Original Article

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Incidence of Extravasation during Norepinephrine Administration via Peripheral Venous Catheter in Emergency Patients

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Abstract:

Objective: To describe the incidence of extravasation resulting from the administration of norepinephrine through a peripheral venous catheter in emergency patients.

Material and Methods: This prospective observational study was conducted on 150 adult patients in the emergency department at Siriraj Hospital, Thailand. Physicians closely monitored patients who received norepinephrine via a peripheral venous catheter examining the intravenous access sites during the period of treatment and for up to 48 hours after discontinuation of treatment. We collected demographic data, norepinephrine administration details, potential risk factors for extravasation, the incidence of extravasation, and mortality rate.

Results: The median age of the patients was 67 years, and 60.7% were male. Most patients (93.3%) received peripheral intravenous norepinephrine for septic shock, administered below the wrist joint (47.3%) through a 22-gauge catheter (82.7%). The median duration of total peripheral intravenous norepinephrine administration was 19.92 hours (interquartile range (IQR) 9.48-38.09). The median maximum dose was 0.07 mcg/kg/min (IQR 0.04-0.10). Extravasation occurred in three patients (2.0%) (95% CI: 0.6 - 6.1), none of which resulted in significant morbidity. The timing from shock diagnosis to peripheral intravenous norepinephrine administration did not statistically differ between survivors and non-survivors at both 7 and 30 days. However, the median time from shock diagnosis to achieve mean arterial pressure (MAP)≥65 mmHg, and time from norepinephrine administration to achieve MAP ≥65 mmHg, was shorter in the survivors compared to the non-survivors.

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Conclusion: Given that the incidence of extravasation events was low and did not result in significant morbidity, we suggest that peripheral intravenous norepinephrine administration is safe under close observation and for a limited duration.

Keywords: emergency department, extravasation, norepinephrine, peripheral vein vasopressor

Introduction

Sepsis and septic shock remain a major healthcare problem in terms of morbidity, mortality, and resource utilization[1]. In Thailand, the mortality rates of sepsis and septic shock are considered high, at 34.3% and 52.6% respectively[2]. Hence, early diagnosis and appropriate management are important strategies for improving patient outcomes.

The 2021 International Guidelines from the Surviving Sepsis Campaign for Sepsis and Septic Shock recommend early and effective fluid resuscitation to stabilize sepsis-induced tissue hypoperfusion in both sepsis and septic shock cases. An initial fluid resuscitation should involve a minimum of 30 mL/kg (based on ideal body weight) of intravenous crystalloids within the first three hours of resuscitation. The target mean arterial pressure (MAP) is 65 mmHg. In situations where the MAP level is low despite adequate fluid resuscitation, vasopressors can be used to achieve the target MAP. Norepinephrine, a potent agonist of α-1 and β-1 adrenergic receptors, results in vasoconstriction and increased MAP, with less effect on the heart rate compared to other vasopressors. Thus, it is usually used as the first-line vasopressor agent[1].

A systematic review and meta-analysis suggest that early initiation of norepinephrine in patients with septic shock is associated with lower short-term mortality (odds ratio [OR]=0.45; 95% confidence interval (CI), 0.34 to 0.61; p-value<0.00001), a shorter time to achieving the target MAP (p-value<0.00001), and lower volume of intravenous fluids within six hours (p-value<0.00001)[3].

The administration of vasopressors in adults with septic shock is advised to commence peripherally to achieve the MAP target, rather than delaying initiation until a central venous catheter is inserted[1]. A systematic review of the safety of peripheral vasopressor administration from seven studies found that norepinephrine was the most commonly administered agent (n=702), with infusion duration of 22 hours (95% CI 8-36). The incidence of extravasation was reported at 3.4% (95% CI 2.5-4.7). All extravasation events were managed either conservatively or treated with a vasodilatory agent with no reported episodes of tissue necrosis or ischemia[4].

However, data on adverse events related to peripheral intravenous norepinephrine administration in emergency departments is limited. This study aimed to describe the incidence of extravasation resulting from the administration of norepinephrine through a peripheral venous catheter in emergency patients at the quaternary emergency room (ER) in Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Material and Methods

Our study had a prospective observational study design, which was approved by the Institutional Review Board (IRB). From July 2020 to July 2022, participants were enrolled in the study after providing informed consent, as approved by the IRB. The inclusion criteria were patients aged 18 or older who received peripheral intravenous norepinephrine, which was infused according to a previously described protocol for administration of norepinephrine via a peripheral venous catheter[5] (Supplementary Table 1). The exclusion criteria were having received central intravenous norepinephrine at the time of vasopressor initiation or having received peripheral intravenous norepinephrine for less than 1 hour. After enrollment, each patient was monitored daily by the study team physicians to examine

Supplementary Table 1 Protocol for administration of norepinephrine via a peripheral venous catheter[5]

Norepinephrine administration protocol
• Double check patient name, type and medication dosage each time
• Norepinephrine must be diluted with a dextrose-containing solvent only
• Compatible solvents are D5W, D5S
• Do not mix in alkaline solutions as it may cause norepinephrine to be oxidized, reducing effectiveness
• Be cautious of extravasation
• The position of the peripheral venous catheter should be documented in large veins, including the antecubital vein and femoral vein.
• Nursing staff should immediately be alerted if an extravasation event occurs and provide prompt local treatment to inhibit complications

the intravenous access sites throughout the period of peripheral intravenous norepinephrine administration and up to 48 hours after discontinuation of treatment or until the patient expired. This protocol was based on studies reporting delayed presentation of complications of up to 48 hours after discontinuation of peripheral intravenous norepinephrine administration[6].

The sample size was calculated based on the estimated proportion of mild complications from norepinephrine administration via peripheral venous catheters of 36%. Based on a 95% CI of 36%±4%, a sample size of 150 patients was required[6].

Data collection included patient demographics, norepinephrine infusion data, such as infusion duration, dose (initial and maximum infusion dose), and site of the peripheral venous catheter (PVC). In addition, we also recorded catheter gauge size, reason(s) for treatment, and time from infusion changed to central venous catheter (CVC) placement, when the signs of PVC insertion problem arise. For extravasation events, the collected data included time from PVC insertion to extravasation, location and gauge of PVC, any corrective measures taken and the severity grade of the event.

The primary outcome of this study was the incidence of extravasation events related to administration of norepinephrine through a peripheral venous catheter. The research physician was trained to identify complications of interest, which were divided into minor complications (drug extravasation, thrombophlebitis and localized cellulitis) and major complications (tissue necrosis and limb ischemia). Extravasation was defined as the extravenous administration of medication or solution with the potential for severe tissue or cellular damage into the surrounding tissue[7,8]. An infiltration scale was employed to grade extravasation events according to infusion nursing standards of Infusion Nurses Society based on the most severe presenting indicator (Table 1).

Table 1 Infusion nursing standards of Infiltration scale[7]

Clinical	Criteria
0	No symptoms
1	Skin blanched Edema <1 inch in any direction Cool to touch With or without pain
2	Skin blanched Edema 1–6 inches in any direction Cool to touch With or without pain
3	Skin blanched, translucent Gross edema >6 inches in any direction Cool to touch Mild–Moderate pain Possible numbness
4	Skin blanched, translucent Skin tight, leaking Skin discolored, bruised, swollen gross edema >6 inches in any direction Deep pitting tissue edema Circulatory impairment Moderate–severe pain Infiltration of any amount of blood product, irritant, or vesicant

Extravasation events were identified by research physician and classified according to the infiltration scale. The role of research physician was entirely observational and did not influence the decisions made by the patient's medical team.

The secondary outcomes were hospital outcomes on 7-day and 30-day mortality, timing from septic shock diagnosis to peripheral intravenous norepinephrine administration, the median time from septic shock diagnosis to achieving MAP≥65 mmHg, and the median time from peripheral intravenous norepinephrine administration to achieving MAP≥65 mmHg. After treatment and discharge from the Emergency Room (ER), hospital outcomes were collected from the patient's medical records for our study.

Data processing was performed using the Statistics Package for Social Sciences (SPSS) statistical software package (version 25.0 for Windows, Chicago, IL). For our descriptive analysis, variables were expressed as median values with interquartile ranges (25^{th} and 75^{th} percentiles).

Results

Patient demographics

A total of 150 patients were enrolled in this study from August 3, 2020, to June 2022. 91 (60.7%) males and 59 (39.3%) females, with a combined mean age of 67, and body mass index of 22 kg/m^2. Approximately half of the patients had a history of hypertension (53.3%), one-third had diabetes mellitus (36.7%), and about one-fourth had coronary disease (23.3%) (Table 2). The most common diagnosis or indication for norepinephrine administration through a peripheral venous catheter was septic shock (93.3%), followed by cardiogenic shock (6.7%), and hemorrhagic shock (4.7%) (Table 2).

All 150 patients received norepinephrine via a peripheral venous catheter at a standard concentration of 4 mg in 250 mL of 5% dextrose in water (D5W). The most common initial infusion was 5 mL/hour (1.33 mcg/min) (90.7%). The maximum infusion dose of norepinephrine was 0.30 mcg/kg/min, with a median infusion dose of 0.07 mcg/kg/min and an interquartile range of 0.04-0.11 mcg/kg/min. The most frequently utilized dosage range was equal to or less than 5 mcg/min, with a median duration of 19.92 hours and an interquartile range of 9.48-38.09 hours. The location of norepinephrine administration was primarily below the wrist (47.3%), followed by the forearm (35.3%), and above the elbow (6.7%). Fifteen of 150 patients required the co-administration of an additional vasopressor agent to maintain adequate perfusion. In this study, 22-gauge PVCs were used in 82.7% of the cases. The most common reason to discontinue the norepinephrine was shock reversal, observed in 105 patients (70%). However, in our study, peripheral norepinephrine treatment was transitioned to central catheter administration in 20 patients (13.3%) (Table 3).

Table 2 Baseline characteristics of study patients (n=150)

Patient demographic data	Number (%)
Male sex [(n, %)]	91 (60.7%)
Age (median, IQR) year	67 (59-79)
Body weight (median, IQR) kg	59 (50-65)
Height (median, IQR) m	1.62 (1.55-1.68)
BMI (median, IQR) kg/m^2	22 (19-24)
Underlying disease	**Number (%)**
None	40 (26.7)
Diabetes mellitus	55 (36.7)
Hypertension	80 (53.3)
Coronary artery disease	35 (23.3)
Cerebrovascular accident	16 (10.7)
Peripheral arterial disease	6 (4.0)
Skin disease	1 (0.7)
Diagnosis/Indication for norepinephrine	**Number (%)**
Septic shock	140 (93.3)
Cardiogenic shock	10 (6.7)
Hemorrhagic shock	7 (4.7)
Adrenal insufficiency	3 (2.0)
Other	4 (2.7)

IQR=interquartile range

Table 3 Details of norepinephrine administration

Parameters	Number (%)
Norepinephrine concentration via peripheral IV	
4 mg in 250 mL of 5% dextrose in water (D5W)	150 (100%)
Initial rate	
5 ml/hours (1.33 mcg/min)	136 (90.7%)
10 ml/hours (2.66 mcg/min)	14 (9.3%)
Median dose	
Median dose (IQR) mcg/kg/min	0.07 (0.04–0.11)
Dose range	
≤5 mcg/min	91 (60.7%)
6–10 mcg/min	49 (32.7%)
11–15 mcg/min	10 (6.7%)
Duration of norepinephrine administration (hours)	
Median hours (IQR)	19.92 (9.48–38.09)
Total patient-hours	3,980.90
Number of patients who achieved MAP ≥65 mmHg within 6 hours of shock diagnosis	21 (14.0%)
Site of norepinephrine administration	
Upper extremity	134 (89.3%)
Above elbow	10 (6.7%)
Forearm	53 (35.3%)
Below wrist	71 (47.3%)
Lower extremity	16 (10.7%)
Above knee	1 (0.7%)
Below knee	10 (6.7%)
Below ankle	5 (3.3%)
Co-administration of another inotrope/vasopressor	
None	135 (90.0%)
Adrenaline	9 (6.0%)
Dopamine	1 (0.7%)
Dobutamine	5 (3.3%)
Size of peripheral venous catheter	
No. 20	10 (6.7%)
No. 22	124 (82.7%)
No. 24	16 (10.7%)
Cannulation difficulty	20 (13.3%)
Reasons for discontinuation of norepinephrine	
Change to central venous catheter	20 (13.3%)
Vasopressor no longer required	105 (70.0%)
Patient expired	15 (10.0%)
Change to another site of peripheral venous catheter	10 (6.7%)
Incidence of peripheral intravenous norepinephrine extravasation	3 (2.0%) (95% CI: 0.6–6.1)

IQR=interquartile range, cannulation difficulty[8]=defined as a catheter insertion condition when the catheter cannot be entered into the vein in one attempt, CI=confidence interval

Primary outcome

In this study of 150 patients who received peripheral administration of norepinephrine, we observed low rates of complications. Only three patients (2%) (95% CI: 0.6–6.1) experienced minor complications, none of which required intervention. These complications occurred during and post–norepinephrine peripheral infusion. The three complications consisted of two instances of extravasation resulting in local erythema, and one case of local thrombophlebitis. (Table 4) In the 15 patients who expired while receiving peripheral norepinephrine therapy, we did not attribute the cause of death to norepinephrine.

The first recorded complication was local thrombophlebitis resulting from norepinephrine administration at the left ankle and wrist, both graded at an infiltration scale of 4. This occurred in an 84–year–old female with underlying conditions, including hypertension, coronary artery disease, asthma, and Parkinson's disease, who presented with urinary– tract– infection (UTI)–induced septic shock. Norepinephrine (4 mg in 250 ml of D5W) was initially administered through a 22–gauge catheter inserted below the ankle. The first period of norepinephrine infusion lasted about 12 hours, at a maximum infusion dose of 0.02 mcg/kg/min, and was stopped upon achieving the MAP target. The second period of norepinephrine administration covered its reintroduction nine hours later–discontinuation due to inadequate MAP, this time through a 22–gauge catheter below the left wrist. This second period of norepinephrine infusion lasted for 70 hours at a maximum infusion dose of 0.07 mcg/kg/min, and was discontinued upon achieving the MAP target. Extravasation occurred at both sites of infusion: at the left ankle 57 hours post–discontinuation, and at the left wrist 1.30 hours post–discontinuation. Both instances of extravasation were categorized as grade 4, based on discolored skin, bruising, gross edema 6 inches in any direction, and moderate pain. No interventions were provided in response to these complications. Although the patient expired during hospital admission, this was not linked to the observed norepinephrine extravasation.

The second complication involved an extravasation of norepinephrine below the right wrist, which was graded 2 on the infiltration scale. The patient was a 64–year–old female with underlying conditions of coronary artery disease and diabetes mellitus, who had presented with septic shock due to a urinary tract infection. Norepinephrine (4 mg in 250 ml of D5W) was administered through a 22–gauge catheter at the right wrist. The total period of norepinephrine infusion was 26.30 hours, with a maximal infusion dose of 0.05 mcg/kg/min. The extravasation occurred five hours post–initiation of norepinephrine administration. Subsequently, the right–side catheter was removed, and a new peripheral site at the left wrist was accessed and used until discontinuation of the norepinephrine. The extravasation was graded as 2, indicating skin blanching, edema spanning 1–6 inches in any direction, and pain. Despite this, no intervention was provided. The patient survived the admission and was later discharged from the hospital.

The third complication was an extravasation of norepinephrine at the right wrist, which was graded 1 on the infiltration scale. The patient, a 46–year–old female, presented with septic shock. Norepinephrine (4 mg in 250 ml of D5W) was administered via a 22–gauge catheter at the right wrist. The norepinephrine infusion lasted for a total period of 8 hours, with a maximal infusion dose of 0.16 mcg/kg/min. The extravasation was discontinued after post–complication recognition, however, discontinuation was not due to this complication but rather because the patient no longer required it. The extravasation was graded as 1, based on the signs of edema of <1 inch in any direction, and pain. No intervention was provided , and the patient survived the admission and was discharged from the hospital. (Table 4)

Secondary outcomes

Our study examined hospital outcomes after admission, including 7-day and 30-day hospital mortality rates . We observed that the time from septic shock to initiation of peripheral intravenous norepinephrine administration did not exhibit a statistcal difference in 7-day mortality between the survivors and non-survivors (p-value=0.51). Similarly, the median time from septic shock diagnosis to achieving MAP≥65 mmHg as well as the median time from peripheral intravenous norepinephrine administration to achieving MAP≥65 mmHg did not show a significant difference in 7-day mortality between the survivors and non-survivors (p-value=0.73 and 0.19, respectively). However, the survivors in the 7-day group achieved a MAP≥65 mmHg or greater from the time of septic shock diagnosis at a median time of 5.25 hours (IQR 3.62-7.96), which was less than the median time of 5.67 hours (IQR 3.17-8.25) for the non-survivors in the same group. Similarly, the median time from peripheral intravenous norepinephrine administration to achieving MAP≥65 mmHg or greater was 2.25 hours (IQR 1.10-4.21) in the survivors and 3.00 hours (IQR 1.45-5.00) in the non-survivors. Furthermore, Patients with a "do not resuscitate" status (DNR), who typically have a higher mortality rate, were excluded from data analysis.Upon this execution, we found no statistically significant mortality difference between survivors and non-survivors at 7 days (Table 5).

Regarding the 30-day mortality group, our data analysis was similar to the 7-day mortality group, with no statistically significant differences observed between the timing of the septic shock diagnoses to peripheral intravenous norepinephrine administration, and 30-day mortality. However, the median time from septic shock diagnosis to achieving a MAP≥65 mmHg was shorter in the survivors within the 30-day group (Table 6).

Table 4 Extravasation cases

Case	Age (years)	Sex	Gauge size	Site of PVC	Duration of pNE (hours)	Max dose (ug/kg/min)	Indication for NE	Infiltration grade	Reason for treatment discontinuation	Extravasation treatment
Case 1	84	Female	22	Below ankle	12	0.02	Distributive shock	4	Achieve MAP	Conservative treatment
			22	Below wrist	70	0.07	Inadequate MAP	4	Achieve MAP	Conservative treatment
Case 2	64	Female	22	Below wrist	26.30	0.05	Distributive shock	2	Change to another site of PVC	Conservative treatment
Case 3	46	Female	22	Below wrist	8	0.16	Distributive shock	1	Achieve MAP	Conservative treatment

PVC=peripheral venous catheter, pNE=peripheral norepinephrine, NE=norepinephrine, MAP=mean arterial pressure

Table 5 Association between time from septic shock diagnosis to peripheral intravenous norepinephrine administration and clinical outcomes

	Calculated with DNR cases(n=139)			Calculated without DNR cases (n=99)		
	Non-survivors at 7 days (n=38)	Survivors at 7 days(n=101)	p†-value	Non-survivors at 7 days (n=16)	Survivors at 7 days (n=83)	p†-value
Time from shock to pNE	1.96 (1.11-3.27)	2.25 (1.28-4.21)	0.51	1.96 (0.83-3.75)	2.25 (1.25-3.83)	0.76
Time from shock to MAP ≥65 mmHg	5.67 (3.17-8.25)	5.25 (3.62-7.96)	0.73	5.67 (2.72-8.25)	5.00 (3.31-7.5)	0.42
Time from pNE to MAP ≥65 mmHg	3.00 (1.45-5.00)	2.25 (1.10-4.21)	0.19	3.00 (1.50-5.17)	2.21 (1.15-3.86)	0.25

Data displayed as median (IQR) hours
pNE=peripheral norepinephrine, DNR=do not resuscitate, IQR=interquartile range, MAP=mean arterial pressure
†p-value calculated by comparing means by one-way ANOVA test

Table 6 Association between time from septic shock diagnosis to peripheral intravenous norepinephrine administration and clinical outcomes

	Calculated with DNR cases (n=130)			Calculated without DNR cases (n=93)		
	Non-survivors at 30 days (n=52)	Survivors at 30 days(n=78)	p†-value	Non-survivors at 30 days (n=27)	Survivors at 30 days (n=66)	p†-value
Time from shock to pNE	1.96 (0.98-3.19)	2.25 (1.25-3.88)	0.51	1.92 (0.58-2.75)	2.13 (1.25-3.71)	0.56
Time from shock to MAP ≥65 mmHg	5.33 (3.25-8.13)	4.50 (3.17-7.92)	0.52	5.29 (2.6-7.63)	4.50 (3.09-7.50)	0.89
Time from pNE to MAP ≥65 mmHg	2.92 (1.48-5.00)	2.17 (1.00-4.09)	0.08	2.58 (1.50-5.04)	2.17 (1.04-4.17)	0.31

Data displayed as median (IQR) hours
pNE=peripheral norepinephrine, DNR=do not resuscitate, IQR=interquartile range, MAP=mean arterial pressure
† p-value calculated by comparing means by one-way ANOVA test

Discussion

The management of patients with septic shock entails interventions including early initiation of appropriate antimicrobials, fluid resuscitation, and prompt commencement of vasopressors. Initiating a vasopressor early can help prevent late organ failure and reverse systemic shock. One study reported a notable association between delayed initiation of a vasopressor and increased mortality[9]. From another study suggests that each 1-hour delay in norepinephrine administration during the first six hours post-septic shock diagnosis is associated with a 5.3% increase in mortality[10].

The Surviving Sepsis Campaign's 2021 International Guidelines for the Management of Sepsis and Septic Shock recommend the peripheral administration of a vasopressor for a short period, typically less than 6 hours[1]. This current study enrolled 150 emergency room patients and found that the total patient-hours of norepinephrine administration via a peripheral venous catheter was 3980.90 hours. The median patient-hours for administering norepinephrine

via a peripheral venous catheter was 19.92 hours (IQR 9.48–38.09), indicating a prolonged administration of vasopressors. However, it was also not possible to establish the median duration of infusion before the development of extravasation events due to wide variations observed in many of the studies[11]. Previous studies have shown that extravasation may occur more frequently when vasopressors are infused distally to the antecubital fossa[6]. A meta-analysis revealed that 85% of reported extravasation events occurred when vasopressors were infused via a catheter located distal to the antecubital fossa[11]. In this study, norepinephrine was administed to half of the patients below the wrist (47.3%) and about a third at the forearm (35.3%), which means that up to 82.5% of the peripheral norepinephrine administrations were below the antecubital fossa. Despite this, we found that the rate of extravasation from norepinephrine administration was relatively low, with only three reported cases. The first reported patient was infused with norepinephrine for a long duration, located distally to the ankle and wrist. The other two patients were infused via catheters located distally to the wrist. This finding is consistent with prior studies indicating a higher incidence of complications when vasopressors are administered distally to the antecubital fossa[6,11,12].

The results of our study indicate a low complication rate for the peripheral administration of vasopressors ,which aligns with reports from other authors[12,13]. Cardenas-Garcia et al. employed a comprehensive safety protocol for the peripheral administration of vasopressor agents, which included ultrasound-guided insertion of peripheral venous catheters into vein more than 4 mm in diameter, use of 18-gauge and 20-gauge PVC in 99% of cases, avoidance of adminstering vasopressor agents in the hand, wrist or antecubital fossa, two-hourly assessments of venous catheter sites, and a maximum infusion period of 72 hours. In their study, out of 734 ICU patients who received peripheral vasopressor agents, 506 received norepinephrine peripherally. The median peripheral norepinephrine duration was 49±22 hours, with a median maximum infusion dose of 0.7±0.23 mcg/kg/min. The extravasation rate was low, with only 19 patients (2%) experiencing complications, of which 16 were associated with the norepinephrine, presenting as local erythema. None required any intervention[13]. Despite the long infusion duration and the larger PVC gauge size used in comparison to our study, their extravasation rate was similary low to our study, which suggests that catheter size might not influence the occurrence of extravasation.

Another prospective observational study conducted in the emergency department (ED) of a tertiary care medical center reported that most of their 55 patients received norepinephrine peripherally. Only three patients (5.45% overall, 6% of patients receiving norepinephrine) reported vasopressor agent extravasation. All complications occurred during norepinephrine infusion, and none required any surgical intervention. Two of the three complications occurred in the hand with infusion being done via a 20-gauge catheter[6]. In comparison, our study reported three complications via a 22-gauge catheter, a smaller gauge than that used in the previous study. Given the small number of complications overall, a definitive recommendation regarding catheter size cannot be made. A further study exploring the relationship between complications and catheter gauge size may provide a more definitive answer.

A recent retrospective observational study investigating the utilization and extravasation of peripheral norepinephrine in an emergency department involved 177 adult participants. The majority of these patients received peripheral norepinephrine for distributive shock. The median duration of peripheral norepinephrine administration was 62 minutes (IQR 32–142). The most common site for peripheral venous catheter placement was above the antecubital fossa, using a 16–20-gauge catheter. The median maximum infusion dose was 10 mcg/min (IQR 5–165). Nguyen et al. reported an extravasation rate of 2.3% without any major

complications, which was similar to the complication rate in our study[14].

In our study, the data were insufficient to determine the relationship between the extravasation event and duration of infusion. For three of our patients, detailed nursing notes documented the extravasation events. The most severe incidents involved skin cooling and skin discoloration, coupled with poor capillary refill. None of these cases required a surgical consultation. Norepinephrine could be reintroduced via alternative peripheral venous catheter sites.

Our secondary outcome found that the median time from shock diagnosis to achieving MAP≥65 mmHg, and the time from norepinephrine administration to achieving MAP≥65 mmHg, was shorter in survivors compared to non-survivors. However, the differences in the times from shock diagnosis to peripheral intravenous norepinephrine administration between the survivors and non-survivors at both 7 and 30 days were not statistically significant, aligning with the findings of previous studies. A double-blind randomized controlled trial study found that early low-dose norepinephrine administration in adults with sepsis and hypotension significantly increased the shock control rate by 6 hours compared to standard care (p-value<0.001). However, there was no significant difference in 28-day mortality between the groups (p-value=0.15)[15].

The 2021 International Guidelines for the Management of Sepsis and Septic Shock of the Surviving Sepsis Campaign advocate the early initiation of vasopressors, which are associated with lower mortality.[1] Our findings align with those from other authors who reported reverse systematic shock, when following these guidelines[1,15]. Permpikul et al. reported the median time from shock diagnosis to achieving MAP≥65 mmHg, as well as the time from norepinephrine administration to achieving a MAP≥65 mmHg, was shorter in survivors compared to non-survivors, which was similar to our study[15].

Limitations

Our study had several limitations. The sample size was relatively small; we collected data from 150 patients, however only three cases had extravasation, and these without major complications. Due to these low numbers, we were unable to employ statistical methods to identify risk factors for extravasation.

Conclusion

In this prospective observational study of 150 patients who received norepinephrine via a peripheral venous catheter, we found an overall extravasation incidence of 2%. None of these events were severe enough to require an antidote or surgical intervention. Our study supports the hypothesis that peripheral administration of norepinephrine is relatively safe, with low complication rates. We support the use of norepinephrine via peripheral venous catheters, as recommended by The Surviving Sepsis Campaign's 2021 International Guidelines.

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Conflict of interest

There are no potential conflicts of interest to declare.

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