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Intraosseous Administration of Drugs in Infants and Children

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Intraosseous (IO) infusion of fluids via the sternum was first suggested by Drinker and colleagues in 1922.[1] The use of the IO route for administration of fluids, drugs, and blood products became relatively common in the 1930's and 1940's, but eventually fell out of favor with improvements in plastic catheters which allowed for more rapid attainment of intravenous (IV) access.[2] The IO route reemerged in the 1980's as an option for fluid and drug delivery during emergencies. In 1986, the American Heart Association (AHA) approved use of the IO route for administration of fluids and medications during pediatric resuscitation.[3] In their 2005 guidelines on pediatric basic and advanced life support, the AHA and the International Liaison Committee on Resuscitation (ILCOR) reiterated the recommendation for establishing intraosseous (IO) access if vascular access is not rapidly achieved in any infant or child requiring IV drugs or fluids.[4,5]

The primary advantage of the IO route is the ease with which access may be obtained. It has been shown that trained health care providers can achieve IO access within 1-2 minutes, with a rate of successful insertion of 80% or greater.[6] In addition to the administration of fluids and medications, IO lines may also be used to obtain mixed-venous samples for blood chemistry, blood gas, and type and cross match studies prior to being used for drug administration.[7]

Technique

Cannulation of the medullary cavity within long bones makes use of their rich vascular supply. With IO administration, fluids and drugs enter the venous sinusoids of the medullary cavity, drain into the central venous channel, and leave the bone through nutrient or emissary veins to enter the systemic circulation.[2,8-10]

In infants and children, the most commonly chosen site for IO catheter insertion is the proximal tibia. The recommended site is the flat area approximately 1 to 2 cm distal to the tibial tuberosity. It has been suggested by some authors that the needle be angled 10 to 15 degrees caudally to avoid injury to the epiphyseal growth plate. The site should be prepped with povidone iodine or a surgical scrub prior to needle insertion. In conscious patients, infiltration of the area with 1% lidocaine is recommended. Intraosseous access should not be delayed in an unconscious patient if access is needed for fluids or medications. Special large-bore (13 to 16-gauge), short-shaft IO needles, as well as auto-injectors, are available for use in older children and adults; but in infants, specifically designed neonatal IO needles should be used. If not available, an 18 or 20-gauge spinal needle may be used. The IO needle should be inserted and advanced to the periosteum, then twisted until a lack of resistance is felt. The stylet is then removed from the needle. [2,8-10]

Verification of proper placement may include visual inspection of the site, aspiration of a small amount of bone marrow through the needle, and/or slow administration of 5 to 10 mL normal saline to ensure lack of resistance. Other sites for IO catheter placement include the distal femur and iliac spine. The sternum has been used in a number of adult cases and some pediatric reports, but is generally not recommended in children because of the risk for damage to the heart and lungs and interference with chest compressions.[2,8-10]

Insertion of an IO catheter is contraindicated in patients with a fracture at the access site. Use of IO may not be appropriate in patients with cellulitis or burns at the access site, inferior vena caval injury precluding adequate blood return, and underlying bone disease, such as osteogenesis imperfecta or osteoporosis. Only one insertion attempt should be made in any one bone.[2,8-10]

Efficacy in Medication Delivery

A variety of fluids, including dextrose and saline solutions, Ringer's lactate, and hydroxyethyl starch, as well as most medications used during cardiopulmonary resuscitation (Table 1) can be administered through IO access.[2,6,8-23] It is generally recommended that standard IV doses be used when administering drugs through the IO route.[9,10]

Bolus administration of medications may result in a depot effect, with drug remaining in the medullary cavity producing lower serum peak concentrations and a longer period of drug distribution compared to IV administration.[9,10] The delay in drug distribution may be offset by the administration of a small (3-10 mL) normal saline flush after drug administration. For continuous infusions, the use of an infusion pump is recommended to maintain adequate rates of drug delivery.[14,22]

Table. Medications for IO administration[9-23]

o Adenosine	o Gentamicin
o Amikacin	o Isoproterenol
o Ampicillin	o Insulin
o Atropine	o Lidocaine
o Calcium chloride	o Mannitol
o Calcium gluconate	o Morphine
o Cefotaxime	o Phenobarbital
o Dexamethasone	o Phenytoin*
o Diazepam	o Sodium bicarb.
o Dobutamine	o Succinylcholine
o Dopamine	o Vancomycin*
o Epinephrine	o Vasopressin

* may result in lower serum concentrations than observed with IV dosing

Utility in Pediatric Emergencies

Since the 1986 AHA recommendation supporting IO as an alternative to IV access in infants and children requiring resuscitation,[3] several authors have reported their experience with this route of administration.[23-30] In 1988, two retrospective studies were published in the *Annals of Emergency Medicine*.[6,24] Glaeser and colleagues at the Children's Hospital of Wisconsin reviewed 93 pediatric cases presenting to the emergency department in 1985.[24] Of the 29 patients who presented in cardiac arrest, 16 received an IO line while the rest received conventional IV access (peripheral or central). There were no significant differences in the time to obtain access; however the time to achieve successful IO access included the time spent initially attempting IV access. Actual time to place an IO catheter was estimated to be 30-60 seconds. Intraosseous access was used in only 2 of the 52 children presenting to the emergency department who were not in arrest. In both cases, the IO route was used only after multiple failed IV attempts. The authors concluded that IO placement was a useful adjunct in the emergency setting.

Brunette and Fischer reviewed 33 cardiac arrest events in the emergency department at Hennepin County Medical Center.[6] The IO route was attempted in 12 cases and successful in 10 (83%). The success rates for other access sites were 78% for central venous access, 18% for percutaneous peripheral access, and 81% for surgical cutdowns. The mean time to establishing access was 4.7$\pm$1.5 min for the IO route, compared to 3.0$\pm$2.0 min for a peripheral line, 8.4$\pm$3.3 min for a central line, and 12.7$\pm$3.2 min for a cutdown. Based on their success rate and the rapid time for placement, the authors recommended that after an unsuccessful attempt at emergency peripheral IV access, practitioners should progress directly to IO placement.

In 1993, Guy and colleagues reviewed 32 cases of IO line placement in 27 pediatric trauma patients.[23] In their sample, the mean patient age was 2.9 years (range 3 months-10 years). Successful placement was achieved in 28 cases. The primary reasons for IO placement were cardiac arrest (in 55% of patients), hypovolemic shock (26%), and neurologic insult (18%). Only seven patients survived. Physicians placed 56% of the IO lines, followed by local paramedics and nurses (44%). The proximal tibia was used in 29 cases, while the distal femur was used in just three cases. As in the previous studies, the authors concluded that IO access was a viable alternative to IV placement in the pre-hospital and hospital setting.

Also that year, Glaeser and colleagues published a five-year review of pre-hospital IO use in patients of all ages in the Milwaukee area.[25] All IO placement was done by trained paramedics. A total of 152 patients, with ages ranging from newborn to 102 years) received IO catheters. The overall success rate was 76% per patient. Success rates were significantly higher in children 3 years of age and younger than in older children and adults ($p = 0.04$). Infiltration occurred in 12% of patients.

In 2005, Fiorito and colleagues reported their experience with IO access used during the transport of critically ill pediatric patients to their institution.[26] Over the period from January 1, 2000 to March 31, 2002, 1,792 transports were completed. During that period, a total of 58 IO lines were placed in 47 children. The patients ranged in age from 3 weeks to 14 years. The majority of the lines were placed by the referring emergency medicine physician (42%), followed by members of the transport team (40%), and other emergency medical personnel (18%). Successful placement of the IO needle occurred on the first attempt in 78% of cases. Access was maintained for an average of 5.2 hours and was used to infuse fluids and medications, as well as obtain blood samples for laboratory values. Complications, consisting of local edema or fluid extravasation, were reported in 7 of the 58 cases (12%). The authors concluded that this was a safe and effective method for vascular access in children requiring emergency transport.

In another retrospective review published last year, Smith and colleagues evaluated data from the Trauma Audit and Research Network in England and Wales.[27] They found that IO access was utilized in only 129 of the 23,489 cases collected between 1988 and 2002. The children most likely to receive IO catheters were those under 7 years of age, as well as the more severely injured. In an accompanying editorial, Colin Graham suggested that early use of IO access should be encouraged and that the skills should be taught to all pediatric health care providers.[28]

Use in Neonates

Intraosseous catheterization has also been used successfully in both term and preterm neonates.[29,30] In 1999, Ellemunter and colleagues at the Innsbruck University Hospital placed 30 IO lines for fluid and drug administration in 27 neonates in whom IV access was not achieved.[30] The needles were left in place for a maximum of 20 hours. All patients were able to be appropriately treated with IO fluid and drug administration. Three patients required placement of a second needle after dislodging the first. One patient developed subcutaneous necrosis after extravasation of a hypertonic glucose solution and one developed a hematoma during blood transfusion.

Complications

Complications have been reported in fewer than 1% of patients after IO infusion. The most commonly encountered complication is extravasation of fluids or drugs. As with extravasation after IV administration, there is a risk for necrosis in surrounding muscle and subcutaneous tissues. Fat embolism has also been reported, but with less frequency.[2,8-10]

Extravasation of fluids under pressure can lead to the development of compartment syndrome. Launay and colleagues described a severe case of compartment syndrome resulting from IO placement in a 7-month-old with shock.[31] The patient developed thrombosis of the popliteal artery, leading to tissue necrosis and eventual amputation.

Infectious complications, including cellulitis and localized abscess formation, have also been reported after IO use.[2,8-10] Osteomyelitis is a rare complication, occurring in less than 1% of patients. In a 1985 retrospective review, Rosetti and colleagues reported 27 cases of osteomyelitis in 4,270 IO infusions (0.6%).[9] Conditions associated with a greater risk for osteomyelitis included prolonged IO use, bacteremia, and the administration of hypertonic fluids. Injection of highly concentrated drugs may also place patients at risk. In 2002, Stoll and colleagues reported a case of osteomyelitis in a 3-month-old after he received high-dose (0.1 mg/kg) epinephrine into the right tibia, using the 1:1000 (0.1 mg/mL) concentration.[32] Localized inflammation was noted within 24 hours of medication administration, with no reaction in the opposite leg, which had also been used for IO access. Cutaneous necrosis developed, with osteomyelitis demonstrated on bone scan. Treatment required surgical removal of the epiphysis and part of the metaphysis. The authors suggest that the administration of high concentrations of epinephrine may have led to the complications seen in this patient.

In rare cases, fractures at the insertion site have been reported.[33] Injury to the epiphyseal growth plate has been considered a risk of IO use in pediatric patients, but this effect has not been demonstrated in radiographic studies.[2,34,35] In 1997, Fiser and colleagues conducted a prospective, blinded observational study of 10 children following IO catheterization to evaluate tibial length discrepancy.[34] The authors found no significant difference between the leg in which the IO line had been placed and the opposite leg up to one year after catheterization. In 2003, Claudet and colleagues found similar results in their prospective, single-blind study.[35] They performed radiographic evaluations in 23 children who had received IO catheters (mean age at IO placement 18.6 months). At follow-up (mean time 29.2 months) when compared to standard tables, all anterior leg lengths were within the 95% confidence interval. There were no significant differences in any other measurements between the procedure and control legs. Both groups concluded that appropriate IO placement appears to have no long-term adverse effects on tibial growth.

Summary

Intraosseous administration is a fast, reliable method to deliver fluids and drugs during pediatric emergencies. Studies conducted in animal models, as well as those done in humans, have demonstrated the efficacy of this route in achieving adequate serum concentrations and pharmacologic response. Disadvantages of IO administration consist primarily of the risk for extravasation and rare cases of osteomyelitis. Appropriate placement of an IO catheter does not appear to adversely affect bone growth. When used by trained health care providers, the IO route can be a valuable tool during pediatric resuscitation.

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Formulary Update

The Pharmacy and Therapeutics Committee did not meet in November. Meetings will resume in January 2007.

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