gel. e Ambu AuraOnce. f Air-Q. g Shiley.

The Supreme LMA is a single-use polyvinyl chloride (PVC) mask with an esophageal drain tube and a firm, curved, and anatomically shaped airway tube designed to achieve easier insertion without any introducer tool or placement by using fingers. The drainage tube emerges proximally as a distinct conduit and runs distally along the anterior surface of the cuff, crossing its distal end to communicate with the upper esophageal sphincter. The drainage tube can be used to pass a gastric tube to the stomach, allowing easy access for evacuation of gastric contents, and it also has another important function: it can be used to verify the correct positioning of the LMA Supreme mask after insertion and, subsequently, to continuously check that the mask remains in place during use.

The Ambu AuraOnce is designed with a rigid pre-inclinated curve in the main tube, which supposedly better replicates the human anatomical airway compared to the classic model, and ensures that the head remains in a natural position when the mask is introduced. The inner part of the tube has a structure that gives it the flexibility to adapt to any individual anatomical variation. The Ambu AuraOnce is provided with an extra-thin 4 mm cuff, so the seal of the cuff adapts perfectly to the shape of the airway with a significant decrease in internal pressure. The cuff, mask and tube are made of one piece.

The Air -Q LMA has a shorter and curved handle, with a claimed advantage that it can be removed after tracheal intubation if unexpected intubation is required.

The I-gel LMA is a second-generation supraglottic device made from thermoplastic elastomer and has a noninflating soft-gel cuff, that creates a perfect anatomical seal of the hypopharynx and allows to reduce soft-tissue trauma. A recent meta-analysis showed that this specific model provides a higher oropharyngeal leak pressure than Classic and ProSeal LMA in pediatric patients, suggesting that it provides an efficient seal (78).

The Shiley LMA has greater tensile strength and lower flexibility, to make insertion easier and decreasing the possibility of occlusion. Initially used in adult and pediatric patients, its effectiveness was later recognized in the neonatal setting as well.

These devices mentioned are made of polyvinyl chloride (PVC) or silicone.

Silicone-based LMAs provide more elasticity to conform to the anatomy and provide higher oropharyngeal seal pressure without the risk of phthalate exposure from PVC. Some of the silicone based LMAs are reusable up to 60 times. In the US, the single-use disposable LMA made of medical-grade PVC is the most commonly available type.

There have been studies conducted to compare the different types of LMAs, but these are mostly manikin-based studies. Micaglio et al. (71) compared the time from insertion to the first inflation of an artificial lung for the LMA Classic and LMA ProSeal and the peak inflation pressures delivered. The study showed an advantage of the LMA Proseal over the LMA Classic in both aspects (higher first insertion success rates and better laryngeal seal during PPV). Trevisanuto et al. (79) compared LMA Supreme, LMA Classic, and LMA ProSeal in a manikin study, to assess the time to establish adequate ventilation and the ease of insertion. The success rate to insertion with the first attempt was comparable in all 3 devices.

1.3.2 LMA insertion technique and functioning

The American Heart Association (AHA) recommends the standard insertion technique for LMA use in neonates (80), described by Brain (67): this technique mimics the action of swallowing a bolus of food, with the operator's index finger pressing the mask against the hard palate, and posterior pharyngeal wall mimicking the action of the tongue (72).

For correct positioning of the LMA in infants, the following steps must be followed (52):

1. Use the correct size of LMA for the patient. Size 1 is suitable for neonates weighing 2.5–5 kg (81). It has been suggested that a smaller size (0.5) may be useful in preterm infants, for example the Air-Q LMA is available as "size 0.5" for infants with a BW <4.0 kg. However, successful use of size 1 has been reported in preterm neonates weighing 0.8-1.5 kg (82,83). An important point to highlight is that there is no manufacturing standard for size 1 designation, so both mask and ventilatory pathway dimensions vary significantly by model

within the same nominal size (27). Nowadays only the classic model is available in a neonatal size (84,85). LMA-ProSeal is currently being evaluated and will soon be suitable in pediatric size.

The choice of mask size is the critical factor for correct positioning and avoiding major and minor complications (86).

2. Fully deflate the cuff and lubricate the back of the mask tip (for neonates in the labour ward, lubrication may not be necessary, as oral and pharyngeal secretions may reproduce this function).

3. Stand at the head end with the infant in a sniffing position (27): press the tip of the LMA against the hard palate with the operator's index finger placed at the junction between the mask and the distal end of the airway tube. Gently advance the LMA with one single movement, applying continuous pressure against the palatopharyngeal curvature. The vector of the force applied must be directed cranially and not caudally. Continue pushing the LMA against the soft palate so that the cuff passes along the posterior pharyngeal wall and the tip locates itself in the hypopharynx. In spontaneously breathing patients, connecting a CO_2 detector to the LMA before insertion facilitates monitoring for development of airway obstruction, which might necessitate slight repositioning of the LMA usually by withdrawing a few millimeters.

4. Inflate the cuff with the minimum air volume necessary to ensure its perfect fit (the maximum insufflation volume for size 1 is 4 ml) and allow the patient to be ventilated up to 20 cmH20 without air leakage (87). Do not hold the tube airway of the LMA during cuff inflation, because it may be move outwards allowing correct positioning.

5. Once the device is fully inserted, the mask lumen sits over the laryngeal opening while the cuff conforms to the contours of the hypopharynx occluding the esophagus with a low-pressure seal. Connect the proximal end of the airway tube to a device (bag, ventilator) for PPV (88).

6. Check the correct LMA positioning can by observing synchronous movements

of the chest and by neck auscultation. After correct insertion and use, the LMA is left in place, until spontaneously ejected by the patient.

One of the main merits of the LMA is that healthcare workers can be easily trained in its insertion with a brief ≤15 min manikin-only training (89).

The tightness of the mask depends on the correct positioning and adequacy of the size used, while it is less dependent on the inflation pressure. The most common problem encountered during insertion maneuver is obstruction at the base of the tongue. In this case, the mask must be removed, and the procedure reviewed in all its phases. If the operator does not follow the recommended insertion technique, malpositioning problems may occur: the epiglottis may be ‘‘downfolded’’, the mask lumen may not be correctly aligned with the laryngeal inlet, or the cuff may fold inwards or lie too high in the pharynx (69,90).

The overall incidence of complications after removal of the LMA is about 10–13%, including coughing, laryngospasm, retching, breath holding (91,92), soft-tissue trauma in the uvula, oropharynx, epiglottis (53,93), regurgitation, vomiting (92), stridor, desaturation, and excessive salivation (85). Many of these complications are caused by overinflation of the LMA cuff and inadequate analgesia, and generally none required intensive care management (94).

There are several alternative techniques of LMA insertion mainly studied in adult patients (95). Variations of the standard technique include inserting the LMA with the cuff partially or fully inflated (96). There are also two rotational techniques, namely 180° and 90° techniques (97). In the 180° technique, an LMA with a fully deflated cuff is inserted back-to-front and then rotated counterclockwise through 180° as it is pushed into the hypopharynx. The 90° rotational technique is similar to the 180◦ technique, except that after the LMA device with a fully deflated cuff is inserted laterally into the mouth, it is rotated counterclockwise through 90° and advanced and straightened out in the hypopharynx. These rotational techniques have been shown to be better than the standard technique in randomized trials in children and adults during anesthesia (98,99). Nevertheless, apart from the standard technique, none of these techniques have been studied in newborn infants during resuscitation.

1.3.3 Comparison of LMA with other neonatal resuscitation techniques

The use of the LMA in neonatal resuscitation was demonstrated over 2 decades ago and has become increasingly important (100,101), because can achieve effective ventilation during neonatal resuscitation in a time frame consistent with current neonatal resuscitation guidelines (102).

LMA is useful because it combines ease of insertion and adequate airway patency (103), so it's more practical than the FM and less invasive than the ETT.

Several studies have compared LMA with FM and ETT, highlighting its advantages:

1. Comparison with FM:
   the use of LMA as an alternative to FM ventilation in neonatal resuscitation was first studied in 1994 (104). Recent studies found that LMA is a safe (105), easy and more effective alternative to FM in terms of shorter resuscitation and ventilation times (52,106). However, in trials comparing LMA with FM, over 80% of infants in both trial arms responded to the allocated intervention. But in infants failing FM in whom LMA was used as rescue, ETT could be avoided in most cases (102). A randomized clinical trial conducted by Trevisanuto and collaborators compares a second-generation LMA having a gastric drain tube with an FM and shows that LMA is more efficacious than FM ventilation in preventing ETT during neonatal resuscitation at birth (107). A similar result was obtained by Schmolzer in 2013 (108). Furthermore, comparing the FM and LMA insertion procedure, we note that the ability to insert and maintain the LMA has a much lower inter-individual variability. FM ventilation is an easy skill, but delivery room studies have shown that mask leakage and airway obstruction are common without regular practice (109,110), especially without a respiratory function monitor (111,112). In addition to poor mask placement skills, several factors can reduce the effectiveness of mask ventilation, such as spontaneous movements of the baby, movements by or distraction of the resuscitator, and procedures like changing the wraps or fitting a hat (113). Various airway maneuvers (e.g. neutral position, chin lift or jaw thrust) can be used to optimize mask ventilation and reduce airway obstruction (114), as

suggested by resuscitation guidelines. Furthermore, the use of excessive pressure with FM may result in injuries to facial soft tissues and nerves (115).

In summary, in term and near-term infants during resuscitation LMA offers many advantages over the face mask (101,116): its use does not require manipulation of the patient's head, neck, and jaw; after positioning, the LMA is quite stable and frees the operator's hands for other important tasks; it also avoids compression of facial nerve; less skill is required to achieve and maintain effective PPV with the LMA compared with the FM (103,117). It has been shown that the incidence of hypoxia is lower in infants with the use of the LMA than with the FM (118). So, LMA is more effective with shorter ventilation time resulting in less need for endotracheal intubation. The introduction of LMA into neonatal airway management policy in Padua NICU in 1997, although historical comparison between no matched pair groups is open to criticism, shows a significant decrease of intubation rate of neonates from 1996 to 2000 (119).

2. Comparison with ETT:

   many studies compared LMA with ETT, such as that of Esmail in 2002 (120), that of Feroze in 2008 (121), that of Yang in 2016 (122).

   These studies showed that the use of LMA was not associated with clinically significant differences in insertion time or failure to correctly place the device. Both techniques provided effective ventilation with no difference in the short-term clinical outcomes observed, suggesting that LMA can be a good alternative to ETT when FM ventilation fails.

   The potential advantages of using LMA for neonatal resuscitation include the ease of insertion without laryngoscopy or other instruments and the fast learning-curve, with a brief ≤15 min manikin-only training (89). This brief training shows high rates of success in the first attempt ranging from 87.5% to 97.5% (74,79). By avoiding laryngoscopy, we can prevent the potential risks of adverse tracheal intubation-associated events, such as cardiac arrest, malpositioning of the tracheal tube in the esophagus or in the bronchial tree (123), airway trauma, laryngospasm, hypotension, and oxygen desaturation (124,125). In comparison with the ETT, the LMA use is associated with a lower hemodynamic stress response during LMA positioning and removal (126,127)

and this could theoretically reduce the incidence of cerebral hemorrhage in neonates.

On the other hand, the ETT application requires long and repetitive training for resuscitators: recent studies, using videotape recordings and respiratory function monitoring during resuscitation, have shown that resuscitators are frequently significantly challenged with regard to ETT placement (128). In a web-based national survey conducted in the UK to assess the experience and training in endotracheal intubation among pediatric trainees and neonatal nurse practitioners (ANNPs), only 18% of the 646 respondents felt completely confident at intubation (129). At least 40 intubations are required to achieve proficiency (130). However, this number is challenging to achieve during pediatric training: less than 50% of general pediatric trainees and ANNPs reported performing >20 neonatal intubations. In the literature, ETT placement failure rates are high: only 50-62% of neonatal intubation procedures were successful on the first or second attempt by pediatric residents, and 35% of the neonates could not be successfully intubated by a pediatric resident, despite four attempts (45). Similarly, another study in 2010 reported the rate of successful intubation between 63% and 69% among pediatric residents and neonatal intensive care unit (NICU) fellows (131).

In summary, the advantages of the LMA over the tracheal tube include: increased speed and ease of placement by anesthetists and non-anesthetist medical personnel and trained non-medical personnel (132), so LMA can largely be used independently of individual operator training levels, providing more reliable support in time-critical situations, such as neonatal resuscitation (72); reduced anesthetic requirements for airway tolerance, e.g. neuromuscular blocking agents are not necessary, diminishing pharmacological risk in neonates; use of a minimally invasive insertion technique without laryngoscopy (133).

Nowadays, the interfaces first used to provide PPV are face mask or an endotracheal tube (52). But both devices have limitations including difficulties achieving effective and consistent tidal volumes, in particular when infants have airway obstructions or craniofacial abnormalities (such as the Pierre Robin sequence) that

obstruct the normal flow of air into their lungs and/or obstructing the view of the airway by the medical personnel attempting intubation (102,134). A further challenge is the requirement for extensive training and practice.

LMA could bypass the problems of insufficient FM ventilation and ETT placement (135), achieving successful resuscitation faster than a bag-mask device or endotracheal intubation, as demonstrated in the 2008 clinical trial comparing FM, LMA and ETT (121). The updated systematic review of the Cochrane database in 2018 (102) concluded that LMA is more efficacious than FM and comparable to ETT as an airway device during delivery room resuscitation of term and late preterm newborns. Its use may be lifesaving in particular in patients with malformations of the upper airway when ETT and FM ventilation fail (136).

1.3.4 Limits and disadvantages of LMA use

The limit of LMA use is that most studies enrolled infants with birth weight over 1500 g or 34 or more weeks' gestation (82,119). The potential use of LMA resuscitation for low-gestation and low-birth-weight infants requires further study (72), in particular there is a lack of evidence of the use of LMA in neonates born before 34 weeks' gestational age or weighing <1,500 g at birth. LMA use has been tested in preterm neonates only in non-resuscitation settings for surfactant administration to avoid endotracheal intubation (137–140).

Potential disadvantages of LMA use are (70,141):

1. Gastric insufflation and aspiration, because LMA does not separate the respiratory and alimentary tracts. This fact may limit the efficacy of ventilation. Some studies report that this consequence can be prevented by meticulous attention to the insertion and fixation of the LMA and by avoiding excessive positive pressure (94).

2. Inadequate alveolar ventilation. The LMA cuff forms a low-pressure seal against the larynx. The maximum seal pressure is 20–25 cm H2O (103), but during the first breaths at birth, or for some specific pulmonary diseases, this

pressure may be ineffective (24,30). The recently introduced LMA-ProSeal, now available for pediatric use, may alleviate this problem.

3. Impossibility of suctioning the airway (in depressed neonates with meconium aspiration syndrome) or administering drugs endotracheally (102,116).

1.3.5 Current LMA use

The LMA is underutilized because of its variable availability in delivery rooms, providers' limited experience, insufficient training, preference for endotracheal tube, and lack of awareness (27,142)**.**

Recently, in 2015, the ERC guidelines suggest LMA use as an alternative to ETT intubation in late preterm (>34 weeks' gestational age), full-term newborns, and/or newborns with a birth weight >2,000 g when FM ventilation is unsuccessful, and recommend it when intubation with ETT is not possible (25,31). It therefore offers an alternate airway device when attempts at inserting endotracheal intubation are unsuccessful during resuscitation (80).

An ILCOR review of 2022 suggests the use of a supraglottic airway device as an alternative to FM during neonatal resuscitation immediately after birth (143). LMA insertion is now being routinely taught as a skill in neonatal resuscitation programs.

However, nowadays guidelines don't recommend routine use of LMA either as a primary airway device (as an alternative to BMV) or as a secondary airway device (as alter- native to ETT).

The advantages of LMA use mentioned above, in particular its brief training time and low invasiveness compared to the ETT, the reduced ventilation time and less need for intubation compared to FM suggest the LMA may be crucial especially in settings where operators' skills and experience on neonatal resuscitation procedures (such as intubation) may be suboptimal (144). LMA could be considered by health care givers of level I-II hospitals for neonatal resuscitation in interhospital care, but literature provides little information on this aspect (145).

1.3.6 LMA use during neonatal transport

Neonatal transport teams can often offer the same advanced respiratory techniques that are currently used in the NICU (16), but airway control during interhospital transport may present more management difficulties, even for experienced personnel (14).

Trevisanuto et al. (11) underline a modification in patient characteristics and respiratory management of neonatal emergency transfers during the last two decades. This change mirror a similar one in neonatal care practice in delivery room and intensive care unit. In particular, these changes, present both at call and during transfer, include:

- the adoption of less-invasive respiratory approaches, such as CPAP, HFNC, nIMV (146,147);
- the administration of lower oxygen concentrations in agreement with increased attention on potential harms caused by oxygen therapy (148,149);

LMA application has been tested in transport context. Five cases of LMA use during neonatal transport have been reported:

- Fraser et al. reported inter-hospital transfer of two infants with type 3 laryngotracheo-oesophageal clefts (150);
- Trevisanuto et al. described two infants with congenital airway malformations during inter-hospital transport (145);
- Brimacombe et al. described a newborn infant with sudden apneic episodes during helicopter transport (151).

In 4 of the 5 cases, the history was positive for polyhydramnios, which suggests that accurate prenatal diagnoses could facilitate the prediction of difficult airways. The median (IQR) gestational age and birth weight of these five infants was 36 weeks and 2800 g, respectively. All five infants required rescue airway management with LMA as both bag and mask ventilation or endotracheal intubation either failed or were not feasible (152). All infants were successfully managed with

a size 1 LMA. In 3 of 5 cases, no sedative and/or anesthetic drugs were used for LMA insertion and placement, so this device can be used for relatively long periods of time. The duration of LMA use ranged from 5 minutes to 4 hours: in 1 case the LMA was used as a rescue device for 90 minutes, from the time of birth to the arrival of the transport team. No complications related to its use were reported, which suggests the safety of this device for both inexperienced and skilled personnel (116). The LMA was positioned at the referring hospital in 4 cases; in 1 case, the LMA was positioned during interhospital helicopter transport.

These cases demonstrate that the LMA may play an important role in airway management in transport process: both during stabilization at the referring hospital (before the arrival of the transport team, when the local health care givers are responsible for the stabilization of the patients), and during the transfer. LMA is especially useful when access to the patient’s airway is limited, such as during air transport where vibration, limited space and access to the infant's head make endotracheal intubation impossible.

So, LMA could be lifesaving in the treatment of sick neonates particularly during interhospital transport, which is considered a dangerous phase in the care of newborns (145).

Chapter 2

Objective

This study aims to review the use of LMA in a large series of neonates who underwent postnatal transfer by an Italian regional service.

Chapter 3

Materials and Methods

3.1 Study Design

This retrospective study evaluated the use of LMA in infants who underwent emergency transport by the Eastern Veneto Neonatal Emergency Transport Service (EV-NETS) between January 2003 and December 2021. The study was enclosed in a project on neonatal transport which was approved by the Ethics Committee of the Azienda Ospedaliera di Padova (Protocol number 0021321). Parents gave their written informed consent for scientific use of clinical records.

3.2 Patients

All transferred neonates between January 2003 and December 2021 were retrospectively evaluated. The only inclusion criterium was receiving LMA during the stabilization immediately before the transport or during the transport. There were no exclusion criteria.

3.3 Data Collection

The information collected concerned the transferred patients (demographics and diagnosis), the transport (referring center, referral center, travel distance), the timing of the use of LMA (during the stabilization immediately before the transport or during the transport) and the outcome. All data were obtained from transport registry, transport forms and hospital charts.

3.4 Statistical analysis

Data were summarized as median and interquartile range (IQR) (continuous data) or frequency and percentage (categorical data). The proportion of transferred neonates who received LMA ventilation was modelled over time using Beta regression and a p-value less than 0.05 was considered statistically significant. Statistical analysis was carried out using R 4.1 (R Foundation for Statistical Computing, Vienna, Austria) (153).

Chapter 4

Results

Overall, 64 out of 3,252 (2%) transferred neonates received ventilation with LMA in 2003-2021 (*Figure 4*). The proportion of transferred neonates who received ventilation with LMA increased over the time period (p=0.001) and ranged from 0.7% to 8.0% according to the referring centers.

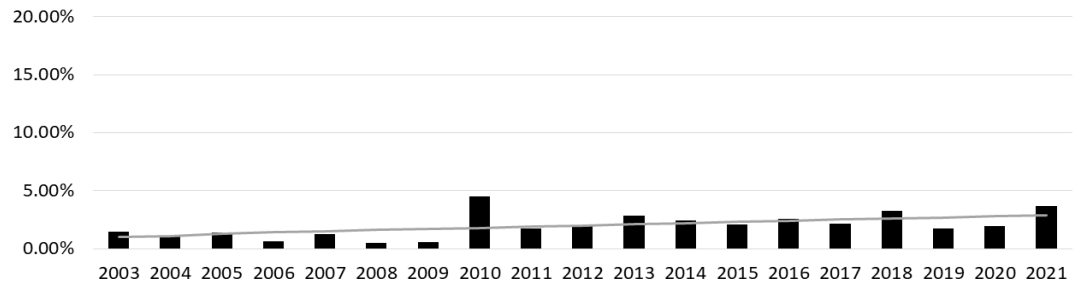

Figure 4. Proportion of transferred neonates who received ventilation with LMA in 2003-2021 (the grey line shows the trend estimate)

Neonatal and transfer information is displayed in *Table 1*. Overall, most neonates were transferred after birth (95%) due to a respiratory or neurologic (asphyxia) disease (95%). Sixty neonates (93%) received ventilation with an LMA only before the transport. Three neonates (5%) presented a severe congenital upper airway malformation (Pierre Robin sequence) which did not allow intubation, hence were treated with LMA before and during the transport. One neonate (2%) with meconium aspiration syndrome was treated with LMA during the transport due to an accidental extubation in the ambulance. Eleven neonates (17%) had gestational age <34 weeks. Mechanical ventilation was included in the respiratory management of 25 neonates before the transport (39%) and 40 neonates during the transport (63%). No device-related adverse effects (such as major bleeding or esophageal lesion) were recorded.

Sample size	N of neonates	64
Neonatal characteristics	Males	38 (59%)
	Gestational age, weeks	38 (34-40)
	Birth weight, grams	2,935 (2,100-3,355)
	Transferred after birth	61 (95%)
Logistics	Level of referring center: Level I Level II Level III	 52 (81%) 12 (19%) 0 (0%)
	Travel distance, km	33 (25-43)
Diagnosis at call	Respiratory Neurologic (asphyxia) Cardiac Surgical	31 (48%) 30 (47%) 2 (3%) 1 (2%)
LMA	Only before the transport Only during transport Before and during transport	60 (93%) 1 (2%) 3 (5%)
Respiratory management before the transport	Oxygen concentration, %	40 (24-100)
	Additional respiratory support: None Non-invasive respiratory support Mechanical ventilation	 28 (44%) 11 (17%) 25 (39%)
Respiratory management during the transport	Oxygen concentration, %	21 (21-39)
	Additional respiratory support: None Non-invasive respiratory support Mechanical ventilation	 16 (25%) 8 (12%) 40 (63%)
In-hospital data	Neonatal temperature at NICU admission, °C	36.7 (35.7-37.0)
	Length of hospital stay, days	16 (6-26)
	Outcome: Discharged Transferred Died	 27 (42%) 34 (53%) 3 (5%)

Table 1. Information on transferred neonates who received ventilation with an LMA in 2003-2021. Data summarized as n (%) or a median (IQR).

After a median length of hospital stay of 16 days (IQR 6-26), 27 neonates (42%) were discharged and 34 (53%) were transferred. Three neonates (5%) died at the referral center: one very preterm infant (30 weeks' gestation and BW 1,190 grams) was transferred for prematurity, asphyxia and renal failure, and died at 10 days of life; one extremely low birth weight infant (25 weeks' gestation and BW 820 grams) was transferred for prematurity and respiratory distress syndrome, and died at 112 days of life; one late preterm infant (34 weeks' gestation and BW 2,500 grams) was transferred for severe perinatal asphyxia, and died at 1 day of life.

Chapter 5

Discussion

This study aims to review the use of LMA in over 3,000 neonates who underwent postnatal transfer by an Italian regional service in 2003-2021.

Discussing the main results obtained:

- *Overall, 64 out of 3,252 (2%) transferred neonates received ventilation with LMA.* This result currently indicates a poor use of the laryngeal mask, in agreement with a recent survey among the directors of 446 European neonatal units: the availability of LMA was reported in 56% of the delivery wards, but only 1% of directors declared to use the LMA as primary interface for initial respiratory support (154). So, LMA is present in the majority of centers, but it's under-used. The percentage difference in LMA use between our study (2%) and the survey (1%) may be partially explained by the inclusion of level III hospitals and the evaluation of LMA as primary interface in the survey.

- In addition*, the proportion of transferred neonates who received ventilation with LMA increased over the time period (p=0.001):* this trend may be associated with the inclusion of LMA among neonatal resuscitation techniques in 2015 ERC guidelines (25,31), and the growing evidence on the role of LMA (102,155): according to updated systematic review of the Cochrane database in 2018 (102) LMA is more efficacious than FM and comparable to ETT as an airway device during delivery room resuscitation of term and late preterm newborns. LMA insertion is now being routinely taught in neonatal resuscitation programs. While we cannot estimate the proportion of neonates undergoing postnatal transfer who would benefit from LMA, it is reasonable to assume a larger use of LMA in the future (143,155).

- Of note, *the proportion of transferred neonates who received ventilation*

with LMA ranged from 0.7% to 8.0% according to the referring centers. This large heterogeneity in LMA use may mirror the different experience of health caregivers on neonatal resuscitation procedures and the professional background (i.e. midwife, anesthesiologist or pediatrician) in level I-II hospitals. Despite such heterogeneity, LMA was *safe as no device-adverse events were recorded*, in agreement with previous studies reporting a rare incidence of such events for both inexperienced and skilled personnel (105,107,116).

These data highlight that LMA could be crucial especially in settings where operators' skills and experience on neonatal resuscitation procedures (such as intubation) may be suboptimal (144). So, LMA is a device that can largely be used independently of individual operator training levels and ensures more reliable support in time-critical situations, such as neonatal resuscitation (42,72). This because of its brief training time (79,89) and low invasiveness (126,127) compared to the ETT: proficiency in LMA positioning can be achieved without the use of instruments and after training on manikins alone, unlike endo-tracheal intubation (89). The LMA also shows advantages over the FM, the main ones are the reduced ventilation time (107,120) and the lower inter-individual variability in inserting and maintaining the device (109).

The retrospective study conducted by Trevisanuto (119) reported that LMA use had a low incidence of failure (1%) and that LMA turned out to be effective in administering PPV in four neonates in whom FM ventilation had proved ineffective: in these infants, the successful use of the LMA removed the risk of endo-tracheal intubation. So, LMA seems to decrease intubation rate of neonates. However, the evidence is still insufficient to recommend the LMA instead of FM or ETT ventilation in the delivery room (72) and larger randomized trials are warranted before the technique can be widely applied. Nowadays guidelines recommend it as a rescue when intubation with ETT is not possible (25,31), but an ILCOR review of 2022 suggests the use of a supraglottic airway device as an alternative to FM during neonatal resuscitation immediately after birth (143).

- *Eleven neonates (17%) with gestational age <34 weeks received effective ventilation with LMA*, in contrast with the recommendation of LMA use in newborn infants with ≥34 weeks' gestation (143)**.** In fact, there is a lack of evidence of LMA use in neonates born before 34 weeks' gestational age or weighing <1,500 g at birth: previous studies enrolled infants with birth weight over 1500 g or 34 or more weeks' gestation (82,119).

- Our study suggests that *the neonatal size-1 LMA* may be used *in neonates with smaller gestational age*, in according to other studies showing successful use of size 1 in preterm neonates weighing 0.8-1.5 kg (82,83). But the small sample size does not provide adequate support on such interpretation and the development of smaller LMA sizes remains a reasonable preference. It should be remembered that the choice of mask size is the critical factor for correct positioning and avoiding major and minor complications (86): in 2011, Trevisanuto (156) reported on an extremely low-birth-weight infant with an upper esophageal lesion following LMA resuscitation, prompting questions regarding the need for smaller devices for the most premature babies and for studies to define the proper cuff inflation level. In fact, a size 0 laryngeal mask for newborns weighing under 1 kg was recently introduced.

- *Most neonates were transferred after birth (95%) due to a respiratory or neurologic (asphyxia) disease (95%).* We can conclude that respiratory disease remained the main reason for neonatal transport, in agreement with recent (11,15) and previous studies (4,22).

- *Sixty neonates (93%) received ventilation with an LMA only before the transport. Three neonates (5%) presented Pierre Robin sequence, so were treated with LMA before and during the transport. One neonate (2%) with meconium aspiration syndrome was treated with LMA during the transport due to an accidental extubation in the ambulance.* So, although LMA was mainly used at the referring hospital, it was sometimes needed during the transport in case of "cannot intubate, cannot oxygenate" situations (neonates

with severe congenital upper airway malformations) and in case of accidental extubation in the ambulance. Such finding confirms that LMA use may be lifesaving specially in patients with malformations of the upper airway, in which ETT and FM ventilation fail (135,136). Trevisanuto et al. (145) had already reported the LMA use during interhospital transport in two infants with congenital airway malformations. In another case mentioned by Brimacombe (151) the LMA was positioned during interhospital helicopter transport, where vibration, limited space and access to the infant's head make endotracheal intubation impossible. Our study contributes to supporting the need to include the LMA in the emergency bag of the neonatal transport team (72,145).

- *After a median length of hospital stay of 16 days (IQR 6-26), 27 neonates (42%) were discharged and 34 (53%) were transferred. Three neonates (5%) died at the referral center.* These results demonstrate that LMA plays an important role in airway management achieving effective ventilation in most cases. In the literature, the other examples of infants ventilated with LMA during transport were all successful (145,150,151).

To our knowledge, this is the first study assessing the use of LMA in neonates who underwent postnatal transfer. It adds new data on LMA use in neonates born in level I-II hospitals and undergoing postnatal transfer and provides useful information to pediatricians and doctors who are involved in neonatal transport. A survey published in 2004 (157) studying current practice and perceived role of LMA by anesthesiologists and pediatricians in forty-three hospitals of Veneto Region, shows that, although the availability of the LMA mask were very high in many hospitals, competence and utilization rates of this device in neonatal resuscitation were low in both groups, especially among pediatricians: only 5% of anesthesiologists and no pediatricians admitted to using the LMA routinely during neonatal resuscitation, 52% of anesthesiologists and 72% of pediatricians had never used the LMA in their practice, only 27% of the anesthesiologists and 5% of the pediatricians considered LMA as an essential device, only 35% of anesthesiologists and 22.5% of pediatricians had attended a course on laryngeal mask airway use. We hope that the implementation of educational courses could help to change current practice and to

include LMA in routinary neonatal care, and then also in neonatal transport.

The limitations of the study included:

- the retrospective design, which restricted the availability of some data such as details on resuscitation interventions and times at birth, as well as experience of health care staff at referring centers;
- the lack of information about LMA being used as primary interface or after failure of previous attempts (using face mask or intubation);
- the limited sample size.

In conclusion, within such limitations, this study shows that LMA may play a role in airway management in transport process: both during stabilization at the referring hospital (before the arrival of the transport team) and during the transfer. In a large series of transferred neonates, LMA use was rare but increasing over time, and showed some heterogeneity among referring centers. However, LMA was safe and useful in “cannot intubate, cannot oxygenate” situations.

Future prospective, multicenter research may provide more detailed insights on LMA use in neonates requiring postnatal transport.

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