Original Article

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North American Survey of Vasopressor and Inotrope Use in Severe Sepsis and Septic Shock

Jaclyn M. LeBlanc, Joseph F. Dasta, Steven M. Hollenberg

Abstract

***Objective*: The primary objective of this study was to characterize how vasopressor and inotropic agents are prescribed and administered in the hemodynamic management of sepsis. Secondary objectives were 1) to evaluate adherence with published guidelines to identify areas of deviation and 2) to describe pharmacists' perceived incidence of adverse drug reactions (ADRs) of vasopressors and inotropes.**

***Design and setting*: Web-based survey.**

***Patients and participants*: Critical care pharmacists.**

***Interventions*: An email invitation was sent to critical care pharmacists asking them to complete a web-based survey. The survey opened September 29, 2004 and closed March 4, 2005.**

***Measurements and results*: Of 1065 pharmacists, 235 (22.1%) responded to the survey. Median hospital and ICU size were 451 and 20 beds, respectively. Primary types of ICUs included general (42.1%), medical (28.5%), surgical/trauma (18.3%), cardiac (9.8%), and other (1.3%). Independent of pulmonary artery catheter (PAC) use, the most common initial vasopressor choice in surgical/trauma ICUs was norepinephrine. In the other ICUs, the most common first-line agent was norepinephrine if a PAC was present and dopamine if a PAC was not present. The most common dosage regimen of vasopressin was a continuous infusion of 0.04 units/min (49.8%). The most commonly used inotrope was dobutamine. Respondents reported using inotropes either sometimes (48.1%) or rarely (34.0%), with therapy continuing 24–48 (54.5%) or 48–72 (26.0%) hours. Commonly associated agents with specific adverse effects included dopamine with tachycardia and norepinephrine with digital ischemia. Much variability was shown in drug concentrations and various dosages of vasopressors and inotropes between institutions.**

***Conclusions*: Despite published guidelines, vasopressor and inotrope use in hemodynamic management of patients with sepsis and septic shock displayed much variability. Perceived incidence of ADRs for these agents also demonstrated inconsistency among respondents. National organizations need to develop recommendations for standardization of concentrations of continuous infusion medications in the ICU.**

Key words: vasoconstrictor agents, inotrope, sepsis, septic shock, parenteral infusions.

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Introduction

Published guidelines analyze and grade the quality of corroborating studies and generate a recommendation based on available evidence. If successfully implemented, peer-reviewed, evidence-based guidelines can help to decrease the variability of practice that exists between hospitals, specific intensive care units (ICUs), and individual clinicians. In addition, these guidelines aid the clinician in making an educated, evidence-based decision for the care of the patient and may potentially help to reduce unnecessary risks or adverse drug reactions (ADRs) from inappropriate use of the high-risk medications.

The care of septic patients has recently come to the forefront in both the medical literature and lay press, with publication of national guidelines, such as the Surviving Sepsis Campaign and the update of the Hemodynamic Support of Sepsis [1,2]. Despite this, little information is known about the current and actual practice of hemodynamic management in patients with sepsis and septic shock. Specifically, there is a paucity of data available with regards to the use of the vasopressors and inotropes in this population.

One of the first steps towards standardizing the approach to managing the septic patient is to document the lack of standardization of continuous infusion medication preparation, dosing, and usage according to guidelines. These findings will also establish key areas for health care professional education development. The primary objective of this study was to characterize how vasopressor and inotropic agents are prescribed and administered in the hemodynamic management of sepsis. Secondary objectives were 1) to evaluate adherence with published guidelines to identify areas of deviation (the ACCM Hemodynamic Guidelines and the 2004 Surviving Sepsis Guidelines, which were both current when this survey was distributed, are summarized in **Table 1** and **2** to describe pharmacists' perceived incidence of ADRs of vasopressors and inotropes.

Materials and methods

Survey Development

The survey was developed to evaluate the objectives by exploring the following domains:

1. Demographic information.
2. Overall hemodynamic management of specified population.
   a. General questions regarding vasopressor and inotropic agents use in the ICU for the hemodynamic management of sepsis and septic shock.
      i. Initiation of therapy (including choice of agents).
      ii. Endpoints and titration of therapy.
      iii. Duration of therapy.
   b. Perceived consequences of sepsis and septic shock (including incidence of low cardiac output and renal failure).
3. Perceived ADRs of various vasopressors and inotropes.
4. Infusion-related information with regards to concentrations of prepared drugs, dosages prescribed and administered, and error dosages (defined as the dose which would require the pharmacist to question the prescriber due to a suspected mistake).

Questions from Domains 1, 2a, and 4 (twenty-four questions) were meant to reflect the environment of the specific ICU the pharmacist was practicing in. Questions from Domains 2b and 3 (eleven questions) were meant to reflect the opinions of the pharmacist, not the ICU as a whole.

The questionnaire was evaluated for face validity by 3 experienced critical care pharmacists and 1 intensivist in the United States (US), who also reviewed the

questions for ambiguity. Appropriate changes were made and the amended questions were entered onto the internet via a web-survey tool (www.zoomerang.com) to allow easy accessibility to respondents and rapid data analysis. This revised internet-based survey was piloted by an additional 4 experienced critical care pharmacists in Canada and the US, and changes were made based on their comments.

Sample and Data Collection

After IRB approval of the research study, critical care pharmacists practicing in an adult ICU in the US and Canada who were members of the American College of Clinical Pharmacy (ACCP), the Society of Critical Care Medicine (SCCM) and/or the Canadian Society of Hospital Pharmacy (CSHP), were invited via email to participate in the survey. A list of pharmacists who were members of the SCCM–Clinical Pharmacy and Pharmacology section and/or the ACCP critical care practice research network (PRN) during the months of August 2004–February 2005 was manually compiled. The assembled list was reviewed and all duplicate e-mails and e-mails of pharmaceutical or device industry employees were purged. The instructions for the survey asked that only one pharmacist per ICU answer the questionnaire, and the lists were also reviewed for potential duplicate practice sites. If a duplicate practice site was noted, one of the names was arbitrarily deleted from the invitation list.

The email invitation was distributed through the CSHP critical care PRN and those members did not receive an individual invitation to the survey. The survey also instructed respondents to answer the survey only once, in the event a duplicate email was missed, or a member of the CSHP critical care PRN received an individual email from the compiled list.

The survey opened on September 29, 2004 and closed March 4, 2005. Prospective respondents were sent up to 4 reminders, and all responses were anonymous.

Data Analysis

The data from the survey tool were downloaded directly into Microsoft Excel, and analysis was completed via Microsoft Excel® and SPSS (version 14.0). Only data from complete surveys (defined as completing ≥75% of the first three domains of the survey) were used in the final analysis. Descriptive statistics were used where appropriate. In the instance where a range of numbers was answered to a question that asked for a specific number, the median of the range was used in statistical analysis. Responses requiring an estimation of a specific number are presented as the median (interquartile range).

Results

Demographics

The survey was sent to 1065 ICU pharmacists, with 302 responses. A total of 67 responses were excluded from the final analysis: 1 for pediatric ICU, 3 for responses from outside North America, and 62 for completing ≤75% of the survey questions, with a final response rate of 22.1% (n=235). Respondents were from the United States (90.6%) and Canada (9.4%). The hospitals were described as teaching (73.2%), non-teaching (8.1%), public (13.2%), private (12.8%), community (35.7%), and government/military (3.8%). Median hospital bed size was 451 (350-696, n =229). ICU classification, as defined by Brilli et al, demonstrated an even distribution of transitional (37.3%), open (31.8%), or closed units (30.9%), and median size of the units was 20.0 (14.0-25.0) beds [3]. The types of ICUs were general (42.1%), medical (28.5%), surgical/trauma (18.3%), cardiac (9.8%), and other (1.3%). Pharmacists estimated there were 10.0 (5.0-18.l) patients with sepsis or septic shock admitted to the ICU per month.

A hemodynamic management algorithm was in place in 13.6% of respondents' ICUs. Pharmacists estimated the percent of patients with various invasive monitoring devices was 95 (70-100, n =215) with an arterial catheter, 30 (10-70, n =213) with a pulmonary artery catheter (PAC), and 0 (0-100, n =175) with no invasive monitoring device.

The most commonly perceived incidence of low cardiac output was between 11-20% (39.2%), although

many respondents believed it was higher (21-30% [16.7%] or 31-40% [16.7%]). Interestingly, 9.1% of respondents felt the incidence was >50%. The percent of patients estimated to have developed acute renal failure during sepsis or septic shock was estimated to occur most often in 41-50% (13.6%) and >50% (37.4%) of patients. The use of low-dose dopamine (defined as a dosage of <3.0 μg/kg/min attempting to augment urine output) in the ICU was reported as never (33.5%), rarely (36.1%), sometimes (22.7%), often (6.4%), or always used (1.3%).

Vasopressors

First- and second-line vasopressors of choice, depending on whether a PAC was present, are shown in **Figure 1**. Independent of whether a PAC was present, the most common initial choice in the surgical/trauma ICU was norepinephrine, with phenylephrine as the second most common initial choice. This was contrasted to the cardiac, general, and medical ICUs where the most common first-line agent was norepinephrine if a PAC was present or dopamine if a PAC was not present. When a second agent was started, the first agent was continued (70.4%), titrated off (25.8%), or some other action taken (3.9%). The most common blood pressure (BP) endpoint used to guide vasopressor titration was mean arterial pressure (MAP) >60 (34.0%), regardless of the type of ICU.

Low-dose vasopressin infusions were initiated before starting an adrenergic vasopressor (5.6%), concomitantly with an adrenergic vasopressor (70.9%), or after adrenergic vasopressors had failed (15.4%); 8.1% indicated they never used low-dose vasopressin for this population in their ICU. The three most common dosage regimens of vasopressin included titration to a maximum of 0.1 U/min (9.8%), titration to a maximum of 0.04 U/min (22.6%), and a constant infusion of 0.04 U/min (49.8%). Other respondents reported using constant infusions of a different dosage of vasopressin (3.8%) and titration to a different maximum dosage (2.1%).

Inotropes

The frequency of inotrope use was reported as sometimes (48.1%), rarely (34.0%), often (12.3%), always (4.3%) and never (1.3%). Although many respondents used clinical signs to determine the need for inotropic therapy such as urine output (18.5%), clinical signs and symptoms (24.7%), and persistent hypotension (27.8%), an even larger proportion used parameters derived from the PAC (oxygen delivery or mixed-venous oxygen saturation (37.0%), and cardiac index or output (71.4%)). The most common inotropes reported to be prescribed were dobutamine (58.1%) and dopamine (20.1%), while norepinephrine (8.1%), milrinone (7.3%), and epinephrine (1.7%) were also used. Endpoints of inotropic therapy are shown in **Figure 2**, with therapy usually continuing 24–48 (54.5%) or 48–72 (26.0%) hours.

Adverse Drug Reactions

Table 2 demonstrates the most common agents pharmacists felt were responsible for specific ADRs, as well as the overall perceived incidence of each effect. The perceived incidence of arrhythmias with dopamine and dobutamine were 6.3±3.5% and 5.6±3.3%, respectively. The most common range estimations of hypotension with dobutamine included 6-10% (27.1%) or 1-5% (24.1%).

Drug Concentrations and Dosage

Table 3 demonstrates the standard and maximum concentrations of vasopressors and inotropes used within the ICUs. Reported starting, average, and maximum dosages, and the dosage at which there would have been considered an error to occur ("Error Dosage") are shown in **Table 4**. The patient's weight used in calculation of the vasopressor dosage varied among ICUs and included preadmission or dry (63.9%), daily (30.0%), calculated (4.7%), or other (1.3%).

Discussion

Discussion

Our main finding was the variability surrounding the initiation, dosage, titration, and discontinuation of

vasopressors and inotropes in patients with severe sepsis and septic shock despite the recent publication of two national guidelines.

An average of 40% of patients were estimated to have a PAC; however, the standard deviation of 33.1 indicated variability between ICUs. The hemodynamic guidelines suggest consideration for a PAC when BP is not at goal after fluid resuscitation [1]. Variability was also echoed in the number of patients with various lines and monitoring devices. These results were expected, as the presence or absence of invasive monitoring devices is usually specific to ICU practice and the patient. However, it raises two questions: whether the range of patients having a PAC was appropriate, or whether there should be more attention to standardized appropriate use of PAC's in this patient population?

The majority of respondents felt the incidence of acute renal failure was >50%. Low-dose dopamine was still being used, although 33.5% reported its use as "never". A 1996 survey of vasopressor and inotrope use showed that 65% of 54 respondents indicated low-dose dopamine was used prophylactically with vasopressors and 29% used it to treat oliguria [4]. Both guidelines discourage the use of low dose dopamine for renal protection [1,2]. Our results suggest that many practitioners are responding to recent data showing "renal dose" dopamine as not helpful, but additional education is needed [5].

No study has documented a preference for norepinephrine in surgical/trauma ICUs, however, our survey suggests it is a first-line choice independent of the presence of a PAC. There was gravitation to dopamine as a first-line agent when a PAC was not present in the other three types of ICUs. Both guidelines suggest that either dopamine or norepinephrine can be used first-line in the setting of sepsis or septic shock, despite some controversy in the literature [1,2,6-8]. This survey has demonstrated the differing opinions as to where each agent is used in the sequence of therapy.

The first-line use of phenylephrine reported in our survey was accounted for most commonly by the surgical/trauma ICU. Although there are a few small trials examining the use of phenylephrine in this patient population, its ultimate role in therapy is unknown [9-11]. The current guidelines suggest this agent as an option in refractory shock, however, lack of data does not allow for a strong recommendation for its place in therapy. The amount of use of phenylephrine reported in our survey suggests that further research is required comparing it to other first-line agents in this patient population. A small percentage of ICUs (5.6%) used vasopressin as the vasopressor of choice, although evidence is lacking to support this. The guidelines currently recommend that vasopressin be considered in refractory shock [1,2]. While approximately 50% of ICUs used a constant infusion of 0.04 U/min of vasopressin, the majority of other ICUs were titrating to a maximum of 0.04 or 0.1 U/min. The Hemodynamic and 2004 Surviving Sepsis Guidelines recommend a low-dose infusion between 0.01-0.04 U/min, but do not address titration within this dosage range [1,2]. It is a concern that 27.6% of ICUs reportedly use vasopressin in a manner outside of approved guidelines. The recent update of the Surviving Sepsis Guidelines, suggest a constant vasopressin infusion of 0.03 U/min, and this will most likely prompt a change of practice for those using non-recommended dosages. More education with regards to existing evidence and potential deleterious effects of vasopressin, including skin necrosis, alterations in liver function, and splanchnic and cardiac hypoperfusion, needs to be disseminated [12-14].

There were varying opinions about the estimates of low cardiac output in these patients. The percent of ICUs using invasive monitoring parameters in determining whether inotropes were warranted was surprisingly high, suggesting that practice is to evaluate patients invasively before starting this therapy. Endpoints of therapy included objective measurements and clinical signs and symptoms; however, the most commonly used endpoint was cardiac index/output (76.6%), indicating that when inotropes were used, a PAC was most likely in place.

Most respondents felt the incidence of arrhythmias with dobutamine and dopamine was between 1-5%.

The potential for these drugs to cause arrhythmias has been documented, although not necessarily in septic ICU patients [15,16]. Response inconsistency in the form of large interquartile ranges of all of the ADRs suggests that a study examining their actual incidence in ICU patients should be conducted. The variability in weight used to calculate different doses of vasopressors is of concern because of the high-risk nature of the medication. A recent study highlighted the potential of medication errors as a result of inaccurate and estimated weights used in the calculation of infusion medications [17]. While guidelines do not suggest which particular weight should be used in calculation of vasopressor and inotrope dosages, there should be a standard from ICU to ICU. This would also allow a more consistent comparison between studies evaluating these agents.

Variability in the way continuous infusion drugs are prepared and dosed was documented throughout the survey. Different dosage units were reported for the same medications between hospitals. For example, the recommended dosage of norepinephrine is reported in μg/min and μg/kg/min, and our results showed that both of these units were used in practice [14,18]. Data have been shown in a study of 100 hospitals' infusion devices where 60% of all medications were found to have more than one continuous dosage unit, and there were high levels of variation in concentrations [19]. Several reports in the pediatric and adult literature have attempted to standardize drug concentrations and infusions in the critical care setting [20-23]. The alarming number of concentrations found for vasopressors and inotropes should serve as an impetus for action with regard to patient safety. A national organization needs to develop a guideline for recommendations of standard concentrations, not only of vasopressors and inotropes, but all continuous infusion medications used in the ICU setting.

Limitations

Because this was an anonymous survey, we were not able to control for non-response error. We were unable to review CSHP list serve emails for potential duplications, and there is the possibility that a small number of respondents received a duplicate invitation to the survey. Because we did not use the ACCP or SCCM list serves to disseminate the survey, we can't be sure that we encompassed every ICU pharmacist member of ACCP and SCCM. As well, using the members of the three organizations (ACCP, SCCM, and CSHP) may have led to a biased sample, as those pharmacists do not necessarily represent all ICU pharmacists in the US and Canada.

Most of the respondents to our survey practiced at teaching or university associated hospitals, where pharmacists may be more likely to be integrated into the ICU. These institutions may have more resources to develop and implement institutional guidelines based on national guidelines. Therefore, our results may not accurately reflect care at smaller and non-university based hospitals. We did not ask questions about pharmacists' specific duties in the ICU, and this may have influenced response as a pharmacist more integrated into the ICU would have a better understanding of the practice in that unit.

Our instructions were for only one pharmacist per ICU to respond; however, since the survey was anonymous, we cannot guarantee complete compliance with this instruction. We did not collect hospital names from respondents, in order to maintain anonymity, and therefore cannot provide the number of hospitals reflected from our results. Finally, our survey was not sent to physicians and nurses to gain an even broader view on the opinion based questions or to verify what the pharmacists reported was occurring in their respective ICUs.

Conclusions

Despite published guidelines, vasopressor and inotrope use in hemodynamic management of patients with sepsis and septic shock displayed much variability. The perceived incidence of ADRs for these agents also demonstrated inconsistency among respondents. Education of current guidelines (including the recently published update to the Surviving Sepsis Campaign) should be reinforced and institutional guidelines adapted to aid in standardization [24]. National organizations need to develop recommendations

for standardization of concentrations of continuous infusion medications in the ICU.

Acknowledgment

At the time of completion of this project, Dr. LeBlanc was a Critical Care Pharmacy Research Fellow at The Ohio State University. All work was conducted at The Ohio State University.

Table 1. CONSENSUS RECOMMENDATIONS FOR VASOPRESSOR SUPPORT IN SEPSIS PATIENTS [25]

ACCM Practice Parameters	Surviving Sepsis Campaign[a]
When fluid administration fails to restore an adequate arterial pressure and organ perfusion, therapy with vasopressor agents should be initiated; vasopressor therapy may also be required transiently to maintain perfusion in the face of life-threatening hypotension, even when adequate cardiac filling pressures have not yet been attained	When an appropriate fluid challenge fails to restore adequate BP and organ perfusion, therapy with vasopressor agents should be started; vasopressor therapy may also be required transiently to sustain life and maintain perfusion in the face of life-threatening hypotension, even when a fluid challenge is in progress and hypovolemia has not yet been corrected
Arterial cannulation should be performed in patients with shock to provide a more accurate measurement of intraarterial pressure and to allow beat-to-beat analysis so that decisions regarding therapy can be based on immediate and reproducible BP information	All patients requiring vasopressors should have an arterial catheter placed as soon as practical if resources are available
Dopamine and norepinephrine are both effective for increasing arterial BP; it is imperative to ensure that patients receive adequate fluid resuscitation; dopamine raises cardiac output more than norepinephrine, but its use may be limited by tachycardia; norepinephrine may be a more effective vasopressor in some patients	Either norepinephrine or dopamine (through a central catheter as soon as available) is the first-choice vasopressor agent to correct hypotension in septic shock patients
Phenylephrine is an alternative to increase BP, especially in the setting of tachyarrhythmias; epinephrine can be considered for therapy of refractory hypotension, although adverse effects are common, and epinephrine may potentially decrease mesenteric perfusion	
Administration of low doses of dopamine to maintain renal function is not recommended	Low-dose dopamine should not be used for renal protection as part of the treatment of severe sepsis
Low doses of vasopressin given after 24 h as hormone replacement may be effective in raising BP in patients refractory to other vasopressors, although no conclusive data are yet available regarding outcome	Vasopressin use may be considered in patients with refractory shock despite adequate fluid resuscitation and high-dose conventional vasopressor therapy; pending the outcome of ongoing trials, it is not recommended as a replacement for norepinephrine or dopamine as a first-line agent; if used in adults, it should be administered at an infusion rate of 0.01 to 0.04 U/min; it may decrease stroke volume

ACCM = American College of Chest Physicians

[a]Recommendations are from the 2004 Surviving Sepsis Campaign. Adapted with permission from Hollenberg SM [25]

Table 2. PHARMACISTS' PERCEPTIONS OF ADRS OF VASOPRESSORS AND INOTROPES

	Agents Associated with Specific ADRs (% Response)			Perceived Overall Percent Incidence of ADRs Associated with Vasopressors or Inotropes (median [interquartile range])
	1st	2nd	3rd	
Tachycardia	Dopamine (35.7%)	Epinephrine (33.6%)	Dobutamine (17.0%)	50 (25-70)
Other arrhythmias	Epinephrine (23.8%)	Dopamine (23.0%)	Dobutamine (19.6%)	15 (10-20)
Digital ischemia	Norepinephrine (36.2%)	Phenylephrine (20.4%)	Epinephrine (20.0%)	10 (5-25) (vasopressors only)
Hypotension	Milrinone (46.0%)	Dobutamine (36.2%)	Dopamine (2.6%)	20 (10-30) (inotropes only)

ADRs = adverse drug reactions

Table 3. REPORTED CONCENTRATIONS OF VARIOUS VASOPRESSORS AND INOTROPES

Medication	# of Std Conc'ns	Range of Std Conc'ns (mg/ml)	Most Common Std Conc'ns (mg/ml)	# of Max Conc'ns	Range of Max Conc'ns (mg/ml)	Most Common Max Conc'ns (mg/ml)
Dopamine	6	0.0064-4.0	1.6	11	0.0064-12.8	3.2
Epinephrine	12	0.004-0.1	0.04	18	0.004-undiluted/none	0.064
Norepinephrine	8	0.008-1.0	0.016	12	0.0128-undiluted/none	0.064
Phenylephrine	15	0.00016-1.0	0.08	20	0.02-undiluted/none	0.4
Dobutamine	8	0.5-16.0	2.0	10	0.5-16.0	4.0
Milrinone	6	0.005-0.4	0.2	6	0.005-0.8	0.2
Vasopressin	12	0.01-1.0	1.0	16	0.01-40	1.0

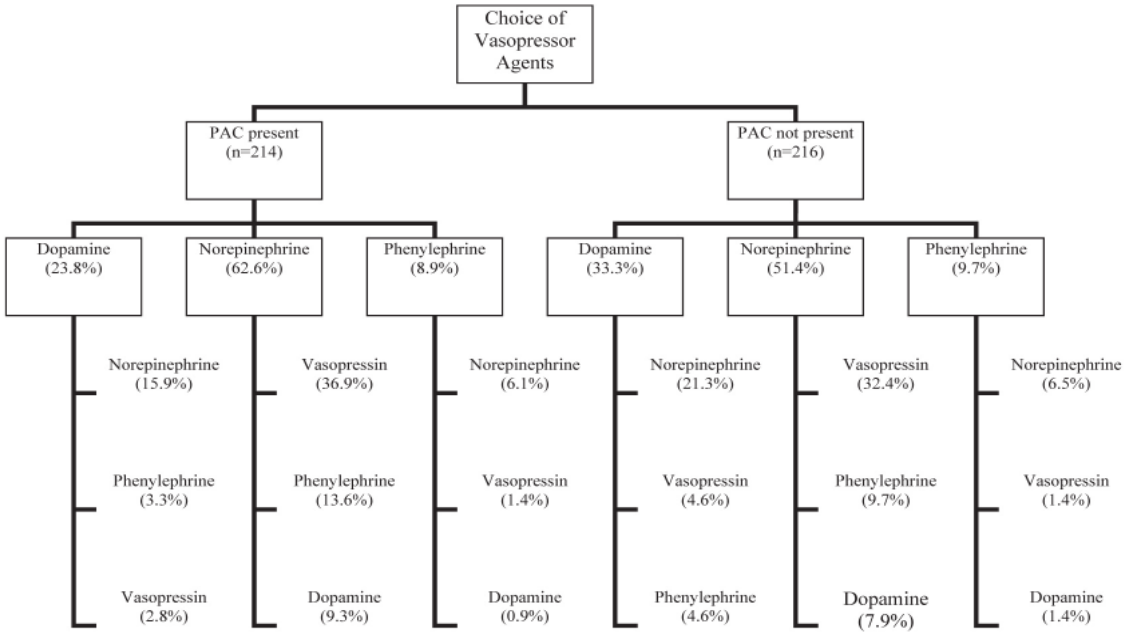
Conc'ns = concentrations, Max = maximum, Std = standard

Table 4. REPORTED DOSAGES OF VARIOUS VASOPRESSORS AND INOTROPES

	Rx Units	Starting Dosage		Average Dosage		Maximum Dosage		Error Dosage[a]	
		#[b]	Range[c]	#	Range	#	Range	#	Range
Dopamine	μg/kg/min	10	0.2 – 10	18	2.0 – 20.0	9	10.0 – 40.0	15	0.1 – 200.0
Epinephrine	μg/kg/min	11	0.01 – 5.0	11	0.05 – 5.0	12	0.05 – 30.0	13	0.05 – 5.0
	μg/min	9	0.01 – 5.0	18	2.0 – 30.0	13	4.0 – 333.0	11	2.0 – 120.0
Norepinephrine	μg/kg/min	9	0.01 – 5.0	9	0.1 – 15.0	7	0.4 – 30.0	9	0.5 – 30.0
	μg/min	12	0.1 – 12.0	15	4.0 – 30.0	13	12.0 – 200.0	14	10.0 – 300.0
Phenylephrine	μg/kg/min	10	0.01 – 50.0	10	0.05–150.0	9	1.0 – 200.0	9	0.1 – 200.0
	μg/min	13	2.0 – 140.0	19	15.0–400.0	15	60.0 – 900.0	14	0.1 – 1000.0
Dobutamine	μg/kg/min	10	0.05 – 5.0	10	2.5 – 20.0	7	10.0 – 50.0	11	10.0 – 80.0
Milrinone	μg/kg/min	7	0.1 – 0.5	7	0.05 – 1.0	6	0.375 – 1.5	8	0.38 – 5.0
Vasopressin	units/min	7	0.01 – 0.3	6	0.01 – 0.2	10	0.04 –1.0	15	0.04 – 10.0
	units/hour	6	0.01 – 2.0	2	2.4 – 4.0	5	0.04 – 60.0	-	

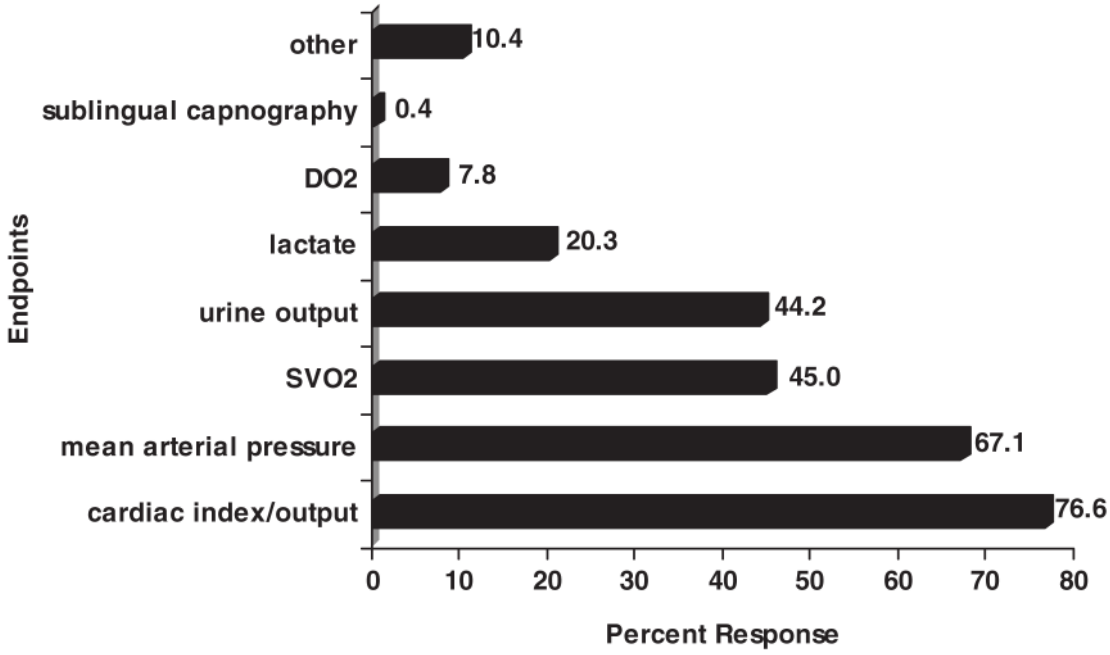
[a]Error dosage was defined as the dose that would require you to question the prescriber due to a suspected mistake.
[b]# refers to the actual number of dosages reported overall by respondents
[c]Range refers to the range of dosages reported overall by respondents

Figure 1. MOST COMMONLY CHOSEN FIRST AND SECOND LINE VASOPRESSORS



The boxes denote the most commonly chosen first-line vasopressors for patients with sepsis and septic shock depending on whether a pulmonary artery catheter (PAC) is present. The vertical trees denote the most commonly chosen second-line vasopressors, depending on the first agent chosen and whether a PAC is present.

Figure 2. CLINICAL ENDPOINTS OF INOTROPE THERAPY



Various endpoints used during inotrope therapy in patients with sepsis and septic shock.

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