REUE | Review Article

Intraosseous infusion of drugs and fluids in critical patients: a systematic review

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OBJECTIVE. To systematically review the literature to identify drugs, fluids, and blood products administered through intraosseous devices during emergencies, and to determine the flow rates used for infusions.

METHODS. We searched the following databases: Dialnet, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Science Direct, the Spanish National Research Council (CSIC), ProQuest, Scopus, LILACS, Current Contents, PubMed, the Cochrane Librarly Plus, and the Spanish Virtual Health Library (BVS), Cuiden, Cuidatge, the Clinical Online Network of Evidence for Care and Therapeutics (JBI Connect +), and the MEDES search engine. In addition we searched databases for doctoral theses and similar texts: Teseo, TDR, and the document repository of the University of Alicante (RUA). Metasearch engines used were the Trip Medical Database and Google Scholar. The following electronic journals were searched directly: *Evidence-Based Nursing*, *Evidence-Based Medicine*, *Enfermería Global*, *Rol de Enfermería*, *Emergencias*, *Nursing Research and Practice*, *NURE Investigation*, *Revista Científica de Enfermería*, *American Journal of Critical Care*, *The New England Journal of Medicine*, and *Journal of Critical Care and Nursing Research*. Publisher and other web portals for journal groups were also consulted: BioMed Central, Directory of Open Access Journals, Nursing Center, Internet Scientific Publications (ISPUB), RACO (Catalan Open Access Journals), Scielo, and Elsevier. This approach followed the PRISMA recommendations for conducting systematic reviews. We analyzed full texts and specified inclusion criteria governing experimental and quasi-experimental research designs and assessed methodological quality. Articles selected could be published between 2000 and 2021 in Castilian Spanish, English, or Catalan.

RESULTS. Twenty-four articles were included. Among the numerous drugs that were administered through an intraosseous access device were epinephrin, dopamine, dobutamine, adenosine, digitalis, heparin, lidocaine, atropine, and fibrinolytics. Fluids (crystalloids and colloids) were also infused. High flow rates were reported. Blood product transfusions were not followed by hemolysis. Use of intraosseous infusion also allowed valid blood samples to be taken for analysis of blood gases and hemoglobin, sodium, potassium, magnesium, lactic acid, and calcium concentrations.

CONCLUSION. Intraosseous infusion is an option to consider when drugs must be administered rapidly in emergencies other than cardiopulmonary resuscitation.

Keywords: Intraosseous access. Emergency health services. Critical care. Pharmacotherapy.

Fármacos y fluidos administrados por vía intraósea en pacientes críticos: revisión sistemática

OBJETIVO. Revisión sistemática de la literatura científica sobre los fármacos, fluidos y productos sanguíneos susceptibles de administrarse a pacientes críticos por un acceso intraóseo (AIO), en situaciones de emergencia.

MATERIAL Y MÉTODO. Se utilizaron las bases de datos Dialnet, CINAHL, Science Direct, CSIC, ProQuest, Scopus, LILACS, Current Contents, PubMed, Biblioteca Cochrane Plus, Biblioteca Virtual en Salud (BVS), Cuiden, Cuidatge, JBI Connect + y MEDES. Las bases de datos de tesis doctorales y trabajos de investigación fueron TESEO, TDR y el repositorio institucional de la Universidad de Alicante (RUA). Los metabuscadores fueron Trip Database y Google Académico. Las revistas electrónicas consultadas fueron Evidence-Based Nursing, Evidence-Based Medicine, Enfermería Global, Rol de Enfermería, Emergencias, Nursing Research and Practice, Nure Investigation, RECIEN, American Journal of Critical Care, The New England Journal of Medicine, Journal of Critical Care y Nursing Research. Portales de revistas BioMed Central, DOAJ, Nursing Center, ISPUB, RACO, Scielo y Elsevier. Se incluyeron los artículos con diseños experimentales o cuasi experimentales y casos clínicos, publicados en texto completo, con calidad metodológica, publicados entre los años 2000 y 2021 en castellano, inglés y catalán.

RESULTADOS. Se incluyeron 24 artículos. Estos indican que es posible la administración de numerosos fármacos, como epinefrina, dopamina, dobutamina, adenosina, digitálicos, heparina, lidocaína, atropina, fibrinolíticos, etc. y fluidos, cristaloides y coloides con tasas de flujo altas y transfusiones sanguíneas sin aumento de la hemólisis. Además, el AIO permite tomar muestras sanguíneas válidas para algunas determinaciones analíticas como gases en sangre, hemoglobina y hematocrito, además de sodio, potasio, magnesio, lactato, y calcio.

CONCLUSIÓN. El AIO es una vía alternativa a tener en cuenta en el tratamiento farmacológico inmediato de pacientes en situaciones de emergencia diferentes a la reanimación cardiopulmonar.

Palabras clave: Acceso intraóseo. Emergencias. Paciente crítico. Tratamiento farmacológico.

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Introduction

The American Heart Association (AHA), the European Resuscitation Council (ERC), and the International Liaison Committee on Resuscitation (ILCOR) recommend establishing intraosseous access (IO) during the resuscitation of a patient in CA when peripheral venous access cannot be obtained within 90 seconds or after three attempts,[1-4] as it allows early administration of the drugs and fluids required for resuscitation,[5-8] which could increase the chances of survival.[9]

The relevance this route has acquired is reflected in the large number of studies published over the past 10 years on various aspects such as the effectiveness of intraosseous devices[10,11] and their learning curves,[12] insertion time,[13-15] as well as their usefulness in many contexts, not limited to CA situations.[16] In adults, the use of IO has increased in recent years thanks to the development of devices capable of penetrating the dense cortical bone and to the technical ease of insertion.[16] Regarding the point of intraosseous cannulation, it has been observed that it does not necessarily need to be a bone containing a medullary cavity.[17] Some bones without a medullary cavity, such as the calcaneus and radius, are composed of cancellous bone, which has a trabecular structure similar to the medullary cavity. These sites also reduce the likelihood of trauma to the lower extremity or pelvis, as well as damage to major vessels. Evidence also exists supporting the usefulness of IO access in special situations in which healthcare professionals must wear chemical, biological, radiological, or nuclear protective equipment, in which obtaining IO access may be even more difficult.[18] IO access can be obtained quickly using this PPE and allows early drug administration.[19,20]

Given the existing literature on all these aspects and the possibilities it offers, the aim of this systematic review was to evaluate the scientific evidence on drugs, fluids, and blood products that can be administered to a critical patient via IO access in emergency situations, and to determine the flow rates achievable through this route.

Material and methods

We conducted a systematic literature review between December 2021 and February 2022; the information sources consulted were classified into specialized databases, doctoral thesis and research repositories, metasearch engines, electronic journals, and journal portals.

The specialized databases consulted were Dialnet, CINAHL, Science Direct, CSIC, ProQuest, Scopus, LILACS, Current Contents, PubMed, Biblioteca Cochrane Plus, Virtual Health Library (BVS), Cuiden, Cuidatge, JBI Connect+, and MEDES. The doctoral thesis and research databases consulted were TESEO, TDR, and the institutional repository of Universidad de Alicante (RUA). The metasearch engines used were Trip Database and Google Scholar. Finally, articles were searched in the journal portals BioMed Central, DOAJ, Nursing Center, ISPUB, RACO, Scielo, and Elsevier.

The following keywords were used: "vía intraósea," "acceso intraóseo," "accesos intraóseos," "perfusión intraósea," "punción intraósea," "infusión intraósea," "infusiones intraóseas," "intraósea," "intraóseo," "intraosseous access," "intraosseous infusion," "intraosseous cannulation," "intraosseous," "emergency," "prehospital," and "out-of-hospital." Searches in Cuidatge and RACO were conducted in Catalan using "intraossi" and "intraossia."

The descriptors used were: "infusions, intraosseous," "infusiones intraóseas," "emergency medical services," "prehospital emergency care," and "emergency treatment." Additionally, a reverse search was performed using the reference lists of the selected studies, following PRISMA recommendations for systematic reviews.[21]

Inclusion criteria were: experimental, quasi-experimental, and observational descriptive studies published in full text whose results provided data on the administration of drugs and/or fluids in adult or pediatric critical patients or CA, flow rates achievable through IO access, and blood products administered via this route; published between 2000 and 2021; in Spanish, English, or Catalan; and peer-reviewed for methodological quality. Single-patient case reports were also included if they passed methodological evaluation.

Exclusion criteria were clinical practice guidelines, editorials, protocols, articles published in languages other than those specified, or published before 2000.

Finally, the scientific evidence[22] of the selected studies was evaluated using the GRADE system.

Results

A total of 517 articles were initially identified. Of these, 6 were found in Dialnet, 63 in CINAHL, 62 in Science Direct, 6 in CSIC, 48 in ProQuest, 45 in Scopus, 1 in LILACS, 14 in Current Contents, 82 in PubMed, 53 in BVS, 3 in Cuiden, 6 in Cuidatge, and 7 in MEDES. No relevant articles were found in Biblioteca Cochrane Plus or JBI Connect+.

No relevant doctoral theses or research papers were found in the corresponding databases.

Fifteen articles were found in Trip Database and 47 in Google Scholar. Fifteen articles were identified in BioMed Central, 18 in DOAJ, 5 in Nursing Center, and 14 in Scielo. No articles were found in ISPUB or RACO. After combining search results and removing duplicates, 203 articles related to IO access remained, of which 156 were excluded for not meeting the inclusion criteria. Of the remaining articles, 23 were excluded for not passing methodological evaluation. Ultimately, 24 articles were included in the systematic review (Figure 1).

The literature review showed that numerous drugs have been administered via IO access, with pharmacodynamic and pharmacokinetic characteristics comparable to those achieved through IV administration (Table 1), including inotropic agents, sedatives, cardiovascular drugs, diuretics, analgesics, and antibiotics. Crystalloid fluids administered via IO were shown to be effective for fluid resuscitation in critically ill adult and pediatric patients, with adequate flow rates. Moreover, IO access allows blood transfusions without increased hemolysis, and in the

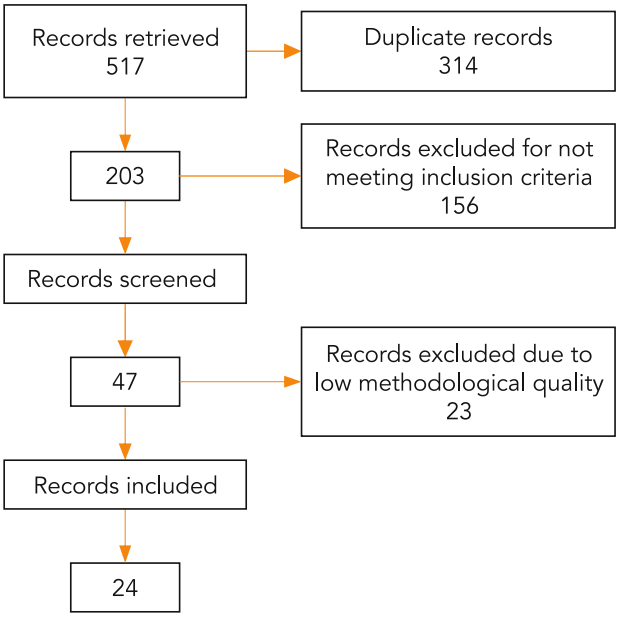

Figure 1. Flow diagram of the systematic review.

study by Ruiz-Hornillos *et al.*,[23] valid blood samples were obtained via IO for some laboratory tests such as blood gases, hemoglobin, hematocrit, as well as sodium, potassium, magnesium, lactate, and calcium (Table 2).

Discussion

IO administration has been documented in published studies in critically ill adult and pediatric patients in emergency situations other than CA, such as severe trauma,[14] acute brain injury with increased intracranial pressure,[24] pulmonary thromboembolism,[25] hypovolemic shock,[26-28] respiratory distress,[11] etc. The most widely used drugs were epinephrine, dopamine, dobutamine, adenosine, digitalis agents, heparin, lidocaine, atropine, sodium bicarbonate, phenytoin, neuromuscular blockers, and antibiotics, requiring the same dose as for IV administration and achieving similar plasma levels. Von Hoff *et al.*[29] observed the bioequivalence of morphine sulfate when administered to adults via IO and intravenously. The intraosseous route also allows early administration of drugs used in cardiopulmonary resuscitation, such as vasopressin or epinephrine.[30,31] Ventura *et al.*[30] conducted a prospective, randomized, double-blind trial comparing the effectiveness of dopamine versus epinephrine in pediatric septic shock, without distinguishing between iv or intraosseous administration. Likewise, it has been demonstrated that intraosseous vasopressin administration achieves concentrations similar to those obtained through an IV route, making IO access very useful when treating a patient in hypovolemic shock.[31]

IO access has also proven useful for fibrinolysis. Cases have been reported of thrombolytic administration—such as Alteplase and Tenecteplase—through this route, achieving results similar to those obtained IV and using the same doses.[23,25,32,33] This represents major progress when treating patients in whom peripheral venous access cannot be established, as central venous catheterization is a relative contraindication in patients requiring fibrinolytic therapy.[23] In the clinical case described by Northey *et al.*,[34] intraosseous thrombolysis was used in a patient on extracorporeal membrane oxygenation (ECMO) with massive acute pulmonary embolism. The risk of local hemorrhage and compartment syndrome is higher with IO thrombolysis,[32] but this adverse effect was not observed. Hydroxocobalamin has proven to be an effective antidote for cyanide poisoning, but cannot be administered intramuscularly due to the large volume of diluent required. The intraosseous route has been shown to be a simple and effective alternative for administering hydroxocobalamin and other antidotes in cases of severe intoxication.[35]

Table 1. Drugs and solutions administered through intraosseous access in humans

Acetylsalicylic acid	Flumazenil
Adenosine	Furosemide
Alteplase and tenecteplase	Sodium heparin
Amiodarone	Insulin
Atropine	Ketamine
Sodium bicarbonate	Lidocaine
Ceftriaxone	Midazolam
Potassium chloride and calcium chloride	Morphine
Dopamine	Naloxone
Ephedrine	Omeprazole
Enoxaparin	Blood products
Epinephrine	Rocuronium
Etomidate	Colloid solutions
Phenylephrine	Crystalloid solutions
Fentanyl	Succinylcholine

Authors' own work.

There is evidence supporting the usefulness of this route for continuous insulin infusion.[36] The efficacy of intraosseous insulin administration has been reported in a patient with diabetic ketoacidosis, achieving correction of hyperglycemia and metabolic acidosis within a time frame similar to that of IV therapy. In diabetic ketoacidosis with severe dehydration, peripheral perfusion may be compromised. In such cases, alternative routes to peripheral venous access—such as intramuscular or subcutaneous administration—are recommended. However, their effectiveness is not proven when peripheral perfusion is decreased; therefore, treatment protocols should be reviewed and the potential role of IO access considered in such cases.

The rapidity with which the drug is released from the bone marrow cavity into the systemic circulation is a major advantage, allowing for rapid and effective administration of medications used for endotracheal intubation.[12,13]

Regarding fluids, several studies have documented the administration of isotonic crystalloid and glucose solutions via IO access. Carness *et al.*[37] compared the administration of a colloid solution (Hetastarch®) and a crystalloid solution (Ringer's Lactate®) through IO access, obtaining greater expansion volumes with the colloid at lower flow rates. Currently, the use of colloid solutions is under review.[38,39]

The flow rates allowed by IO access are high and permit infusion of the necessary volume for resuscitating critically ill patients,[40] although to maintain optimal flow,

Table 2. Characteristics of the studies included in the systematic review

Study	Sample	Objective	Variables	Results	Limitations
Gazin *et al.*, 2011[11]	25 adults and 5 children	To test the efficacy and safety of the EZ-IO device in cases of CA (25 adults and 5 children), shock (4 adults), coma (2 adults), and respiratory distress (3 adults).	Drugs. Fluids.	An average of 680 mL of fluids, epinephrine, and drugs required for rapid sequence intubation were administered via IO. The authors conclude the device is safe and has a high success rate in out-of-hospital emergencies in both children and adults.	Small sample size.
Schalk *et al.*, 2011[13]	69 adults and 5 children	To study the effectiveness of the EZ-IO device in out-of-hospital emergency services in patients with CA, polytrauma, and other critical conditions.	Drugs. Fluids.	IO infusion of analgesics or narcotics, cardiovascular drugs (inotropes, beta-blockers, vasoconstrictors), naloxone, and isotonic fluids.	Non-randomized observational cohort study.
Santos *et al.*, 2013[14]	58 individuals	Prospective observational 3-year study of patients who received intraosseous access in the prehospital setting using the EZ-IO device, compared with available literature.	Drugs.	EZ-IO was used in CA (74%), major trauma (12%), and shock (5%). Drugs administered included epinephrine, atropine, and amiodarone. No complications were reported.	
Ruiz-Hornillos *et al.*, 2011[23]	64-year-old man	To describe the case of a 64-year-old man with acute coronary syndrome.	Drugs. Fluids. Blood products	IO access allowed administration of tenecteplase, unfractionated heparin, and amiodarone at the same doses used intravenously. IO access also allowed blood sample collection.	Single case report.
Lawson *et al.*, 2019[24]	5 adult patients	Prospective case series of critically ill neurological patients without central venous access who required 3% hypertonic saline administered intraosseously.	3% hypertonic saline.	IO administration of 3% hypertonic saline was feasible, producing an adequate rise in serum sodium levels.	Small sample size.
Spencer *et al.*, 2013[25]	36-year-old woman	To describe a case of a 36-year-old woman with massive pulmonary embolism and hemodynamic instability, treated with thrombolytics via IO access.	Drugs.	Treatment was effective and no complications were observed.	Single case report.
Burgert *et al.*, 2009[26]	79-year-old woman	To describe the case of a 79-year-old woman who developed hypovolemic shock from postoperative hematemesis. IO administration included epinephrine, 1 unit of packed RBCs, 2 units of fresh frozen plasma, crystalloids, and colloids.	Drugs. Fluids. Blood products.	IO administration of crystalloids, colloids, blood products, and drugs stabilized the patient's hemodynamic status with no complications.	Single case report.
Torres *et al.*, 2013[27]	107 individuals	To test the effectiveness of the EZ-IO intraosseous infusion device in critically ill patients with oxygen saturation < 80% after oxygen therapy, Glasgow Coma Scale < 8, systolic BP < 90 mmHg, hypovolemic shock, or CA.	Drugs. Fluids.	EZ-IO provided vascular access for administering various drugs: saline, dextrose solution, bicarbonate, epinephrine, atropine, fentanyl, dopamine, vecuronium, adenosine, enoxaparin, midazolam, acetylsalicylic acid, omeprazole, and amiodarone.	
Ngo *et al.*, 2009[28]	24 individuals	To compare infusion flow rates using the EZ-IO device in tibial vs humeral insertion sites in critically ill adults with: O_2 saturation < 80%, GCS < 8, systolic BP < 90 mmHg, hypovolemic shock, or CA.	Flow rate.	Flow rates were significantly faster with a pressure bag. Tibial flow: 204.6 mL/min with pressure bag vs 68.2 mL/min without (difference −129.5 mL/min; 95%CI, −218.2 to −40.3). Humeral flow: 148.1 mL/min with pressure bag vs 81.8 mL/min without (difference −69.6 mL/min; 95%CI, −113.9 to −25.3). Differences between tibia and humerus with vs without pressure bag were not significant (p = 0.157).	Small sample size. Did not analyze flow rates with colloid solutions.

(Continued)

system pressure must be kept above approximately 300 mmHg, achieving infusion rates of up to 129 mL/min at this pressure.[25,41-43] This overcomes the pressure inside the bone, allowing fluid to enter without difficulty.[44] Sontgerath *et al.*[45] observed an inverse relationship between the duration of 10 mL saline flushes used to verify vascular access patency and intraosseous pressure. Therefore, they recommend extending the duration of the flush for several seconds, thereby limiting high intramedullary pressures, which may contribute to fat embolization in the bone marrow and to the pain experienced by patients during IO infusion.[32] It is also recommended to administer a 20–50 mg bolus of 2% lidocaine to conscious patients to prevent pain.[13,14,23,25,42]

There is evidence that blood samples obtained through IO access are valid and allow certain laboratory measurements such as blood gases, hemoglobin, hematocrit, as well as sodium, potassium, magnesium, lactate, and calcium.[21] Blood transfusions can also be performed[14,23,41,45-49] without increased hemolysis, although transfusion time may be longer. In a reported case, Weiser *et al.*[50] transfused blood via an intraosseous route in a patient younger than 1 year.

The main limitation of this review was the high heterogeneity of the included studies, discordant patient characteristics, and investigations performed in different contexts, which prevented a quantitative synthesis. Another major limitation was the exclusion of many clinical trials conducted in animal models, which do not yet allow safe extrapolation to humans. Finally, due to the infrequent situations in which the technique is indicated, the sample sizes of the included studies may be insufficient.

Table 2. Characteristics of the studies included in the systematic review (Continued)

Study	Sample	Objective	Variables	Results	Limitations
Von Hoff *et al.*, 2008[29]	14 oncology patients	To compare the pharmacokinetic properties of IV vs intraosseous morphine sulfate. Prospective, randomized, crossover study. Each subject randomly received a 5 mg bolus of morphine sulfate via IV or IO.	Drugs.	Among all pharmacokinetic parameters, only the central compartment distribution volume showed a statistically significant difference, likely due to less deposition near the IO port or in bone marrow. Results support the bioequivalence of IO and IV administration of morphine sulfate in adults.	Small sample size.
Ventura *et al.*, 2015 [30]	120 children younger than 15 years	Prospective, randomized, double-blind controlled trial.	Drugs.	Early administration of peripheral or intraosseous epinephrine was associated with higher survival in this population.	No statistical analysis comparing IV vs IO administration.
Landy *et al.*, 2011[32]	53-year-old man	To describe a case in which CA caused by pulmonary embolism was reversed, as well as subsequent complications.	Drugs.	Asystole due to pulmonary embolism was reversed 5 minutes after administering Alteplase (0.6 mg/kg) via IO.	Single case report.
Valdés *et al.*, 2010[33]	25-year-old woman	Case report of a 25-year-old woman in cardiogenic shock who developed prehospital CA.	Drugs.	Fibrinolytic therapy was administered via IO with effective results. The patient had no sequelae after 39 days of hospitalization.	Single case report.
Northey *et al.*, 2015[34]	34-year-old woman	Patient with massive acute pulmonary embolism on ECMO support.	Drugs.	Thrombolysis with a 10 mg Alteplase bolus administered over 2 minutes via an IO needle in the left proximal tibia, as adjunctive ECMO therapy, with successful outcome.	Single case report.
Alawi *et al.*, 2008[36]	5-year-old boy	Case description of a 5-year-old child with diabetic ketoacidosis.	Drugs.	IO access allowed insulin administration, achieving correction of hyperglycemia and metabolic acidosis comparable to IV therapy.	Single case report.
Alawi *et al.*, 2008[36]	10 individuals	To compare IO access with central venous access.	Drugs. Fluids. Blood products.	IO access allows administration of crystalloid and colloid solutions, packed red blood cells, and fresh frozen plasma. Doses and onset of action were equivalent to IV administration.	Small sample size.
Carreras González *et al.*, 2011[41]	22-day-old neonate	Case report of a neonate admitted to the emergency department in CA.	Drugs. Fluids.	Epinephrine, diluted bicarbonate, and crystalloids were infused. Sinus rhythm recovered after 10 minutes. Hypotension and metabolic acidosis required vasopressors and bicarbonate via IO. Complication: major soft tissue necrosis from drug extravasation through IO access.	Very small sample size. Does not analyze flow rates for colloid solutions.
Stoll *et al.*, 2002[42]	3-month-old infant	To describe resuscitation of a 3-month-old infant using IO access and subsequent osteomyelitis from high-dose epinephrine administration.	Drugs. Fluids. Flow rate.	IO administration of epinephrine (1:10,000 and 1:1,000), 5% human albumin (150 mL), sodium bicarbonate 1 mEq/mL (50 mL), Ringer's lactate, and 5% dextrose solution (140 mL).	Single case report.
Tan *et al.*, 2011[43]	22 individuals	To compare flow rates obtained from proximal vs distal tibial IO access in adult patients.	Flow rate.	IO access allows administration of epinephrine, atropine, ceftriaxone, and allows blood transfusions. Flow rates were significantly faster with a pressure bag. Proximal tibia: 6.36 mL/min with pressure bag vs 3.96 mL/min without. Distal tibia: 3.28 mL/min with pressure bag vs 1.72 mL/min without.	Small sample size. Does not analyze flow rates with colloid solutions.

(Continued)

Conclusions

Multiple drugs administered intravenously, as well as fluids, can be safely and effectively administered via IO access, including epinephrine, dopamine, dobutamine, adenosine, digitalis agents, heparin, lidocaine, atropine, sodium bicarbonate, phenytoin, neuromuscular blockers, antibiotics, crystalloids, colloids, and blood products, using the same doses as for IV administration and achieving similar plasma levels.

In addition, IO access allows for the collection of blood samples for certain laboratory analyses, such as blood gases, hemoglobin, hematocrit, sodium, potassium, magnesium, lactate, and calcium.

IO access is an alternative to consider for the treatment of critically ill patients in emergency situations other than CA, although clinical trials are needed to strengthen the available evidence.

Table 2. Characteristics of the studies included in the systematic review (Continued)

Study	Sample	Objective	Variables	Results	Limitations
Ong *et al.*, 2009[44]	24 individuals	To compare flow rates and insertion success rates between femoral and tibial IO access using the EZ-IO device.	Flow rates.	No significant differences were found between humeral and femoral IO access. 95%CI.	Small sample size.
Villena *et al.*, 2012[46]	49 individuals	To evaluate the effectiveness of the EZ-IO device in out-of-hospital emergency situations.	Flow rate.	Applying a pressure infuser around the IV bag, or a sphygmomanometer above 300 mmHg, overcomes intra-bone pressure and increases flow rate.	No statistical data provided.
Bjerkvig *et al.*, 2018[48]	30 volunteer individuals	To compare reinfusion flow rates of 450 mL autologous blood and hemolysis using two IO devices (sternal) and IV access.	Flow rates. Blood products.	Mean reinfusion rates: 46.2 mL/min (FAST1), 32.4 mL/min (EZ-IO T.A.L.O.N.), and 74.1 mL/min (IV). Results suggest IO blood transfusion is safe, reliable, and provides adequate flow for resuscitation.	Non-randomized observational study; small sample size.
De Vogel *et al.*, 2011[49]	42-year-old woman	Case report of a woman who developed postpartum hemorrhage 45 minutes after delivery and entered CA.	Drugs. Fluids. Blood products.	Estimated blood loss: 12 L. IO access delivered 75% of total infusion volume: 20 U packed RBCs, 10 U FFP, 20 platelet units, desmopressin 0.4 µg/kg, 3,000 U factor II/VII/IX/X, 3 L colloids, and 5 L crystalloids. Resuscitation drugs (epinephrine, amiodarone) were administered via IO.	Single case report.
Weiser *et al.*, 2013[50]	5-month-old infant	To describe the case of a 5-month-old infant with traumatic brain injury and epidural hemorrhage. Venous access was lost; the patient developed severe hypovolemic shock. IO insertion (15-gauge) allowed infusion of 100 mL packed RBCs every 10 minutes.	Blood products.	Rapid hemodynamic stabilization. According to the authors, after literature review, this is the first successful reported case of IO packed RBC transfusion in a child under 12 months.	Single case report.

CA: cardiac arrest; IOA: intraosseous access; IO: intraosseous; ECMO: extracorporeal membrane oxygenation.

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