Original Research

Use of Vasopressors in Septic Shock (VISS) "A Multi-National Survey to Know the Practice Pattern"

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Abstract

Objective: Despite the widespread compliance of surviving sepsis guidelines, heterogeneity may exist in clinical practice while using vasopressors in ICU setting. Due to paucity of clear-cut evidences and recommendations in some areas of management of septic shock, this multinational survey was conducted to know how physicians use vasopressors and inotropes to manage patients with septic shock.

Method: The survey consisted of nine questions pertinent to use of vasoactive drugs and one question about country of responder. Data were collected automatically using SurveyMonkey Inc. (www.surveymonkey.com). The survey link (https://www.surveymonkey.com/r/JN5GMPX) was distributed by e-mail, text message, and WhatsApp to qualified medical practitioners that treat critically ill patients.

Results: A total of 142 physicians from ten countries participated in the survey. Majority of the responders start vasopressor before completion of fluid bolus, through a peripheral venous access and use vasopressin infusion as second line vasopressor. But opinions are divided at what dose of norepinephrine infusion, vasopressin and steroid are added and how to de-escalate vasopressor after resolution of septic shock.

Conclusion: This survey reveals that some areas in the management of septic shock need uniformity in clinical practice and require further research.

Introduction

Intravenous fluids, vasopressors and inotropes are the cornerstones in the management of patients with septic shock. Surviving sepsis Campaign guidelines and its recent updates in 2018 laid down following salient recommendations regarding use of vasopressors and inotropes.[1,2]

It recommends rapid administration of intravenous fluid at 30ml/kg in case of hypotension or when lactate is more than 4mmol/L. Vasopressor should be started if a patient remains hypotensive after fluid resuscitation to maintain MAP > 65 mmHg. Norepinephrine should be used as the first choice vasopressor. Vasopressin or epinephrine should be added to norepinephrine with the intent of raising MAP to target MAP, or vasopressin (up to 0.03 U/min) is added to norepinephrine to decrease norepinephrine dosage. Dopamine should be used as an alternative vasopressor agent to norepinephrine only in highly selective patients. Dobutamine should be used in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and use of vasopressor agents. Intravenous hydrocortisone at a dose of 200 mg per day should be used when septic shock persists despite adequate fluid resuscitation and vasopressor therapy.

Recent studies have questioned some of the recommendations of these guidelines. Three large randomized control trials did not find benefit with early goal directed therapy over standard therapy.[3,4,5] Another study showed that early norepinephrine use was significantly associated with increased shock control by 6 hours. [6]

Despite the widespread compliance of surviving sepsis guidelines, heterogeneity may exist in clinical practice while using vasopressor in ICU setting. This is because some key issues are still not clearly addressed by the guidelines. For instance, it is not known whether to start vasopressor simultaneously with fluid administration or after fluid resuscitation. Septic shock is basically a vasodilatory shock, not hypovolemic shock. It is not clear at what dose of norepinephrine, vasopressin or epinephrine is to be added. Similarly, there is no recommendation regarding how to de-escalate vasopressors.

Due to these lacunae in the guidelines, this multinational survey was conducted to know how physicians use vasopressors and inotropes to manage patients with septic shock.

Methods

The survey consisted of 9 (nine) questions pertinent to use of vasoactive drugs and 1 (one) question about the country of responder. Ethical approval was not requested as this was a voluntary survey, and no individual patient data was collected.

The questionnaire was formulated by NSC, AG and SKD. Data was collected automatically using SurveyMonkey Inc. (www.surveymonkey.com). The survey link (https://www.surveymonkey.com/r/JN5GMPX) was distributed by e-mail, text message, and WhatsApp to qualified medical practitioners who treat critically ill patients. No personal information was collected, other than the country where the responder practices and no login was required to participate. Completion and submission survey was confirmed by an alert after the questionnaire was submitted. It was not possible to review and change the given answers after submission. If someone did not respond the first time, an automatic reminder was sent after a week. The 10-question questionnaire and the responses are provided in Table 1. The survey was conducted between February 2020 and October 2020. The study participation was voluntary and no incentives were offered for participation.

The methodology and results of the questionnaire are reported according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) statement.[7]

Results

A total of 142 physicians from ten countries participated in the survey. 59.62% participants were from India, rest were from Afganistan, Algeria, Australia, Bangladesh, Ethiopia, Indonesia, France, United Kingdom and Belgium. 22% participants did not disclose their country.

One hundred and forty participants responded to the first query. 63.7% responders administer vasopressor after initial fluid bolus and the rest start vasopressor simultaneously with initial fluid resuscitation.

82.42% responders administer vasopressor with peripheral venous access and 17.58% wait for insertion of central venous catheter.

Majority i.e. 88.76% dilute 4mg norepinephrine in 100 ml of intravenous fluid whereas 11.24% dilute 2mg norepinephrine in 100 mL of intravenous fluid.

72.29% of the responders use vasopressin as second vasopressor in septic shock not responding to norepinephrine alone; 19.28% responders use epinephrine; 4.82% responders use dopamine and 3.61% responders use dobutamine as second line of vasopressor or inotropes. None uses Levosimendan as a second vasopressor/inotrope.

Considerable heterogeneity exists with regards to infusion dose of vasopressin. 10.23% add at the dose of 0.05U/kg/min, 22.73% at 0.1U/kg/min, 17.05% at 0.15U/kg/min, 23.86% at 0.2U/kg/min and 26.14% add vasopressin when norepinephrine infusion dose is more than 0.2mcg/kg/min.

37.21% responders start epinephrine when infusion dose of norepinephrine is 0.2mcg/kg/min. 19.77%, 12.79% and 30.23% start epinephrine at norepinephrine infusion dose

of 0.3mcg/kg/min, 0.4mcg/kg/min and 0.5mcg/kg/min respectively.

28.05%, 29.27%, 14.63% and 28.05% start steroid at norepinephrine infusion dose of 0.1mcg/kg/min, 0.2mcg/kg/min, 0.3mcg/kg/min and 0.4mcg/kg/min respectively.

Majority of the responders i.e. 45.78% do not use inotropes like dobutamine or levosimendan in the management of septic shock. 32.53% responders use inotropes to increase cardiac contractility and peripheral perfusion.

While de-escalating vasopressor, 30.34%, 38.2% and 31.46% responders first withdraw vasopressin, epinephrine and norepinephrine respectively.

Discussion

VISS survey observed considerable lack of uniformity while using vasopressor and inotropes in the management of septic shock. Although majority of the responders in our survey start vasopressor infusion after initial fluid bolus, the recent CENSER study found that early use of norepinephrine is associated with better resolution of septic shock in six hours.[6] Early epinephrine use may correct hypotension faster, increase cardiac output, improve microcirculation, prevent fluid overload and improve patient outcome.[8]

Vasopressor medications have traditionally been administered via central venous catheters, due to concerns of peripheral extravasation of vasoconstrictive medications leading to tissue necrosis and limb ischemia. However systematic review of seven studies analyzing 1381 patients found no tissue necrosis or limb ischemia while using vasopressor through peripheral access.[9] Majority of the responders in this survey initially start vasopressor through peripheral access.

Despite the absence of proven outcome benefits in large randomized controlled trials comparing vasopressin with norepinephrine, vasopressin is recommended as a second-line vasopressor by the surviving sepsis guidelines.[10,11,1] Majority of the responders in the survey use vasopressin as second line vasopressor although considerable difference exists among the responders when to start vasopressin. Some responders prefer epinephrine but epinephrine is known to be associated with serious side effects such as tachycardia, tachyarrhythmias and increased blood lactate levels.[12]

Surviving sepsis guidelines recommend hydrocortisone infusion at a dose of 200 mg per day when septic shock persists despite adequate fluid resuscitation and vasopressor therapy. Recent adrenal trial showed that hydrocortisone did not decrease 90 days mortality but helped early resolution of shock. Our survey showed that there was lack of uniformity in responses regarding timing of steroid administration.

Although majority of the responders avoid inotropes like dobutamine or levosimendan, 32.5% use inotropes to increase cardiac contractility and peripheral perfusion. Recent surviving sepsis guidelines do not support use of dobutamine or levosimendan in septic shock.[1] A meta regression analysis of 11 studies showed that dobutamine seems to have a positive effect on cardiovascular parameters in septic shock.[13] A meta-analysis of 10 studies analyzing 1036 patients found no sufficient evidence to support levosimendan as superior to dobutamine or as an optimal adjunct in severe sepsis and septic shock.[14]

De-escalation of vasopressor after resolution of shock is an important consideration to prevent tissue hypoperfusion and vasopressor associated side effects. The opinions of the responders were divided regarding this issue.

Physicians from eleven countries responded to this study. So, the survey may be a true reflection of the current clinical practice across the globe. The survey also revealed areas in management of septic shock that need uniformity and further research. The survey has several limitations. The survey had limited queries and sample size is definitely low. Physicians of many countries did not take part in the survey. Every question had limited option for response. There may be different practices that is not covered in the responses.

VISS survey revealed many areas in management of septic shock that need extensive research. Due to the lacunae in evidence, there is lack of uniformity in clinical practice.

Conflict of Interest: Not declared

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