Neonatal Surgery

Contemporary Strategies from Fetal Life to the First Year of Age

Mario Lima
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Editors

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1 Introduction to Neonatal Surgery

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In 1989, the British National Confidential Enquiry into Perioperative Deaths (NCEPOD) ruled "that pediatricians and general surgeons must recognize that small babies differ from other patients not only in size and stated that they pose quite separate problems of pathology and management" [1].

As pediatric surgeons, we are convinced that children are not just small adults. This is all the more true for neonates. Neonates have some unique problems that require very special knowledge, special surgical managements, and facilities specifically designed for them. Pediatric surgeons must understand their special needs and that of their relatives. They must learn team working with other specialists. They have to create the conditions to follow their patients from birth into adulthood as the treatments do not end with the healing of the problem but once the child has become an adult.

With the rapid advances in fetal diagnosis, babies are no longer referred at the time of birth, but when prenatal diagnosis is made even if termination of pregnancy is planned because of an expected poor prognosis. Direct contacts between the prenatal team, the neonatologists, and the pediatric surgeons are also highly recommended to ensure continuity in the messages delivered to the parents.

We live now in the era of evidence-based medicine (EBM), and best evidences are generated from prospective trials. Unfortunately, when compared with adult general surgeons who may operate hundreds of similar cases, pediatric surgeons perform a great variety of different procedures but few of each. Consequently, the indications for surgery and the type of procedure performed in neonates are rarely supported by randomized controlled trials, the majority being supported by retrospective studies and surgeon's preferences. Hall and Pierro have tried to summarize what was the EBM randomized controlled trial (RCT) (level I evidence) of some of the most common neonatal procedures (esophageal atresia, congenital diaphragmatic hernia (CDH), bowel atresia, anorectal malformations, anterior abdominal wall defects, congenital lung lesions, Hirschsprung's disease, inguinal hernia, necrotizing enterocolitis, pyloric stenosis). Their review highlights the fact that a quality evidence base supporting many of these interventions is lacking. Only a few randomized controlled trials have been done in neonatal diseases such as congenital diaphragmatic hernia, necrotizing enterocolitis, pyloric stenosis, and inguinal hernia. All of these trials have been based on collaboration between pediatric surgical units convinced by the importance of networks to promote multicenter prospective studies [2].

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In 1999, Hardin and Stylianos undertake to study the current state of the pediatric surgery literature and its value in determining best clinical practice. As of March 1, 1998, they found 9373 references provided through Medline. After review, only 34 studies (0.3%) were classified as prospective, randomized, controlled studies [3]. Twelve years later, Ostlie and St Peter have done a similar study in 2010, collecting all randomized controlled trials from January 1999 through December 2009 published in the English literature excluding transplant, oncology, and the other non-general subspecialties, to conclude that randomized controlled trials represent less than 0.05% of all publications involving pediatric surgery in the 26 journals with at least one trial (<1 trial for every 200 articles) [4]. It is concerning that they document a similar lack in the twenty-first century, despite the increased educational and public expectations placed on EBS.

In a recent lecture, Juan Tovar advocated to which extent pediatric surgery needs to base its therapeutic attitudes and operations on a solid research background [5]. This is particularly difficult on the field of clinical research because of the low prevalence of many of the conditions involved and also because of the fact that patients are minors that are not entitled to give informed consent by themselves for randomized studies. As regards laboratory research, this specialty is scarcely interesting for basic scientists. This situation can only be improved by prospective randomized studies performed in network collaboration with other hospitals/countries and by basic research conducted by pediatric surgeons and/or in association with other scientists [5].

Among the three particularly relevant recommendations that NCEPOD made in the report on perioperative pediatric deaths [1], the first one was: "surgeons and anesthetists should not undertake occasional pediatric practice". This was also a statement of the European Union of Medical Specialists (EUMS) in 1995: "Surgeons taking care of children should have adequate training in a pediatric surgical unit. They should also continue to have regular exposure to this type of patients." Neonatal surgery should only be carried out by surgeons and anesthetists whose pediatric workload is of adequate volume to maintain a high level of surgical competence and to allow the training of the residents. Congenital birth defects complicate 3–6% of pregnancies leading to live birth. As for example of the structural birth defects associated with significant mortality/morbidity, CDH is among one of the most common anomalies, occurring in about one per 2000–3000 live births. Consequently, the opportunity of training—and to keep his expertise—on a CDH is low. Added to these facts, the combination of a shortened training period and the "new deal" on junior doctors about the number of hours has serious implications for training.

This means that neonatal malformations need to be concentrated in some centers to allow sufficient case load. There are arguments for and against such large regional specialist pediatric centers. The benefits of centralization include concentration of expertise, more appropriate consultants on call, development of support services, and training. The disadvantages include children and their families far from their homes and the loss of expertise at a local level. The benefits of centralization far outweigh the adverse effects of having to take children to a regional pediatric intensive care center [6]. Unfortunately, in many places, politicians favor the multiplication of small regional centers to satisfy their voters who are poorly informed of the cold hard facts.

Nowadays, it is unacceptable to train on real patients. The new technologies, namely, minimal invasive surgery and simulators, have been of great help using simulation technology to reduce risks to both students and patients by allowing training, practice, and testing in a safe environment prior to real-world exposure. This is supported by interest in quality of care, restrictions on the use of animal models, limited number of cases, medicolegal pressures, and cost-effective performance. Many models are available. The usefulness of mechanical simulators with faithful models have been proven efficient: hypertrophic pyloric stenosis (Plymale, 2010), closure of patent peritoneo-vaginal tract (Breaud, 2014), pyeloplasty (Breaud, 2014), esophageal atresia (Maricic and Bailez, 2012; Barsness, 2014), and

CDH (Barsness, 2013). They have shift to realistic interactive models. Computerized modern technology with electronically assisted devices and virtual reality environment has provided new tools to the mechanical simulators.

We have now the tools to evaluate cognitive/clinical skills, technical skills, and social/interactive skills as we have seen how important this could be in neonatal surgery. Surgical simulators (mechanical, computerized, virtual) and models (animals and interactive) are the appropriate tools to learn, to train, to assess surgical skills, and to keep his expertise, in spite of the small number of cases.

Becoming a pediatric surgeon requires completion of one of the longest training programs among the medical systems and probably the widest as they have to learn a great variety of procedures but few of each. While specialization among adult surgeons usually focuses on a particular organ or region of the body, pediatric surgery deals with a defined age group. Pediatric surgeons are trained to operate anywhere on the body, and thus they appear to be probably the last general surgeons. They must ask their authorities to provide them modern tools to avoid training on real babies. Undoubtedly, this is expensive, but as said by Bok Derek at Harvard Law School, "If you think education is expensive, try ignorance!" They have to learn teamwork and multicenter collaboration. This will be the challenge of the new generation of pediatric surgeons to promote collaboration between pediatric surgical units and to create networks as to publish multicenter prospective studies with adequate sample sizes.

In spite of these daunting challenges, they remain some courageous volunteers as you probably are, you reader of this book. We need neonatal surgeons, motivated, well trained, wishing to transmit their skills and their knowledge to the future one.

References

1. NCEPOD (National Confidential Enquiry into Perioperative Deaths). Health Serv Manage. 1990;86(5):203.
2. Hall NJ, Eaton S, Pierro A. The evidence base for neonatal surgery. Early Hum Dev. 2009;85:713–8.
3. Hardin WD, Stylianos S, Lally KP. Evidence-based practice in pediatric surgery. J Pediatr Surg. 1999;34(5):908–13.
4. Ostlie DJ, St Peter SD. The current state of evidence-based pediatric surgery. J Pediatr Surg. 2015;45:1940–6.
5. Tovar JA. Research in pediatric surgery. E-Mem Acad Natl Chir. 2016;15(3):67–70. http://www.academie-chirurgie.fr/ememoires/005_2016_15_3_067x070.pdf.
6. Arul GS, Spicer RD. In where should paediatric surgery be performed? Arch Dis Child. 1998;79(1):65–70; discussion 70–2.

Part I

General

2 Anesthesiological Considerations: Stabilization of the Neonate, Fluid Administration, Electrolyte Balance, Vascular Access, ECMO, Bronchoscopy, and Pain in Neonates

Fabio Caramelli, Maria Teresa Cecini, Monica Fae, Elisa Iannella, and Maria Cristina Mondardini

2.1 Introduction

Despite progress in anesthesiology, neonatal anesthesia today still represents one of the most challenging areas in this field for the anatomical, physiopathological, and pharmacological features of newborn babies and requires not only highly specialist knowledge but also manual and technical skills, owing to the size and fragility of these patients.

The mortality rate linked to anesthesiological problems has fallen dramatically in neonates and infants from 1/10,000 in the 1960s to 1/100,000 (1/1,000,000 in healthy patients) today, but it is considerably higher than the equivalent rate in adults.

This proves the particular vulnerability of this patient group, mainly due to difficulties in airway management, the presence of congenital lesion or syndromes, coexisting pathologies, and, potentially, prematurity.

Furthermore, the developing brain seems to be susceptible to the damaging effects of the anesthetic drugs. Extensive literature from laboratory and animal studies [1, 2], as well as some epidemiological and cohort studies in humans [3–6], provide evidence of neurotoxic (apoptotic) effects of anesthetics during the synaptogenesis, which can induce long-term neurocognitive deficits.

On December 14, 2016, the Food and Drug Administration (FDA) issued a warning statement for the USA regarding the use of anesthesia or sedation in children less than 3 years of age [7]. Nevertheless, the hypothesis of anesthetic neurotoxicity has not been confirmed in humans, at least for a single and short-term anesthesia [8, 9]; therefore, the FDA warning is not shared by several Anesthesia European Societies [10].

At the same time, the focus is actually concentrating also on the need to ensure the newborn a safe conduct of general anesthesia and good perioperative clinical practice. The Safetots initiative (http://www.safetots.org/) highlights that there is a casual relationship between poor anesthetic conduct and risk of neuromorbidity.

In fact, several perioperative events may cause cerebral morbidity. The concept of 10-N has been proposed by the Safetots initiative to prevent neurological injury. The **10-N** principles provide a simple matrix of clinical goals: **N**o fear, **N**ormovolemia, **N**ormotension, **N**ormal heart rate, **N**ormoxemia, **N**ormocapnia, **N**ormonatremia, **N**ormoglycemia, **N**ormothermia, and **N**o postoperative discomfort [11]. It is recommended

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that the 10-N be applied to maintain physiological homeostasis.

The development of pharmacological knowledge, the availability of new smaller medical devices, the doubts related to the aforementioned safety of anesthetic agents, and, above all, the increased spread of ultrasound in the field of anesthesia have led to a progressive increase in the use of locoregional anesthesia techniques even in babies.

These safe and effective techniques can be easily used in selected cases, even without sedative drugs, employing non-pharmacological techniques of distraction, as demonstrated by preliminary report of the ongoing GAS trial [8].

In the following pages, only certain aspects of the anatomy and physiology of the newborn and their changing features over time will be touched on briefly within each individual topic, apart from those of fluid balance and body composition.

2.2 Surgical Emergencies and Stabilization

With the advances in care of the newborn over the last 20 years, most of the surgical pathologies that were emergencies in the past no longer require immediate surgery.

This change in the approach toward the surgical neonate was also born from the evidence that adequate stabilization time before the operation is able to improve outcomes, leading the patient to the surgery in the best possible conditions.

The stabilization of the patient is even more important if he has to be transferred, given that the transport is challenging for the physiologic reserve of the critically ill newborn.

In fact there is greater risk for babies requiring neonatal intensive care who are transferred ex utero than those transferred in utero [12].

Stabilization is optimization of clinical conditions and physiologic functions on the basis of the underlying pathology and its pathophysiology, targeting the therapy also on coexisting diseases (e.g., CHDs), as failure to do so may mean futile every other efforts.

The fundamental concepts of the stabilization are always the same in medical and surgical emergencies—detailed medical history, exhaustive physical exam, and management of ABCDE—such as maintaining correct body temperature, fighting respiratory insufficiency, optimizing blood volume, and cardiac output.

Monitoring, respiratory and cardiac support, fluid and electrolyte replacement, and optimal analgesia are the cornerstones of this process, and this strategy should be carried on also in the operating theater to avoid any clinical deterioration.

In fact, as already mentioned, maintenance of physiological homeostasis is key for the safe conduct of anesthesia. Experience is recommended to avoid or minimize complications and adverse events, especially in neonates, which are prone to hypotension, desaturation, and effects of anesthetics.

During the perioperative period, it is important to avoid not only hypotension, hypocapnia, and hypoxemia but also hyperoxemia and hyponatremia, especially in neonates. All these events can cause subclinical neuronal damage: hypotension and hypocapnia can lead to cerebral hypoperfusion; hypoxemia is tolerated only for a short time because neonates have higher oxygen demand and lower oxygen reserves [13].

Congenital diaphragmatic hernia (CDH) is prototype of this changed paradigm.

Approximately 1 in 3000 babies is born with a congenital diaphragmatic hernia [14].

The disorder is characterized by herniation of the abdominal viscera into the thoracic cavity and pulmonary hypoplasia. This one, with associated pulmonary hypertension and ventricular dysfunction/hypoplasia, is key factor which contributes to the morbidity and mortality associated with CDH (30–40%).

The current strategy to postpone surgery until the cardiorespiratory function is stabilized reflects the idea that surgery cannot correct these factors [15].

Firstly, after delivery, the infant should be intubated immediately without bag and mask ventilation, and a nasogastric tube should be positioned to avoid bowel distension that can limit the expansion of the lung [15].

Routine use of surfactant is not recommended [16], and conventional ventilation seems to offer better results in comparison with high-frequency oscillatory ventilation (HFOV) regarding time on mechanical ventilation, need of extracorporeal membrane oxygenation (ECMO), inhaled nitric oxide (iNO), sildenafil, inotropes, and numbers of failed treatment, as shown by the recent VICI (Conventional mechanical ventilation versus high-frequency oscillatory ventilation for congenital diaphragmatic hernia: a randomized clinical trial (the VICI-trial)) [17].

These results probably suggest that minimizing lung injury is much more important than the used strategy to reach it.

However, ventilation is not the only way to improve blood oxygenation. Inotropes and pulmonary vasodilators are also needed to maintain better systemic/pulmonary blood pressure (BP) and to counteract right-to-left shunting across the ductus.

Extensive use of echocardiography can not only give several prognostic factors [18, 19] but also helps in clinical management, allowing for monitoring of pulmonary hypertension, diastolic function of the right ventricle, dysfunction/hypoplasia of the left ventricle, and response to the therapy.

iNO, the most frequently used pulmonary vasodilators [20], failed to improve survival or reduce the need for ECMO, but, in some cases, an increase in PaO_2 was observed [21].

Pulmonary hypertension may also be treated by several other agents (Milrinone, sildenafil, PGI_2, inhaled iloprost, bosentan) even if there is limited evidence of positive effects on primary outcomes [22–26].

However, the hemodynamics, the cardiac insufficiency, and the pulmonary hypertension should be managed simultaneously, as previously described, in order to progressively obtain the better oxygenation and perfusion with the lesser ventilatory insult during the stabilization phase.

From this point of view, prostaglandin-E $(PGE)_1$ can also be used to improve the hemodynamics, employing the ductus as a ventricular vent in case of severe pH and right ventricular dysfunction [27, 28].

There are no standard criteria to define physiologic stabilization, but also our group has proposed the trend and the value of five different respiratory and blood-gas-derived indices to guide the timing of surgery [29]. The reliability of these indices may probably be increased by the use of echocardiography [30, 31].

2.3 Fluid Administration and Electrolyte Balance in Neonate in the Perioperative Period

Fluid and electrolyte therapy is an essential component of the care of the neonatal surgical patient, and an accurate understanding of the changing requirements of growing is fundamental in appreciating the many important pharmacokinetic changes that occur from birth to childhood.

There are developmental considerations that anesthesiologists should consider.

Total body water (TBW) content changes remarkably from before birth until 1 year of age. At 24 weeks' gestational age, a baby's TBW content is close to 85% of total body weight (BW), which is due to a large extracellular fluid (ECF) volume of 40–50% of BW (in comparison with 20% in adults) [32]. This percentage decreases to 75% of total BW for a term newborn but small for gestational age (SGA); preterm infants have an even higher TBW content than appropriate for gestational age babies (AGA) [33].

After birth, the excess of TBW is mobilized and excreted, and the newborn may lose up to 10–15% of its weight (in preterm babies) in the first week of life. Then, the intracellular fluid (ICF) compartment progressively increases at the expense of the ECF compartment. This means that extracellular water content falls in parallel with TBW content, from 45% at term to 20–25% at 1 year of age. The ECF is further divided into plasma volume (intravascular fluid, equal to 4–5% of BW and proportionally similar at all ages) and the interstitial fluid.

There is a similarity in extracellular and intracellular electrolyte composition in children and adults, but, due to the higher ECF volume in infants, there is more sodium and chloride per kilogram and less potassium in infants than in adults.

Furthermore, newborns carry a lower liver mass (glycogen stores) and muscle mass (protein stores) and, therefore, are less able to maintain the normoglycemia during fasting through glycogenolysis and gluconeogenesis.

The postnatal shift in body fluid is principally mediated through the regulation of water and sodium excretion by the kidneys (due to the increase in atrial natriuretic peptide (ANP) secretion and tubular insensitivity to aldosterone) [34, 35].

A term newborn's glomerular filtration rate is about 25% of that of an adult, and this impairs the ability to excrete a water load. Renal function is not completely developed, and, in particular, sodium clearance is limited. Therefore, the neonate's kidneys have limited capacity to excrete both concentrated and diluted urine so are unable to concentrate urine despite dehydration [36, 37].

Neonates also have large blood volume, high metabolism, and high fluid turnover rates relative to their body weight. These changes have important implications for drug therapy, fluid management, electrolyte needs, and glucose requirements in the perioperative period.

In particular, neonates undergoing major surgery are at greater risk of developing dehydration, hyponatremia, and alteration in blood glucose level [38].

Hyponatremia is the most frequent electrolyte disorder in the postoperative period [39]. Recent studies have shown that hyponatremia is due to the administration of hypotonic solutions and the presence of multiple non-osmotic stimuli for antidiuretic hormone (ADH) release [40]. Severe hyponatremia leads to cerebral edema, the main clinical signs being a decreasing level of consciousness, disorientation, and, in the most severe cases, seizure, permanent handicap, or death [41]. Therefore, avoiding infusion of hypotonic fluids, during surgery and in the early postoperative period, should prevent hyponatremia [42].

Fluid requirement can increase due to high liquid loss during the perioperative stage, caused by prolonged fasting, vomit, diarrhea, fever, and major tissue exposure occurring during abdominal and thoracic surgery. Therefore, fluid administration for the neonatal surgical patients must be aimed at supplying basal metabolism requirements (maintenance fluids), compensating preoperative fasting and fluid losses (deficit fluids) and replacing losses during surgery (replacement fluids).

Conceptually, this distinction between maintenance requirements, deficits, and replacement loss is helpful to plan any intraoperative fluid management. Although the pathophysiological bases are well-investigated, some aspects still remain controversial, mainly in newborn infants.

The goal of infusion therapy is to maintain or reestablish the neonate's normal physiological state in blood volume, tissue perfusion, metabolic function, electrolyte, and acid-base balance [43].

The optimal regimen of fluid management is still a matter of debate, and great concerns remain about the type of fluids, the ideal composition of solutions, and the amount of fluids that should be administered [44].

In any event, the neonatal anesthesiologist must bear in mind that the preoperative fasting times for patients should be as short as possible to prevent newborn dehydration, ketoacidosis, and discomfort [45].

In line with the European Consensus Statement Guidelines, recent literature recommends the use of low glucose (1–2.5%) isotonic balance solutions during neonatal surgery. These types of fluids have been shown to maintain acceptable glucose levels and prevent electrolyte imbalances in the perioperative period [46].

Due to the renal function immaturity, the majority of synthetic colloids should not be used. The colloid molecules are large and cannot be filtered by the kidneys; therefore, they remain in plasmatic volume for an unpredictable time.

Albumin 5% has been considered the gold standard for the maintenance of colloid osmotic pressure in neonates and continues to be the most frequently used fluid in volume replacement therapy.

The "right amount" of fluid administration still remains uncertain; however, a fluid infusion rate of approximately 10 mL/kg/h is required in neonates [47].

The most useful parameters that assess the efficacy of the intraoperative infusion therapy are mean arterial blood pressure, heart rate, capillary refill time, core-peripheral temperature gradients, base deficits, and blood glucose levels. Measurement of central venous pressure and diuresis do not predict the real fluid responsiveness.

In case of major surgery, regular (hourly) blood gas analyses should be performed to assess the acid-base status (base excess, lactate) and blood glucose level. It is recommended to use a syringe pump or infusion pump in order to avoid accidental overload fluid infusions during neonatal intraoperative fluid therapy.

In the postoperative period, neonates on intravenous fluid therapy need to be evaluated regularly with daily weight measurements, fluid balance assessment, plasma electrolytes, and glucose concentrations.

2.4 Pharmacology

The pharmacokinetics and the pharmacodynamics in neonates are often difficult to predict; there are considerable interindividual differences and variability related to gestational age, postnatal age, coexisting diseases, and different genetic polymorphisms. Indeed, pharmacological data is often lacking and extrapolated from adults by allometric equations with corrective factors for the maturation of metabolic functions [48] (Box 2.1).

Not only is distribution volume increased in neonates but also metabolic/elimination ability is reduced at birth; this depends on postconceptional age and changes quite rapidly over time [49, 50].

Pharmacodynamics of anesthetics is also affected by rapid changes in neuronal connections, functional interrelationships, regional blood flow, and number of γ-aminobutyric acid type A ($GABA_A$) receptors in the developing human brain [51].

Often the use of drugs is off-label in neonates; only a minority (<5%) of the medications used in hospitalized neonates had been approved by the FDA, and no anesthetics had updated labeling for premature babies above 29 weeks of GA [52, 53].

Neonates have narrower margins of error in drug delivery and dilution as well as a higher incidence of drug substitution and drug dosage errors in comparison with adults, increasing the clinical risk of drugs with a low therapeutic index, like anesthetics [54].

Furthermore, adult monitoring systems of anesthesia levels are not validated for use in neonates, making the measurement of the pharmacodynamics anesthetic targets impossible [55].

Therefore, clinical evaluation maintains a pivotal role in the management of anesthesia.

In this setting, inhalation agents usually remain the preferred choice of neonatal anesthesiologists for their versatility, predictability, and singular pharmacokinetics, independent of the different organ functions.

2.5 Vascular Access in Neonates

Adequate vascular access is often challenging in neonates [56] but is fundamental in modern emergency and intensive care and plays a decisive role in stabilization of the patient.

Nowadays, the use of ultrasound (US) has greatly increased the percentage of success in gaining vascular access [57], but, given the size of neonatal structures, equipment with a small linear probe at high frequency (>10 MHz) is needed. Furthermore, it should include Doppler, which allows screening for occlusion and thrombosis, and zoom functions.

The vessel can be visualized in the short-axis view (SAX), where the probe is placed transversally to the direction of the vessel, which is seen in cross section, and in the longitudinal view or long-axis view (LAX), where the probe follows the direction of the vessel, which is seen in its length.

According to the chosen visualization approach, the progression of the needle will be placed in the US beam, so called in-plane (IP) or will cross it perpendicularly, so called out-of-plane (OOP).

Obviously, in the first case, the movement and position of the needle can be seen clearly, but it is not simple to keep the needle in the US beam.

2.5.1 Peripheral and Central Venous Catheterization

Several different approaches are possible, and the choice among these different options is made on gestational age, size, site availability, underlying pathology, and, above all, duration of and indication for vascular access.

They can be classified on the basis of site of access and tip position (umbilical, peripheral, central peripherally inserted, and central) and of expected length of use (short term, long term, and permanent).

2.5.1.1 Umbilical Catheters (UC)

The umbilical vein is the recommended emergency access for neonatal resuscitation, and catheters can easily be positioned in the first few days of life, sometimes up to the end of first week. It is to consider as any other central line but must be removed after 5–7 days [58].

Indications for positioning of UC are low GA (<29 weeks) or higher GA (>29 weeks) but needing mechanical ventilation (MV), total parenteral nutrition (TPN), hemodynamic support, or intravenous infusion in cases of difficult peripheral access [59].

The choice of size according to ultrasound measurement of the diameter of the inferior vena cava and ecographic evaluation of tip position are strongly recommended. A high position is optimal, where the catheter is advanced through the ductus venosus into the IVC. If a radiological check is carried out, the optimal response is the T6–T9 space, above the diaphragm. The tip of a UC in the heart may result in perforation, pericardial effusion with cardiac tamponade, potentially fatal arrhythmias, endocavitary thrombosis, or pleural effusion.

A UC placed in the portal system can lead to necrotizing enterocolitis, colonic perforation, necrosis and hepatic hematomas, hepatic cysts perforating vessels of the portal system, and portal hypertension. Future perspective is to follow the catheter under echographic vision along its progression up to the optimal point. UC migrations have been demonstrated in 50% of patients in the first 24–48 h.

2.5.1.2 Peripheral Venous Catheters (PC)

They are generally inserted at the level of superficial veins of the upper limbs, lower limbs or, in certain cases, at the level of the scalp. They are indicated in preterm births >31 weeks. GA or at term which should receive non-hyperosmolar fluid therapy for a short period of time (maximum 6 days).

In addition to needle cannulas, long cannulas (mini-midline) and long peripheral catheters (midline) may be used, and, in these cases with peripheral access, it is possible to advance and position the catheter up to a great vessel, which allows for it to be kept in place for a longer period of time and to be used for endovenous solutions with higher osmolarity.

Peripheral access can also be gained by using a surgical venous cutdown (the saphenous vein is the usual primary choice). This method, frequently used in the past, today has a limited role only in emergency situations when other peripheral, central, and intraosseous attempts fail.

Intraosseous Catheters

Intraosseous catheters still have a major role in life-threatening emergency situations when other access methods fail and when time is of the utmost importance.

In neonates, the preferred choice is the proximal tibia, but other sites are the distal tibia and distal femur [60].

The pediatric resuscitation guidelines from the American College of Surgeons Advanced Trauma Life Support (ATLS) manual recommend that intraosseous access should be established in the newborn in case of circulatory collapse if umbilical venous access cannot be rapidly achieved [61].

2.5.1.3 Peripherally Inserted Central Catheters (PICC)

In the same way, as described above for midline catheters, the tip can be placed in a central position (at the junction of the superior vena cava with the right atrium).

Usually, a suitable vein is selected under US guidance, and the skin is carefully cleaned and draped. The vein is cannulated using a removable needle, a peelable cannula, or semi-Seldinger technique. The catheter is then inserted into the vein and slowly advanced up to the desired length. Correct catheter tip location must be verified either radiologically or ultrasonographically or using intracavitary electrocardiography.

PICCs combine the advantages of peripheral catheters (less infection risk, fewer complications