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COMPARISON OF ONSET OF EPINEPHRINE EFFECTS BETWEEN INTRAVENOUS AND TIBIAL INTRAOSSEOUS ADMINISTRATION IN A PEDIATRIC PORCINE MODEL

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INTRODUCTION

Over one million people died in the wars in Iraq, Afghanistan, Pakistan, and Syria many of whom were children.[1-4] Currently, thousands of children have died because the horrific events in Israel and Gaza. Also, thousands of individuals die each year because of disasters.[5,6] It is estimated that 15,000 pediatric patients have cardiac arrest just in the United States alone.

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According to the European Committee for Resuscitation (ECR) and the American Heart Association (AHA), the administration of epinephrine is essential for patients who have cardiac arrests and should be initiated as quickly as possible.[7-10] For every minute of delay in resuscitation, there is a decrease of 9 percent in achieving success.[11,12-17] Both the ECR and AHA state that the intravenous (IV) administration of epinephrine is the route of choice, and if not accessible, the intraosseous (IO) routes can be used. These include the sternal IO, humerus IO, and Tibia (TIO). Intraosseous access is a fast and reliable route to give medications in situations when vascular access cannot be rapidly achieved. However, it is not known what the onset of epinephrine is relative to TIO versus IV administration of the drug.

Objective

The objective of this study was to compare the onset of epinephrine by the IV versus the TIO route in a normovolemic pediatric model. Few studies have examined the onset of any drug when comparing IV and IO routes, and it is not known if a significant difference in onset exists. If a significant difference does not exist, this would support obtaining TIO access sooner when IV access cannot be established. TIO was chosen since it is the preferred site of IO access in pediatric emergencies.

Methods

Design: This was an experimental study. **Setting:** Tri-Service Research Facility was used. **Subjects:** 18 swine weighing between 20-40 kilograms, which is representative of a 6–8-year-old child. **Measures:** G-Power was used to determine the number of subjects. A multivariate analysis of variance (MANOVA) was used to analyze the pretest data to determine equivalence of the groups. An Independent T-Test was used to analyze the difference in onset between the groups. **Intervention:** The pigs were randomly assigned to the IV or TIO group. Swine were anesthetized, and after 15-minute stabilization, baseline blood pressure and pulse were recorded for each subject. Epinephrine 1:10,000 was then administered at a dose of 0.01 mg/kg followed by a 10 mL flush of 0.9% normal saline. This is the recommended dose for pediatric patients according to both the ACR and AHA. A stopwatch was started after administration and stopped once a 10% increase above the baseline pulse and/or blood pressure was achieved. This value was the operational definition of onset of effect.

RESULTS

Similar studies were used to calculate a large effect size, 0.6. Using a power of 0.80, an effect size of 0.6 and an alpha of 0.05, we calculated a sample size of 9 in each of the IV and TIO groups. A MANOVA indicated that

there were no significant differences between the IV and TIO groups relative to weight, blood volume, systolic blood pressure, or pulse indicating that the groups were equivalent on these variables ($p > 0.05$). The initial systolic blood pressures and pulses by group are reported in means ± standard deviations (SD). The systolic blood pressures were as follows: TIO: 99.4 ± 27.7; IV 97.3 ± 16.0. The initial pulses were as follows: TIO: 83 ± 21.0; IV pulse: 88 ± 8.7. An independent t-test indicated that there was a significant difference in time to onset ($p = 0.002$). The means ± SD of time in seconds to increase systolic blood pressure and/or pulses by 10% were as follows: TIO: 14 ± 4; IV: 8 ± 2.

DISCUSSION AND CONCLUSION

The ECR and AHA recommend using the IV route, if available, for epinephrine administration; however, this recommendation is based primarily on expert opinion, rather than on research data. The difference in onset of action of epinephrine between IV and TIO was statistically significant, although this was not clinically significant. Clinicians can be confident that the administration of epinephrine by the TIO route is efficacious. **Relevance:** Initial placement of an IV may delay epinephrine administration. A TIO is easier and faster to place in a pediatric patient and can be inserted while CPR is being administered. Given the clinical similarities in time of onset of epinephrine in the IV versus TIO route, the faster placement of TIO may result in improved outcomes in pediatric arrest in terms of odds and time to return of spontaneous circulation. **Limitations:** Swine may not be generalizable to humans; however, they do have similar cardiovascular systems and bone structure. Another limitation to this study was the small sample size, although the power was large enough to find a statistically significant difference. **Recommendations for Future Research:** Future studies should include a larger sample size and other IO sites. Measuring peak and duration as well as time for elimination ($t_{1/2}\beta$) from the body should also be investigated.

Conflict of interest

The authors declare that they have no conflict of interest. The views expressed are those of the authors and do not necessarily reflect those of the US Army or the Department of Defense.

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