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IPHMI Literature Review

Keeping You Up To Date with Current EMS Literature and Studies

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1. **Efficacy of bolus-dose epinephrine to manage hypotension in the prehospital setting.** Weant KA, French DM. *Am J Emerg Med.* 2021;50:71-75.

Prehospital hypotension (systolic blood pressure [SBP] < 90 mmHg) results in a demonstrated increase in in-patient mortality rates of 33-52%. When fluid boluses and blood products, as necessary, fail to raise systolic blood pressure, vasoactive agents are often used in an attempt to normalize blood pressure in patients experiencing both transient and pathogenic hypotension.

Traditionally, vasopressors have been administered via IV infusion through an infusion pump or controller. IV pumps are not required equipment in many EMS systems. Emergency physicians have begun to adopt the anesthesiologists' practice of administering bolus-dosed epinephrine (BDE) to quickly and effectively raise SBP. Epinephrine is a commonly used and readily available emergency medication. It has a short onset of action, usually less than one minute, and is therapeutic for 5-10 minutes. Epinephrine raises SBP by increasing both heart rate (Beta) and vasoconstriction (Alpha).

Weant and French conducted an IRB approved, two-year (2019 – 2020) retrospective review of a single, academic medical center's patients that received protocol-permitted BDE from a single, urban EMS agency. The primary goal was to assess the effect of BDE on prehospital SBP. Additionally, they looked at changes in heart rate, the incidence of severe hypertension (SBP > 220 mmHg), and dosing relationship to SBP. Patients were excluded if they received BDE while in cardiac arrest or for anaphylaxis where doses were equal to, or greater than, 0.3 mg.

Two hundred and eighty-seven patients received 993 doses of epinephrine, 5 to 20 mg every 2 to 5 minutes. Two hundred and thirty-two of those patients were excluded due to receiving the exclusion dose of epinephrine (n=222) or for incomplete documentation (n=10). A total of 55 patients, who received 96 doses of BDE were included for analysis. The median age of study patients was 61 years of age. The most common demographics were hypotensive, unresponsive white males post cardiac arrest.

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The most commonly administered dose was 10 mg, with 45.5% of the patients receiving multiple PDE boluses. Systolic blood pressures in these patients increased following PDE administration from the initial average of 70 mmHg. The median increase was 14.0 mmHg. Patients that received greater than 10 mg of BDE experienced a significantly higher increase in SBP (30 mmHg). No significant increase in heart rate was found and no patients had a documented severe hypertensive episode.

This study was retrospective in nature and practitioners were following an already established protocol. The authors concluded that while needing additional studies to determine the best dose range, BDE appropriately elevated the SBP in this size limited patient group. This study was limited by the fact that there were no patient outcome data. The authors did not make any conclusion if the use of prehospital BDE effected overall patient outcomes or length of hospital stay.

Bolus-dosed epinephrine may be beneficial for EMS agencies that don't have access to IV infusion pumps or as a bridge to elevate SBP while vasoactive agents are mixed and primed through existing IV infusion pumps. It may also have a place in treating pre- and immediate post intubation hypotension. The authors did describe in some detail how standard dose epinephrine is drawn up and diluted for use just prior to administration. Before implementing BDE in practice, all providers will need to be skilled and practiced at accurately obtaining and administering the small doses needed during emergent, high acuity, low occurrence, hypotensive patient encounters.

2. Video Laryngoscopy for Out of Hospital Cardiac Arrest. Huebinger RM, Stilgenbauer H, Jarvis JL, Ostermayer DG, Schulz K, Wang HE. *Resuscitation* 2021;162:143-148

A standard benchmark in modern EMS is Return of Spontaneous Circulation (ROSC) post cardiac arrest. One of the most highly studied and debated interventions in the prehospital management of cardiac arrest is airway management, more specifically, endotracheal intubation. The authors of this retrospective study review data that compare the use of video laryngoscopy (VL) versus direct laryngoscopy (DL) on first pass success rates and ROSC.

Data were obtained from ESO inc. a large electronic patient care report company based in the USA that uses National Emergency Medical Services Information System (NEMSIS 3.0) date point definitions.

For the calendar year 2018, there were 70,867 cardiac arrests identified in the data set. After excluding patients that did not meet study criteria, 22,132 patients were enrolled into the study. Exclusions included traumatic cardiac arrest, supraglottic airway use prior to intubation, incomplete documentation and no advanced airway used.

Of the 22,132 patients, 5702 (25.7%) had VL as the primary first intubation attempt, while 16,430 (74.2%) received DL. Those patients intubated using VL demonstrated a higher first pass success rate compared to DL (75.1% vs. 69.5%, $p < 0.001$). However, there was no demonstrated difference between airway techniques when it came to ROSC. On the other hand, first pass success, regardless of the method of intubation, was associated with improved ROSC when compared to multiple intubation attempts.

The authors list limitations that are related to documentation provided by the field provider and the inability to identify the blade or VL type used. The data set did not allow for analysis of AED use and did not include information on survival to hospital discharge which is a more important outcome measure than ROSC.

Prehospital cardiac arrest management should be based upon studies conducted in the field and not just extrapolated from in-hospital studies. While this study demonstrated a better first pass intubation rate with VL, there was no difference between VL and DL as far as ROSC. Bigger questions in prehospital cardiac arrest management should be the timing of when intubation should take place regardless of the technique used to accomplish it and the ultimate improvement in survival to hospital discharge, not just ROSC.

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3. Physician-staffed Ambulance and Increased In-hospital Mortality of Hypotensive Trauma Patients Following Prolonged Prehospital Stay: A Nationwide Study. Yamamoto R, Suzuki M, Yoshizawa J, Nishida Y, Junichi S. *J Trauma Acute Care Surg.* 2021;91:336–343

The EMT and paramedic have been the standard prehospital healthcare providers in the United States since the 1970s. In many other countries around the world, ambulances are staffed with physicians. Studies show conflicting results in terms of benefit for one model versus the other based on patient populations, criticality, resource availability etc. Retrospective studies in Germany and the Netherlands reported no survival benefit when severe injuries were treated by physician staffed ambulances. Conversely, a study in France reported a reduced risk of mortality in trauma patients treated by physician staffed ambulances. They also note that more than half of the recent studies looking at physician staffed ambulances targeted patients with isolated traumatic brain injury.

The authors hypothesized that prolonged scene time with physician staffed ambulances, leading to delayed definitive control of bleeding, would have a negative effect on the outcomes of hypotensive trauma victims. They conducted a retrospective cohort study that looked at trauma patients that were hypotensive at the scene (BP less than 90 mm Hg systolic) and were transported by ambulances between January 2004 and March of 2019. Data were obtained from the Japan Trauma Databank. Of 14,652 patients included in the study, 738 patients were transported by physician staffed ambulances and the remainder by non-physician staffed ambulances.

Patients transported by the physician staffed ambulances had higher in-hospital mortality (28.8% [201/699]) versus (17.5% [227/13,090]) when transported by EMS personnel staffed ambulances. The physician staffed ambulances also had longer total prehospital time, averaging 50 (36-66) minutes versus EMS personnel averaging 37 (29-48) minutes.

Longer prehospital times with the physician staffed ambulances affected the survival of hypotensive trauma patients. It is likely that since this study only included hypotensive trauma patients, their instability was due to massive hemorrhage that required surgical intervention and was negatively affected by prolonged field time. In addition, physician specific therapeutic interventions for this patient population were few. Therefore, when a physician is dispatched with EMS, prolonged prehospital time must be avoided, particularly with hypotensive trauma patients

The results do not negate the potential usefulness of physician staffed ambulance systems. In the case of trauma patients, physician triage has been reported to decrease the undertriage of major traumatic injuries. However, the results of this study, as do others, makes the critical point that if the needs of the patient are considered, there are limited interventions that can be done for massive bleeding in the field and reducing total prehospital time by expediting transport to an appropriate trauma center will positively affect outcomes.

4. Out-of-Hospital Ketamine: Indications for Use, Patient Outcomes, and Associated Mortality.

Fernandez AR, Bourn S, Crowe RP, et al. *Ann Emerg Med.* 2021;78:123-131.

4.1. Accompanying Editorial: Ketamine: Focusing on the Facts and Forgetting the Fiction

Klein LR, Cole JB. *Ann Emerg Med* 2021;78:132-139.

Ketamine has become a popular choice for prehospital analgesia and sedation. However, as a result of a number of incidents that have garnered significant media attention, there has been a growing amount of controversy concerning ketamine and its use by prehospital care providers.

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The authors sought to describe the effect of ketamine on patient outcome and its potential to contribute to patient death. To accomplish this they conducted a retrospective analysis of prehospital ketamine administration by ESO Data Collaborative agencies, a consortium of 1,322 EMS agencies distributed across the United States during the calendar year 2019. Data reviewed included the indications for ketamine, dose administered, transport disposition, development of hypoxia or hypercapnia after ketamine administration, and mortality (both prehospital and in-hospital).

A total of 11,291 patients received ketamine in the field. Indications included trauma/pain = 5,575 (49%), altered mental status/behavioral indications = 3,795 (34%), cardiovascular/pulmonary indications = 1,454 (13%), seizure = 248 (2%), and 219 (2%) categorized as other. Over 90% of the patients were transported to the hospital.

Hypoxia developed in 897 (8.4%) patients and hypercapnia was noted in 1,131 (17.2%) patients following ketamine administration. There were eight deaths on scene and, of 2,030 hospital patients with available data, and additional 120 deaths that were reviewed. After review, ketamine could not be excluded as a contributing factor in two of the on scene deaths (0.02% of all patients receiving ketamine in this study) and in 6 of the in-hospital deaths (0.3% of the total patients receiving ketamine).

The study has a number of important limitations. The study did not look at known complications of ketamine use including respiratory depression, the need for active airway management (either in the field or in the hospital), hypersalivation, or emergence reactions. In addition, 82% of the cases did not have ED/hospital linked records; although the authors state that the linked and non-linked groups were demographically similar. They did note that this was more than twice the rate that reported to the National EMS Information System.

Ketamine, as with all medications, has its indications for use and, like all medications, its associated complications. All healthcare providers, whether prehospital or hospital, must be aware of and remain vigilant for these potential complications. Based on this study of over 11,000 patients, ketamine could not be ruled out as a contributing factor in 8 deaths (0.07%) of all patients receiving ketamine, although it is important to note that this association does not imply that ketamine actually caused the deaths. Ketamine was administered for a variety of clinical indications in this study and overall, appears relatively safe. Further research to determine the complete safety profile for Ketamine is still needed to answer some of the lingering doubts about its use.

4.1. Accompanying Editorial: Ketamine: Focusing on the Facts and Forgetting the Fiction

Klein LR, Cole JB. *Ann Emerg Med* 2021;78:132-139.

In this editorial accompanying the ketamine review by Fernandez, the authors describe the current situation regarding the way the media and lay press report about the use of ketamine and how it differs from scientific peer reviewed research. Further they express concern over how public opinion is formed about advances in medicine through these same media and lay press without the same rigorous scrutiny applied by scientific publications.

The recent coverage of two very different incidents in 2018 and 2019 illustrates this concern. The first involved a patient death following administration of ketamine during a police encounter and the second involved a sedation protocol used by a regional EMS agency and the data collected. The controversy stemmed from the perception that Ketamine was used as an adjunct to law enforcement rather than treatment for an acute behavioral emergency. Negative media coverage of both of these incidents sometimes contained demonstrably false information as the coverage rose to an international scale.

They appropriately point out that there are risks associated with nearly any medications and those risks are considered in the risk-benefit profiles that determine the utility and safety of all

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medications. The authors describe several possibilities as to why this concept goes unrecognized when ketamine is being discussed.

First, to people who have no experience treating these patients, the concept of life-threatening behavioral emergencies is an elusive one. They go on to say “Nearly every experienced emergency physician has seen a patient with acute agitation suffer respiratory failure or cardiac arrest”. The morbidity associated with these situations is difficult for the public to comprehend. The situation is further complicated by “experts” cited in the news stories about ketamine who generally did not have the field experience with these types of patients to support their opinions.

Second, they point out that many of the situations in which ketamine is used are often complex. The patients are agitated possibly with metabolic or traumatic etiologies but often due to intoxication or psychiatric illness. As a result, ketamine is disproportionately administered to a vulnerable population of patients in emergency situations

Third, it is important to recognize how the media chooses to report on ketamine. While they generated a large uproar over the two incidents described earlier, the use of ketamine in facilitating the rescue of 12 critically ill children in the Tham Luang cave rescue was celebrated. In other instances, ketamine has been referred to as a date rape drug (erroneously) and an animal tranquilizer.

The authors applaud the efforts of the Fernandez research paper stating that while there is a need for more study, Fernandez et al “provide us with a robust, global sense of Ketamine’s safety in a very broad patient population and not just those that are at high risk of imminent clinical deterioration, as in many of the previous agitation and sedation trials we have seen.” Ketamine may be the best choice for many of these patients in the many diverse situations encountered in the prehospital setting but the decisions made on which medication to administer or when to use it should be informed by evidence and data and not on fiction.