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Progress in anesthesia and management of the newborn surgical patient

Mary Ellen McCann, MD, MPH, FAAP[a,b,*], Sulpicio G. Soriano, MD, FAAP[a,b]

[a] Department of Anesthesiology, Perioperative and Pain Medicine, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115
[b] Department of Anaesthesia, Harvard Medical School, Boston, MA

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ABSTRACT

Ongoing advances in the perioperative management of the newborn have undoubtedly decreased the incidence of morbidity and mortality of this vulnerable patient group. The introduction of new surgical techniques and more comprehensive understanding of the effects of varied anesthetic drugs and techniques on the surgical newborn present many challenges for pediatric surgeons and anesthesiologists. Thorough preoperative evaluation and open communication between members of the health care team are important. A basic understanding of age-dependent variables and the interaction of anesthetic and surgical procedures is essential in minimizing perioperative morbidity and mortality.

Introduction

The first year of life represents the most vulnerable period, with approximately two-thirds of infant deaths occurring in the first month of life.[1] The leading cause of mortality in infants in 2011 was congenital anomalies at a rate of 126.1/100,000 births followed by premature births at a rate of 104/100,000 live births.[2] Fortunately, the infant mortality rate has declined in the USA ninefold from 1935 to 2011.[1,2] Although, the reasons for this drop are multifactorial, advances in neonatology, pediatric surgery, and pediatric anesthesiology have been certainly instrumental in improving survival and outcomes. Previously, survival after surgery was a cause for celebration, but today the goals have broadened to ensure that neonates are not harmed from the acute derangements in homeostasis during neonatal surgery that may lead to impaired neurological outcomes.[3] Although all organ systems are affected by perioperative alterations in physiology, the neurologic system in particular may be susceptible to neurotoxic and ischemic damage during general anesthesia. In this review, we will discuss some of the relevant anesthetic concerns in surgical neonates.

Prematurity

Closed claim analysis studies have revealed that neonates and infants are at higher risk for morbidity and mortality than any other age group, which is the result of respiratory and cardiac-related events.[4,5] When assessing the anesthetic risks of young infants, it is important to classify them as neonates who are in their first month of life or infants who are in the first year of their life. Furthermore, the risk of anesthesia is greater in preterm neonates who are less than 37 weeks postmenstrual age (PMA). Infants who were born preterm but have reached a chronological age that makes them greater than 37 weeks PMA are considered ex-preterm infants. These distinctions are important when determining which infants are appropriate for ambulatory cases. The rates of prematurity have risen recently in the United States and developed world, in part, because of a higher incidence of multiple births and maternal older age. Premature infants are particularly vulnerable during general anesthesia because of their immature organ systems. Infants born with congenital anomalies are more likely to require both surgical procedures and to have concomitant congenital cardiac defects, which can complicate the conduct of anesthesia.

Cardiac function is limited and is heart rate dependent in healthy newborns because the immature myocardium has limited compliance.[6] Therefore, bradycardia must be aggressively treated to ensure adequate systemic and cerebral perfusion. A very common cardiac abnormality in premature infants is patent ductus arteriosus (PDA), which can lead to either left to right or right to left cardiac shunting, depending on the pulmonary vascular resistance. It is customary to place two pulse oximeters on infants with a known PDA to measure preductal (right upper extremity) and postductal (left upper and both either lower extremity) oxygen saturations during surgical procedures. Intraoperative hypoxia, hypercarbia, acidosis, hypothermia, and surgical stress can lead to ductal reopening. Neonates may need vasopressors such as

* Corresponding author at: Department of Anesthesiology, Perioperative and Pain Medicine, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115.
E-mail address: mary.mccann@childrens.harvard.edu (M.E. McCann).

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dopamine or additional fluids to maintain normotension during general anesthesia. The parasympathetic system is predominant in preterm and term infants; thus stimulation of the vagus nerve by laryngoscopy or the stress of hypoxia can cause bradycardia. Many pediatric anesthesiologists will routinely administer an anticholinergic agent before manipulating the airway of a neonate.

The respiratory system is also affected by prematurity. Although the type II pneumocyte begins to differentiate by 24 weeks' gestation, adequate surfactant is not created until about 34–36 weeks' gestation. Maternal treatment with betamethasone before birth and the administration of surfactant immediately after birth improve respiratory mechanics but many preterm infants still require respiratory assistance such as additional oxygen, continuous positive airway pressure, or mechanical ventilation.[7] Preterm infants have a very high rate of oxygen consumption (more than twice that of adults per body weight) and low pulmonary functional residual capacity. Therefore they are at high risk for oxygen desaturation with any interruption of ventilation. Anesthetic inductions can be complicated by tracheomalacia, which makes mask ventilation difficult. Furthermore indiscriminant mask ventilation results in abdominal distension, which in turn impedes diaphragmatic excursion.

Premature infants are at higher risk for postoperative apnea after general anesthesia, with a reported rate between 5% and 50%, depending on the method of measuring apnea.[8] Studies using clinical measures such as nursing observation with or without impedance pneumonography report rates between 5% and 10%, with anemia, lower gestational age, and length of surgery being risk factors.[8] There is some evidence that regional anesthesia has a lower rate of postoperative apnea but regional anesthesia supplemented with sedatives has a reported rate of postoperative apnea greater than general anesthesia alone.[9,10] Since neonates can have obstructive, central, or mixed apnea, with most episodes occurring in the first 12 hours postoperatively, most pediatric anesthesiologists recommend at least a 12-hour apnea-free period before discharge for former preterm infants who have undergone surgery.[11] The risk of postoperative apnea persists until the infants reach a postmenstrual age of 60 weeks.[8]

Preterm infants are also at risk for retinopathy of prematurity, a progressive overgrowth of retinal vessels, which can lead to intraocular hemorrhage, retinal detachment, and blindness. Although it has been reported in term infants who were not given supplemental oxygen, it is typically found in preterm infants exposed to supplemental oxygen.[12] It is important for anesthesiologists to limit the inspired oxygen for infants less than 46 weeks postmenstrual age and aim for oxygen saturation percentage in the range of low 90s.[12] This may be difficult to do in situations where the respiratory dynamics are altered during thoracic or abdominal surgery.

The immature renal and hepatic systems affect fluid and electrolyte management and alter the metabolism of common anesthetic medications and antibiotics during the perioperative period. Neonates have a lower glomerular filtration rate and urine concentrating ability. This leads to impaired renal clearance of solutes and drugs. Drug metabolism and protein binding are also diminished due to immature hepatic function in the neonate. Therefore it is also important to regulate fluid and drug administration carefully in these patients.

Their surface area is larger per body weight and thus they are susceptible to evaporative losses both through surgical wounds as well as their skin, and their renal system is unable to concentrate their urine to compensate for fluid losses. The larger surface area also puts neonates and premature infants at higher risk for significant temperature fluctuations during surgical procedures. Hypothermia can stress the infant leading to respiratory failure and the need for postoperative ventilation. On the other hand, it is important to not overheat premature infants while in the operating rooms. There are many stressors that may be unavoidable such as episodes of hypotension, hypoxia, or hypocarbia that occur during surgery. The potential for cerebral damage of these stressors is exacerbated by hyperthermia.

Neurotoxicity

General anesthetics in vivo and in vitro experiments have been shown to have neurotoxic effects on the developing central nervous system. These effects include decreased neurogenesis, abnormal dendrite formation, decreased glial cell formation, and increase in neuroapoptosis in both the brain and spinal cord.[13–15] Neuroapoptosis or programmed cell death occurs normally during fetal development as part of cerebral and neuronal maturation. It differs histologically from ischemic cell death in that there is no inflammation, and it tends to occur in isolated cells rather than regionally. However, anesthetic exposure during vulnerable periods in laboratory animals has been shown to lead to a marked increase in apoptotic cell death and subsequent learning deficits, especially in the domain of executive function in animals allowed to mature. The general anesthetics found to cause this neurotoxicity include most of the commonly used agents such as those that block N-methyl-D-aspartate (NMDA) glutamate receptors (ketamine and nitrous oxide) and those that are gamma-amino butyric acid (GABA) agonists (volatile anesthetics, benzodiazepines, and barbiturates). The period of maximal vulnerability in the neuroapoptotic effects of anesthetics in animals seem to correspond with the time of maximal synaptogenesis. For rodents, this is day 7 of life, for rhesus monkeys, it is day 122 of gestation up to day 5 of life with no excessive apoptosis seen on day 35.[16,17] The neurotoxic effects of anesthetics on animals are also dose and duration dependent. Extrapolations of these preclinical studies to humans are fraught with uncertainty because of physiological differences between species and difficulties in physiologic monitoring for glucose, blood pressure, and respiration in very young and small mammals.

The issue of anesthetic neurotoxicity is further muddled by the fact that in some circumstances such as cerebral ischemia general anesthetics can be protective. Isolated pain or surgical stress can lead to increased neuroapoptosis in animals and surgical stimulation has been found to lessen the amount of apoptosis seen after anesthetic exposure in young animals.[18,19]

The susceptibility of human neonates to the neuroapoptotic effects of general anesthesia has not been elucidated. The potential period of vulnerability might be the period of maximal synaptogenesis during fetal and early postnatal development, which in humans occurs between the third trimester of gestation to about 36 months of age. However, there is controversy in this area, with some researchers using neuroinformatic analysis of brain development across mammalian species concluding that the relevant period during human development is 17–20 weeks' gestation.[20,21] This is roughly the same time period of maximal human susceptibility to fetal alcohol syndrome, which is caused by in utero exposure to ethanol, which is an NMDA antagonist and a GABA agonist.[22]

Retrospective epidemiologic evidence clearly supports an association between surgery at a young age and later poor neurodevelopmental outcomes in humans. The infant's underlying pathology; the type, duration and scope of the surgery; and the conduct of the general anesthetics inevitably confound these studies. A case–control study in infants born at 23–27 weeks' gestation found there is an association between the need for surgery and general anesthesia and later abnormal sensory–neural outcomes. The surgeries included PDA ligations, inguinal