Title:

Septic Shock and Vasopressor Therapy: The Impact of Excessive Mean Arterial Pressure Values

Barbara Clark Mims, MSN
School of Nursing, The Catholic University of America, Bartonville, TX, USA

ACCEPTED

Session Title:

Rising Stars of Research and Scholarship Invited Student Posters

Slot:

RS PST1: Sunday, 17 November 2019: 11:45 AM-12:15 PM

Applicable Category:

Clinical, Students, Researchers

Keywords:

septic, shock and vasopressors

References:

1. Koczmara, C, St-Arnaud, C, Martinez, HQ, et al. Vasopressor stewardship: a case report and lessons shared. Dynamics 2014; 25:25-29.

2. Levy, M. The cardiac and vascular factors that determine systemic blood flow.

3. Rivers, E, Nguyen, B, Havstad, S, et al. Early goal directed therapy in the treatment of severe ssepsis and septic shock. The New England Journal of Medicine 2001; 345:1368-1377.

4. Lamontagne, F, Meade, MO, Hebert, PC, et al. Higher versus lower blood pressure targets for vasopressor therapy in shock: a multicenter pilot randomized controlled trial. Intensive Care Medicine 2016; 42:542-550.

5. Lamontagne, F, Cook, DJ, Meade, MO, et al. Vasopressor use for severe hypotension-a multicenter prospective observational study. PloS ONE 2017;12:e0167840

6. Kurniati, AP, Hall, G, Hogg, D, et al. Process mining in oncology using the MIMIC-III dataset. Journal of Physics: Conference Series 2018; 971: doi:10.1088/1742- 6596/971/1/012008

7. Johnson, AEW, Pollard, TJ, Shen, L, et al. Data descriptor: MIMIC-III, a freely accessible critical care database. Scientific Data 2016; 3:doi: 10.1038/sdata.2016.35

8. Rhodes, A, Evans, LE, Alhazzani, W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock. Intensive Care Medicine 2017; 43:304-377.

Abstract Summary:

A retrospective, correlational, longitudinal study explores relationships between excessive mean arterial pressure values and adverse outcomes during septic shock. These include duration of vasopressor exposure, duration of mechanical ventilation, length of ICU stay, length of hospital stay, and mortality at 28 days, 90 days, and one year after hospital discharge.

Content Outline:

Septic Shock and Vasopressor Therapy: The Impact of Excessive Mean Arterial Pressure Values

I. Introduction

A. Purpose

Determine short and long-term impact of excessive mean arterial pressure values during vasopressor therapy for patients in septic shock.

B. Background

1. Importance and significance

a) Septic shock involves life-threatening circulatory failure due to infection.

b) Incidence of 20% in patients in ICU.

c) Mortality rate of approximately 40%.

d) Significant sequelae in survivors of septic shock.

i) Cardiovascular impairment

ii) Cognitive dysfunction

iii) Impaired quality of life

2. Vasopressor therapy is mandatory for patients in septic shock

a) Mediator-induced vasodilation

b) Four out of six vasopressors are adrenergic agents

i) Stimulate alpha receptors

ii) Causes therapeutic narrowing of blood vessels

iii) High doses often required due to downregulation of alpha receptors

iv) May cause harm, especially with higher doses

Cardiac dysfunction

Arrhythmias

Ischemia

Others

c) Continuous dosage adjustment is required to provide therapeutic response without harm.

d) Provider specifies the target MAP value to guide vasopressor administration (international guidelines have specified MAP ≥ 65 mmHg for decades)

e) Critical care nurse adjusts the dose to maintain MAP above the target value

f) Maximum MAP is not specified in provider's orders

g) Nursing judgment significantly influences the patient's actual MAP value maintained (above 65 mmHg)

h) Evidence indicates lack of consistency in nursing practice related to vasopressor

C. Problem

1. MAP values often significantly exceed the recommended titration target value of 65 mmHg and may contribute to adverse outcomes.

2. Nurses use independent judgment in adjusting the dose.

3. Aim is to maintain MAP above target MAP (typically 65 mmHg)

4. Noncompliance only occurs if MAP is maintained below the target.

5. When nurses maintain MAP significantly above the target, compliance with providers' exists, but patient harm may occur.

II. Body

A. Research design

1. Retrospective, correlational, longitudinal

2. One research question

3. Seven hypotheses

4. Sample of 214 participants (critically ill adults)

5. Explores relationships between excessive MAP values and adverse outcomes, including:

a) Duration of vasopressor exposure

b) Duration of mechanical ventilation

c) Length of ICU stay

d) Length of hospital stay

e) 28-day mortality

f) 90-day mortality

g) One year mortality

B. Conceptual Framework

1. Levy's Conceptual Model of the Cardiovascular System

a) Depicts heart and vasculature as continuous system.

b) Change in one provokes changes in the other.

c) Dynamic equilibrium normally exists.

d) Effects of vasopressors may disrupt equilibrium and cause harm.

C. Research Question

In adults undergoing vasopressor therapy during septic shock, is there an association

between excessive MAP values and adverse outcomes?

D. Covariates in hypotheses include:

1) Age

2) Race

3) Gender

4) PaO2/FiO2 ratio (in ventilated patients)

5) APACHE-III score at ICU admission

6) SOFA scores at ICU admission

E. Literature Review

Actual MAP values often exceed recommended or ordered target levels during vasopressor

therapy in septic shock.

F. Protection of Human Subjects

1. A secondary database is used.

2. Data were deidentified before being entered into the database.

3. IRB of The Catholic University of America granted and IRB exemption.

G. Instrument and Procedures

1. Meticulous review of each participant's medical record.

2. Data entered into Case Report Form.

3. Electronic queries used to extract data when possible.

H. Data Analysis

1. Descriptive analysis

a) Demographic data

b) Details about vasopressors received and MAP values achieved.

2. Inferential analysis

a) Multiple linear regression

b) Cox proportional hazards model regression

c) Adjusted odds ratio with 95% confidence intervals (CI) for each predictor variable

d) Adjusted hazards ratio with 95% CI for each of three hypotheses exploring mortality

e) Multivariate analysis will be done if indicated.

III. Significance and Originality

A. Evidence and international guidelines predict more conservative use of vasopressors in septic shock

B. This study offers first nursing study exploring impact of nurses' decisions and independent actions related to manipulation of vasopressors in septic shock.

C. Potential to Expand Critical Care Nursing Knowledge

1. Support critical thinking and independent nursing action.

2. Provide evidence base for practice

3. Promote minimization of vasopressor exposure of patients in septic shock.

Topic Selection:

Rising Stars of Research and Scholarship Invited Student Posters (25201)

Abstract Text:

Purpose: To determine the short and long-term impact of excessive mean arterial pressure (MAP) values during vasopressor therapy for patients in septic shock.

Background: The life-threatening disorder known as septic shock consists of circulatory failure secondary to infection. Individuals with septic shock account for an estimated 20% of patients admitted to Intensive Care Units annually, and of those, about 40% do not survive. Those who do survive experience long-lasting and often devastating sequelae, including cardiovascular impairment, cognitive dysfunction, and impaired quality of life. In septic shock, hypotension ensues from mediator-induced vasodilation, requiring administration of powerful vasoconstrictive drugs. Four of the six vasopressors used in the United States are catecholamines, with norepinephrine designated as the first-line vasopressor in septic shock. These drugs mimic endogenous epinephrine by stimulating adrenergic receptors, with activation of alpha receptors on the blood vessel walls producing therapeutic narrowing of the blood vessel diameter. Patients in septic shock often require substantial vasopressor doses in order to counteract down-regulation of the vasoconstrictive receptors. Vasopressor-dependency characterizes all patients in septic shock, and while necessary and life-sustaining, vasopressors may cause harm, especially with delivery of higher doses. Potential serious adverse effects of vasopressors such as cardiac dysfunction, arrhythmias, excessive vasoconstriction resulting in ischemia, and others have been documented in the literature. Unlike most drugs, vasopressors require continuous dosage adjustment in order to achieve the desired clinical effect, which includes maintaining a sufficient but not excessive mean arterial pressure value. While the response to vasopressors varies among patients, obtaining higher MAP values requires higher vasopressor doses. The provider typically specifies the drug, concentration, MAP target, starting dose, frequency and amount by which the dose may be increased, and the maximum allowable dose. The maximum MAP level is not typically part of the provider's order. Administering and adjusting the dose is the responsibility of the patient's nurse. This approach to ordering and titrating leaves the nurse with considerable discretion regarding the dose delivered and the MAP value maintained. For more than a decade, clinical guidelines recommended a MAP value of

≥ 65 mmHg as the target value for patients in septic shock, yet evidence demonstrates no consistency in nursing practice related to vasopressor titration. However, evidence does exist wherein physicians in both practice and research settings report instances of observing actual patient MAP values significantly higher than the titration target value.[1]

Problem: *During vasopressor therapy for patients in septic shock, actual MAP values often exceed the recommended titration target value of 65 mmHg and may contribute to adverse patient outcomes.* In the ICU environment, critical care nurses adjust the provider-ordered starting dose using independent judgment, aiming to maintain the actual MAP no lower than the ordered MAP target value. Failure to follow the provider's order occurs *only* if the MAP is maintained *below* the target MAP value. When nurses adjust the dose within the provider's order but allow the MAP to remain higher than the target value, the potential for patient harm exists.

Research Design: Utilization of a retrospective, correlational, longitudinal design aims to answer one research question and test seven hypotheses in a sample consisting of 214 critically ill adults diagnosed with septic shock. The study explores relationships between actual MAP values > 65 mmHg and adverse outcomes. These include duration of vasopressor exposure, duration of mechanical ventilation, length of ICU stay, length of hospital stay, 28-day mortality, 90-day mortality, and one year mortality in adults receiving vasopressors during septic shock.

Conceptual Framework: Levy's Conceptual Model of the Cardiovascular System depicts the heart and peripheral vasculature as a continuous system, with changes in one component provoking changes in the other.[2] According to the model, a dynamic equilibrium exists between the heart and peripheral vasculature, which explains both beneficial and adverse effects of vasopressor therapy in septic shock. This dynamic interplay between the heart (the pump) and the peripheral vasculature (the resistance) underpins the challenge of maintaining sufficient, but not excessive, vascular tone during titration of vasopressors**.**

Research Question: The research question for this study is: *In adults undergoing vasopressor therapy during septic shock, is there an association between excessive MAP values and adverse outcomes?*

Hypotheses: H_1: While controlling for age, gender, race, PaO_2/FiO_2 ratio (in ventilated patients), APACHE-III score at ICU admission, and SOFA score at ICU admission, actual MAP values exceeding 65 mmHg are associated with increased duration of vasopressor exposure. The six additional hypotheses consist of the aforementioned covariates and independent variable, and the following dependent variables; H_2 duration of mechanical ventilation, H_3 length of ICU stay, H_4 length of hospital stay; H_5 28-day mortality, H_6 90-day mortality, and H_7 one-year mortality.

Literature Review: Medical literature dating back to at least 2001 indicates that actual MAP values often exceed recommended target values in patients undergoing vasopressor administration in septic shock. The early goal-directed therapy protocol developed by Rivers and colleagues specified a target of 65 to 90 mmHg, but reported MAP values of 95 ± 19 mmHg.[3] In a later multicenter, randomized controlled trial, researchers found that 68.5% of actual MAP values violated the MAP range ordered in the research protocol, with 80-88% of the violations reflecting actual MAP values exceeding the upper limit of the range.[4] Recently, a multicenter, prospective, observational study of patients undergoing vasopressor therapy in septic shock showed that MAP values ranged from 65 to 80 mmHg most of the time.[5] However, over the course of the study, values ranged from approximately 40 mmHg to 115 mmHg, with 39% of patients exhibiting average MAP values greater than 75 mmHg, exceeding the prevailing recommendation by 10 mmHg.

Protection of Human Subjects: This study employs the widely used, rigorous secondary database entitled the MIMIC-III, which contains detailed medical information regarding 38,597 critically ill adults cared for in the Beth Israel Deaconess Medical Center in Boston.[6.] The sample includes 214 patients, consistent with a calculated value of 178 using Power Analysis and Sample Size (PASS[14]) software to obtain 80% power at a significance of 0.05, plus 20% oversampling in case of missing data in the secondary database. During preparation of the MIMIC-III database, the scientists who created and managed the database carefully deidentified all patient records using data shifting and data cleansing.[7] The Institutional Review Board at The Catholic University of America granted an IRB exemption for this study.

Instrument and Procedures: Data collection involves meticulous review of each participant's medical data, followed by entry of relevant information entered into a Case Report Form formatted as a Microsoft™ Office 365 Excel spreadsheet. Extraction of data from the MIMIC-III and transfer into the CRF occurs via electronic queries in so far as possible.

Data Analysis: A descriptive analysis will describe the sample in terms of demographic data and provide details about the vasopressor(s) received and MAP values achieved. Inferential analysis of individual

hypotheses will include multiple linear regression and the Cox proportional hazards model regression. Results of the multiple linear regression will include an adjusted odds ratio (OR) for each predictor variable, with 95% CI calculated for each OR. The Cox proportional hazards model for three hypotheses exploring mortality will produce an adjusted hazards ratio, with 95% CI for each hazards ratio. Multivariate analysis will also be done if indicated.

Significance and Originality: An abundance of recent medical research studies, along with a slight modification of the MAP target value for use when administering vasopressors presented in the most recent edition of the international Surviving Sepsis Campaign guidelines, herald a more conservative use of vasopressors during septic shock.[8] The proposed study offers the first nursing research study exploring the potential impact of critical care nurses' decisions and independent actions related to manipulating vasopressor doses for patients in septic shock. The expansion of the body of critical care nursing knowledge will support critical thinking and independent nursing action when providing vasopressor therapy and provide an evidence base for clinical practice related to minimizing vasopressor exposure of patients in septic shock.