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HYDROCORTISONE IN SEPTIC SHOCK: A CROSS SECTIONAL STUDY ON VASOPRESSOR REQUIREMENTS & HEMODYNAMIC STABILITY

Original Article (ID: 456)

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ABSTRACT

Background: Septic shock is a critical condition marked by persistent hypotension, tissue hypoperfusion, and the need for vasopressors despite adequate fluid resuscitation. Hydrocortisone is commonly used when shock remains refractory, as it may improve vascular responsiveness and reduce catecholamine exposure. However, local evidence regarding its effect on vasopressor requirements and early ICU outcomes remains limited, particularly in public-sector tertiary-care settings where septic shock burden is high and resources are often constrained.

Objective: To evaluate changes in mean arterial pressure and norepinephrine-equivalent vasopressor requirements after intravenous hydrocortisone administration and to assess the association of early hemodynamic stability with ICU outcomes among adults with septic shock.

Methods: This prospective observational cohort study was conducted in the Medical ICU of Jinnah Postgraduate Medical Centre, Karachi, over six months after IRB approval. Adult patients aged 18–60 years with septic shock who received vasopressor support and intravenous hydrocortisone were enrolled using non-probability consecutive sampling. Hydrocortisone was administered as 50 mg intravenously every six hours. Mean arterial pressure and norepinephrine-equivalent vasopressor dose were recorded at hydrocortisone initiation and at 6, 12, 24, and 48 hours. Outcomes included hemodynamic stability, shock reversal, ICU mortality, and ventilator dependency beyond day 7. Data were analyzed using SPSS version 25, and $p<0.05$ was considered statistically significant.

Results: A total of 62 patients were included, with a mean age of 44.6±9.8 years. Males accounted for 59.7% of cases. Pneumonia was the most common source of sepsis, reported in 41.9% of patients. Mean arterial pressure increased from 58.3±6.1 mmHg at initiation to 68.7±5.4 mmHg at 24 hours and 70.4±5.0 mmHg at 48 hours ($p<0.001$). Norepinephrine-equivalent dose decreased from 0.42±0.11 mcg/kg/min to 0.19±0.08 mcg/kg/min at 24 hours and 0.11±0.06 mcg/kg/min at 48 hours ($p<0.001$). Hemodynamic stability at 24 hours was achieved in 66.1% of patients. Shock reversal occurred in 64.5%, ICU mortality was 27.4%, and ventilator dependency beyond day 7 was 21.0%. Stability at 24 hours was significantly associated with higher shock reversal ($p<0.001$) and lower ICU mortality ($p=0.045$).

Conclusion: Septic shock patients receiving intravenous hydrocortisone showed improved mean arterial pressure and reduced vasopressor requirements during early ICU monitoring. Hemodynamic stability within 24 hours was associated with better early ICU outcomes. Larger controlled studies are required to clarify the independent effect and safety profile of hydrocortisone in local ICU settings.

Keywords: Critical Care; Hemodynamics; Hydrocortisone; Intensive Care Units; Norepinephrine; Septic Shock; Vasoconstrictor Agents.

INTRODUCTION

Septic shock remains one of the most challenging and life-threatening conditions encountered in intensive care units. It is characterized by severe circulatory and metabolic disturbances in which patients continue to have hypotension requiring vasopressor support to maintain a mean arterial pressure of at least 65 mmHg, despite adequate fluid resuscitation, along with evidence of tissue hypoperfusion (1). Although early recognition, timely antibiotics, source control, fluid resuscitation, and vasopressor therapy have improved the management of septic shock, many patients continue to experience persistent hemodynamic instability, prolonged vasopressor dependence, organ dysfunction, and high mortality (2). This burden is even more concerning in resource-limited healthcare settings, where delayed presentation, limited intensive care capacity, and variation in protocol-based management may contribute to prolonged shock and poorer clinical outcomes (3). A major clinical problem in septic shock is reduced vascular responsiveness to catecholamines. Norepinephrine is recommended as the first-line vasopressor; however, some patients require escalating doses to achieve and maintain the target mean arterial pressure (4). Higher catecholamine exposure may increase the risk of adverse effects such as tachyarrhythmias, excessive vasoconstriction, and impaired microcirculatory perfusion. One proposed mechanism behind vasopressor resistance is critical illness-related corticosteroid insufficiency, in which endogenous corticosteroid activity becomes inadequate for the severity of illness. Inflammatory mediators may also impair adrenergic receptor function and vascular smooth muscle responsiveness, leading to persistent vasodilation and reduced sensitivity to vasopressor therapy (5).

Hydrocortisone has therefore been used as an adjunctive treatment in patients with refractory septic shock. Its potential benefit is thought to arise from its anti-inflammatory effects and its ability to restore vascular tone and improve responsiveness to catecholamines. Evidence from international trials suggests that corticosteroid therapy may shorten the duration of shock and reduce vasopressor requirements, although its effect on mortality remains variable across different patient populations and clinical settings. In line with this evidence, current guidelines recommend considering intravenous hydrocortisone in patients with septic shock who remain hypotensive despite adequate fluid resuscitation and vasopressor support (6). In routine intensive care practice, hydrocortisone is commonly initiated when vasopressor needs remain high, mean arterial pressure is difficult to maintain, or shock persists after initial resuscitative measures (7). Despite its widespread use, local evidence regarding the hemodynamic response to hydrocortisone in septic shock remains limited. Most available data are derived from large international trials, which may not fully represent the clinical realities of tertiary-care public-sector hospitals in Pakistan. Differences in infection patterns, severity at presentation, comorbid conditions, ICU resources, and timing of intervention may influence both vasopressor requirements and patient outcomes (8). Generating local observational data is therefore important to understand how hydrocortisone performs in real-world ICU practice, particularly in relation to vasopressor dose reduction, mean arterial pressure stabilization, shock reversal, ventilator dependence, and short-term mortality.

The research question underlying the present study is whether septic shock patients receiving intravenous hydrocortisone demonstrate reduced vasopressor requirements and improved hemodynamic stability during ICU care. It is hypothesized that hydrocortisone use is associated with better early hemodynamic control, reflected by improved mean arterial pressure and reduced vasopressor dependence. Therefore, the objective of this cross-sectional study is to evaluate vasopressor requirements, hemodynamic parameters, and early ICU outcomes among septic shock patients receiving intravenous hydrocortisone in a tertiary-care public-sector ICU, and to determine whether early hemodynamic stability is associated with short-term clinical outcomes.

METHODS

This prospective observational cohort study was conducted in the Medical Intensive Care Unit of Jinnah Postgraduate Medical Centre (JPMC), Karachi, over a period of six months after approval from the institutional ethical review committee. Written informed consent was obtained from the patient or from the legally authorized attendant when the patient was unable to provide consent because of critical illness. Adult patients admitted with septic shock, diagnosed according to Sepsis-3 criteria, were enrolled through non-probability consecutive sampling. Patients were included if they required vasopressor support and received intravenous hydrocortisone as part of standard ICU management. A total of 62 patients fulfilling the eligibility criteria were included in the study. Patients were excluded if they had known adrenal insufficiency, had received systemic corticosteroids within the preceding seven days, were pregnant, or had a documented do-not-resuscitate status. These criteria were applied to reduce clinical confounding and to ensure that the observed hemodynamic response was assessed in patients receiving hydrocortisone for septic shock rather than for a pre-existing steroid-dependent condition.

Data were collected using a structured proforma from ICU monitoring charts, medication records, and clinical files. The initiation of hydrocortisone therapy was considered the index time. Hydrocortisone was administered intravenously at a dose of 50 mg every six hours according to routine ICU practice. Vasopressor requirement was recorded as norepinephrine-equivalent dose in mcg/kg/min at the index time and at predefined observation points of 6, 12, 24, and 48 hours after hydrocortisone initiation. Hemodynamic stability was defined as achievement or maintenance of mean arterial pressure of at least 65 mmHg at the time of observation. Shock reversal was defined as discontinuation of vasopressor support with persistent mean arterial pressure of at least 65 mmHg for a minimum of 24 hours after vasopressor withdrawal. Additional clinical outcomes included ICU mortality and ventilator dependence after day 7 of ICU admission. Data were entered and analyzed using SPSS version 25. Continuous variables were assessed for distribution and summarized

as mean ± standard deviation for normally distributed data or median with interquartile range for non-normally distributed data. Categorical variables were presented as frequencies and percentages. Changes in vasopressor dose and hemodynamic parameters across repeated observation points were analyzed using appropriate paired or repeated-measures statistical tests, such as repeated-measures ANOVA for normally distributed data or the Friedman test for non-parametric repeated observations. Associations between categorical variables, including hemodynamic stability, shock reversal, ventilator dependence, and ICU mortality, were assessed using the chi-square test or Fisher's exact test where appropriate. A p-value of less than 0.05 was considered statistically significant. As this was an observational cohort study conducted under routine clinical practice, the findings were interpreted as associations and were not considered evidence of direct causality.

RESULTS

A total of 62 adult patients with septic shock who received intravenous hydrocortisone were included in the study. The mean age of the study population was 44.6 ± 9.8 years, and 37 patients were male, representing 59.7% of the cohort. Pneumonia was the most common suspected source of sepsis, reported in 26 patients, accounting for 41.9% of cases, followed by intra-abdominal infection in 17 patients, accounting for 27.4%. At the time of hydrocortisone initiation, the mean arterial pressure was 58.3 ± 6.1 mmHg, indicating that the target MAP of ≥65 mmHg had not been achieved at baseline. Mean arterial pressure increased progressively during the subsequent observation period and reached 70.4 ± 5.0 mmHg by 48 hours. During the same period, the norepinephrine-equivalent vasopressor dose decreased from 0.42 ± 0.11 mcg/kg/min at the index time to 0.11 ± 0.06 mcg/kg/min at 48 hours. The overall changes in mean arterial pressure and norepinephrine-equivalent vasopressor requirement across the recorded time points were statistically significant ($p<0.001$).

By the 24-hour observation point, 41 patients achieved hemodynamic stability, defined as MAP ≥65 mmHg, representing 66.1% of the total cohort. Shock reversal during ICU stay was documented in 40 patients, accounting for 64.5%. ICU mortality was recorded in 17 patients, representing 27.4%, while 13 patients remained ventilator-dependent beyond day 7, accounting for 21.0%. Patients who achieved hemodynamic stability within 24 hours had higher rates of shock reversal compared with those who did not achieve stability at 24 hours. Shock reversal occurred in 33 of 41 stable patients, representing 80.5%, compared with 7 of 21 patients, representing 33.3%, in the non-stable group ($p<0.001$). ICU mortality was lower among patients who achieved 24-hour hemodynamic stability, with 8 deaths among 41 stable patients, representing 19.5%, compared with 9 deaths among 21 non-stable patients, representing 42.9% ($p=0.045$). Ventilator dependency beyond day 7 was also lower in the stable group, occurring in 6 of 41 patients, representing 14.6%, compared with 7 of 21 patients, representing 33.3%, in the non-stable group ($p=0.048$).

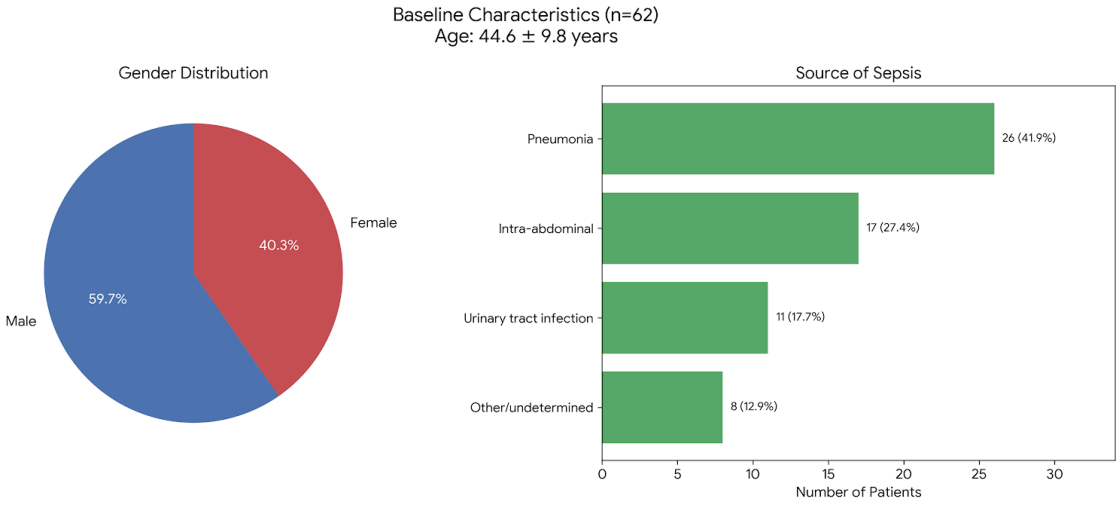

Figure 1: Baseline Characteristics of the Study Cohort.

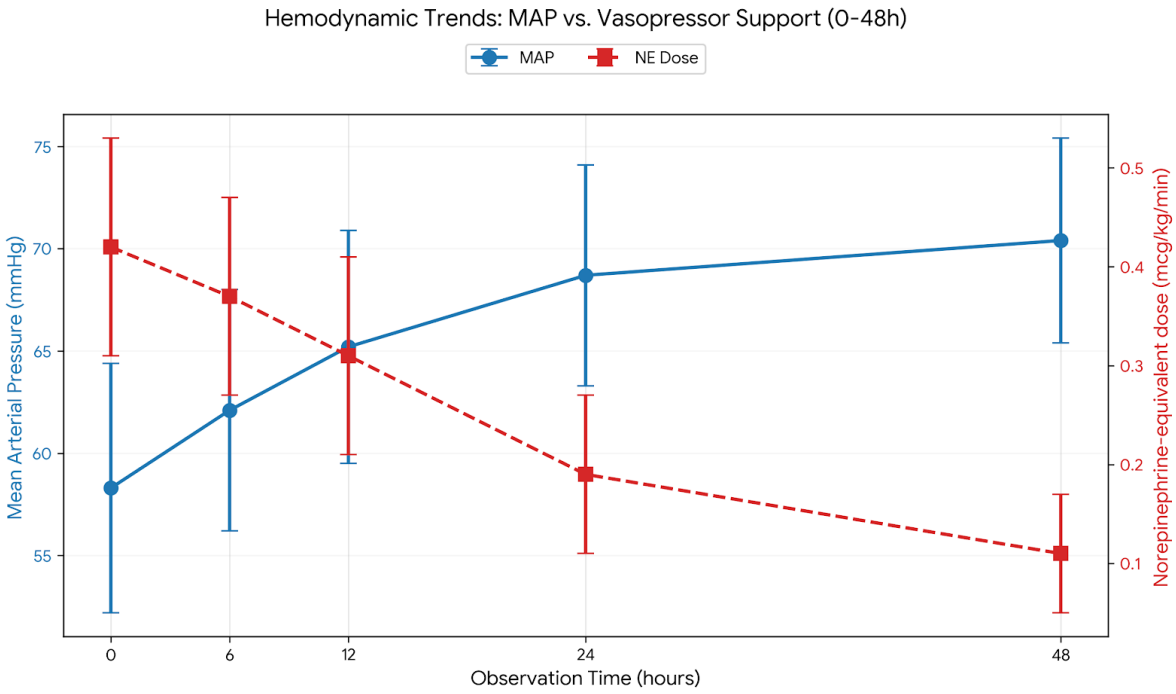

Figure 2: Temporal Trends in Mean Arterial Pressure (MAP) and Vasopressor Requirement.

Table 1: Early ICU Outcomes (n=62)

Outcome	n (%)
Hemodynamic stability by 24 h observation (MAP ≥65 mmHg)	41 (66.1)
Shock reversal documented during ICU stay	40 (64.5)
ICU mortality	17 (27.4)
Ventilator dependency beyond day 7	13 (21.0)

Table 2: Association of Hemodynamic Stability at 24 Hours with Early Outcomes (n=62)

Outcome	Stable MAP ≥65 at 24 h (n=41)	Not stable at 24 h (n=21)	p-value
Shock reversal, n (%)	33 (80.5)	7 (33.3)	<0.001
ICU mortality, n (%)	8 (19.5)	9 (42.9)	0.045
Ventilator dependency >7 days, n (%)	6 (14.6)	7 (33.3)	0.048

DISCUSSION

This prospective observational cohort study evaluated hemodynamic trends, vasopressor requirements, and early ICU outcomes among patients with septic shock who received intravenous hydrocortisone in a tertiary-care public-sector intensive care unit. The main finding was that mean arterial pressure increased progressively after hydrocortisone initiation, while norepinephrine-equivalent vasopressor requirements decreased over the early observation period. By 48 hours, the mean arterial pressure had reached the recommended target range, and vasopressor dose had declined substantially. These findings supported the clinical observation that patients receiving hydrocortisone as part of standard septic shock care often demonstrated early improvement in circulatory stability and reduction in catecholamine requirement (9,10). The observed improvement in mean arterial pressure and reduction in vasopressor dose were

consistent with previous evidence suggesting that corticosteroids may improve vascular responsiveness in patients with refractory septic shock. Earlier clinical studies reported that hydrocortisone could reduce the duration of shock and facilitate earlier withdrawal of vasopressor support, particularly in patients who remained hypotensive despite adequate fluid resuscitation and catecholamine therapy (11,12). The biological explanation for this response is clinically plausible, as corticosteroids may enhance vascular tone, improve adrenergic receptor sensitivity, reduce excessive inflammatory activity, and counter relative corticosteroid insufficiency during critical illness. However, the present findings were interpreted cautiously because all patients received several concurrent ICU interventions, including antibiotics, fluid optimization, ventilatory support, and source control where indicated. Therefore, the hemodynamic improvement observed in this cohort reflected the combined effect of standard sepsis management in patients who received hydrocortisone rather than the isolated effect of hydrocortisone alone.

Another important finding was the association between hemodynamic stability at 24 hours and better early ICU outcomes. Patients who achieved a mean arterial pressure of at least 65 mmHg within 24 hours had higher rates of shock reversal and lower rates of ICU mortality and ventilator dependency beyond day 7. This finding was in line with the broader understanding of septic shock, in which early restoration of adequate perfusion is closely linked with improved organ function and clinical recovery (13). Early stabilization may indicate better vascular responsiveness, effective resuscitation, timely antimicrobial therapy, or adequate control of the infectious source. In routine ICU practice, achieving the target mean arterial pressure within the early treatment window may allow clinicians to reduce vasopressor exposure and shift attention toward ongoing organ support, infection control, nutrition, ventilation strategies, and prevention of ICU-related complications (14,15). Despite improvement in hemodynamic parameters, ICU mortality remained considerable. This finding emphasized that septic shock outcomes are not determined by blood pressure stabilization alone. Mortality is influenced by several interrelated factors, including severity of organ dysfunction, baseline comorbidities, timing and appropriateness of antibiotics, adequacy of source control, lactate clearance, renal and respiratory failure, secondary infections, and complications related to prolonged ICU care (16). Similarly, the presence of ventilator dependency beyond day 7 in a subset of patients indicated that circulatory recovery did not always translate into complete clinical recovery. This observation was important because it highlighted the multidimensional nature of septic shock, where improvement in one physiological domain may coexist with persistent respiratory, metabolic, renal, or neurological dysfunction.

The clinical relevance of this study lies in its local context. Most evidence on hydrocortisone in septic shock has been generated from large multicenter trials conducted in healthcare systems with different ICU structures, staffing patterns, infection profiles, and resource availability. The present study provided real-world data from a public-sector tertiary-care ICU, where patients may present late, infection burden may be high, and resource limitations may affect monitoring and implementation of sepsis bundles. Such local data are useful for understanding practical ICU outcomes, especially in relation to vasopressor trends, early hemodynamic response, shock reversal, mortality, and prolonged ventilator support. A strength of this study was its prospective observational design, which allowed systematic recording of hemodynamic parameters and vasopressor requirements at predefined time points after hydrocortisone initiation. The use of norepinephrine-equivalent dosing also improved comparability of vasopressor requirements across patients. In addition, the study focused on clinically meaningful outcomes, including hemodynamic stability, shock reversal, ICU mortality, and ventilator dependency, making the findings relevant to bedside ICU decision-making.

However, several limitations were present. The absence of a non-hydrocortisone comparison group limited the ability to determine whether the observed improvements were directly attributable to hydrocortisone. The observational design also introduced the possibility of confounding by indication, as hydrocortisone may have been started in patients with greater shock severity or persistent vasopressor need. The study was conducted in a single center with a relatively small sample size, which may limit generalizability. Important clinical variables such as baseline severity scores, lactate levels, timing of antibiotics, timing and adequacy of source control, comorbid conditions, renal replacement therapy, glycemic control, and steroid-related adverse events were not fully described. These missing variables may have influenced both hemodynamic response and clinical outcomes. Furthermore, because multiple ICU interventions occurred simultaneously, the associations observed in this study did not establish causality. Future research should include larger multicenter cohorts with matched comparison groups or randomized study designs to better evaluate the independent effect of hydrocortisone on vasopressor requirements and patient outcomes. Future studies should also incorporate standardized illness severity scoring, serial lactate clearance, detailed infection source documentation, antibiotic timing, source control status, and adverse-event monitoring, including hyperglycemia, secondary infections, gastrointestinal bleeding, and ICU-acquired neuromuscular weakness. Longer follow-up after ICU discharge would also help determine whether early hemodynamic stabilization was associated with sustained recovery, survival, and functional outcomes. Overall, the findings suggested that early hemodynamic stability among septic shock patients receiving hydrocortisone was associated with favorable short-term ICU outcomes, while also reinforcing the need to interpret these associations within the broader context of bundled sepsis care and observational study limitations (17-19).

CONCLUSION

This study concluded that septic shock patients receiving intravenous hydrocortisone demonstrated improvement in mean arterial pressure and a reduction in vasopressor requirements during early ICU monitoring. Early achievement of hemodynamic stability was

associated with better short-term clinical outcomes, including greater shock reversal and lower adverse ICU outcomes. These findings highlight the practical importance of close hemodynamic surveillance, timely vasopressor adjustment, and structured septic shock management in resource-limited intensive care settings. However, larger controlled studies are needed to clarify the independent effect of hydrocortisone, identify patients most likely to benefit, and evaluate safety concerns such as hyperglycemia and secondary infections.

AUTHOR CONTRIBUTION

Author	Contribution
Dr Muhammad Hassan	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Dr Zeeshan Ali Junejo	Methodology, Investigation, Data Curation, Writing - Review & Editing
Dr Ramsha Habibullah Mangrio	Investigation, Data Curation, Formal Analysis, Software
Dr Waseem Abbas	Software, Validation, Writing - Original Draft

REFERENCES

1. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock 2021. Crit Care Med. 2021;49(11):e1063-e1143. doi:10.1097/CCM.0000000000005337.
2. Ragoonanan D, Allen B, Cannon C, Rottman-Pietrzak K, Bello A. Comparison of early versus late initiation of hydrocortisone in patients with septic shock in the ICU setting. Ann Pharmacother. 2022;56(3):264-70. doi:10.1177/10600280211021103.
3. Jochheim L, Jochheim D, Habenicht L, Herner A, Ulrich J, Wiessner J, et al. Adjunctive Hydrocortisone Improves Hemodynamics in Critically Ill Patients with Septic Shock: An Observational Study Using Transpulmonary Thermodilution. J Intensive Care Med. 2023;38(8):717-26.
4. Lenney M, Kopp B, Erstad B. Effect of fixed-dose hydrocortisone on vasopressor dose and mean arterial pressure in obese and nonobese patients with septic shock. Am J Health Syst Pharm. 2022;79(Suppl 3):S94-s9.
5. Jha AK, Kumar R, Goenka MK, Dayal VM. Emerging Treatment and Prevention Strategies against COVID-19: A Brief Update. J Dig Endosc. 2020;11(1):69-72.
6. Petros S. [Fluid and vasopressor therapy in sepsis]. Med Klin Intensivmed Notfmed. 2023;118(2):163-71.
7. Annane D, Renault A, Brun-Buisson C, Megarbane B, Quenot JP, Siami S, et al. Hydrocortisone plus Fludrocortisone for Adults with Septic Shock. N Engl J Med. 2018;378(9):809-18.
8. Heming N, Renault A, Kuperminc E, Brun-Buisson C, Megarbane B, Quenot JP, et al. Hydrocortisone plus fludrocortisone for community acquired pneumonia-related septic shock: a subgroup analysis of the APROCCHSS phase 3 randomised trial. Lancet Respir Med. 2024;12(5):366-74.
9. DeMillard L, Thuyns M. Implementation and Evaluation of Weight-Based Vasopressors in Intensive Care Units. J Pharm Technol. 2024;40(1):23-9.
10. Jakowenko ND, Murata J, Kopp BJ, Erstad BL. Influence of Timing and Catecholamine Requirements on Vasopressin Responsiveness in Critically ill Patients with Septic Shock. J Intensive Care Med. 2022;37(11):1512-9.
11. Costa NA, Pereira AG, Sugizaki CSA, Vieira NM, Garcia LR, de Paiva SAR, et al. Insights Into Thiamine Supplementation in Patients With Septic Shock. Front Med (Lausanne). 2021;8:805199.
12. Ndomba N, Soldera J. Management of sepsis in a cirrhotic patient admitted to the intensive care unit: A systematic literature review. World J Hepatol. 2023;15(6):850-66.
13. Der-Nigoghossian C, Hammond DA, Ammar MA. Narrative Review of Controversies Involving Vasopressin Use in Septic Shock and Practical Considerations. Ann Pharmacother. 2020;54(7):706-14.
14. Endo A, Yamakawa K, Tagami T, Umemura Y, Takahashi K, Nagasawa H, et al. Optimal target blood pressure in elderly with septic shock (OPTPRESS) trial: study protocol for a randomized controlled trial. Trials. 2022;23(1):799.
15. Albertson TE, Chenoweth JA, Lewis JC, Pugashetti JV, Sandrock CE, Morrissey BM. The pharmacotherapeutic options in patients with catecholamine-resistant vasodilatory shock. Expert Rev Clin Pharmacol. 2022;15(8):959-76.
16. De Backer D, Cecconi M, Chew MS, Hajjar L, Monnet X, Ospina-Tascón GA, et al. A plea for personalization of the hemodynamic management of septic shock. Crit Care. 2022;26(1):372.
17. Schlapbach LJ, Raman S, Buckley D, George S, King M, Ridolfi R, et al. Resuscitation With Vitamin C, Hydrocortisone, and Thiamin in Children With Septic Shock: A Multicenter Randomized Pilot Study. Pediatr Crit Care Med. 2024;25(2):159-70.
18. Russell JA. Vasopressor therapy in critically ill patients with shock. Intensive Care Med. 2019;45(11):1503-17.
19. Puntillo F, Giglio M, Pasqualucci A, Brienza N, Paladini A, Varrassi G. Vasopressor-Sparing Action of Methylene Blue in Severe Sepsis and Shock: A Narrative Review. Adv Ther. 2020;37(9):3692-706.

