Guideline

Guidelines for the Use of Vasopressin in Adult Patients with Septic Shock in the ICU

Document Reference #:	5540
Version #:	2
Originally Issued:	Not Set
Last Revision:	12/29/2021
Last Review:	06/23/2022
Next Review:	06/23/2025
Approved:	06/23/2022

BACKGROUND

Many patients with sepsis require vasopressor support to maintain a sufficient mean arterial pressure (MAP) for perfusion.[1] Septic shock is defined as sepsis accompanied by refractory hypotension despite appropriate fluid resuscitation.[2] The 2021 Surviving Sepsis Campaign Guideline recommends norepinephrine as the first line vasopressor, followed by the addition of vasopressin to increase the MAP to goal.[14] Vasopressin can also be used to decrease norepinephrine requirements, and the combination of norepinephrine plus vasopressin is associated with a lower risk of atrial fibrillation.[2,3]

As a second line vasopressor, the optimal dosing of vasopressin has been controversial due to the absence of high quality evidence. A recent study, including more than 1600 critically ill patients, demonstrated a median norepinephrine dose of 20 mcg/min (equivalent to 0.22 mcg/kg/min in a 90kg patient) at the time of vasopressin initiation in survivors, compared to a median starting dose of 30 mcg/min (equivalent to 0.33 mcg/kg/min in a 90kg patient) in non-survivors.[15] The authors also found a 20.7% increase in in-hospital mortality for every 10 mcg/min (equivalent to 0.11 mcg/kg/min in a 90kg patient) increase in norepinephrine, up to 60 mcg/min (equivalent to 0.67 mcg/kg/min in a 90kg patient), at the time of vasopressin initiation. In addition, recent studies suggest that discontinuing vasopressin prior to norepinephrine may increase the incidence of hypotension, but this has not been associated with an increase in ICU mortality or hospital length of stay.[4-13]

PURPOSE

The purpose of this guideline is to standardize vasopressin initiation and discontinuation in adult patients with septic shock in the intensive care unit (ICU). This guideline provides evidence-based recommendations to optimize vasopressin use in patients with septic shock by utilizing dosing thresholds of norepinephrine. Recommendations for initial fluid resuscitation in patients presenting with septic shock is outside the scope of this guideline. This guideline is not meant to replace clinical judgement and

individual patient characteristics may alter the management of vasopressor dosing strategies in certain situations.

ABBREVIATIONS

Epi = epinephrine
HR = heart rate
ICU = intensive care unit
MAP = mean arterial pressure
NE = norepinephrine
PE = phenylephrine

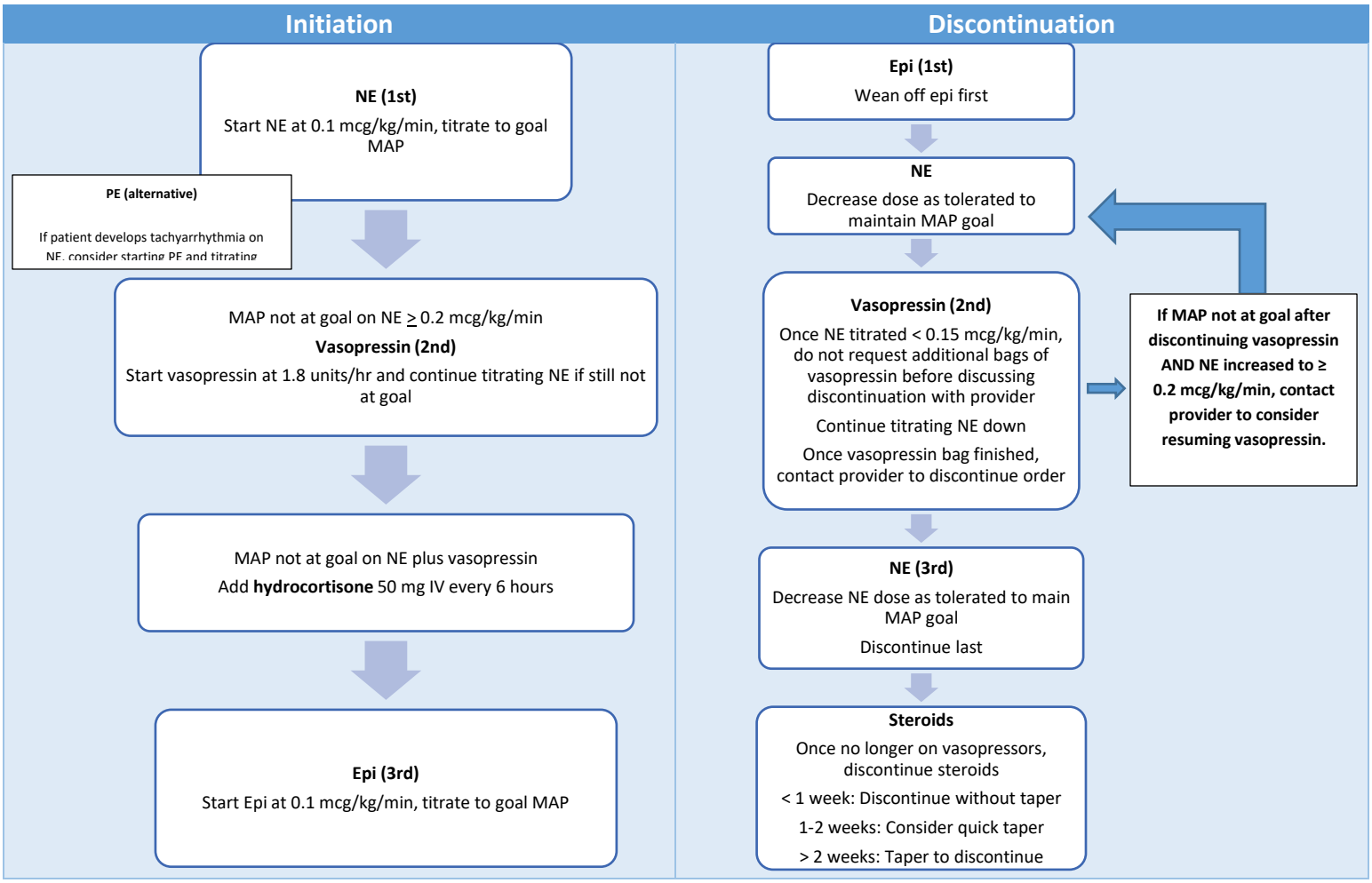
PROCEDURES

1. Initiation
    a. If MAP is not at goal of >65 mmHg, start **norepinephrine** (NE) IV as first line vasoactive medication[14]
        i. Initiate at 0.1 mcg/kg/min then titrate per Adult Critical Care Intravenous Titration Protocol to goal MAP
        ii. Max dose is 3 mcg/kg/min (contact provider if rate is > 1 mcg/kg/min)
    b. If MAP is not at goal on NE $\geq$ 0.2 mcg/kg/min, **add vasopressin**[15] IV
        i. Start vasopressin at ordered dose (1.8 units/hr without titration)
        ii. If MAP goal not reached after starting vasopressin, continue titrating NE to goal MAP
        iii. The provider may increase vasopressin to a max rate of 2.4 unit/hr if the MAP goal is not achieved within 4 hours of initiating vasopressin
        iv. It may be reasonable to start vasopressin sooner in the following situations: HR > 110, pH < 7.15, or weight > 120 kg
    c. Consider adding hydrocortisone 50 mg IV every 6 hours if the patient is on two or more vasopressors[14]
    d. If MAP is still not achieved on max dose NE and vasopressin, **add epinephrine** IV as third line[14]
        i. Consider initiating sooner if myocardial dysfunction is present
        ii. Initiate at 0.1 mcg/kg/min then titrate per Adult Critical Care Intravenous Titration Protocol to goal MAP
        iii. Max dose is 2 mcg/kg/min (contact provider if rate is > 1 mcg/kg/min)
    e. In patients who develop a tachyarrhythmia on NE, consider starting **phenylephrine** (PE) IV and titrating down NE
        i. Initiate at 0.1 mcg/kg/min then titrate per Adult Critical Care Intravenous Titration Protocol to goal MAP
        ii. Max dose is 10 mcg/kg/min (contact provider if rate is > 6 mcg/kg/min)
    f. In patients with measured or suspected low cardiac output and adequate left ventricular filling pressure, consider adding **dobutamine**[14] IV
        i. Initiate at 2.5 mcg/kg/min
        ii. May only be titrated by provider
        iii. Max dose is 40 mcg/kg/min
    g. In patients with a low risk for tachyarrhythmias and have absolute or relative bradycardia, consider using **dopamine**[14] IV
        i. Initiate at 5 mcg/kg/min

ii. May only be titrated by provider
iii. Max dose is 20 mcg/kg/min

2. Discontinuation
    a. Titrate off epinephrine, dobutamine, and/or phenylephrine first
    b. Decrease dose of NE as tolerated to maintain goal MAP
    c. When NE dose is **< 0.15 mcg/kg/min**, do not request additional bags of vasopressin[15]
        i. Contact provider to confirm it is acceptable for vasopressin to stop
        ii. Continue to titrate NE down
    d. If MAP is not at goal after stopping vasopressin and NE is increased to ≥ 0.2 mcg/kg/min, consider resuming vasopressin[15]
    e. Decrease NE as able to maintain goal MAP
        i. NE should be discontinued last (after vasopressin)
    f. Once the patient is no longer on vasopressors, discontinue steroids
        i. < 1 week: Discontinue without taper
        ii. 1-2 weeks: Consider quick taper
        iii. > 2 weeks: Must taper to discontinue

Figure 1. Vasoactive Medication Titration in Septic Shock



NE = norepinephrine; PE = phenylephrine; Epi = epinephrine; MAP = mean arterial pressure

RELATED PROTOCOLS

Adult Critical Care Intravenous Titration Protocol

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