CONTROVERSIES IN NEONATAL RESUSCITATION

Maria Fernanda Branco de Almeida,1 Ruth Guinsburg2

Abstract

Objective: To describe the main controversies surrounding newborn resuscitation procedures.

Sources: Systematic review of articles from Medline, Lilacs and Cochrane Library, and of abstracts published in Pediatric Research, using the keywords resuscitation, asphyxia neonatorum, and newborn infant.

Summary of the findings: The effectiveness of hypothermia and ambient air ventilation has been under study. The reduction of barotrauma and volutrauma in the ventilation of preterm infants is still a challenge. The indication of endotracheal intubation in preterm infants based only on their extremely low weight is not a general agreement, except if the use of exogenous surfactant is required. There is still some uncertainty about the ideal dosage of intravenous or endotracheal adrenaline and the need of sodium bicarbonate, mainly in preterm infants. The ethical dilemma includes the decision on whether or not resuscitation should be used in circumstances related to gestational age, birth weight and severe congenital anomalies.

Conclusions: Only the results obtained through animal experiments and randomized controlled clinical trials, with a follow-up of the development of newborn infants submitted to certain resuscitation procedures, will allow changing currently used therapies.


Introduction

The objective of the present article is to discuss the main controversies concerning neonatal resuscitation reported in the literature during the past 10 years. In addition, we will present a brief description of the procedures employed along the centuries to receive children at birth. Finally, we will briefly describe the procedures used for resuscitation in our setting so as to illustrate the discussion concerning controversies.

A history of neonatal resuscitation

Neonatal resuscitation is as old as medicine - however, the procedures currently employed have been developed over the past 40 years. Centuries have gone by before physiological and technological notions were applied to the resuscitation of newborns. In old times, most physicians and midwives knew that stimulation and expansion of the lungs were required to stimulate breathing. However, the methods used for stimulation were often cruel, inefficient, and even fatal. Those methods ranged from violent shaking, beating, electrocution, and hanging the child upside down to press or squeeze the chest.1


In ancient times, neonatal care was mainly associated with principles such as cleaning and avoiding cold weather, which were considered as initial steps, followed by an elaborate ritual of cutting the umbilical cord. Immersion in lukewarm or cold water, started in the 18th century, was used until the 1930s. Intense friction, slapping, rectal dilation, and traction of the tongue to stimulate breathing have also been employed for three decades, and were abandoned in the 1930s. Cleaning of the oropharynx was performed exclusively with the fingers from 1910 until the 1950s. In addition, mouth-to-mouth ventilation had been used for many centuries before being officially recognized in the second half the 18th century. This technique was used until the 1970s.

The introduction of surgical anesthesia in 1840 and its application to obstetrics led to a decrease in intrapartum maternal mortality, and consequently in the time devoted by physicians and midwives to the newborn. In the end of the 19th century, several apparatuses were developed to expand the lungs rhythmically and allow prolonged ventilation. The Scottish obstetrician Blundell (1790-1878) was the first to use a “silver tube” for tracheal intubation of newborns. He introduced air in the tube around 30 times per minute until heart beats were observed, and was able to save hundreds of neonates.

The first apparatus used for intermittent positive pressure ventilation was the “aerophore pulmonaire,” developed by French obstetrician Gairal and made known to the public in 1897. This rubber balloon was connected to a J tube, placed in the upper airways, and pressed to introduce air into the airways.

The use of oxygen was introduced in 1889 to treat weak premies; however, its application did not become routine until the 1920s. Only in 1940 did mobile oxygen tanks appear, allowing this resource to be used in the delivery room. In 1917, Yilppo recommended the intragastric administration of oxygen via a catheter. This practice continued until the mid-1950s, when Virginia Apgar and her colleagues demonstrated that gastrointestinal absorption of oxygen was insignificant.

In 1923, Sidbury made the first umbilical vein catheterization to perform a blood transfusion. Before then, the administration of fluids was performed intraperitoneally and through the sagittal sinus, via the anterior fontanel. In the mid-1960s, closed-chest cardiac massage was introduced, and in 1963, Redding used epinephrine for cardiac reanimation/resuscitation in adults. That author later demonstrated that the intracardiac administration of diluted epinephrine and closed-chest cardiac massage were able to save over 90% of patients with asphyxia.

It was Virginia Apgar, an obstetric anesthesiologist, who introduced the modern era to neonatal resuscitation. In 1953, she publicized a score to classify depressed newborns at birth, taking into consideration five clinical parameters at 60 seconds of life: respiratory effort, heart rate, color of mucosa and extremities, muscle tone, and reflex activity.2 Due to its simplicity, this score has been used for three decades in making decisions concerning the need to resuscitate newborns in the delivery room.

With the expansion of neonatology in the 1960s and 1970s, neonatal resuscitation became a priority. It was taught in conferences covering variable contents catering to professors and teaching institutions. In the 1980s, the American Academy of Pediatrics and the American Heart Association began an effort to establish uniform standards for neonatal resuscitation. These organizations published the first neonatal resuscitation manual in 1987, when the efficacy of several of the recommendations had not been established by scientific evidence, and a large portion of the text was based only on consensus. A new edition of this manual was released in 1990 and 1994, with small changes in the recommended procedures.3 Since the proposed techniques could be easily carried out in a systematic manner, and due to the low cost of the procedures recommended in the American Academy of Pediatrics/American Heart Association Neonatal Resuscitation Program, many countries adopted the program in the past decade, especially developing countries, including Brazil.

At the end of the 1990s, several international organizations met to discuss the need to make recommendations that were based on updated scientific evidence concerning neonatal resuscitation.4 Specialists evaluated each practice and classified it according to the type of evidence available, based on the design (randomized, controlled, prospective or retrospective, case-control, with animals, extrapolations, common sense) and on the quality of the methodology employed (population, technique, presence of bias, etc.) for data collection. In September 1999, a conference gathered to discuss the number and quality of studies, the consistency of conclusions, prognostic assessment, and magnitude of the benefits. In February 2000, several neonatal resuscitation committees (American Academy of Pediatrics, International Liaison Committee on Resuscitation, American Heart Association, and World Health Organization) elaborated a consensus document addressing the indication and performance of more efficacious procedures to resuscitate newborns based on research data, knowledge, and experience.5

Current practice in neonatal resuscitation

Currently, the procedures carried out during neonatal resuscitation aim at 1) maintaining the permeability of airways by the adequate positioning of the head and neck, by suctioning of the mouth, and, if necessary, of the trachea; 2) initiating breathing through tactile stimulation and positive pressure ventilation using a balloon and mask or balloon and tracheal catheter; 3) maintaining circulation by means of cardiac massage; and 4) administering medication or fluids.6
The beginning of reanimation is no longer based on the Apgar score.\(^2\) Immediately after birth, the need for reanimation depends on a quick and simultaneous assessment of presence of meconium, crying or breathing, muscle tone, color, and on whether the baby was born at term or before term. After that, the procedures to be carried out are based on the integrated assessment of three signs: breathing, heart rate, and color.

**Maintenance of temperature**

The first step on receiving a newborn in the delivery room is to maintain the body temperature using heated fields and radiant heat. The process of drying, in addition to preventing heat loss due to evaporation and conduction, also promotes tactile stimulation that induces breathing.\(^5\)-\(^6\) Premature babies have a high body surface/weight ratio, and therefore are highly susceptible to the stress caused by cold, which may cause hypothermia, hypoxemia, and acidosis. To decrease heat loss in babies weighing less than 1,000g, transparent PVC film has been used. After being dried with heated fields under radiant heat, the neonate is wrapped in PVC film, except for the face; after that, resuscitation procedures can be carried out.\(^7\) In addition, heat loss in patients with 23 to 27 weeks of gestational age has been controlled by involving the trunk and limbs in a polyethylene bag (20 x 50 cm) immediately after birth.\(^8\) These are low cost practices, which are easy to perform and do not interfere with resuscitation procedures.

Whatever the technique used for maintaining the neonate’s temperature, hyperthermia must be avoided, since it is associated with respiratory depression.\(^9\),\(^10\)

**Airway suctioning**

To achieve airway permeability, the baby’s head must be positioned with a light neck flexion. If necessary, secretions are removed. The mouth, followed by the nostrils, is delicately aspirated with a bulb or tracheal catheter (number 8 or 10) connected to a vacuum aspirator, under a maximum suction pressure of 100 mmHg. Aggressive suction of the larynx may cause laryngeal spasm and vagal bradycardia,\(^11\) delaying the start of breathing. Vigorous term newborns without meconium-stained amniotic fluid usually do not require airway suctioning.\(^12\)

In the presence of meconium-stained amniotic fluid, regardless of consistency, suctioning of the mouth, the pharynx, and the nostrils with a tracheal catheter number 12 or 14, as soon as the infant’s head reaches the perineum, is recommended. This procedure decreases the risk of meconium aspiration syndrome.\(^13\),\(^14\)

Despite the suctioning of airways, about 20 to 30% of neonates with meconium-stained amniotic fluid also present meconium in the trachea, suggesting the need for tracheal suctioning after delivery. Therefore, in cases when the neonate presents apnea or irregular breathing, a decrease in muscle tone and/or heart rate lower than 100 bpm immediately after birth, the pediatrician removes the residual meconium from the hypopharynx and performs intubation and suctioning of the trachea.\(^15\) Currently, the endotracheal instillation of saline solution to fluidify meconium is not recommended, since this procedure seems to be ineffective to decrease the severity of aspiration pneumonia and may result in worsening of lung mechanics.\(^14\)

In relation to vigorous meconium-stained newborns, there is evidence that tracheal suctioning does not alter prognosis, and may in fact cause intubation-related complications.\(^16\) At the moment, this is considered to be an acceptable and safe recommendation.\(^4\)-\(^6\)

It is believed that the procedures followed in the delivery room are crucial to ensure a good clinical evolution in most newborns with meconium-stained amniotic fluid. However, in neonates with severe intra-uterine asphyxia or massive intrauterine meconium aspiration, the benefits of the procedures described above may be small.

**Oxygenation and ventilation**

After the measures taken to maintain temperature and airway permeability, if the neonate presents spontaneous breathing, heart rate higher than 100 bpm and central cyanosis, inhaled oxygen is indicated. This can be offered though a mask with side orifices, anesthetic balloon or through a catheter connected to the oxygen source with a flow of 5 l/minute.\(^4\)-\(^6\)

If the newborn presents at least one of the following: apnea, gasping, heart rate lower than 100 bpm or persistent cyanosis despite the administration of inhaled oxygen, positive pressure ventilation through a balloon and face mask is indicated. For this procedure, a self-inflating balloon (maximal capacity 750 ml) is connected to the oxygen source with a flow of 5 l/minute and to a reservoir to achieve an oxygen concentration of 90 to 100%. Balloons must also have a safety mechanism, that is, a pressure release valve that is, a pressure release valve gauged at 30-40 cm H\(_2\)O and/or a manometer to prevent the excess pressure applied to the balloon from being transmitted to the patient’s lung, causing barotrauma and volutrauma.\(^5\),\(^6\),\(^17\)

The face mask must be made of clear or semi-clear flexible material, cushioned and planned so as to have a dead space of less than 5 ml. In general, round masks adjust to the face better in premies, whereas anatomical masks are the best suited for term newborns.\(^18\)

Ventilation is carried out at a frequency of 40 to 60 movements/minute. Although the pressure required for lung expansion is variable and unpredictable, it may initially be higher than 40 cm H\(_2\)O, with a longer inspiratory interval in the first ventilations.\(^19\) After that, adequate ventilation is ensured by continuous observation of thoracic expansion through inspection and auscultation.\(^5\),\(^6\)
Ventilation with balloon and catheter is indicated if ventilation with balloon and mask is prolonged or ineffective, if cardiac massage and/or medications are required or if there is suspicion or diagnosis of diaphragmatic hernia. Tracheal intubation is also considered in premature extreme low weight newborns. This maneuver is carried out with a laryngoscope coupled to a straight number 0 blade for premies and number 1 for term newborns, with tracheal catheters of uniform diameter (2.5 - 3.0 - 3.5 - 4.0 mm).5,6

Following intubation, ventilation is started with the self-inflating balloon in the same frequency and pressure described for balloon-mask ventilation. Positioning of the catheter is ensured by inspection of the chest, auscultation of the axillary and gastric regions, visual inspection of condensation in the tracheal catheter, and observation of vital signs and activity of the newborn. Improvement is defined as presence of spontaneous and regular breathing movements and heart rate higher than 100 bpm. In this situation, ventilation is interrupted, and inhaled oxygen is administered through a catheter, with gradual weaning.

Ventilation is the most effective and efficient procedure for neonatal resuscitation. Most patients requiring ventilation can be adequately ventilated with a balloon and face mask.5,6,20

Cardiac massage

Cardiac massage is initiated only if, after 30 seconds of ventilation and 100% oxygen, the newborn develops or presents persistent heart rate below 60 bpm. Chest compression is performed in the low third of the sternum using the two-thumb or two finger (second and third fingers) techniques. The first technique seems to be more efficient, since it generates a higher peak of systolic pressure and coronary perfusion. It is also the technique favored by most physicians.22 Although there are no data relating to the neonatal period, it is recommended that the deepness of the compression encompass about one third of the antero-posterior thorax, so as to produce a palpable pulse.5,6

Ventilation and heart massage are performed in synchronicity, with a rate of 3:1.23

Improvement is defined as a heart rate higher than 60 bpm after ventilation associated with heart massage. At this point, massaging is interrupted. In the presence of regular and spontaneous breathing and heart rate higher than 100 bpm, ventilation is also interrupted. Then, inhaled oxygen is administered through a catheter with gradual weaning based on the color of the mucosa.

Drug therapy

The need for drugs during resuscitation in the delivery room is an exception if ventilation and, if necessary, cardiac massage, are carried out in an effective manner.20,24 neonatal bradycardia usually results from insufficient lung expansion and/or marked hypoxemia.

The preferred path for drug infusion in the delivery room is the umbilical route. The intravenous route is rarely used in the neonatal period because the bones are fragile and the intravenous space is narrow, especially in premies. This route can be used in neonates when other routes are not accessible.25

Epinephrine is indicated in the presence of a heart rate lower than 60 bpm after at least 30 seconds of positive pressure ventilation and 100% oxygen, along with cardiac massage. Its main action seems to be peripheral vasoconstriction, improving the supply of oxygen to the heart and brain during cardiac massage.26 The usual dose is 0.1-0.3 ml/kg/solution at 1/10,000 (0.01 - 0.3 mg/kg) given endotracheally or intravenously.

Volume expanders may be required to resuscitate newborns with hypovolemia. Hypovolemia is suspected when the response to resuscitation procedures is not adequate, if there is loss of blood, or if there are signs of hypovolemic shock, such as paleness, poor perfusion and weak pulse. The expander of choice is isotonic crystalloid fluid - physiologic solution at 0.9% or ringer-lactate - and the initial dose is 10 ml/kg administered endovenously through the umbilical route in 5 to 10 minutes. Albumin should not be used due to its restricted availability, to the risk of infection and to the association between myocardial lesion and increase in neonatal mortality.27,28

Sodium bicarbonate is indicated only during prolonged reanimation, when the newborn has not responded to other measures. In this situation, it is essential to ensure the presence of adequate ventilation and circulation. The dose to be infused for at least 2 minutes is 2 mEq/kg of a 4.2% (0.5 mEq/ml) solution.6

Naloxone is indicated in the presence of respiratory depression, when the mother used opioids or opioid derivatives in the last four hours before the birth. It is important that adequate ventilation be maintained at all times before and during administration of the drug. The dose to be used is 0.1 mg/kg at a 0.4 mg/ml concentration through an endotracheal or endovenous route.6 Naloxone should not be administered to newborns whose mothers have a history of opioid dependence, since it may trigger withdrawal syndrome with seizures.29

Other procedures

Other procedures may be required to resuscitate the newborn in special situations, such as thoracocentesis, cases of pneumothorax or pleural effusion, and paracentesis in patients with ascites. The use of a Guedel sound may be indicated in choanal atresia.5,6

Controversies in neonatal resuscitation - Almeida MFB et alii

With the dissemination of the American Academy of Pediatrics/American Heart Association Neonatal...
Resuscitation Program, millions of newborns in several countries have been resuscitated at birth following the routines described above. However, there is controversy concerning the application of some of these procedures in the neonatal period, since some are based on clinical experience and studies carried out in animals and adults. Below is a description of the main points that are currently being submitted to laboratory investigation and clinical assays.

Hypothermia

The maintenance of temperature is the first step in the care of newborns in the delivery room. It is well-established that hyperthermia must be avoided, since it triggers respiratory depression. On the other hand, hypothermia may be a promising treatment for hypoxic-ischemic encephalopathy.

Some studies in animals and human beings suggest that hypothermia may reduce brain damage in birth asphyxia. However, this form of treatment may have adverse effects. Term newborns with clinical encephalopathy on electroencephalography until 6 hours of age, when submitted to superficial cooling of the trunk or selective head cooling for 72 hours present cardiovascular alterations. A decline in heart rate is observed, as well as an increase in blood pressure when rectal temperature reaches 33.3-34.5°C, with a return to normality during re-heating. These effects, in association with certain drugs, such as anticonvulsivants, may cause hypotension and compromise the evolution of asphyxiated newborns.

To investigate whether systemic hypothermia, initiated before 6 hours after birth and maintained for 72 hours reduces mortality and/or developmental alterations, a study is under way since November 1999. This multicentric study carried out in the United States includes term neonates presenting mild to severe hypoxic-ischemic encephalopathy. The investigation is assessing 200 newborns randomized to receive systemic hypothermia or conventional treatment, with a follow up of 18 months, until 2004 (LA Papile, personal communication). At the present moment, hypothermia should not be implemented, until the results of these controlled and randomized clinical trials become available.

Oxygen concentration

One of the main controversies investigated in the last decade refers to the minimal concentration of oxygen required to resuscitate newborns at birth. Some authors have questioned the need for the 100% oxygen concentration that is currently recommended based on animal studies and studies with human newborns, due to the potential toxicity of oxygen.

Following long hypoxia periods, the level of hypoxanthines in tissue is increased. When hypoxanthines combine with oxygen in the presence of xanthine-oxidase, a large number of free radicals is generated. This can cause enzymes to be oxidated; in addition, it may inhibit protein and DNA synthesis, decrease the production of surfactants, and cause lipid peroxidation, with consequent tissue damage. These free oxygen radicals - superoxide, hydrogen peroxide, and peroxide radicals - have been associated with the pathogenesis of several disorders affecting the lungs, the brain, and other systems in the newborn, especially preterm newborns. These are especially vulnerable to the pulmonary lesion induced by free radicals, since the antioxidant system develops during the last trimester of pregnancy. This system includes the enzymes catalase, superoxid dismutase and glutathione reductase and free radical scavengers, such as vitamins A, E and C, beta-carotene and glutathione, whose levels are low in premature newborns. Therefore, the amount of free oxygen radicals may exceed the antioxidant capacity of the newborn and trigger a diffuse lung lesion that may lead to the development of diffuse alveolar damage and progressive lung dysfunction. It is possible that the use of a low oxygen concentration during neonatal resuscitation may lead to the production of small amounts of free radicals and reduce tissue damage after reperfusion.

Since the 1960s, studies carried out in rabbits have shown that the increase in oxygen arterial pressure from 50 mmHg to several hundred mmHg causes little change in pulmonary vasodilation, as far as there is no lung malformation of immaturity, and that ventilation with room air is adequate to ensure alveolar diffusion of oxygen into blood. In addition, studies in pigs have shown that resuscitation with room air decreases vascular resistance in the lungs similarly to 100% oxygen.

In human beings, the first pilot study to assess the effect of oxygen concentration during resuscitation was carried out in India and included 84 newborns weighing more than 1,000 g, presenting gasping or heart rate below 80 bpm at birth. Forty-two patients were ventilated with room air, and 42 with 100% oxygen. Both groups were similar in terms of Apgar score at the 1st minute, heart rate, acid-base balance and blood gases during the first 10 minutes after birth, as well as in terms of survival and neurological development at 28 days after birth. The same investigators carried out a clinical trial in 1 center from six countries, involving 288 neonates resuscitated with room air and 321 with 100% oxygen. Again, there was no difference between the groups in terms of the outcomes analyzed in the pilot study. The time until start of crying and first breath was shorter, and the Apgar score at the 1st minute was higher in patients ventilated with room air when compared to patients ventilated with 100% oxygen. At seven days after birth, the incidence of hypoxic-ischemic encephalopathy (11% with air vs. 15% with 100% oxygen) and lethality (14% with air vs. 19% with 100% oxygen) were similar in both groups. However, the long term evolution of these children was not assessed.
In favor of the administration of high concentrations of oxygen at birth, in addition to the presence of lung vasodilation, is the fact that some animal studies confirm the reduction in the extent of infarction in rabbits with transitory myocardial ischemia, the increase in blood flow in ischemic skeletal muscle in rats and brain ischemia in adult cats.33

Since the existing studies are not sufficient to prove the efficacy and safety of oxygen concentrations lower than 100% in delivery rooms, it is recommended that oxygen be used in concentrations close to 100% to ensure a rapid turnaround of hypoxia during neonatal resuscitation. In cases when oxygen is not available and positive pressure ventilation is required room air may be used.5,6

**Positive pressure ventilation**

In addition to the questions concerning the ideal concentration of oxygen to resuscitate newborns, another concern relates to the effects of applying pressure and of the volume during manual ventilation, especially in premies.

Barotrauma, a term that refers to lung lesion induced by pressure, occurs during ventilation as a result of high inspiratory pressure peaks, and is considered an important cause of acute and chronic pulmonary lesion in preterm neonates. Therefore, it is recommended that self-inflating balloons should have both an escape valve regulated at 30-40 cm H2O and a connection to a manometer, so that the pressure to be administered can be monitored and the risk of hyperdistention and alveolar lesion minimized. In addition, animal studies suggest that the excessive variation in lung volume, known as volutrauma, may be the main mechanism causing lung lesions. Since the capacity of the chest to expand is inversely proportional to gestation age, the risk for volutrauma in extreme premies is higher than in larger premies. Therefore, inspiratory pressure peaks considered satisfactory may produce excessive current volumes, hypocapnia, and lung lesion. Recent evidence has also shown an association between hyperventilation and hypocapnia in preterm newborns, and abnormal neurological development with presence of periventricular leukomalacia and cerebral palsy.17,37

The strategy used in ventilation may also reduce the efficacy of endogenous and exogenous surfactant. Studies in premature sheep have provided evidence that only six manual inflations of 35 to 40 ml/kg, carried out before the administration of surfactant and before mechanical ventilation are sufficient to compromise the efficacy of surfactant replacement. These sheep presented more lung lesions, more compromise of lung mechanics and less gas exchange when compared to those that did not receive manual ventilation at birth.42 In addition, there is concern about the fact that manual ventilation at birth in neonates weighing 600 g can supply up to 40 ml/kg (functionally), and also that during the first 5 minutes of life premies with very low birthweight receive more than 100 breathing movements with such elevated current volume values. More pronounced volutrauma occurs when collapsed alveoli are hyperdistended during the manual application of assisted ventilation, in which continuous positive airway pressure (CPAP) and current volume are difficult to control.37

These observations may have important clinical implications for the resuscitation of premature newborns in the delivery room. Ideally, volutrauma should be prevented through the normalization of the residual functional capacity, improved insufflation, and lung blood flow, using as little ventilatory support as possible to ensure liberation of oxygen for tissues. However, these objectives are hard to measure at the moment of birth. Some questions are being debated in the literature, such as: would it be possible to start the resuscitation of extremely low weight newborns with CPAP and controlled volume ventilation? Should high frequency ventilation be started in the delivery room for neonates presenting clinical evidence of respiratory distress syndrome? While these questions are not answered, the smallest possible pressure and volume should be used to achieve adequate ventilation, with continuous monitoring of thoracic expandability.

**Tracheal intubation**

Certain aspects related to the indication for tracheal intubation at birth are also controversial. Tracheal intubation in the delivery room based only on the extreme low weight of newborns is not unanimously accepted. Studies carried out in Germany have compared mortality and morbidity in newborns with gestational age higher than 23 weeks and weight at birth lower than 1,000g receiving care at the delivery room in two different moments (1994 and 1996), following different routines immediately after birth. In the first moment, all the neonates (n=56) with signs of mild respiratory distress were intubated at birth. In the second moment, all patients (n=67) received continuous pressure of 20 to 25 cm H2O through a nasopharyngeal catheter followed by 4 to 6 cm H2O CPAP to establish the residual functional capacity and avoid intubation and mechanical ventilation. None of the 123 patients received prophylactic surfactant in the delivery room. In 1994, 84% of the neonates were intubated in the delivery room and 7% did not require intubation or mechanical ventilation during admission; in 1996, 40% of the neonates were intubated in the delivery room, and 25% never required intubation or mechanical ventilation. In this last group, 35% received mechanical ventilation due to respiratory distress syndrome. The introduction of a new routine in the delivery room did not increase morbidity and mortality. The authors conclude that the strategy of intubation in the delivery room must be individualized and restricted to those patients requiring this measure. In addition, they speculate that the administration of prophylactic surfactant could alter these results due to the needs of immediate intubation.7
The indication to intubate a newborn in the delivery room must always take into consideration the ability of the person in charge of resuscitation and the possibility of complication, including the appearance of hypoxemia, apnea, bradycardia, pneumothorax, soft tissue laceration, tracheal perforation, and increased risk of infection.

Still concerning intubation, some authors mention that measuring the amount of expired carbon dioxide may be helpful to determine if the catheter is adequately positioned.43 However, there are few data concerning the sensibility and specificity of end-tidal carbon dioxide detectors in newborns.44 Data from other age groups should not be extrapolated to newborns due to the peculiarities of neonatal physiology, including inadequate lung expansion, reduced lung blood flow, and low current volumes, which may influence the interpretation of the data obtained.

In cases of failure in tracheal intubation or ineffective ventilation with the balloon and mask, ventilation with a laryngeal mask has been proposed in term newborns.45 However, the application of this technique cannot yet be recommended routinely, since there is little experience in the neonatal period, especially in preemies.46 In addition, the technique requires specific training, it cannot be used for tracheal suctioning in fetuses with meconium-stained amniotic fluid and its effectiveness has not yet been established.5,6

Exogenous surfactant in the delivery room

Meta-analyses of randomized and controlled clinical trials have show that prophylaxis with exogenous surfactants decreases in 40% the neonatal mortality in comparison to late therapy in preemies submitted to mechanical ventilation with a clinical and radiological diagnosis of respiratory distress syndrome.47,48 In addition, its early use, until 2 hours after birth in patients presenting this disorder and submitted to mechanical ventilation decreases in 13% the risk of neonatal mortality in relation to patients receiving the surfactant later on.49 However, there are no studies comparing the efficacy of late prophylaxis in relation to early prophylaxis.50

The benefits of surfactant prophylaxis using a tracheal catheter at birth are maintained until 10 minutes after birth. Such benefits probably occur because the surfactant mixes with lung fluid and reaches the alveoli before the onset of lung lesion. Kendig et al., in a study carried out in three U.S. maternity wards, randomized 651 preemies with gestational age estimated between 240/7 and 286/7 weeks in two groups, before birth. The first group included patients receiving 3 ml (105 mg) of natural surfactant bolus endotracheally immediately after birth and before the beginning of positive pressure ventilation. The other group was submitted to tracheal intubation after a maximum of 5 minutes after birth and to other resuscitation procedures if required. At 10 minutes, these babies received 3 ml of surfactant divided into four aliquots of 0.75 ml. All the patients received a maximum of three additional doses of therapeutic surfactant when they developed respiratory distress syndrome. Survival until hospital discharge was similar in both groups (76% vs. 80%), as well as the need for oxygen therapy until 36 weeks of post-conceptual age (18% versus 13%). Those authors recommend the use of a post-ventilatory strategy at 10 minutes after birth for the administration of surfactant prophylaxis in premies with gestational age of less than 29 weeks.51

A disadvantage of the use of prophylactic surfactant is the need for submitting the patient to tracheal intubation. However, the complications associated with this procedure may be minimized by having well-trained personnel to perform neonatal resuscitation in the delivery room. Another disadvantage is the significant number of patients that would not develop respiratory distress syndrome, that is, 35% to 55%, and that would receive a costly treatment without requiring it.

Wolkoff and Davis make the following recommendations for the administration of surfactant in the delivery room: to identify surfactant deficiency before birth, by obtaining the lecithin/sphingomyelin ratio; to test the presence of phosphatidylglycerol; to administer the first surfactant dose (100 mg/kg) few minutes after delivery in newborns with less than 29 weeks of gestational age, especially if the mother did not receive corticoids and started premature labor suddenly.52

Dose and route of administration of epinephrine

The dose and route of epinephrine administration during neonatal resuscitation have been discussed by some authors. Experiments in adult animals show that the main benefit of epinephrine is mediated by alpha-agonist activity with vasoconstriction, rather than by beta-agonist property with a consequent increase in contractility and heart rate. In adult animal models, and in adult human beings, an epinephrine dose 10 times higher than the dose usually recommended improves brain blood flow, debt repayment, and coronary perfusion, as well as time until return of spontaneous circulation during ventricular fibrillation. Despite all that, since no prospective and controlled studies have been carried out, an initial dose of 1.0 mg is still recommended in adults.24

There are several differences between adults and newborns in terms of the use of epinephrine. First, 80% of the neonates do not develop ventricular fibrillation as a terminal cardiac activity. Newborns present bradycardia, and high doses of epinephrine have no effect on this condition. Also, in adults with cardiac arrest due to coronary disease, high doses of epinephrine may be helpful in myocardial perfusion, which is vital for the restoration of spontaneous circulation. However, in the neonate, the terminal heart rate results from hypoxia, despite the transitory
increase in heart rate and myocardial blood flow. Therefore, in this age group, the increase in coronary flow through high epinephrine doses is not critical for the success of resuscitation, contrarily to what happens in adults.

In newborn sheep with asphyxia-induced bradycardia, a 0.05 to 0.1 mg/kg dose increases blood pressure and heart rate more than a 0.01 mg/kg dose, however with less volume and cardiac debt. Therefore, a dose of 0.1 mg/kg epinephrine may be deleterious to the neonate. A greater concern exists in relation to premies, since those may develop intraventricular hemorrhage due to the hypertension that follows hypotension, especially if receiving epinephrine doses that are higher than those currently recommended.53

Based on the lack of knowledge concerning the dose-response effect of epinephrine in neonates, on the absence of evidence showing the efficacy of high doses during symptomatic bradycardia, on the lack of knowledge the importance of coronary pressure in newborns, and on the risk associated with high doses of epinephrine, it is recommended that doses of 0.01 to 0.03 mg/kg be used at a concentration of 1:10,000.24

In terms of administration path, the same effects are obtained by tracheal infusion of a 0.1 mg/kg dose or endovenous administration of 0.01 mg/kg; however, the cardiovascular repercussions are different, and may have important implications for neonatal resuscitation, especially in premies. The peak and duration of blood hypertension are higher when a dose of 0.1 mg/dl is administered tracheally when compared to a dose of 0.01 mg/dl administered by endovenous infusion. As previously stressed, high levels of blood pressure in preterm newborns may predispose to intraventricular hemorrhage. The fact that the lung is hypoperfused does not compromise the endotracheal absorption of epinephrine, as shown in the lungs of newborn sheep with hypoxic lung vasoconstriction and a 30% decrease in lung blood flow.54

Therefore, when considering the deleterious effects associated with high doses of epinephrine administered tracheally to premature or term newborns, a dose of 0.01 to 0.03 mg/kg or 0.1 to 0.3 ml/kg at a concentration of 1:10,000 is recommended; this is the same dose administered endovenously.5,6,24,54

**Administration of sodium bicarbonate**

Another medication involved in controversy in neonatal resuscitation is sodium bicarbonate, since there is no convincing evidence supporting its use, especially in premature newborns with less than 32 weeks of gestational age.

For many years, acidosis was corrected with bicarbonate before the administration of epinephrine, due to the decreased response to catecolamines during acidosis. However, several studies have raised doubts about the use of bicarbonate during hypoxic lactic acidosis, since this medication may lead to the decrease in cardiac debt, blood pressure, and intramyocardial pH. The correction of acidosis depends on the removal of CO2; if CO2 remains in the circulation, it will cross the cellular membranes, increasing the formation of hydrogen radicals with worsening of intracellular acidosis and myocardial activity, even with increase in arterial pH. The elimination of CO2 depends on ventilation and lung blood flow. When sodium bicarbonate is administered in patients with inadequate ventilation, there will be an accumulation of CO2. If there is cardiorespiratory arrest, venous pH will increase and a small amount of blood will reach the lungs to eliminate CO2. In addition, hypercapnia hinders the elimination of CO2, which results in more intracellar acidosis. Therefore, the administration of sodium bicarbonate must always be accompanied by efficient ventilation.24

Other potential complications of sodium bicarbonate infusion include hypernatremia and intraventricular hemorrhage in premature newborns.55 Non-diluted sodium bicarbonate solution contains 2000 mOsm/l, which is extremely hypertonic and independently associated with increased mortality, even after successful resuscitation. Hyperosmolarity may cause a decrease in aortic diastolic pressure, increase in right atrium pressure and decrease in lung perfusion.56 In addition, the sudden elevation of CO2 pressure may act on brain arterioles causing an increase in brain perfusion and consequent hemorrhage. Some authors consider that adequate volume infusion corrects metabolic acidosis as efficiently as bicarbonate, without the risk for sodium overload and hyperosmolarity, and suggest that sodium bicarbonate should not be used in neonatal resuscitation.57

Taking into consideration the risk and laboratory evidence of the deleterious effects of sodium bicarbonate during resuscitation, it is suggested that sodium bicarbonate be used only in cases of prolonged resuscitation, when other measures are not successful. It is reasonable to administer this solution very slowly in well ventilated patients if an adequate response is not achieved after administration of epinephrine and volume expanders.4,6

**Ethical aspects**

The advances of obstetric interventions and the introduction of new technologies have resulted in increased survival for extreme premies. At the same time, these advances have allowed the development of more newborns with altered neuropsychomotor development. Several of these babies who were not previously considered to viable currently survive. These aspects call for an ethical discussion concerning the decision to perform resuscitation procedures in the delivery room. Such a discussion involved moral and legal considerations about the high emotional and financial burden that may be placed on the family, health professionals, and society.58
The resuscitation of extreme low weight neonates becomes more controversial the lower the weight and the gestational age at birth. Although the minimum weight to start resuscitation in the delivery room varies from institution to institution, the probability of survival may be better estimated when the gestational age is also known. Despite the fact that weight is a precise measure, which can be obtained immediately after birth, its reliability to predict viability is limited. For example, a premie weighing 750g may be considered adequate for 22 to 26 weeks of gestational age, but this difference of four weeks is associated with a wide variation in survival rates - from 0 to 66% according to U.S. data. Therefore, gestational age is a better indicator of viability than weight at birth.

Although there is no consensus concerning “how small is small,” a survey carried out with U.S. neonatologists revealed that those physicians were unanimous in relation to the absence of viability for a gestational age of less than 23 weeks during parent counseling. Hack et al. report that none of 47 premature children with 21 weeks survived and only one out of 27 babies born alive at 22 weeks of gestational age survived. Another study also reports that none of 22 babies born alive at 22 weeks of gestational age survived. Statistical data from the past decade show that survival varies from 5% to 41% at 23 weeks, from 33% to 57% at 24 weeks, and from 60% to 79% at 25 weeks of gestation. Survival is between 71 and 78% at 26 and 27 weeks of gestational age.

Data obtained at a public university hospital maternity ward in the city of São Paulo suggest that the limit for viability is around 25 weeks. After analyzing survival in the years of 1993, 1995 and 1997, the authors conclude that all the efforts must be placed on delivery care and resuscitation of neonates with less than 27 weeks, whereas in babies with 25 to 27 weeks of gestational age, the presence of other factors must be weighed before a more aggressive strategy is adopted.

Unfortunately, in daily practice, the precise gestational age is unknown in a significant portion of cases. In addition, the neonatal clinical assessment of gestational age using the new Ballard score for age between 22 to 28 weeks may also be imprecise in 1.3 to 3.3 weeks. It is important to stress that the clinical sign of fused eyelids may be present in about 20% of babies born alive with gestational age between 24 and 27 weeks. These facts may complicate decision-making in the delivery room. Thus it seems prudent to recommend that reanimation must be instituted if gestational age cannot be determined. The “wait and see” strategy before starting resuscitation must be abandoned, since delaying the beginning of resuscitation procedures may result in lesions associated with cold-related stress, hypoglycemia, hypotension, and hypoxemia, increasing mortality and morbidity.

Data from several countries support the notion that resuscitation should not be indicated for a confirmed gestational age of less than 23 weeks or weight at birth below 400g. Passed this cutoff point, if time allows, parents should receive orientation so that they can understand the implications of resuscitation, including the probability of sequelae from diseases associated with a specific gestational age. In addition, the evolution of neonates at a certain institution should also be weighed in the resuscitation decision. Each clinical case should be individualized, trying to establish adequate communication between parents, obstetricians, and pediatricians with the aim of deciding if resuscitation applies. However, it is important to stress that most physicians agree that the delivery room is the most adequate site for making life-death decisions.

In 1987, Avery reported, with some apprehension, some aspects of resuscitation in newborns weighing less than 750g, taking into consideration U.S. culture: to establish institutional routines for reanimation of extremely low weight premature babies; to discuss the situation with the family, if possible before delivery, and to take into consideration the wishes of the family; to institute ultrasonography between 10 and 20 gestational weeks to establish gestational age more precisely; not changing decision not to resuscitate once it is taken; initially, give the newborn the benefit of doubt; make decisions taking into consideration the values of the physician and the institutional routines. Besides extreme prematurity, other diseases that may have to be considered when making not-to-resuscitate decisions in the delivery room include congenital anomalies with fatal prognoses. Advances in the detection of chromosomal defects and hydrocephaly, among other serious complications, provide support for a poor prognosis, although this is often uncertain. A confirmed diagnosis of trisomy 13 or 18 and anencephaly is considered by some investigators as sufficient basis for do-not-resuscitate decisions, since death or survival with severe alterations is very likely. However, such decision must be discussed with the parents, taking into consideration cultural, religious, moral and legal aspects.

In our setting there are no specific recommendations elaborated by bioethical committees concerning minimal gestational age or presence of congenital anomalies to orient resuscitation decisions in the delivery room. Maternity wards should compile information concerning the success or failure of resuscitation procedures in their delivery rooms, as well as survival data according to gestational age, weight at birth and presence of congenital anomalies, so as to compare them with data available in the literature and thus discuss and determine their own routines in relation to these patients.

Another ethical aspect that should be considered refers to the interval before resuscitation procedures are interrupted in the delivery room in relation to gestational age. A retrospective analysis carried out between 1989 and 1992 including 156 patients with weight equal to or less than 1,000g revealed that among babies weighing less than 750g and requiring cardiac massage with or without medication,
none survived. All the newborns weighing between 751 and 1,000g submitted to heart massage and not requiring medication survived, whereas half of those who received heart massage and required medication died.58

The experience of the Vermont Oxford Network, which encompasses 196 neonatal units with 27,707 premies between 401 and 1,500g, assessed between 1994 and 1996, reports on survival in relation to the administration of cardiac massage and/or epinephrine during resuscitation in the delivery room. This multicentric study shows that, among those submitted to these procedures, 24% of the neonates with weight between 401 and 500g and 63% of those with weight between 501 and 1,500g survived, in comparison to 17% to 88% in the same weight groups for babies not submitted to these resuscitation procedures. For neonates weighing less than 1,000g, survival was 54% in those submitted to survival maneuvers, compared to 75% without maneuvers. In addition, survival without severe intraventricular hemorrhage (grades III and IV) occurred in 52% of the babies submitted to massage and/or epinephrine in comparison to 81% in neonates not submitted to these procedures. This study emphasizes that most extreme low weight neonates who received heart massage survived, and that at least half survived without severe intraventricular hemorrhage.69

Data from the literature reveal that resuscitation of a newborn after 10 minutes of asystolia is unlikely to result in survival or survival without profound alterations.57,70-72 Resuscitation may be interrupted after 15 minutes if heart rate is still absent even if all resuscitation procedures were carried out adequately.5,6

**Final considerations**

The existence of many controversies and the lack of scientific knowledge concerning several resuscitation procedures currently used in newborns stimulate the performance of experiments in neonate animals and of controlled and randomized clinical assays focusing on development. The aim of these investigations should be to show the efficacy, effectiveness, and efficiency of certain resuscitation procedures, and may alter the routines currently adopted.

**References**


