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ANESTHESIA FOR NEWBORNS AND INFANTS

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Abstract

One of the most difficult andthe most challenging assignments for anesthesiologist is providing safe and effective treatment for newborns and infants during operation.

When performing endotracheal intubation, we must consider specific anatomical differences of this age: larger head, flexible longer and larger epiglottis, voluminous tongue and high larynx position. The data from the literature suggest that the safest position for intubation is “neutral position” of the body with light head flexion towards the chest. However, some pediatric anesthesiologists are preferring the “sniffing position” that is reached by setting a soft roll under the shoulders (1). All newborns with body weight<1kg should be intubated with 2.5 cuffless endotracheal tube, and newborns with body weight >2.5kg with 3.0 cuffless endotracheal tube. Current protocols are suggesting the routine use of video-laryngoscopy for elective intubation of all children <1year and body weight <10kg (2).Due to small compliance of the neonatal myocardium, the minute volume at this age is more dependent of the hearth rate. The newborns have less ability to compensate the blood loss because of the less efficient vasoconstriction.

Children at this age have decreased ability to metabolize and eliminate drugs. The renal and hepatic function reaches the adult levels approximately after 6 months, and in preterm babies even later. Glomerular filtration rate in the 25th week of gestation is only 10% of adult levels, while at birth reaches only 35%. Drugs have larger volume of distribution due to higher percentage of total body water and extracellular water content (2). The nerve routes are completely myelinated all the way to the thalamus by the end of the 30th week of gestation, so all the babies, even premature newborns, are feeling pain at birth. Therefore, all newborns and infants are requiring careful pain treatment for all painful procedures (1).

Conclusion: It is very important to have good knowledge of the dynamic process of the development of the physiological functions and the specific pharmacodynamics of drugs in the early life of the newborns. The safe treatment of this highly vulnerable age population requires experience, continuous education and excellent manual skills.

Key Words: *anatomical differences, infants, newborn, pediatric anesthesia.*

1. Introduction

One of the most difficult and the most challenging assignment for anesthesiologist is providing safe and effective anesthesiology treatment for newborns and infants during operation. At the same time,this part of our clinical practice frequently is reason for worry and uncertainty even for experienced practitioners. The reason for this is the fact that newborns are not “small adults” and protocols and dosage of drugs for anesthesia cannot simply be transferred to this age group. The main characteristicof this age is the dynamic process of adaptation to extra-uterine life in the form of physiological development changes of different organs. In this process of adaptation, the respiratory and the cardiovascular system are susceptible to the biggest changes. Anesthesiology strategy must be made individually through tight understanding of these physiological processes.

2. Respiratory System

The breathing activity starts with sporadic movements of the diaphragm by the end of the 1st trimester and is gaining stability during late pregnancy. At term the breathing activity reaches 30-60% of the normal values. One very important characteristic of the neonatal age is the presence of ”Hypoxic respiratory depression”, a reflex that can persist up to 6 months after birth. The initial stimulation of the respiration during hypoxia is quickly converted to respiratory depression to levels of ventilation below the normal oxygenation level. Immaturity of the respiratory control is also manifested with the presence of apneas and periodic breathing. Laryngeal and pharyngeal protective reflexes (laryngospasm, glottic spasm, expiratory reflex, coughing, sneezing, apneas and spasmodic breathing) are present in early life but with certain degree of hyperactivity. There are not enough scientific data regarding the development dynamic of these reflexes after the birth. It is understood that the process of maturation of central synapses leads to disbalance of the excitatory and inhibitory control of the central nervous system. The presence of the “Trigeminus-cardiac reflex” is presented with severe bradycardia and prolonged apneas after the stimulation of the stretch receptors of trigeminus nerve. In newborns,it is essential to select the right size and the correct form of the face maskand to avoid excessive pressure on the face. The “Hering-Beuer reflex” results in the depression of the inspiratory activity and prolongation of respiratory cycle after overdistension of the lungs caused by high inspiratory volume and increase in the inspiratory muscle activity after severe deflation of the lungs.

The supraglottic airways in newborns are narrow and soft and can easily collapse during forced inhalation (1). Epiglottis of the newborn is bigger and has a different shape compared to adults (narrow and longer) and has higher position with more vertical presentation. The tonsils and adenoids are disproportionally big and determine the size of upper airways. Their size is continuously increasing until school age and the involution doesn’t start until adolescence. The length of the trachea at birth has 40% of the adult value, but at the same time it reaches only 10-15% of the internal lumen compared to adults. The tracheal diameter is the best correlated with the age, but the length of the trachea correlates with the height of the baby. Cartilaginous rings are soft at birth and gain solidity later.

The main objective of all anesthesiology techniques is to maintain open upper airways and to provide adequate gas exchange. The obstruction of the airways in newborns most often originates from the supraglottic segment and the pharyngeal tissues. Short periods of airway obstruction will lead to the development of severe hypoxemia, bradycardia and if not corrected to cardiac arrest. The positioning of the head and the neck is playing a vital role in prevention, and also the treatment of airway obstruction. Opposite to school children where in supine position and a light extension of the head is suggested, at this age it is the safest to maintain neutral position of the head and neck, with light flexion towards the chest. The simple method to de-obstruct the upper airway is the “chin lift and jaw trust” maneuver. “Lateral position”is considered the safest for all children from 2-12 years that receive any form of analgesia-sedation and are breathing spontaneously (2).

Alveolarizationis the process of the formation of new alveoli and starts at the beginning of the 1st trimester. This process is followed by parallel forming of capillary vessels, the production of surfactant and progressive thinning of the interstitial tissue and alveolar walls.To the purpose of easy and efficient passing try the narrow and rigid birth canal, the rib cage of the newborns is more flexible and with lower degree of calcification. But at the same time the lungs consist of high percentage of immature alveoli that contain less elastin. The combination of soft and flexible rib cage and solid and relatively inelastic lungs parenchyma, leads to higher closing volume of the lower airways and is creating conditions for collapsing and interruption of ventilation. This is happening in the periods of the decreased minute ventilation. It takes a long period for recruitment of the collapsed alveoli to re-open and again take part in the gas exchange. During spontaneous ventilation, babies are dynamically compensating for this immaturity of the tissues by maintaining a higher respiratory rate and shortened expiratory pauses. This creates conditions for diffuse air movement and increased resistance during exhalation, which is helpful in maintaining open alveoli during all phases of the respiratory cycle.

The main determinant of the diffusion capacity of the lungs is the ventilation/perfusion relation (V/Q). While in adults, V/Q relation is mainly dependent on the gravitation force, in newborns ventilation is directed to the non-dependent parts of the lungs. For this reason, the V/Q relation at this age is unfavorable for efficient gas exchange. As the child is approaching school age the V/Q is becoming more efficient. The newborns also have lower and relatively instable value of the functional residual capacity (FRC). There are developed defense mechanisms at this age for maintaining adequate value of FRC, such as: post-inspiratory activity of the diaphragm and inter-costal muscles, higher respiratory rate, and short exhalation phase (auto PEEP) and adduction of the larynx during forced exhalation (functional PEEP). General anesthesia (GA) and deep sedation are lowering the effectiveness of these defense mechanisms. The literature shows that in the most children < 3years old, atelectasis will develop after the induction in GA and giving muscle relaxant (1). The use of positive pressure (PEEP) and recruitment maneuvers is helpful in re-opening of the collapsed alveoli and recovering of the FRC. Volatile anesthetics decrease the activity of the respiratory muscle activity, and consequently lower the FRC. This effect is higher in young newborns that have high compliance of the chest wall. Propofol given to spontaneously breathing children is causing dose-dependent reduction of FRC, decreased V/Q and non-homogenous ventilation. Midazolam given as premedication is causing decreased lung compliance and decreases also the FRC value. Ketamine, even in high doses,doesn't have clinically relevant effect on the FRC and V/Q relation, but we should always be careful of the unpredictable influence on the respiratory rate and the depth of breathing. Opioids have the potential to cause activation of the intercostal and abdominal muscles, which can lead to clinically significant rigidity of the chest wall. This phenomenon is less present in small children. However, we should be always aware of the possibility of difficult face mask ventilation in newborns after administration of opioids. Babies in the first months of life have higher rate of oxygen consumption in accordance with body mass and body surface area compared to adults (6ml/kg/h vs 3ml/kg/h) (3). Higher alveolar ventilation, that has almost double value compared to adults, is effectively compensating for the high oxygen consumption. Increased alveolar ventilation offers advantage for the anesthesiologist and provides fast and predictable inhalator induction in GA due to fast absorption of volatile anesthetics. On the other hand, the standard practice of administration of high levels of oxygen (FiO_2) during the induction in anesthesia and reanimation, can lead to de-recruitment of alveoli, atelectasis and inhomogeneous ventilation with unstable V/Q relation. The data are showing that prolonged periods of FiO_2>80% during GA and postoperatively can result in low breathing volumes that can persist up to 24 hours after extubating the newborn (2). At the same time, we need to be aware of the rapid desaturation that can happen after short apneas even after period of adequate pre-oxygenation with 100% FiO_2.

Small babies have very soft supraglottic airways that are susceptible to obstruction. They have big tongue, voluminous tonsils and adenoids, developed fatty tissue in the cheeks and bigger and horizontal epiglottis. For that reason, they are considered to be "obligatory nasal breathers". Great care should be taken to maintain open nasal cavities and airways for the whole period of hospitalization, pre and postoperatively.The positioning of the infants on the operational table and endotracheal intubation are in the center of every anesthesiologic plan and require certain knowledge and experience. To the purpose of easy passing, try the rigid birth canal the bones of the skull have lower degree of calcification and are considered soft and flexible. Therefore, during the positioning of the head on the operational table in supine position, we need to provide soft surface and adequate fixation of the head and the neck in the neutral position. The newborns have small body surface area which makes the correction of the head and body position very difficult once the site of operation is covered with sterile sheets. It is very important before the sterilization of the operational site to secure and fixate: all the iv lines, endotracheal tube, nasogastric tube, the lines of the hemodynamic monitoring.

The latest reports from the literature are suggesting that the use of video-laryngoscopy for all routine elective endotracheal intubations for newborns < 1 year and body weight < 10kg, will increase the safety and will decrease the rate of unsuccessful intubations (2,3). The experience is showing that the safest position for face mask ventilation and for endotracheal intubation after birth and in the 1st year of life, is the "neutral position" of the head, while the baby is in supine position. Some anesthesiologists prefer light flexion of the head towards the chest wall in early age, as it provides better route for placing the ET. Some pediatric anesthesiologistson the other hand prefer the “sniffing position” that is accomplished by putting a soft roll under the shoulders of the newborn, as well as small flat pillow under the head. All newborns with body weight <1kg should be intubated with 2.5 cuffless endotracheal tube, and newborns with body weight >2.5kg with 3.0 cuffless endotracheal tube. In terms of the correct depth of the ET at this age, there are several orientation formulas for the calculation of the distance to which the tube should be fixated. The famous “7-8-9 formula of Tochen” is calculating the adequate ET tube depth by adding 6cm to the current weight of the child in kilograms. The safest and the most reliable method to determine the correct position and the depth of the ET after intubation in all age groups is, of course, the bilateral auscultation of the lungs and careful monitoring of the end-tidal CO_2 curve during mechanical ventilation. During the mechanical ventilation at this age even small variations of the minute volume can lead either to atelectotrauma, or overdistension and volume trauma of the lung parenchyma. After careful tunning of the respiratory rate, we need to limit the upper value of the tidal volume (6-8ml/kg) and choose the lowest safe margin for FiO_2 in order to avoid oxygen toxicity. Permissive hypercapnia ($PaCO_2$ 45-55mmHg) will contribute to decreased possibility of lung trauma. The current recommendations are suggesting that peripheral saturation (SAT) should be maintained between SAT 89-95% for all newborns, while high value in the operation room should be limited on SAT – 95%, as it will prevent all the possibility of oxygen toxicity (2,3).

3. Cardiovascular System

The circulatory system undergoes dramatic changes in the period of adaptation from the fetal circulation to the extrauterine life. Certain perinatal complications (meconium aspiration, asphyxia and septicemia) can prevent or postpone this transition of circulation and potentially lead to “persistent fetal circulation” that can result with increased pulmonary vascular resistance and raised BP. Clinically this condition is manifested as moderate to severe hypoxemia, right ventricle dilatation and circulatory collapse. Because of the high risk of perioperative complications in this group of newborns, it is recommended that all elective operations should be postponed until this hearth condition is treated (2).

Myocardium of the newborn has smaller compliance and lower ventricle filling pressures. Hearth myocytes after birth are less elongated and have agreater percentage of non-contractile elements, whereas the contractile elements have irregular organization. Based on the findings from animal studies, the Sarco-plasmatic reticulum (SR) and the T-tubular system are immature at birth. Myocardium contraction is less efficient and more dependent on calcium levels, and for this reason, it is very important to monitor and maintain adequate circulatory level of calcium in the first 4 weeks of life. The neonatal myocardium in early life is less responsive to changes in preload which is described as flattening of the Starlings curve. When filling volumes of the ventricles are increased, the pressure on the ventricle wall increases up to the levels when the coronary circulationsdecrease (3). For these reasons the minute volume (MV) in newborns is highly dependent on the hearth rate. This should always be kept in mind, and the mandatory part of all perioperative protocols is continuous monitoring and control of the hearth rate of the newborn.Autonomic control of the circulation is present at birth but is still immature. The data from the literature show that immediately after birth the responses of the autonomic nerve system are limited and the sympathetic component is more reactive. However, quickly after birth (in the first couple of weeks) the parasympathetic becomes dominant component, and this ratio is maintained until school age. Consequently, we can see that instead of acceleration of the hearth rate, every stimulation of the circulation results in a paradox deceleration of the hearth rate and further decrease of the MV. The administration of anesthetics in the circulation is compromising and reducing the autonomic nerve system responses to changes in the blood volume and makes newborns even more vulnerable to bleeding and fluid loss. Due to unstable sensitivity of the baroreceptors, the vascular resistance cannot adequately respond to fall in the BP either with increase in hearth rate or vasoconstriction. Decrease of blood volume of 10% at this age can lead to fall in mean arterial pressure (MAP) for 15-30% (3). At the same time newborns have high circulating blood volume (90-100ml/kg) compared to adults, which means that term newborn with body weight of 3.8kg has blood volume of 320ml. Recommendations suggest that blood transfusion should be initiated when approximately 20% of blood volume is lost, or after loss of 50-75ml of blood. It is also recommended that strategies should be adopted in the direction of monitoring of the blood loss and timely substitution (2). At all stages of the treatment of hypovolemia we should take into account the developmental physiology of the neonatal myocardium and the circulatory system. At this age the myocardium cannot adequately respond to increased preload, and excessive administration of fluids in the circulation can lead to increased filling volume of the right ventricle and even heart failure. The modalities of treatment of hypovolemia in newborns and infants consist of administration of crystalloids (to restore adequate blood volume) and inotropes and vasoconstrictors (to improve minute volume and the hearth rate). Administration of catecholamines has the effect of rise in the MAP and improved perfusion of the coronary circulation and other vital organs. The developmental changes are making myocytes highly vulnerable to high doses ofcatecholamines. It has been confirmed that high doses can lead to decrease in the levels of adenosine triphosphate (ATP) and low energetic depos in the cells and even structural damage of the hearth muscle. Modern recommendations suggest that the use ofcatecholamines in newborns is necessary in the treatment of hypovolemia and shock, but with special care to the administered dose, and we should always be aware of their potential to cause cell damage and decreased energy levels of the hearth (3).

4. Pharmacotherapy

There are limited data regarding the metabolism of different drugs and anesthetics in newborns and infants. The volume of distribution at this age is significantly higher due to a higher percentage of total body water (75-80% of body weight compared to 60% in adults), as well as extracellular fluid content. Consequently, in newborns a higher initial dose of the drug is required for therapeutic concentration in the serum to be reached. We should always keep in mind that it is not possible to simply transfer the protocols and the dosage of the drugs according to body weight. Main routes for elimination of anesthetics and their metabolites are hepato-biliary, renal system and lungs. All these systems are undergoing process of adaptation and maturation in early life. Renal and hepatic function usually reach adult levels of activity in terms of metabolism and elimination of drugs around 6^{th} month of life (4). Glomerular filtration rate (GFR) at term is relatively small and is doubled after 2 weeks of life. At the end of 25th week of gestation, GFR has the activity of 10% of adult values, while at term GFR reaches around 35%. At the end of the 1st year, the GFR has the activity of around 90% and it not reaches full adult activity until the end of the 2nd year of life. . Hepatic route of metabolism and elimination through the activity of P450 isoenzymes is present at birth and reaches approximately 85% of the adult values by the end of 44th week of gestation. The ability for bonding to the plasmatic proteins, albumin and α1 glycoproteins is reduced due to lower circulatory concentration of these proteins in the serum. As a result, we can see higher concentration of free “unbound” fraction of the drugs in the circulation, which is increasing the danger of unwanted effects and complications. The values of proteins in the circulation is stabilized in the 6th month of life.

Minimal alveolar concentration (MAC) is used to express the potency of volatile anesthetics. MAC of all volatile anesthetics is lower in preterm babies but is significantly higher in all other term newborns (3). High values of MAC are maintained until the 6th month and are then starting to decrease, but MAC doesn’t reach adult values until adolescence. For example, MAC of Sevoflurane after birth is 3.2% and this high value is stable in the first 6 months of life.

Intravenous anesthetics are a fundamental part of the anesthesia plan in newborns. After the introduction of secure iv line, we need to establish a clear plan regarding the types of drugs and their doses and dosage intervals respectively. The administration of anesthetics should be adapted to the specific developmental physiology of renal and hepatic systems, as well as the levels of circulatory proteins.The pharmacodynamics of opioids is probably the best understood at this age, probably because of the most frequent use (4). All newborns, as well as premature babies, are experiencing pain that if left untreated can lead to serious stress response in form of: metabolic acidosis, hyper or hypoglycemia, cardiovascular instability or electrocytes abnormality. Therefore, all infants have the need for active treatment of pain (1). Morphine is still the most frequently used opioid worldwide, but the data are showing that there is high dependency from the renal route of elimination, and when administered in clinically significant doses we can expect prolonged half-life in circulation and pronounced hypotension. Synthetic opioid fentanyl has less effects on the cardiocirculatory system and is safe solution for the treatment of surgical pain at this age. Propofol has broad use as secure drug for intravenous induction of anesthesia mainly due to positive pharmacodynamic profile. The drug is highly liposoluble and when administered in doses sufficient for the induction in anesthesia, it has prolonged redistribution and longer elimination times from the plasma. Consequently, we can expect the effects of accumulation of the drug and prolonged activity. High doses can lead to deep hypotension and circulatory instability. Although hypotension is transitory, reversible and self-limited, it is important to note that it is more frequent in newborns compared to adolescent and adult population. The use of depolarized muscle relaxant (Succinylcholine) in infants is reserved for providing fast muscle relaxation for endotracheal intubation. Due to high volume of distribution, the dose needed for intubation is higher (2mg/kg) compared to adults (1mg/kg). Despite the high dose, the effect of muscle relaxation is not prolonged because of the fast plasmatic clearance through the activity of plasma esterase enzymes. The response in terms of the length of muscle relaxation of non-depolarizing muscle relaxants is much less predictable and highly variable. All agents from this group have a large volume of distribution and decreased plasmatic clearance. At the same time the neuro-muscular bonds in newborns have increased sensitivity to the presence of these drugs. This is making the clinical use of non-depolarizing muscle relaxants very unpredictable. Historically, the most used drug from this group was pancuronium, mainly because of its capability to decrease vagal activity and increase the hearth rate. But the prolonged muscle relaxation has limited its clinical use. Vecuronium and rocuronium exert less effecton the vagal activity but are also producing much shorter periods of muscle relaxation. It should be emphasized that the length of muscle relaxation in newborns and infants is longer compared to adults and can surpass 60 minutes. All guidelines for pediatric anesthesia are strongly limiting the use of muscle relaxants in the operation room, where the complete equipment for endotracheal intubation and mechanical ventilation is present and ready for use (2,4).

5. Conclusion

Newborns and infants cannot be treated as “small adults”. Therefore, the protocols and anesthetic treatment regarding the plan of perioperative care and dosage of anesthetics and other drugs cannot be simply mirrored from adults to this age group of patients. The perioperative treatment of newborns requires significant knowledge of the dynamic process of postnatal adaptation of different organ systems because these physiological changes are carrying significant specific to the creation of the anesthetic plan for every individual patient at this age. Only by careful planning and strictly following the established anesthetic plan, we can be sure to provide safe and effective care to this highly vulnerable population. Also, the recommendations suggest that the most experienced anesthesiologist in pediatric anesthesia should always perform all techniques in newborn babies. This strategy has been proven to minimize the risk of potentially fatal incidents.

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