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Abstract: PURPOSE OF REVIEW Difficulties to establish a venous access may also occur in routine pediatric anesthesia and lead to hazardous situations. Intraosseous infusion is a well tolerated and reliable but rarely used alternative technique in this setting. RECENT FINDINGS According to recent surveys, severe complications of intraosseous infusion stay a rare event. Minor complications and problems in getting an intraosseous infusion started on the other side seem to be more common than generally announced. The EZ-IO intraosseous infusion system has received expanded EU CE mark approval for an extended dwell time of up to 72 h and for insertion in pediatric patients in the distal femur. Key values of blood samples for laboratory analysis can be obtained with only 2 ml of blood/marrow waste and do also offer reliable values using an I-Stat point-of-care analyzer. SUMMARY Most problems in using an intraosseous infusion are provider-dependent. In pediatric anesthesia, the perioperative setting should further contribute to reduce these problems. Nevertheless, regular training, thorough anatomical knowledge and prompt availability especially in the pediatric age group are paramount to get a seldom used technique work properly under pressure. More longitudinal data on large cohorts were preferable to further support the safety of the intraosseous infusion technique in pediatric patients.

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Intraosseous infusion in elective and emergency pediatric anesthesia: when should we use it?

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Summary
Most problems in using an intraosseous infusion are provider-dependent. In pediatric anesthesia, the perioperative setting should further contribute to reduce these problems. Nevertheless, regular training, thorough anatomical knowledge and prompt availability especially in the pediatric age group are paramount to get a seldom used technique work properly under pressure. More longitudinal data on large cohorts were preferable to further support the safety of the intraosseous infusion technique in pediatric patients.

Keywords
difficult venous access, emergency, intraosseous infusion, pediatric anesthesia

INTRODUCTION
Timely establishment of an intravenous access can be very demanding also in routine pediatric anesthesia patients. Depending on the situation and the provider’s skills, alternative techniques like central venous catheterization or venous cutdown are not an option. Delay in parenteral access can be associated with a higher morbidity [1].

The intraosseous infusion technique is a generally acknowledged alternative for parenteral therapy in various difficult-venous-access situations. It therefore also has its eligibility as a ‘Plan B’ in the perioperative care of pediatric patients. Nevertheless, it still seems to be vastly underutilized [2,3] and some clinicians still have strong reservations using it [4].

Purpose of this review therefore is to describe a reasonable application of the intraosseous infusion technique in pediatric anesthesia.

HISTORICAL ASPECTS
Knowledge about the correlation between bone marrow and systemic circulation goes back to the year 1922. It was then, that the idea to apply fluids for the systemic circulation via the intraosseous pathway first arose [5,6]. In the 1940s, the intraosseous infusion became the standard method to systemically apply drugs and fluids in pediatric care [7–9]. In the 1950s, however, the advent of flexible plastic cannulas for intravenous injection soon replaced the intraosseous infusion technique. It therefore fell into oblivion for several decades.

INTRAOSSEOUS MATERIAL
Medical device manufacturers offer many different specialized systems to establish an intraosseous
infusion. These are either manual needles or assisted devices.

Manual devices are cheaper and do not depend on energy supply but tend to have several other disadvantages: it takes longer until the infusion can get started (30–60 s); they tend to produce a less stable, beveled drill hole; they tend to break under effort and are said to be more painful and even are associated with fractures at the puncture site [10,11].

The EZ-IO Intraosseous Infusion System (Vida-care, San Antonio, Texas, USA) as an assisted device however is one of the market leaders and proofed to outplay several competitive products [10,12,13] especially in pediatric patients.

Which technique finally comes into action is eventually depending on individual resource background.

Hamed et al. [14] from Baghdad just recently described successful and uneventful placement of intraosseous infusions in 30 critically ill infants using simple 18-G intravenous catheters.

**PUNCTURE TECHNIQUE**

Some general principles while inserting an intraosseous needle are equally important, no matter which technique is used. These are hygienic handling of all material, thorough localization of the puncture site according to the anatomical landmarks, a firm fixation of the needle in the bone and injection without paravasation and swelling. The process of intraosseous puncture at the proximal tibia, the way it would be performed with the EZ-IO system or a manual needle is described as follows:

1. Identify anatomical landmarks (e.g. tuberositas tibia: two patient fingers caudal and one finger medial).
2. Skin disinfection and sterile handling.
3. Consider peristomal local anesthesia (if appropriate/necessary).
4. Intraosseous puncture:
   a. Fix bone firmly between thumb and index finger of nondominant hand
   b. Prick needle through skin without rotation
   c. Verify contact with the bone surface
   d. Drill until loss of resistance after penetrating cortex
   e. Check that needle is firm into the bone (must not move)
   f. Aspiration of bone marrow is ‘nice to have’ but not required
   g. Consider intramedullary local anesthesia (if appropriate/necessary)
   h. Inject saline bolus (5–10 ml), make sure no paravasation.
5. Fix needle with stabilizer.
6. Check regularly for dislocation, paravasation, compartment syndrome.

Although many puncture sites are described in literature, the tibial bone seems to be the preferred location for intraosseous infusion in pediatric emergency care [15,16]. In school-age children, its puncture sites are relatively easy to identify and to palpate, as described in the process of intraosseous puncture at the proximal tibia described above. In infants and toddlers, subcutaneous tissue makes proper palpation sometimes impossible. In these situations, the proximal puncture site can be found, starting palpation from proximally, thumb and index finger on the condyls, going downwards where the bone is still clearly cone-shaped. The puncture site is then in the middle of the still cone-shaped antero-medial edge (before reaching the cylindrical diaphysis) strictly between thumb and index finger (Fig. 1).

In 2011, the EZ-IO intraosseous infusion system has received expanded EU CE mark approval for insertion in pediatric patients in the distal femur. According to a Vidacare Cooperation Internal Study, the distal femur target area is said to be relatively large (measuring approximately 3 cm in length and 2 cm width for a newborn infant) and the landmarks (superior patella and distal femur) can easily be identified [17]. Actually, there are only very few clinical reports of its use in pediatric patients possibly because that information has not yet spread into a clinical daily routine. Nevertheless, one drawback might be that the tissue layer coating the bone might often require a 25-mm needle.

A recently published study proposed Doppler ultrasound technique to confirm intraosseous flow after intraosseous needle placement. It may also be able to verify whether an intraosseous device is still adequately working after transportation or patient positioning [18]. Point-of-care sonographic
technique may therefore support conventional indirect methods of needle position as mentioned in the process of intraosseous puncture at the proximal tibia described above.

In a conscious patient, pain on puncture might become an issue [19–21]. The provider must distinguish between local periostal anesthesia and endostal medullary anesthesia. Penetration of the cortex seems to be less painful than intramedullary injection. Moreover, local anesthesia in a conscious child can be uncomfortable or even painful itself and might render the child even more uncooperative toward the provider’s attempts. A better approach might be distraction of the child’s attention, firm fixation of the leg and an experienced provider with an advanced technique. Together, they seldom produce significant pain. Therefore, local periostal anesthesia is rarely recommended by the author. Intramedullary injection otherwise can be very painful and should initially be performed slowly, after preparing the patient by explaining what will happen or after injection of a small amount of local anesthesia into the medullary cavity before starting injection or infusion.

**COMPLICATIONS AND GENERAL CONSIDERATIONS**

The most dreaded complication is osteomyelitis. Prior studies [7,22] report an incidence of 0.6%. A very recent investigation from Denmark described a 0.4% incidence rate for osteomyelitis in 1802 patients [23]. However, three smaller retrospective pediatric cohort studies [19,24,25] report no such severe complication. It seems that osteomyelitis is a very rare complication if stringent hygienic standards and modern puncture devices are applied. In the author’s institution, a single shot of an adequate antibiotic is additionally considered, applied directly through the intraosseous needle especially, when hygienic conditions were suboptimal or in patients with pre-existing bacteremia.

In 2011, the EZ-IO intraosseous infusion system has received expanded EU CE mark approval for an extended dwell time for up to but no longer than 72 h. Nevertheless, the author recommends using the intraosseous infusion only as a bridging technique and replacing it as soon as possible by an intravenous access.

Epiphyseal plate injury as another potentially severe complication seems to be of little clinical relevance, as it is rarely mentioned in literature. Claudet et al. [26] described normal development of the extremities after intraosseous infusion in a longitudinal investigation. Correct landmarks and proper evaluation of the puncture site are nevertheless paramount to avoid damage of the epiphyseal plate.

Bone fractures are reported using manual needles with too much force. Modern techniques and regular training should take pressure out of intraosseous puncture and reduce providers’ stress.

In his recent Scandinavian study, Hallas et al. focused on ‘real life use’ of 1802 intraosseous infusions. He described a relatively high rate of ‘minor’ problems when using an intraosseous infusion that is not adequately addressed in teaching the intraosseous infusion technique [23]. Among them are the difficulty to penetrate the cortex, broken needles, difficulties to aspirate, displacement and paravasation. Paravasation seems to be a quite frequent problem and occurs because of primary or secondary needle displacement. It can lead to malfunction of the intraosseous infusion or result in compartment syndrome with dramatic complications. In order to avoid these problems, an intraosseous infusion must never be left unmonitored, especially with pressure cuff infusion. During transportation and in the operating room, the extremity has to be checked regularly for swelling, paravasation or newly occurred pain. In the author’s institution, EZ-IO needles have to be fixed with an EZ-Stabilizer that provides an additional fixation of the system to the extremity (Fig. 1b, c).

![FIGURE 1.](a) Intraosseous infusion puncture with EZ-IO System. EZ-Stabilizer before connecting (b) and after connecting (c) a suitable infusion line (fix line with tape to skin).
Removal of an EZ-IO needle with ‘bare fingers’ sometimes is astonishingly difficult because of its tight fixation in the bone. Connecting a 50-ml syringe with luer-lock to the needle neck stabilizes the grip on the needle and facilitates its removal.

After removal of the intraosseous infusion needle, the puncture site should be covered with sterile dressing for 48 h and checked regularly for signs of wound infection afterwards. Mild pain on palpation might occur for the first days after removal and is no cause for concern. To avoid paravasation, no further puncture should be performed at the same metaphysis within these 48 h.

Intraosseous blood can also serve for blood analysis even with I-Stat point-of-care technology [27,28]. There is a repeatedly proofed significant correlation between intravenous and intraosseous infusion samples for hemoglobin, hematocrit and red blood cell counts as well as for glucose, blood urea nitrogen, creatinine, sodium, chloride, total protein and albumin. Discrepancies are confirmed in white blood cell and platelet counts as well as potassium, blood gases, base excess and lactate levels [27]. I-Stat point-of-care analyzers seem to be a convenient and reliable system, bypassing the proposed problem with bone marrow contents threatening to damage conventional laboratory equipment [28]. At least 2 ml of bone marrow aspirate should be discarded before taking a sample.

CONTRAINDICATIONS

In principal, there are very rare contraindications for insertion of an intraosseous needle, if a patient urgently requires vascular access. Nevertheless, some situations need consideration.

Absolute contraindications are situations with local fracture or (recent) orthopedical manipulation at the site of needle insertion and a prior unsuccessful/lost intraosseous needle, as the penetrated cortex will allow extravasation of the applied medication or situations that impede venous backflow of that extremity.

Relative contraindications are: local infection at the site of the planned needle insertion, osteogenesis imperfecta, osteopetrosis and thermal injury at the puncture site. In that case, the same bone’s other metaphysis might be used for infusion or any other adequate alternative puncture site.

INTRAOSSEOUS INFUSION IN PEDIATRIC ANESTHESIA

Difficult venous access, especially in pediatric care, is an ongoing topic. No anesthesia provider or emergency medicine caregiver will escape the repeatedly occurring ‘no-veins’ situation [4]. Professional experience does definitely improve this problem, but extreme situations, caused by anatomy or emergency, will again and again reveal our limits and necessitate a strategy for a ‘Plan B’ [29–32].

Lots of alternatives are available in a situation with difficult venous access. Central venous catheterization, intramuscular sedation, bedside ultrasound and transillumination do all have their advantages depending on the situation and the qualification of the caregiver.

Central venous catheterization, even catheterization of the vena femoralis, goes along with a certain morbidity and cost [33] that might not be adequate for several patients. Moreover, it needs a high level of qualification, especially if the patient is quite young or only superficially sedated (e.g. nonfasted patient after intramuscular ketamine). Ultrasound is not everywhere available and transillumination does only help in small infants. The intraosseous infusion on the other side proofed to be easy to learn and to provide [34–36] and offers a wide range of advantages [15,30,33,37,38], combined with a relatively low rate of severe complications [23,24,26].

Therefore, there are more and more case reports and recommendations for its use not only in the prehospital emergency situation but also for perioperative pediatric anesthesia care [14,22,29,31,32,34,39–46]. As a consequence of these reports and in order to provide a structured approach, the German Scientific Working Group for Pediatric Anesthesia published working guidelines in 2011 for the use of intraosseous infusion in the pediatric perioperative setting [37]. Indications and clinical examples for the perioperative intraosseous cannulation according to the German Scientific Working Group for PediatricAnesthesia (modified from [37]) are as follows:

1. Immediate indication/life-threatening emergency (early or primary intraosseous infusion cannulation)
   a. Cardiac/respiratory arrest, acute shock (e.g. meningococcal sepsis)
   b. Hypothermia, obesity, edema, thermal injury
   c. Critical hemodynamic instability before or during anesthesia induction
   d. Process compromising the airway (e.g. severe laryngospasm, bleeding).

2. Urgent indication (timely intraosseous infusion cannulation after unsuccessful venous punctures)
   a. Relevant dehydration (e.g. gastrointestinal infection)
(b) Urgent induction of anesthesia in a non-fasted child.
(3) Semi-elective indication (intraosseous infusion cannulation after unsuccessful venous punctures and thorough risk–benefit analysis)
(a) Elective surgery, after inhalational induction.
(b) Mandatory ‘intravenous’ induction (e.g. malignant hyperthermia).

Three possible indications are suggested. Indication 1 describes acute life-threatening emergency situations during induction, maintenance or emergence from anesthesia. Although indication 1 is quite rare, indications 2 and 3 describe more common ‘urgent’ or ‘semi-elective’ situations with an individual risk-benefit analysis. They normally occur during anesthesia induction. Here, the low-risk profile of an intraosseous infusion, its minimum of procedural preparation and the low need for operator experience have to be weighed against the risk profiles of alternative, more invasive and time-consuming techniques. The urgent indication as well as the semi-elective indications can be performed under well prepared clinical circumstances. That should contribute to the anyway low rate of complications associated with the intraosseous infusion technique. As already mentioned earlier, Hamed et al. [14] recently described successful and uneventful placement of an intraosseous infusion in 30 critically ill infants in a perioperative ‘urgent indication’ setting according to the German Scientific Working Group for Pediatric Anesthesia classification. Owing to political circumstances (Teaching Hospital, Baghdad, Iraq), the authors were forced to use simple 18-G intravenous catheters. Nevertheless, the only described complications were two dislocations at first attempt and one cellulitis postoperatively.

In elective patients, especially in ASA 3 patients, prolonged searching for a vein might influence a lot of consecutive parameters. Prolonged mask ventilation might result in deterioration of pulmonary parameters like oxygenation, ventilation, gastric insufflation and atelectasis, as in these situations often the more experienced team member usually cares for the venous access, whereas the less experienced member takes over the mask ventilation. Additional problems might occur like decreasing core body temperature, a significant time delay for consecutive patients and last but not least parents claiming an unnecessary high number of puncture wounds. In the author’s institution, there is an unwritten ‘3–3–1’ rule: three punctures for the first provider, three more for the next more experienced provider and one last puncture for another experienced provider (all with additional technical help of course, like transillumination). Until then, the most preferred puncture sites might have been ruined and we seriously consider an intraosseous needle as the next alternative.

Like in airway management, the establishment of parenteral access sometimes needs to stay flexible, speedy and efficient as underestimating the need for parenteral access has been shown to be one of the leading causes of intraoperative cardiac arrest in children [1,47]. ‘Task fixation’ and the anesthetists’ pride to manage a difficult-venous-access situation [34,39,43] should no longer delay a reasonable onset of therapy. Therefore, ‘a change of approach is required rather than repeated use of a technique that has already failed’ [15,48]. Every pediatric anesthetist has to consider and evaluate the situation according to his given ‘standard operating procedures’ and his own experience and expertise. A ‘Plan B’ and a ‘Plan C’ should be part of the training of every actual and future medical caregiver. Regular training and prompt availability of the material in every workplace where children are clinically cared for (Fig. 2) are important requisites to develop reliable skills that also work under pressure and allow us to ‘exercise independent judgment in order to make appropriate decisions in the face of complex and often unstable circumstances’ [49].

A special consideration in pediatric anesthesia might be the child with a known difficult venous access. In these patients, multiple puncture attempts and the possibility of an intraosseous infusion should preoperatively be discussed with the parents. They should be informed about how many peripheral punctures might be necessary and about the complications of an intraosseous puncture before the start of anesthesia.

CONCLUSION
Difficult venous access can delay onset of necessary therapy also in pediatric anesthesia. Intraosseous
Intraosseous infusion in pediatric anesthesia
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Intraosseous vascular access is safe, adequate alternative pathway for parenteral access. No matter which technique is to be used, regular training, thorough anatomical considerations and prompt availability of the material are absolute requirements when dealing with pediatric patients.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES