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Short paper

Peri-arrest bolus epinephrine practices amongst pediatric resuscitation experts

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Abstract

Aim: To describe current practices of peri-arrest bolus epinephrine use amongst pediatric resuscitation experts in a multinational survey.

Methods: A 9-question survey was developed and electronically distributed to pediatric critical care physicians who are site investigators for the Pediatric Resuscitation Quality Collaborative (pediRES-Q) network. Institutional demographics were collected through the American Hospital Association 2018 Annual Survey and linked to responses. Descriptive statistics were used to characterize closed-ended responses, and qualitative content analysis to analyze open-ended responses.

Results: Of the 63 collaborative members invited to participate, 49 (78%) responded, representing 35 institutions in 9 countries. Forty-six of the 49 respondents (94%) reported that they would consider using peri-arrest bolus epinephrine during critical situations in patients *not* requiring cardiopulmonary resuscitation. Initial dosing strategies ranged from 0.1mcg/kg to 10mcg/kg, with the most commonly reported initial dose of 1mcg/kg by 25 of the 37 (68%) respondents who answered this question. Three of the 49 (6%) participants indicated that they would generally avoid using peri-arrest bolus epinephrine, citing lack of evidence to support its use.

Conclusions: In this multinational survey of pediatric resuscitation experts, endorsement of peri-arrest bolus epinephrine use was nearly universal, though a few clinicians cited lack of evidence to support this practice. There was a 100-fold dierence in the range of initial weight-based doses reported, as well as a minority of clinicians who reported using non-weight-based dosing. Further research is needed to determine best practices, standardization of initial dosing, clinical factors that may warrant dosing modifications and associations with clinically important outcomes.

Keywords: Peri-arrest bolus epinephrine, Hypotension, Pediatric, Critical Care

Introduction

The clinical practice of administering low-dose peri-arrest vasopressor boluses for acute hypotension (commonly known as "push-dose", "bolus-dose", "dwindle" or "spritzer" vasopressors) has been reported across a variety of hospital settings and geographic regions.[1–16] While commonly reported in obstetric anesthesia and adult emergency medicine, use of peri-arrest pressor boluses in the pediatric intensive care unit (ICU) is rarely reported.[1,3,4] Given

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the paucity of data in the pediatric literature, understanding current practice patterns may support the development of guidelines for this potentially life-saving therapy. Therefore, we aimed to describe the use of peri-arrest bolus epinephrine amongst pediatric resuscitation experts through a multinational survey.

Methods

The Institutional Review Boards at Boston Children's Hospital and Children's Hospital of Philadelphia determined that this study did not constitute human subjects research.

Survey development

Because there were no existing instruments to measure peri-arrest bolus epinephrine practice patterns, we created a survey for this study. We followed steps for survey design as described by Artino et al.[17] After an extensive literature review to identify possible practice variation surrounding PBE, authors (CER, MMH, AMS) developed an initial survey and sought feedback from local experts in survey design and pediatric and adult critical care. We conducted cognitive interviews with 4 local pediatric intensivists to maximize clarity.[18] Pilot testing was done with 10 pediatric intensivists to ensure survey functionality was preserved. The final questionnaire consisted of 9 questions (Supplementary File 1). Survey questions included demographics and personal practice details surrounding the first dose of peri-arrest bolus epinephrine given during a critical event not involving cardiopulmonary resuscitation. The survey included both closed-ended and open-ended items, with open-ended items inviting respondents to describe specific circumstances in which they would consider giving different initial doses and general comments on their experiences with peri-arrest bolus epinephrine.

Population

Pediatric ICU physicians with expertise in resuscitation science were identified from the Pediatric Resuscitation Quality Collaborative (pediRES-Q). pediRES-Q is a clinical research network including over 40 international sites of diverse size and geographic location, with Children's Hospital of Philadelphia serving as the coordinating center. Site investigators were contacted via email by the pediRES-Q principal investigator and program director prior to receiving the electronic questionnaire link. If the original recipient of the email invitation reported that they were not an ICU physician (required for Question 1), they were asked to forward the unique survey link to an appropriate ICU clinician within their institution.

Data collection

The survey and study data were collected and managed using Research Electronic Data Capture (REDCap; Vanderbilt University, Nashville, TN) hosted at the Children's Hospital of Philadelphia. The survey was distributed September 9th, 2020 and closed November 10th, 2020. Institutional demographics were collected through the American Hospital Association 2018 Annual Survey[19] and were linked to participants by a 3rd party to maintain blinding of the research team to the respondents' identities. All survey responses remained de-identified throughout the survey distribution period and during all analyses.

Data analysis

Descriptive statistics are presented as counts with relative frequencies, medians with interquartile ranges (IQRs). We applied methods of qualitative content analysis to analyze the open-ended responses; specifically, the first and last authors independently reviewed all open-ended responses and grouped them into categories, met to review and discuss results, and resolved any differences by consensus. Responder bias was assessed by comparing hospital characteristics between responders and non-responders.

Results

Of the 63 site investigators invited to participate, 49 (78%) responded, representing 35 institutions in 9 countries. One (2%) of these was completed by an alternate participant designated by the original survey recipient. The participants reported a variety of years of experience and types of ICUs in which they practiced (Table 1). Hospital characteristics of non-responders did not significantly differ from responders (Supplementary Table 1).

Forty-six of the 49 respondents (94%) reported that they would consider using peri-arrest bolus epinephrine during critical situations in deteriorating patients *not* requiring cardiopulmonary resuscitation. Of these, most clinicians (63%) reported administration of epinephrine using a 10mcg/mL solution (for reference, standard "code dose" epinephrine in the United States is 100mcg/mL solution). About half (54%) of those using a reduced concentration (below 100mcg/mL) reported dilution at the bedside during the event as opposed to it being prepared ahead of time by pharmacy (46%).

Initial dosing strategies ranged from 0.1mcg/kg to 10mcg/kg (100-fold difference), with the most commonly reported initial dose of 1mcg/kg in 25 of the 37 (68%) respondents who answered this question. Nineteen of 46 (41%) participants who use peri-arrest bolus epinephrine said that they would consider modifying their *initial* dose based on a variety of clinical factors (Table 2).

Three of the 49 (6%) participants indicated that they would generally avoid using peri-arrest bolus epinephrine, citing lack of evidence to support its use (3 of 3) and unfamiliarity with the practice (1 of 3). Twenty-nine (59%) participants commented in open-ended format regarding their thoughts on their personal or institutional experiences with peri-arrest bolus epinephrine: major categories included endorsement of peri-arrest bolus epinephrine as a means to avert cardiac arrest (10%) and ensuring that peri-arrest bolus epinephrine was at bedside for high-risk patients and/or procedures (12%). Participants also conveyed concerns over practice variability (6%), non-standard nomenclature (4%) and dosing errors (6%).

Discussion

In this multinational survey of pediatric resuscitation experts, the vast majority of respondents indicated that they would consider using peri-arrest bolus epinephrine in critical scenarios not requiring cardiopulmonary resuscitation. There was considerable variability in the initial dosing strategy reported, with a 100-fold difference in the range of weight-based doses reported, as well as clinicians who reported using non-weight-based dosing. The minority of intensivists who reported avoiding peri-arrest bolus epinephrine cited lack of supportive evidence as the major reason for avoidance.

Table 1 – Baseline characteristics of pediatric resuscitation expert survey respondents.

Characteristic	All (n = 49)
Baseline Characteristics	
Years in practice, No. (%)	
0 to 5 years	12 (25)
6 to 10 years	13 (27)
11 to 15 years	12 (25)
>15 years	12 (25)
Type of ICU	
Pediatric cardiac ICU	6 (12)
General pediatric ICU without surgical cardiac patients	25 (51)
Combined general and cardiac pediatric ICU	18 (37)
Global hospital region, No. (%)	
Australia/New Zealand	1 (2)
Asia	4 (8)
Canada	3 (6)
Europe	3 (6)
United States	38 (78)
US Geographic Region*, No. (%)	n = 38
New England	4 (11)
Northeast	11 (29)
Mideast	3 (8)
Southeast	8 (21)
Midwest	3 (8)
South	4 (11)
West	5 (13)
Number of pediatric ICU beds, median (IQR)**	41 (13, 54)
Number of total hospital beds, median (IQR)***	546 (406, 673)

* As reported by the American Hospital Association.[19] The authors chose more meaningful labels to represent region codes as follows: New England = Region 1; Northeast = Region 2; Mideast = Region 3; Southeast = Region 4; Midwest = Region 6; South = Region 7; West = Region 9

** Limited to US hospitals with available data, n = 35.

Table 2 – Personal practice characteristics of peri-arrest bolus epinephrine use amongst pediatric resuscitation expert survey respondents.

Practice Characteristic	All (n = 49)
Use of peri-arrest bolus epinephrine, No. (%)	n = 49
Would consider using	46 (94)
Would generally avoid using	3 (6)
Concentration, No. (%)	n = 45
100 mcg/mL	9 (20)
10 mcg/mL	29 (64)
1 mcg/mL	4 (9)
Other	3 (7)
Dilution preparation, No. (%)	n = 36
At the bedside during the event	20 (56)
In the pharmacy prior to use	16 (44)
Dosing strategy	n = 45
Weight-based	39 (87)
<1 mcg/kg	5 (11)
1 mcg/kg	25 (56)
>1 and $\leq$ 5 mcg/kg	7 (16)
>5 mcg/kg	2 (4)
Non-weight-based	6 (13)
1 mcg	1 (2)
10 mcg	5 (11)
Dosing modifications	n = 46
Would consider modifying the initial dose in certain circumstances	19 (41)
Reasons for modifying the initial dose*	
Degree of hypotension / peri-arrest state	12 (26)
Concerns for adverse effects (hypertension, arrhythmia)	4 (9)
Pre-existing vasoactive infusion	4 (9)
Patient size (neonates and adolescents)	2 (4)
Other	2 (4)

Percentages based on the number of respondents for a given question (n).

* Open-ended responses categorized by theme. Some responses included multiple themes and therefore the sum exceeds the total number of responses for this question.

The widespread use of peri-arrest bolus epinephrine coupled with highly variable dosing strategies reported here highlights the need for more research to support standardization of peri-arrest bolus epinephrine in the pediatric ICU. To date, only two studies have described the physiologic effects of peri-arrest bolus epinephrine in the pediatric ICU, both of which report wide dosing ranges used, despite each being performed at a single center.[3,4] Importantly, these studies showed conflicting results in whether blood pressure response to peri-arrest bolus epinephrine is dose dependent. Clinicians' choice of initial dosing strategy would ideally result in a consistent blood pressure response while avoiding overshooting to extreme hypertension. It is not clear if modifications are warranted in certain clinical scenarios as was reported by several of our respondents. Additionally, the appropriate dosing for patients at the extremes of pediatric size/weight (i.e. neonates and adult-sized adolescents) should be explored, as we note that the most commonly reported dose of 1mcg/kg in an adult-sized patient would result in a significantly higher peri-arrest bolus epinephrine dose than the 5-20mcg *total* doses reported in adult studies.[5,20]

The preparation of peri-arrest bolus epinephrine reported was also variable, with over half of participants reporting bedside dilution from a standard concentration. This may be of concern, as the practice of bedside dilution, especially in critical situations by physicians or nurses who do not routinely mix drug products, is prone to significant dosing errors.[2] However, many of our respondents reported having pre-mixed diluted epinephrine readily available at their institutions.

Finally, we note that our respondents (as well as published literature) used a variety of terminology to refer to this practice, with at least 7 unique terms used in the free text responses (Supplementary Table 2). As two of our participants suggest, standardized nomenclature should be established to reduce clinical errors and enhance communication amongst researchers. To this end, we have updated our terminology to refer to this practice as "peri-arrest bolus epinephrine" (formerly "bolus dilute epinephrine") to more accurately reflect the clinical scenario in which it is used.

The results of this survey should be interpreted in the context of several limitations. First, participants were asked to answer survey questions based on their own personal practice style, and therefore their answers may not represent the responders' institutional practice surrounding PBE. Second, the survey participants were geographically diverse, but all were members of the pediRES-Q quality collab-

orative. Therefore, commonalities in knowledge, background and practice styles within the group may have influenced the responses to appear more uniform than what occurs in pediatric ICUs outside of this network. For this reason, the true proportion of pediatric intensivists who endorse using peri-arrest bolus epinephrine may be overestimated in the current study, while the variability in dosing strategies may be underestimated. Finally, though we did not find evidence for responder bias by hospital characteristics, individual participant characteristics were not available for comparison.

CONCLUSIONS: In this multinational survey of pediatric resuscitation experts, endorsement of peri-arrest bolus epinephrine was near-universal; however, a minority of respondents reported abstaining from peri-arrest bolus epinephrine due to lack of supportive evidence. There was a 100-fold difference in the range of initial weight-based doses reported, as well as a minority of clinicians who reported using non-weight-based dosing. Further research is needed to determine best practices, standardization of initial dosing, clinical factors that may warrant dosing modifications and associations with clinically important outcomes.

Conflict of interest

None.

CRediT authorship contribution statement

Catherine E. Ross: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft. **Margaret M. Hayes:** Conceptualization, Methodology, Writing – review & editing. **Monica E. Kleinman:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Michael W. Donnino:** Conceptualization, Writing – review & editing, Supervision. **Amy M. Sullivan:** Conceptualization, Methodology, Validation, Writing – review & editing, Supervision.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2021.100200.

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