Chapter 9

Neonatal Care for Anesthesiologists

Esra Caliskan

Additional information is available at the end of the chapter

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Abstract

In recent years, developments in obstetrics and neonatology have significantly improved the survival and quality life time of neonates. Therefore, anesthesiologists are more confronted with these patients due to surgical and non-surgical procedures. For a safe anesthetic approach and safe care, anesthesiologist must have necessary knowledge and equipment on the physiology of the newborn and should be better understand how immature organs respond to surgery and anesthetic. The purpose of this section is to present spot information that will allow clinicians and anesthesiologists to better understand the problems of neonatal patients and to perform safe care for these patients in the light of the physiologic characteristics of neonates. General principles of anesthetic management of neonatal patients are also reviewed and discussed.

Keywords: neonatal physiology, anesthetic management, perioperative evaluation, postoperative care, neonatal surgery

1. Introduction

Differently from the adult patients, pediatric, especially neonatal age group is a patient population that is difficult to assess. It should not be forgotten that children are not miniaturized adults. Therefore, the preoperative evaluation of the neonate is admittedly the most important part of anesthetic evaluation. The developments in the field of neonatal medicine over the past two decades have increased our probability of encountering a healthy and unhealthy neonatal population [1]. Surgical procedures especially emergency surgical conditions can be represent a significant anesthetic challenge and life threatening in neonatal period [2, 3].

Therefore, the anesthetist needs to take into account the immature function of many vital organ systems, the normal course of development, the effects of the underlying pathologic disease processes, which can frequently lead to serious physiological instability [4, 5].

In this chapter will be discussed issues that related to the anesthetic approach and postoperative care to neonatal patients.

2. Physiological feature in neonatal period

2.1. Organ and system differences in neonate

The neonatal period shows anatomical and physiological differences when compared to adult period. In this section, will be mentioned to physiological characteristics of neonates, also anatomical differences of neonates will be discussed in the part of anesthetic management.

It is important to know the anatomical airway differences between adults and children and newborns for a complete anesthesia assessment [6]. These differences can be listed as follows:

- Proportionately larger head and tongue,
- Narrower nasal passages,
- An anterior and cephalad larynx,
- A longer epiglottis,
- Shorter trachea and neck.

Because of these anatomical features, nasal breathing is dominant in neonates and infants until about 5 months of age [6].

In the newborn period, many vital organ and system functions are immature [7]. In respiratory system, high pulmonary vascular resistance (PVR) which is characteristics in fetal circulation decreases by approximately 10% after labor, but the apparent decrease occurs with the first breath [8, 9]. When the transition period to the adult circulation is examined, pulmonary blood flow, increased alveolar and arterial PO_2 appear to be important factors.

The characteristics of the neonatal respiratory system can be listed as follows: [1, 6].

- Immature hypoxic response, lower functional residual capacity (limits oxygen reserves during period of apnea, rapid desaturation in prolonged intubation attempt),
- Central control of ventilation is not fully develop,
- Peripheral feedback mechanisms are not sufficiently mature,
- Neonatal oxygen consumption 6 cc kg^{-1} per minute is twice that of resting adult (this value increases 10 cc kg^{-1} in the first week of life).

Cardiovascular system changes are also observed during neonatal period. The circulation of a newborn infant is a dynamic state which may revert to a transitional characteristic at any time. This means that the adult series circulation accompanies fetal parallel circulation [10].

The onset of spontaneous breathing is the main factor that reduces high PVR which is characteristic of fetal circulation. This decrease in pulmonary pressure is followed by an increase in systemic vascular resistance and left atrial pressure. Some clinical situations such as hypoxia and acidosis may lead to reduction of pulmonary blood flow which causes a return the fetal circulation features that is called persistent fetal circulation (PFC) [11].

Cardiac function is heart rate dependent in healthy neonates because the immature myocardium has limited compliance [2, 12].

The parasympathetic system is predominant in neonates [10], so that vagal stimulus by laryngoscopy and hypoxia may cause bradycardia. Therefore, it should be avoided bradycardia and treated aggressively when it is observed.

Liver and kidney function are also closely related to the anesthetic management of neonates. In the neonatal period, both organs have not yet completed maturation. The liver serves a critical role in carbohydrate, protein, lipid metabolism, coagulation. And is the primary site for biotransformation of drugs [13]. Hepatic oxidation, reduction and hydrolysis maturation process is rapid and these functions reaches adult rates around 6 month of ages [14]. Because of this, newborns may metabolize drugs (include anesthetic drugs) and toxins less efficiently than adults in the early months of their lives, as the pathway of degradation is immature [1]. Also, one of the changes in early infancy is the lower concentration of total serum protein, albumin and α1-acid glycoprotein. These proteins reach the adult level at about 1 year old [14].

One of the main routes of clearance of drugs and metabolites are the kidneys too. Glomerular filtration rate (GFR), active secretion and passive reabsorption are functions that determine renal excretion of drugs [15].

The kidneys also play an important role in the maintaining of acid base homeostasis and fluid electrolyte balance. GFR and reabsorption are increase age dependent manner. A neonate's kidney takes approximately 6–12 months to achieve adult performance.

In the perioperative period, fluid electrolyte balance is affected and the metabolism of commonly used anesthetic drug altered [10]. Drug metabolism and protein binding are also reduced due to immature organ (hepatic and renal) function [16].

Maturational physiologic changes are most prominent in neonatal period and infancy. The distribution of total body fluid component in neonates is different from adults. Body fluid constitute a greater proportion of body weight in the neonate (approximately 70–75%) and higher than adults. In neonate, the intracellular and extracellular fluid compartments are approximately 45 and 33% of body weight, respectively [17]. These body component changes affect volumes of distribution of drugs.

2.2. Thermoregulation

The newborn baby has a greater surface area relative to weight and a thin layer subcutaneous fat tissue [3]. These properties cause more heat loss to the environment in neonates than older

children and adult. Nonshivering thermogenesis is regulated by brown fat is the primary mechanism in heat generation in the neonates [1]. Brown fat tissue is located in the posterior neck along the interscapular and vertebral regions and it is responsible for heat generation in newborns.

There are four different mechanisms of heat loss [18]:

- Evaporation,
- Convection,
- Conduction,
- Radiation,

Cold intravenous fluids, exposure to cold sterilization solutions, drying of anesthetic gases and the direct effect of anesthetic agents on temperature regulation are the factors that increase this loss.

For this reason mentioned above, caution should be exercised in serious temperature changes in the perioperative period. Hypothermia may cause undesirable effects such as acidosis, myocardial depression, and delay recovery from anesthesia [19, 20].

Maximum precautions should be taken to prevent hypothermia in the perioperative period. These precautions are mentioned in the intraoperative management section.

Characteristics of neonates and infants that differentiate them adult patients are summarized in **Table 1**.

Anatomical differences	**Physiological differences**	**Pharmacological differences**
Head and neck • Relatively larger head and tongue • Narrower nasal passage • Anterior and cephalad larynx • Relatively longer epiglottis and shorter trachea Circulation • Left ventricle –noncompliant • Transitional circulation Respiratory • Weak intercostal and diaphragmatic muscles • Increased resistance to airflow	Increasing parameters • Heart rate (dependent cardiac output) • Respiratory rate • Metabolic rate • Total body water content • Chest wall compliance • Ratio of body surface area to body weight Decreasing parameters • Blood pressure • Functional residual capacity • Lung compliance	Hepatic function • Immature biotransformation • Decreased protein, decreased binding for drug Respiratory changes • More rapid rise in *FA/FI • more rapid induction and recovery from inhaled anesthetics • Increased minimum alveolar concentration Body fluid changes • Relatively larger volume distribution for water- soluble drugs • Immature neuromuscular junction

*FA/FI: Fractional alveolar concentration/fractional inspired concentration.
Table has modified by Lange Clinical Anesthesia 2015.

Table 1. Characteristics of neonates and infants that differentiate them adult patient.

3. General principles of anesthesia in neonate

Neonatal period, which is the most vulnerable time period in terms of anesthetic risk and perioperative mortality, is a challenging period for pediatric anesthetists.

Drug interactions, physiological and anatomical differences, and knowledge of risk factors are also important to reduce these risks.

What are the risks associated with neonatal anesthesia? In addition to the neonatal differences, prematurity, congenital anomalies, asphyxia at birth, and emergency situations that required surgery are risk factors. At the same time, there is a very narrow margin of error, including airway management, vascular access and drug administration. Some of these risk factors are summarized in **Table 2**.

Therefore, a safe aesthetic approach depends on a good understanding of the variables and physiological and anatomical changes taking place in the transition from fatal to neonatal life.

Anatomical differences
Airway anomalies
Difficult airway: Micrognathia, macroglossia, cleft palate-lift
Prematurity, Immature organ and system function
Respiratory
Apnea (especially premature neonates)
Respiratory failure, mechanical ventilatory support, supplemental oxygen
Oxygenation: avoid high FiO_2 (high FiO_2 risk of retinopathy, NEC)
Cardiac
Transitional circulation
Persistent pulmonary hypertension
Immature myocardium
Parasympathetic dominance
Neurological problems
Intraventricular/periventricular hemorrhage (IVH, PVH)
Congenital syndromes and disorders (especially associated with risk of difficult airway, comorbidities of cardiac defect)
• Pierre-Robin syndrome
• Treacher-Collins syndrome (mandibulofacial dysostosis)
• Goldenhar syndrome
• Klippel-Feil syndrome
• Down syndrome
Pharmacological differences
Anesthetic drugs – dilutional changes, prolonged effect
Fluid management
Glucose: avoid hypoglycemia
Intolerance for rapid fluid infusion
Problems of vascular access
Temperature management
Prevent hypothermia
Emergency surgery

Table 2. Risk factors in neonatal anesthesia.

3.1. Effects of anesthetic drugs and inhalation anesthetics on neonates

Effective and safe drug administration in neonates should be based on detailed knowledge on the physiological characteristics of the neonates and pharmacokinetics and pharmacodynamics of given drug. Clinical pharmacology in neonates is recognized with extensive variability. The effect of anesthetic agents varies with organ maturation, body water content and metabolic differences and, coexisting disease in neonatal patient population.

Inhalation anesthesia is a commonly used anesthetic technique in neonatal population. However, intravenous and regional anesthesia methods also can be applied as anesthetic technique in this patient population. The minimum alveolar concentration (MAC) of an inhaled anesthetic is the alveolar concentration that prevents movement in 50% of patients in response to a standardized stimulus (e.g., surgical incision) and changes with age [1, 6, 21]. MAC for inhalational agents is less in neonates than in infants (up to 6 months of age [12, 21]. In newborns, cardiac and respiratory functions and blood pressure are very sensitive to volatile anesthesia. Immature myocardium and less developed compensatory mechanisms are responsible for this result. Therefore, these anesthetics can cause dose dependent cardiac and respiratory depressant effect and can be seen bradycardia, hypotension and postoperative apnea. These effects are more pronounced during the induction period [12, 22].

Intravenous anesthetic agents may be used for induction of anesthesia when inhalational anesthetics are not preferred and/or not practices.

Factors affecting the administration of intravenous anesthesia can be listed as follows:

- Larger intravascular and extracellular fluid compartments,
- Immaturity of hepatic biotransformation pathways,
- Decreased protein binding,
- Increased organ blood flow,
- Higher metabolic rate.

These factors mentioned above affect the properties of the intravenous anesthetics such as duration of effect (onset and termination), doses and toxicity limits of drugs.

An opioid agent causes fewer hemodynamic changes but it should be noted that increase the risk of postoperative apnea and late-onset re-sedation in recovery in preterm and term neonates [2, 4].

Thus, it is crucial that intravenous lines are flushed and cleared of any medication (e.g. opioid, neuromuscular blocker).

Muscle relaxant may be required for some surgical procedures (especially abdominal surgical procedures such as necrotizing enterocolitis, abdominal wall defect). The response of neonates to nondepolarizing muscle relaxant is quite variable. Neuromuscular junction is immature in preterms and this increases the susceptibility to muscle relaxants. However, the large

extracellular distribution volume will dilute the drug concentration, while those metabolized in the liver will prolong the duration.

4. Anesthesia preparation in neonates before surgical procedure

4.1. Preoperative evaluation

Anesthetic management in neonatal patients can be challenging but careful preoperative assessment means that a safe and smooth preparation process for the neonates and anesthetic team. This evaluation is also an approach that encourages confidence for their parents.

A careful preoperative examination allows the anesthetist to determine the risk of anesthesia based on the general state of health of newborn. It is aimed to establish an appropriate plan for anesthesia, postoperative care and analgesia in the light of acquired information.

Preoperative assessment in neonates should include a comprehensive examination of the neonate's perinatal history (such as prematurity, apnea-hypoxic episode history, duration of oxygen dependency, neurological damage etc.), congenital anomalies, previous anesthesia applications, and general state of health (acute, chronic lung disease, cardiac pathologies, etc.) [23].

Premature, ex-premature and term neonates are highly heterogeneous group within newborn period and needs various surgical interventions. Most of them come directly from the neonatal intensive care unit (NICU) and require urgent intervention. Many unusual congenital syndromes occur in childhood. These congenital anomalies in newborn period may accompany emergency surgical procedures [24]. Congenital anomalies that may cause difficult intubation should be noted and the anesthesia plan should be made accordingly.

In addition, a more detailed examination should be performed to reveal early postnatal problems that may be seen (such as hypoglycemia, infection and sepsis, etc.).

Risk factors which are important in neonatal anesthesia are summarized in **Table 2**.

A systematic approach to preoperative evaluation will prevent important problems from being overlooked. Many healthy neonates undergoing elective simple surgery and procedures are fit and do not require compressive physical examination. However, evaluation of the head and neck (such micrognathia, limited neck mobility, macroglossia, etc.) and cardiorespiratory examination (cardiac congenital anomalies, breathing sounds, respiratory pathologies associated with increased secretion and inflammation etc.) should be performed before surgical procedures. Also in cardiac examination, previously undiagnosed murmur with pathological qualities (e.g. loud, continuous, diastolic and or/associated with a trill) may be noticeable.

Evaluation of the airway is critical to the delivery of safe anesthesia. In neonates with a syndrome associated with airway anomalies, the potential presence of a difficult airway (**Table 2**) (*e.g. Pierre-Robin, Goldenhar, Treacher-Collins Syndrome, cleft palate and lip, maxilla mandibular synechia, etc.*) can be identified preoperatively.

It is also important to identify any concomitant (such as necrotizing enterocolitis, hyaline membrane syndrome, cardiac pathologies, sepsis, etc.) disease which might increase the risk of anesthesia and surgery. Familial, genetic, and neuromuscular diseases are important for anesthetic management. The presence of these diseases should be questioned.

Body weight, height, head circumference size must be recorded in order to evaluate newborn's physical status. For example, microcephaly is associated with some genetic disorders and may cause neurological sequel, which may pose a risk for anesthesia.

In laboratory evaluation, a baseline hemoglobin measurement should be obtained for minor surgical procedures [24]. If there is no indication for emergency surgery, anemia should be treated before surgical procedure. Because, even if it is a minor surgery, anemia may precipitate postoperative apnea and bradycardia in neonate. In addition to hemoglobin, in infants with fluid and electrolyte deficit, initial electrolyte values are also important. In major surgeries (e.g. oesophageal atresia, necrotizing enterocolitis, congenital cardiac surgery, neurosurgery) full blood count, blood electrolyte values, renal function and clotting test are recommended [25].

Fasting time before elective surgery should be pointed out. Clear liquid, breast milk and formula milk intake should be prohibited at according to the recommended fasting times (2 hours for clear liquids, 4 hours for breast milk, 6 hours for formula/non-human milk) before elective surgery [12, 14, 25]. Since prolonged period of fasting time pose a risk for hypoglycemia and dehydration, dextrose containing intravenous maintenance fluids should be instituted early period.

A systematic approach the preoperative assessment is summarized in **Table 3**.

Gathering of patient information
History of neonate
Perinatal
Medical conditions (co-morbidities, congenital syndromes, genetic disease)
Medications
Previous anesthesia and surgical experience
Examination
Body weight, height
Physical observation
Airway (especially pathologies that can cause difficult intubation, micrognathia)
Respiratory System
Prematurity
Bronchopulmonary dysplasia
Laryngeal pathologies, stridor
Breathing sounds
Cardiovascular system
Auscultation of heart
Neurological (intracranial hemorrhage history-treatment, seizure activation)
Previous resuscitation history
Previous anesthesia experience
Optimize medical condition
Determination of anesthesia risk
Determination of anesthetic plan

Table 3. Systematic approach to preoperative assessment.

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4.2. Preparation of the operating theater

Anesthesia preparation should be based on the information obtained from the preoperative visit. But, anesthesia preparation does not include preparation of anesthetic equipment, drugs and anesthesia station only. It also includes preparations for the operating theater, such as proper heating of the surgery room, preparations for aspiration materials and arrangements for the patient's position.

The newborn baby has a high ratio surface area to body weight and a thin layer subcutaneous fat tissue. Therefore, neonates lose heat rapidly more than older children and adult [1]. The operating room temperature must be set to maintained neonate's thermoneutral temperature in order to minimize heat loss. In addition, the following applications can be used to reduce heat loss:

- Humidify and warm inspired anesthetic gases
- Many devices such as warmed blanket, overhead radiant heater, a forced air warmer mattress, clear plastic drapes
- Using heating solution for cleansing the skin
- Warm blood and intravenous solutions
- Transport the neonate in a heated incubator

Gas resources and suction materials must be checked.

The patient position is one of the issues to be considered. Different materials such as soft foam padding, rolls and tapes can be used safely for the position.

4.3. Assessment of patient and anesthetic equipment

Proper anesthesia preparation is very important for safe anesthetic management. This is one of the goals of the preoperative visit.

4.3.1. Airway

No matter what anesthetic method is used (sedation or general anesthesia), the airway must be guaranteed in every situation. Difficult, immature airway and respiratory system can lead to airway obstruction during sedation or mask ventilation. Therefore, appropriately size face mask, oropharyngeal airway, laryngoscope blades, endotracheal tube and suction catheters must be available. The use of transparent face masks are recommended for early recognition of cyanosis, vomiting and secretions.

Endotracheal Intubation Study Group [26] demonstrated that the use of Microcuffed tracheal tubes is effective and safe in neonates and young children. But, most anesthetist prefer to use according to the clinical condition of the patient rather than routine.

The laryngeal mask airway (LMA) can be used as an alternative to endotracheal intubation in the presence of difficult airway and for some short surgical procedures. Against possibility of

difficult pediatric airway, advanced airway devices (such as Glidescope, Airtraq) which allow indirect visualization of the larynx should be available [27].

4.3.2. Anesthesia devices

The anesthesia device must be pre-checked before surgical procedure and anesthesia practice. It is essential that the anesthesia ventilator has the ability to provide neonatal compliance, small tidal volume (usually in pressure controlled ventilator mode) and positive end-expiratory pressure [24]. In recent years, new generation anesthesia machines have been developed which is able to small tidal volumes [28] and to provide the ability to ventilate using pressure support ventilation (PSV) [29].

4.3.3. Monitoring

Heart rate-electrocardiography, non-invasive blood pressure, pulse oximetry, and temperature monitorizations are sufficient for basic monitorizations in a healthy newborn.

In neonates whom more risky for surgical procedures, in major surgical procedures and a special circumstances (such as congenital cardiac surgery, oesophageal atresia, congenital diaphragmatic hernia, expected ventilation-perfusion anomalies, hemodynamic changes, and acid-base imbalance), invasive arterial blood pressure and central venous pressure should be monitored.

Two oxygen saturation probes (the right arm probe – pre ductal, the leg probe - post ductal) must be plugged. This approach may provide the diagnosis as, with reverting to transitional circulation and is important to evaluate possible PDA mediated shunt development.

In last three decades, continuous monitoring of respiratory gases (inspiratory oxygen and expiratory end-tidal carbon dioxide and monitoring of gas flows) and continuous use of ventilator disconnection devices are observed routinely in most anesthesia clinic [27].

The precordial oesophageal stethoscope is a traditional and still valid method of monitoring the newborn. With this method, changes in heart rate and respiratory parameters can be identified in early phase.

5. Intraoperative management of anesthesia

5.1. Induction of anesthesia

The anesthesia station is the working area of the anesthetist. Before the surgical procedure, all drugs and equipments required for anesthetic administration should be checked. The neonate should be properly monitored and placed on a forced-air warming mattress before the induction of anesthesia. A safe intravenous access should be established for drug use and fluid therapy. The use of a topical anesthetic such as EMLA cream facilitates awake placement of intravenous cannula [30].

In addition to routine monitoring, direct observation of the neonate is also an important monitoring method. This observation allows the anesthetist to recognize early signs of certain clinic situations (such as cyanosis and pallor).

Inhalation agents or intravenous anesthetics may be used for induction of anesthesia. Although depending on the choice of anesthetist, induction with inhalation anesthetics is a more preferred method. One of the characteristics of the newborns that are different from older children and adults is that they have relatively high alveolar ventilation but low functional residual capacity [6, 14, 24]. This higher minute ventilation to FRC ratio with relatively higher blood flow to vessel rich organs contributes to a rapid increase in alveolar anesthetic concentration. These features enable rapid induction and rapid recovery in general anesthesia [6].

Inhalational induction has the advantage of protection of spontaneous ventilation (especially, important in neonates with potentially difficult airway).

With the advantages we have mentioned above, volatile anesthetics cause dose dependent cardiac and respiratory depressant effect in neonates. These effects can result bradycardia, hypotension and postoperative apnea. This hypotensive effect is also more pronounced in neonates and preterms with cardiovascular instability than older children.

Also, immature airway and respiratory system may cause airway obstruction in mask ventilation during induction phase. Laryngospasm is a frequent occurrence in neonatal anesthesia in this period [31] and if it is intervened early is usually easy to manage. However, laryngospasm, hypoventilation, hypoxia are among the causes of apnea during induction (especially in cases of late notice) [32].

In short surgical procedures, mask ventilation or laryngeal mask airway may be suitable to support respiration. However, endotracheal intubation is frequently performed in patients with emergency surgical procedures, long and major surgical interventions, conditions that requiring muscle relaxation and aspiration risk.

In situation that where inhalation anesthetics are contraindicated or not preferred, intravenous anesthetics may be used to induce and maintain anesthesia.

As we have already mentioned, total body water and extracellular fluid are increased in neonates [16]. These different fluid component affect volumes of distribution of intravenous anesthetic drugs (this means increasing the volume of distribution, especially for water-soluble drugs).

In addition, due to the immaturity of hepatic functions, duration of action will be prolonged in neonates if the drug depends on hepatic metabolism [6].

Muscle relaxant may be required for some neonatal surgical procedures. However, due to immaturity of the neuromuscular junction, neonates have an increased sensitivity to the effects of nondepolarizing neuromuscular blocking drugs [33]. For this reason, prolonged effects may occur at additional doses.

5.2. Intraoperative period

Balanced general anesthesia management is usually achieved by inhalation anesthesia supplemented with different class and wide range of drugs and/or muscle relaxants and regional techniques or achieved by total intravenous anesthesia.

Barbiturates, opioids, propofol, ketamine listed among these intravenous drugs [14]. Long-acting agents such as morphine should be avoided especially in day-case surgery or procedures and postoperative apnea risk should be kept in mind.

In neonatal patients, reduced hepatic glycogen stores, inadequate muscle glycogen reserve and gluconeogenesis enzyme activity require close monitoring of blood glucose concentration [34].

Intravenous glucose infusion may be required to maintain normoglycemia (serum glucose concentration of 40–90 mg dL [1, 24].

All maintenance fluids and blood products used intraoperatively must be warmed before use. Intravenous fluids should be titrated with an infusion pump or a fluid-adjusted burette to avoid excessive fluid loading and to give a controlled fluid.

Following the first few days of baby's life, in all newborns of gestational age, adequate intake of sodium is essential for continued normal developmental activity [1]. In full term neonates, it is not usually necessary to add sodium in maintenance fluids in the first 24 hours of life. However, sodium is added to the maintenance fluids after the second day to replace the sodium losses from the renal and gastrointestinal tract [35]. Also, non-hypotonic, dextrose-containing fluids for sodium replacement may also be used. But, hypotonic fluids should be avoided. These fluids are most common cause of potentially lethal postoperative hyponatremia [35, 36].

Intraoperative fluid requirement should also be met, depending on pre-existing fluid deficits, quality and duration of operation, and the extent of blood loss.

It should not be allowed hypothermia during the intraoperative period. Hypothermia may cause stress in the newborn, leading to postoperative respiratory insufficiency and ventilatory support [10]. On the other hand, the only stressor factor that to avoid in newborns is not hypothermia. Many stress factors (such as hypotension episodes, hypoxia, hypercapnia, acidosis, anemia) can occur during intraoperative period. These factors leads increase PVR and can cause return of the transitional circulation [Ivanova-24]. Different therapeutic maneuvers such as hyperventilation, deepening anesthesia, increased inspired oxygen, and volume expansion may also help in treatment [10].

5.3. Postoperative period and pain practices in neonate

Many neonates undergoing day-case surgery can be anesthetized using mask ventilation and/or LMA by continuing spontaneous breathing without the use of muscle relaxants and intubation.

However, in some situations (such as in major surgical procedures, urgent surgery, full stomach, etc.) endotracheal intubation must be done to secure the airway.

In these patients, in these patients there are many factors that determine postoperative extubation (including surgical conditions).

In major surgeries, (such as NEC, oesophageal atresia, diaphragmatic hernia) endotracheal intubation safer for these neonatal patients. In these neonates usually require elective postoperative mechanical ventilator support in early postoperative period in NICU.

Estuation period is a critical as intubation. Likewise, it requires to be careful and attentive.

It should be take care with regard to residual neuromuscular block and the neuromuscular blocker drugs should be reversed. In extubation period, we may encounter with side effects such as bradycardia, hypoxia, bronchospasm, which can be seen in induction of anesthesia. Intubation equipments and drugs should be available in the anesthesia theater for immediate intervention.

Post-conceptional age (PCA) is important factor in ex-premature babies, for day case surgical procedures. Most ex-premature babies are suitable for day case surgical procedures at greater than 60 weeks post-conceptional age (PCA). Prior to 60 weeks PCA, especially in premature infants less than 44 weeks PCA, postoperative apnea risk increased. In these neonates is recommended postoperative saturation and apnea monitoring in postoperative 24 hours period.

Pain in neonatal patients has for many years been ignored. However, the theory that newborns do not feel pain has become a subject that has lost its validity nowadays.

Recent studies have shown that neuroanatomical and neuroendocrine systems of premature newborns are sufficient for the transmission and perception of pain [37].

Untreated pain causes restlessness, increased oxygen consumption, ventilation/perfusion deficiency, and reduced food intake in early period of neonatal life. Long-term effects are learning disability and developmental retardation. Surgical trauma causes pain and a hormonal stress response that is directly related to the severity and urgency of surgery. Opioids (such as fentanyl, ultra-short acting remifentanil or traditional longer acting morphine) reduce the stress response and catecholamine release in response to painful stimuli. In addition, opioids provide effective pain control so decrease the pulmonary vasoconstrictor responses to painful stimuli in NICU.

In recent years, intravenous paracetamol has begun to be used in the treatment protocol of pain in neonates [38].

6. General anesthesia and developing brain. A special highlight for neonatal anesthesia

One of the most interesting topics in the last 20 years is the general anesthetic effect on the developing brain and neurocognitive functions.

Animal studies show that exposure to general anesthetics (especially these acting through the NMDA and GABA receptors) during the critical period of neuronal development in the developing brain leads to an apoptotic cell death and neurocognitive impairment especially in immature brain [39, 40]. It is reported that this effect to be related to drug dosages and exposure time.

Long-term neurobehavioral effects of sedative and anesthetic agents should be supported by long-term human studies. In recent years, early results of international, multidisciplinary, prospective clinical trials such as GAS and PANDA have begun to be published [41, 42].

In these studies and in Wilder et al. study, it has been reported that multiple exposures to anesthesia, rather than single exposure to anesthesia, pose a risk factor for later development learning disability in children [41–43].

However, to withhold sedation and anesthesia when necessary, would result in ethical consequences, in addition will trigger many negative consequences of painful stimulation in neonatal patients.

7. Conclusion

Approximately 1.5 million neonates receive general anesthesia each year for a surgical procedure according to literature data on neonatal patients [44].

In recent years, it has seen significant improvements in pediatric and neonatal anesthesia practice such as patient safety, advanced monitoring methods and new anesthesia equipments. Nevertheless, the neonatal period is still challenging for the anesthesiologist.

Anesthetic approach in neonatal population has to take into consideration the many immature vital organ functions as well as the effects of the underlying disease processes, which can frequently lead to severe physiological derangements.

Therefore, reliable anesthesia management is possible with a good understanding of the anatomical, physiological and pharmacological differences of the neonatal period.

Also, basic understanding of risk factors in neonatal anesthesia is a starting point for the reduction of risk. A careful preoperative examination of the child and the child's medical record, careful and close perioperative monitoring and follow-up and effective pain treatment would reduce mortality and morbidity.

The basics of safe anesthetic management in neonatal patients are summarized in this chapter, based on feature of neonatal period. The approach in neonatal emergency surgical procedures has not been mentioned in this chapter, since it was described another chapter.

Author details

Esra Caliskan

Address all correspondence to: duru5654@gmail.com

Department of Anesthesiology and Reanimation, Baskent University Faculty of Medicine, Ankara, Turkey

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