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Original Contribution

Intravenous vs. intraosseous access and return of spontaneous circulation during out of hospital cardiac arrest☆,☆☆,★

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ABSTRACT

Introduction: Guidelines endorse intravenous (IV) and intraosseous (IO) medication administration for cardiac arrest treatment. Limited clinical evidence supports this recommendation. A multiagency, retrospective study was performed to determine the association between parenteral access type and return of spontaneous circulation (ROSC) in out of hospital cardiac arrest.

Methods: This was a structured, retrospective chart review of emergency medical services (EMS) records from three agencies. Data was analyzed from adults who suffered OHCA and received epinephrine through EMS established IV or IO access during the 18-month study period. Per regional EMS protocols, choice of parenteral access type was at the provider's discretion. Non-inferiority analysis was performed comparing the association between first access type attempted and ROSC at time of emergency department arrival.

Results: 1310 subjects met inclusion criteria and were included in the analysis. Providers first attempted parenteral access via IV route in 788 (60.15%) subjects. Providers first attempted parenteral access via IO route in 552 (39.85%) subjects. Rates of ROSC at time of ED arrival were 19.67% when IV access was attempted first and 19.92% when IO access was attempted first. An IO first approach was non-inferior to an IV first approach based on the primary end point ROSC at time of emergency department arrival ($p = 0.01$).

Conclusion: An IO first approach was non-inferior to an IV first approach based on the end point ROSC at time of emergency department arrival.

1. Introduction

Prehospital advanced life support (ALS) has been shown to improve survival for patients suffering from out of hospital cardiac arrest (OHCA) [1]. This is critically important because patients who are not successfully resuscitated in the field are unlikely to be resuscitated in the emergency department [2]. Administration of parenteral epinephrine (epinephrine) is part of the standard advanced life support treatment of OHCA [3], and is associated with an increase chance of return of spontaneous circulation (ROSC) [4]. Parenteral prehospital medications are typically administered via the intravenous (IV) route. Unfortunately, IV access may not be practical or possible in all patients. Establishing IV access may be particularly difficult in patients in cardiac arrest [5].

In emergency conditions, intraosseous (IO) access may be utilized as an alternative to IV access [6,7]. IO access has been recommended in pediatric advanced life support since 1988 [8]. With the development of new devices, its use has become more prevalent in adult patients [6]. IO access can be established faster than IV access and has higher first-attempt success rates [5]. Moreover, serum drug concentrations for medications administered through IO sites were shown to be equivalent to those administered through peripheral IV lines [9,10].

The 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science state, "It is reasonable for providers to establish IO access if IV access is not readily available (Class IIa, LOE C)." The AHA cited eight studies in making this recommendation, none of which included human subjects

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in cardiac arrest [11]. In 2011, Reades published a randomized controlled trial comparing IV and IO access in the treatment of out of hospital cardiac arrest. However, the study did not look at return of spontaneous circulation (ROSC) or survival [5]. This recommendation was not reviewed in the 2015 AHA update [3].

Given the paucity of evidence to support this recommendation, a study comparing the effect of IV vs. IO access in the treatment of OHCA is needed. We performed a multiagency, retrospective study to determine the effects of the parental access type in the treatment of OHCA, using ROSC at time of emergency department arrival as the primary end point.

2. Material and Methods

2.1. Study Design

This was a structured, retrospective, chart review designed to evaluate the effects of IV vs. IO access on ROSC at time of emergency department arrival in patients receiving parenteral epinephrine for the treatment of OHCA.

2.2. IRB Approval

This study was granted exempt status by the University's Health Sciences Institutional Review Board.

2.3. Study Setting

Data were collected from three large, commercial ALS agencies in New York State. These agencies collectively respond to nearly 260,000 requests for service each year, and follow similar regional ALS protocols. All of these protocols leave the route of parenteral access in cardiac arrest up to the discretion of the provider and use a standard 1 mg dose of epinephrine 1:10,000 for the treatment of cardiac arrest based on AHA guidelines [3]. All study agencies utilize Zoll Electronic Patient Care Record (ePCR) for creation and maintenance of patient care records. All agencies require, but cannot assure, that providers document procedures including parenteral access and medication administration using predefined data fields in the interventions section of the ePCR.

2.4. Case Selection Criteria

Participating agencies ran electronic queries for the predefined intervention administration of epinephrine 1:10,000 in ePCR for the study period. Agencies accessed patient care records and submitted them in electronic form to the study group. Patient records were reviewed by the study team for inclusion/exclusion criteria. The inclusion criteria was adult patients who received parenteral epinephrine 1:10,000 for the treatment of out of hospital cardiac arrest. Cases where epinephrine 1:10,000 was administered for a patient who was not in cardiac arrest, cases where the patient was less than 18 years of age, cases where no parenteral doses of epinephrine were administered (including endotracheal administration only), cases where epinephrine was given via a previously established IV or central line, and cases where key data points were missing or could not be determined were excluded. When two patient care records existed for a single patient encounter (such as a paramedic ambulance and paramedic first response unit), the two patient records were considered as a single subject and data were extracted from both. Study inclusion/exclusion criteria are demonstrated in Fig. 1.

2.5. Data Extraction

All reviewers were trained by the primary investigator to familiarize them with patient care record format and study procedure. They were required to demonstrate proficiency in abstracting data from at least ten subject records before being able to work independently. Reviewers communicated with the primary investigator frequently to review issues. A primary reviewer reviewed each record for the primary variables, secondary variables and primary outcome.

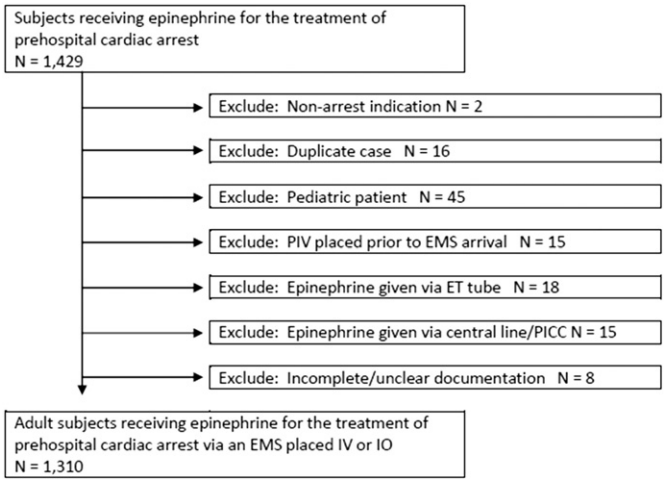

Fig. 1. Exclusion flow chart.

The primary variables were first access type attempted and route of administration for first dose of parenteral epinephrine. If the route of administration of the epinephrine was still unclear after using the above process, it was coded on the basis of the available route of access at the time of administration. The primary outcome was ROSC at the time of emergency department arrival.

Secondary variables included patient age, patient gender, bystander witnessed, bystander CPR, EMS crew witnessed, initial ALS rhythm, parenteral access attempts and success, advanced airway attempts and success. ROSC at any time was also a secondary endpoint. Data was extracted into a standardized Excel spreadsheet with predefined fields.

2.6. Missing and Conflicting Data

The study protocols included a hierarchy of data sources in the case of conflicting data. The free text narrative took precedence over data from other sections of the chart. Next, the procedures section of the PCR and, finally, the other sections of the PCR were reviewed. If ambiguities existed in the record they were settled in favor of the documentation contained in the narrative first and the procedures section second. Data points that remained unclear were entered as unknown. Any case where the first access route attempted, first route administered or ROSC at time of emergency department arrival could not be determined was excluded from the analysis.

2.7. Data Validation

A secondary reviewer reviewed each record in regards to the primary variable (IO or IV administration of first dose) and the primary endpoint (ROSC at time of emergency department arrival). The secondary reviewer was blinded to the study objectives and the results of the primary review. Any disagreements between reviewers were referred to the primary investigator for final coding. Disagreements between the first and second reviewers were reported as kappa scores. Disagreement between the first reviewer and final coding was reported as overall percentage.

2.8. Statistical Analysis

Rates of attempts, success and route of epinephrine administration for IO and IV access were calculated. Other variables such as age, bystander witnessed arrest, bystander CPR and initial rhythms were reviewed to examine for bias between the groups. The primary analysis was a non-inferiority model using first access type attempted as the primary variable and ROSC at time of emergency department arrival as the primary endpoint. In a preplanned secondary analysis, the odds ratio for the effect of the route of first epinephrine administered (IV or IO), regardless of first access type attempted, on ROSC at time of emergency department arrival was calculated. In another preplanned secondary analysis, the odds ratio for the effect of the route of first epinephrine administered (IV or IO), regardless of first access type attempted, on ROSC at time of emergency department arrival was calculated. Finally, the association between the first access type attempted and the first type of advanced airway attempted was determined. Statistical analysis was performed using SAS.

2.9. Sample Size Calculation

Prior to the start of the study a sample size calculation was performed to determine study feasibility. Model assumptions were made based on prior quality assurance reviews. Sample size requirements for a non-inferiority comparison were calculated using the following assumptions: alpha 0.05, beta 80%, clinically significant difference of 5% increase in ROSC and 20% ROSC rate for both arms. Assuming the sample has an equal number of subjects in each arm, the study would need to include at least 792 subjects per arm (1584 total) to reach statistical significance. Based on this model, it was estimated that 18 months of data would be sufficient to obtain the required sample size.

3. Results

From November 2013 to April 2015, 1429 subjects receiving epinephrine 1:10,000 were identified. 1310 subjects received epinephrine 1:10,000 through an EMS established IO or IV route for the treatment of cardiac arrest, met the inclusion criteria and were included in the analysis. The inclusions and exclusions are demonstrated in Fig. 1. Both groups were similar in terms of gender, bystander witnessed arrest, bystander CPR and initial rhythms as demonstrated in Table 1.

3.1. First Access Type Attempted

Providers first attempted parenteral access via the IV route in 788 (60.2%) subjects, with a success rate of 81.6%. Providers first attempted parenteral access via the IO route in 552 (39.9%) subjects, with a first attempt success rate of 94.8%. Among first access type attempted, the success rate for IO access was superior to IV access ($p < 0.01$). Rates of ROSC at time of emergency department arrival were 19.7% when IV access was attempted first and 19.9% when IO access was attempted first. An IO first approach was non-inferior to an IV first approach based on the end point ROSC at time of emergency department arrival ($p = 0.01$). The flow of subjects from first access type attempted, first access type successful, and first epinephrine administered is demonstrated in Fig. 2.

Table 1
Characteristics of subjects with first attempt IV vs IO.

	IV	IO	
Bystander witness[a]	37.0%	37.9%	$p = 0.78$
Bystander CPR[a]	25.7%	28.6%	$p = 0.27$
EMS witnessed	11.9%	10.9%	$p = 0.58$
Initial shockable rhythm	14.3%	16.3%	$p = 0.32$
ROSC at any time	25.2%	24.7%	$p = 0.84$
Male gender	66.2%	61.5%	$p = 0.08$
Mean age	63.0	59.8	$p < 0.01$

[a] Among cases not witnessed by EMS.

3.2. First Epinephrine Administered

Epinephrine was administered first via the IV route in 674 (51.5%) subjects. Epinephrine was administered first via the IO route in 636 (48.6%) subjects. As demonstrated in Fig. 2, rates of ROSC time of emergency department arrival were 20.9% when epinephrine was administered via the IV route first and 18.6% when epinephrine was administered via IO route first (OR 0.86; 95% CI: 0.66–1.13).

3.3. Additional Findings

Success in obtaining the first access type (IV or IO) attempted was associated with an increased chance of ROSC at time of emergency department arrival (OR 1.92; 95% CI: 1.20–3.07). Subjects that were treated with an IO attempt first, were more likely to have an alternate airway attempted first than those where IV was attempted first ($p = 0.02$).

3.4. Data Validation

Agreement between first and second reviewers was very good for first attempt type (kappa = 0.92; 95% CI: 0.90–0.94), route of first administration (kappa = 0.97; 95% CI: 0.96–0.98) and ROSC at time of emergency department (ED) arrival (kappa = 0.84; 5% CI: 0.80–0.88). A third reviewer reviewed all discrepancies between the reviewers. The final coding rarely differed from the first reviewers' coding, with 98.7% overall agreement for these three data points.

4. Discussion

This study demonstrates that treatment with an IO first approach was non inferior to an IV first approach in patients receiving parenteral epinephrine for the treatment of OHCA. This represents some of the strongest published evidence to date in support of the use of IO in the treatment of human cardiac arrest.

In this data set, IO had superior first attempt success rates compared to IV. The findings were similar to other published studies demonstrating IO success rates of 80–100% [7,12-14]. These findings demonstrated a superior IV success rate compared to other published studies demonstrating of success rates of 70–74% [13,15,16]. This study used crossing over to a different access type as a marker of failure. It is possible that this data set underestimated the true difficulty of obtaining IV access as a provider may have made multiple attempts before successfully obtaining IV access and still be classified as first attempt success as long as they did not cross over to an IO attempt.

First attempt failure with either device was associated with a significant decrease in the rate of ROSC. This effect is likely multifactorial. One potential explanation may be that a failure was associated with a delay in providing parenteral epinephrine or a distraction from performing other essential functions. It is also possible that the procedural failure may potentially be a marker for a less skilled clinician or a subject with a more challenging body habitus which may be associated with similar difficulty performing other critical tasks. Additional study to further explore this association would be useful.

During the study period, only one of the three agencies allowed humeral head IO placement. IO attempts were predominantly at the tibia site. The humeral head position has been shown to provide superior medication delivery [13,17-19], but may have lower first attempt success rates[25] compared to the proximal tibia position. The benefits of superior medication delivery must be balanced against the harm associated with unsuccessful attempts.

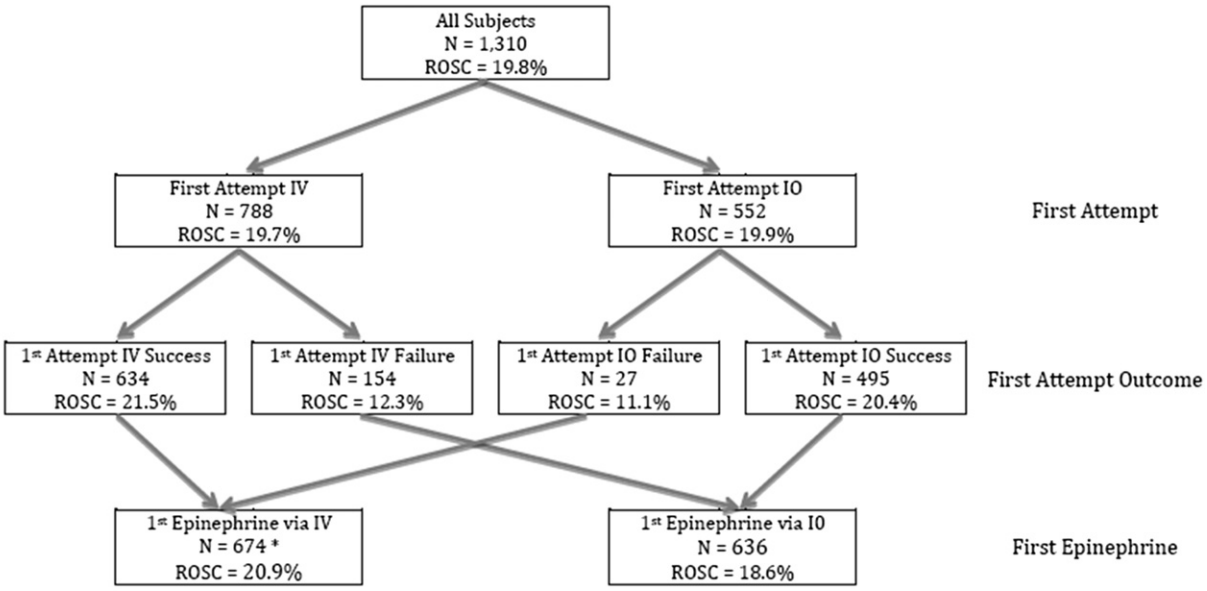

Fig. 2. Intervention flow chart.

Patients treated with an IO first approach were more likely to be treated with an alternate airway first approach than those treated with an IV first. Alternate airways, like IO access, is a newer modality in cardiac arrest management. Both may be used when the more standard techniques of ET intubation or IV access have failed or are determined to be too difficult. However, both may be used as primary devices in these systems. The correlation may be due to patients whom the providers judge to be technically difficult (such as morbidly obese), or this relationship may be based on provider preference.

4.1. Limitations

An important limitation of this study is that access type was at the discretion of the provider. The motivation of a provider in choosing a particular device is outside the scope of this study and poorly understood in the literature.

The value of obtaining vascular access is based on the assumption that the medications delivered have efficacy in the treatment of OHCA. The literature includes conflicting studies on the effect of epinephrine in the treatment of OHCA [4,20-24]. Rare but serious complications associated with emergency vascular access have been previously described in the literature, but were outside the scope of this study [25,26].

Finally, our study used ROSC at the time of emergency department arrival. ROSC is necessary but not sufficient for ultimately surviving with a good neurological outcome. The results of this study should be interpreted with caution as prior studies of high dose epinephrine showed an increase in ROSC, but a decrease in discharge with satisfactory neurological outcome [22]. Further studies with outcomes of neurologic function at discharge would better elucidate the efficacy of this intervention.

5. Conclusion

An IO first approach was non-inferior to an IV first approach based on the end point ROSC at time of emergency department arrival. This represents important evidence in support of the AHA's recommendation. A randomized controlled trial using cerebral performance category (CPC) at time of hospital discharge would be helpful to better understand this relationship.

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