Review Article

Push-dose vasopressors in the Emergency Department: a narrative review

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Background and Objective: Much of the efficacy and safety data behind push dose pressors has been extrapolated from anesthesia literature, but the literature examining the use push-dose pressors in the Emergency Department is lacking. There are many proponents of bolus vasopressors in the field of emergency medicine, but there have been no large-scale trials to support their use. This paper seeks to determine the efficacy and safety of use of push dose pressor in the Emergency Department by review of published literature.

Methods: We conducted a literature search using 8 keywords within Cochrane Library and PubMed. Articles were limited to English language and emergency (including pre-hospital/emergency medical services), critical care, or anesthesia settings. The articles were assessed by three separate reviewers, and pertinence was determined by collective consensus in accordance with the Preferred Reporting Items for literature reviews.

Key Content and Findings: A total of 529 articles met criteria, and after further review, 24 were included in this paper. The data comprised critical care, operative, and pre-hospital push-dose pressor use. An overwhelming majority of articles were observational studies, the exception of several small, anesthesia based, randomized trials.

Conclusions: This review emphasized the paucity of research behind push-dose vasopressors. Their use has been perpetuated without a full scope of knowledge surrounding the effectiveness and safety profile. Clinical trials should be performed prior to accepting the common practice of push-dose vasopressors in emergency medicine.

Keywords: Push dose pressor; bolus dose pressor; push dose vasopressor; bolus dose vasopressor

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Introduction

The use of push-dose vasopressors in emergency medicine is a widely accepted clinical practice, however there is negligible data to support this utilization (1). While research has been performed by anesthesiology examining the use in sedation and intubation related hypotension, these patient populations and clinical scenarios significantly differ from those encountered in the Emergency Department (ED) (1-7). Anesthesia studies generally examined either elective surgical procedures (such as spinal surgery) or obstetrical patients, who would be expected to be younger and healthier than the average hypotensive ED patient (1-7). The hemodynamic profiles of these operative patient populations cannot be extrapolated to those in shock in the emergency room. Up to this point, the endorsement of push-dose pressors (PDPs) has been overwhelmingly based on anecdotal or observational data (8), and multiple authors have suggested the urgent need for deeper examinations of

Table 1 Search strategy summary

Items	Specification
Date of search (specified to date, month and year)	August 15th, 2021
Databases and other sources searched	PubMed, Cochrane
Search terms used (including MeSH and free text search terms and filters)	Push dose pressor* OR push-dose pressor* OR bolus dose pressor* OR bolus-dose pressor* OR push dose vasopressor* OR push-dose vasopressor* OR bolus dose vasopressor* OR bolus-dose vasopressor*
Timeframe	No limitation
Inclusion and exclusion criteria (study type, language restrictions, etc.)	Limited to English language, emergency/critical/anesthesia settings, excluded pediatric (age <18 years)
Selection process (who conducted the selection, whether it was conducted independently, how consensus was obtained, etc.)	Three authors conducted search independently and each created list of pertinent articles. Results compiled and all authors reviewed each article for relevance. Article was included if all authors felt it met search criteria

the practice (9-20). Our goal is to determine the efficacy and safety of use of push dose pressor in the ED. We present the following article in accordance with the Narrative Review reporting checklist (available at https://jeccm.amegroups.com/article/view/10.21037/jeccm-21-98/rc).

Methods

This study evaluated publications regarding the clinical use of push-dose vasopressors in the ED. Using the Cochrane Database and PubMed, literature was reviewed based on the following keywords: push dose pressor* OR push-dose pressor* OR bolus dose pressor* OR bolus-dose pressor* OR push dose vasopressor* OR push-dose vasopressor* OR bolus dose vasopressor* OR bolus-dose vasopressor*. Refer to *Table 1* for full search strategy summary. These databases were last reviewed in August 2021. Inclusion criteria was determined based on a consensus of pertinent information, including pre-hospital articles and in-hospital critical care settings. A total of 529 articles met criteria, and after evaluation by three different reviewers, 24 relevant articles were identified. Several of the papers identified were single case or editorials. Control/case series trials found are summarized in *Tables 2,3*.

Results

There are multiple vociferous proponents of push dose pressors in the emergency medicine world. However, articles cited by Weingart *et al.* do not provide a direct correlation with the use of push-dose vasopressors and patient outcomes (8). The article by Cole *et al.* from 2018 found only 2 studies regarding push dose pressor use in the ED (9). Panchal *et al.* analyzed 20 hypotensive patients receiving bolus-dose phenylephrine in the peri-intubation period. They found improvement in blood pressure by 20 mmHg systolic and 10 mmHg diastolic, but no significant outcome benefit by any other clinical parameters (10). Schwartz *et al.* assessed bolus-dose phenylephrine efficacy based on the need for patients to receive continuous vasopressor infusion (CVI) within 30 minutes of bolus dose administration. Out of 73 patients, 34 required CVI (46.6%). The patients who were considered to have an adequate preload of intravenous fluids received fewer doses of push dose pressors and were less likely to require a CVI. There was a 20.5% adverse event rate, including reactive hypertension in 8.2% of patients, ventricular tachycardia in 2.7% of patients, and bradycardia in 9.6% of patients. The authors suggested that the reliance on push dose pressors may mask inadequate fluid resuscitation and preload expansion thereby causing harm to the patient (11).

Tilton *et al.* warns of the high risk of medication errors in the high risk, high stress situations that push dose pressors are often used (12). Rotando *et al.* retrospectively analyzed the efficacy of phenylephrine 1,000 g/10 mL or ephedrine 50 mg/10 mL in a clinical area outside of the operating room. Vitals were monitored in 80 patients before and after administration of PDP, which showed a mean increase 26 mmHg in systolic blood pressure (SBP) and 13 mmHg in diastolic blood pressure (DBP). However, adverse events occurred in 17 out of 146 patients, including SBP increases by >100%, heart rate (HR) changes of >30%, or dysrhythmias. In addition, 13 out of 116 patients received

Table 2 Studies found that looked at push dose pressors in the Emergency Department

Study	Setting	Study type	Population	N	Medications	Findings	Outcomes	Complications
Patrick 2020	Ground EMS transport	Retrospective, observational	Non-cardiac arrest, hypotensive due to presumed non-traumatic cause while transported via EMS	42 patients	Epinephrine 20 mg IV Q2m PRN	Median SBP 78 mmHg (pre) to 93 mmHg (post), MAP 58 mmHg (pre) to 69 mmHg (post)	Not reported	54.8% required >2 doses, 1 patient with severe hypertension (SBP >180 mmHg) post-PDP
Clifford 2021	Emergency Department	Prospective cohort	Consecutive patients with hypotension from an acute drug overdose and circulatory shock	55 patients	Phenylephrine, epinephrine	PDP used in 32 of 55 patients (12 phenylephrine, 20 epinephrine)	11/12 phenylephrine survived; 4/20 epinephrine survived	None noted
Nowadly 2020	Emergency Department	Case report	n/a	Single patient	Vasopressin 1-unit IVP	BP 80/51 mmHg (pre), 141/102 mmHg (immediately post), gradual decline over 92 min until vasopressor drip started	Discharged after 30 days in hospital	None noted
Guyette 2019	Prehospital critical care transport	Retrospective, case cohort pre- and post-protocol comparison	Patients with documented SBP <70 mmHg undergoing critical care transport	574 patients	Epinephrine 100 µg	Patients receiving PDP were more likely to have both hypotension (68.4% *vs.* 49.4%) and hypertension (2.63% *vs.* 0.99%), less likely to have a perfusing rhythm (63.9% *vs.* 93.0%)	PDP patients less likely to be alive at 24 h (64.6% *vs.* 82.2%) and 30 days (37.9% *vs.* 56.3%)	None noted
Nawrocki 2020	Prehospital critical care transport	Retrospective, observational	Patients documented as receiving at least one dose of PDP epinephrine for SBP <90 mmHg or MAP <65 mmHg	52 patients	Epinephrine 10–20 µg	Use of PDP increased mean MAP by 13 mmHg, hypotension resolved in 58.5% of recipients. Repeat PDP dose administration required in 42 instances	Data only available for 38 patients. 11/38 (28.9%) survived to discharge	Severe HTN (SBP >180 mmHg) in 1/94 (1.1%) administrations
Rotando 2019	Any clinical area outside of the OR	Retrospective, observational	Patients documented as receiving bolus dose pressor in EMR	146 patients (155 PDP events)	Phenylephrine, ephedrine	Mean SBP 80 mmHg (pre) to 106 mmHg (post), DBP 48 mmHg (pre) to 61 mmHg (post), HR 93 beats/min (pre) to 99 beats/min (post)	Not reported	17 (11.6%) adverse hemodynamic events, 13 patients (11.2%) with medication dose error

Table 2 (*continued*)

Table 2 (*continued*)

Study	Setting	Study type	Population	N	Medications	Findings	Outcomes	Complications
Hardwick 2018	Medical evacuation during disaster response	Case series	Hypotensive patients requiring intubation in a pre-hospital transport environment	2 patients	Epinephrine bolus and/or "ad hoc" drip	Improvement in SBP/MAP pre and post intubation	Both patients admitted to ICU	None noted
Gottleib 2018	Emergency Department	Case series	Refractory post arrest hypotension	3 patients	Epinephrine	Improvement in SBP/MAP until vasopressor infusion initiation	2 of 3 patients survived	Nonattributable to PDP use
Schwartz 2016	Emergency Department	Retrospective, observational	Documented use of bolus dose phenylephrine	73 patients	Phenylephrine	Patients receiving adequate fluid resuscitation required fewer PDP doses, 34 (46.6%) patients were initiated on a continuous vasopressor infusion within 30 minutes of initial PDP dose, patients receiving adequate fluid less likely to require vasopressor drip initiation	Not reported	6 (8.2%) reactive hypertension, 2 (2.7%) ventricular tachycardia, 7 (9.6%) bradycardia
Panchal 2015	Emergency Department	Retrospective, observational	Hypotensive patients receiving bolus dose phenylephrine in the peri-intubation period	20 patients	Phenylephrine	Mean SBP 73 mmHg (pre) to 93 mmHg (post), mean DBP 42 mmHg (pre) to 52 mmHg (post), 13 (65%) received multiple PDP doses, 14 (70%) required initiation of vasopressor infusion	Not reported	None noted

EMS, emergency medical services; EMR, electronic medical record; IV, intravenous; Q2m, every 2 minutes; PRN, as needed; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PDP, push-dose pressor; BP, blood pressure; IVP, intravenous push; HR, heart rate; ICU, intensive care unit.

Table 3 Studies found that used adverse events as a main outcome

Study	Setting	Study type	Population	N	Medications	Findings	Survival
Swenson 2018	Emergency Department	Retrospective, observational	Patients receiving pre-mixed bolus dose phenylephrine	181 patients	Phenylephrine	80 patients received additional vasopressor infusion, 27 received more than 2 additional vasopressor infusions. 5 patients with adverse hemodynamic event—3 with hypertension, 2 with bradycardia	Not noted
Cole 2018	Emergency Department	Retrospective, observational	Patient documented as receiving bolus dose pressor in EMR	249 patients	Phenylephrine, epinephrine	Adverse hemodynamic events (HR >140 or <60 beats/min, hypertension, ventricular tachycardia) occurred in 98 (39%), 30 (27%) phenylephrine, 68 (50%) epinephrine, human/ dosing error in 47 patients, 140 patients required >2 doses	120 (49%) survival to discharge, 70 (64%) phenylephrine, 50 (36%) epinephrine

EMR, electronic medical record; HR, heart rate.

>200 µg phenylephrine or >25 mg ephedrine, which was classified by the authors as a medication error (13).

Nowadly *et al.* reported that as of last year, there had not been a single case report published describing the use of push-dose vasopressin in the setting of the ED. Their case report followed a septic patient whose blood pressure improved from 80/51 to 141/102 within 1 minute of administration of 1unit push bolus vasopressin. She subsequently required CVIs 1 hour after push-dose administration (14). Other case reports have been published describing the use of bolus dose epinephrine in hypotensive patients following cardiac arrest. Gottlieb *et al.* in 2021 authored a case series describing blood pressure improvement in three patients after up to 12 doses of push dose epinephrine during central line placement (15).

An article by Acquisto *et al.* presented cases of dosing errors, as well as adverse events associated with the use of phenylephrine and epinephrine in the ED. Reports included that of hypertensive episodes to >300 mmHg, ST depressions, and QTc prolongation (16). Ross *et al.* retrospectively followed pediatric intensive care unit (ICU) patients who received pre-arrest bolus dose epinephrine. Their data showed that 9% of patients experienced reactive hypertension, while 14% and 4% experienced relative tachycardia and bradycardia, respectively (17). Swenson *et al.* performed a retrospective chart review, showing overall mean arterial pressure (MAP) improvement in 147 patients in ED with 5 out of 181 patients experiencing adverse reactions in the form of hypertensive crises (18). Clifford *et al.* presented a prospective cohort study of ED patients in circulatory shock following a drug overdose, for which they observed statistically significant in-hospital mortality in 8% of patients who received push-dose phenylephrine and 80% of patients who received push-dose epinephrine (19).

An examination of pre-hospital literature did not yield much additional evidence to support broad usage. A retrospective emergency medical services (EMS) chart review by Patrick *et al.* showed SBP improvement in 86% of patients, but errors in dosing were specifically excluded in the study analysis (20). Guyette *et al.* provided a retrospective case cohort, prehospital transport study that concluded the use of bolus-dose epinephrine had a lower 24-hour and 30-day survival rate in patients treated with push dose pressors versus those who were not (21). The Nawrocki *et al.* retrospective observational study showed 1 out of 52 push dose pressor administrations resulted in transient extreme hypertension, 3 out of 52 cardiac arrest events occurred within minutes of receiving push dose epinephrine, and one incident of dosing error (22). Finally, Hardwick *et al.* presented two aeromedical cases during the Puerto Rican disaster response in which field expedient vasopressors successfully hemodynamically stabilized patients (23).

Some proponents cite the safety and efficacy profile of push dose pressors in anesthesia literature, extrapolating the similarity to use in the ED. Seven anesthesiology articles

met relevance, looking first at the Wang *et al.* review on rescue bolus phenylephrine compared to norepinephrine. This article emphasized the lack of quality data surrounding bolus norepinephrine use in obstetric anesthesia (1) and reiterated the points made by Ngan Kee *et al.* regarding negative side effects of even the well-researched vasopressor, phenylephrine (2).

A significant amount of the anesthesia published literature on this topic is conflicting. Wang *et al.* showed that the hemodynamic profile for bolus norepinephrine is safer than phenylephrine and ephedrine during cesarean deliveries of women with preeclampsia (3). Hassani *et al.* shared support for the efficacy of norepinephrine, but this randomized control trial differed in its population by studying hypertensive patients undergoing spinal surgery (4). Xia *et al.* also evaluated spinal surgery patients undergoing anesthesia, concluding that a bolus injection of ephedrine best counteracted hypotension while prone (5). The randomized double-blind dose-finding study Mohta *et al.* revealed that the incidence of reflex bradycardia was similar in both phenylephrine and norepinephrine when treating post-spinal hypotension during a cesarean section. They expanded upon the adverse side effect profile of bolus dose phenylephrine in their double-blind study Mohta *et al.*, which called for more studies to evaluate its use in the higher dose range (6,7).

Discussion

The majority of PDP literature has been published by anesthesiologists within the context of hypotension in the operating room. Repeatedly, these reviews suggested the acknowledgment of safety considerations when administering push-dose vasopressors in critical care settings due to the adverse event profile. The demand for randomized trials was made evident, as many of our relevant articles included isolated case reports or literature reviews. Our research indicates that there is limited data on the implementation and efficacy of push-dose vasopressors in the ED.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://jeccm.amegroups.com/article/view/10.21037/jeccm-21-98/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jeccm.amegroups.com/article/view/10.21037/jeccm-21-98/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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