Sepsis is frequent in initially non-critical hypotensive emergency department patients and is associated with increased mortality

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ARTICLE INFO

Article history:
Received 28 April 2019
Received in revised form 8 July 2019
Accepted 21 July 2019

Keywords:
Sepsis
Hypotension
SOFA score
Emergency department

ABSTRACT

Objective: Hypotension, defined as a mean arterial pressure of maximum 70 mmHg, is associated with significant morbidity and mortality. The objective of this study was to determine in initially non-critical hypotensive adult patients the proportion of sepsis and if septic patients had different outcome and clinical factors than non-septic patients.

Methods: This retrospective observational study was conducted over a year on adult hypotensive emergency department patients initially considered by triage as non-critical. Patients were separated into three groups: hypotensive septic patients (HSP), hypotensive non-septic infected patients (HNSIP), and other hypotensive patients (OHP). Clinical scores, signs, length of stay (LOS), and mortality were compared using analysis of variance for continuous variables and chi-square analysis for categorical variables.

Results: There were 136 (35.5%) septic patients, 37 (9.7%) with non-septic infection, and 210 (54.8%) with another cause of hypotension. Overall in-hospital mortality was 12.0% and total mortality was greater in HSP than in HNSIP (20.6% vs. 5.4%, p = 0.031) or OHP (20.6 vs. 7.6%, p < 0.001). LOS was greater for HSP when compared to HNSIP (median(IQR): 9(6–17) vs. 6(1–13), p = 0.004) and OHP (median(IQR): 9(6–17) vs. 3(1–8) days, p < 0.0001).

Conclusion: Sepsis in a priori non-critical hypotensive adult patients, when compared with other causes of hypotension, is associated with significantly higher mortality and increased LOS. Patients that present to the emergency department and have a MAP of 70mmHg or less must be rigorously evaluated and have consistent follow-up.

1. Introduction

Sepsis is a potentially lethal syndrome that appears following an infection and is the consequence of the host’s altered physiological and chemical responses [1]. Although it is a leading cause of mortality and morbidity worldwide, its incidence remains elusive and early treatment remains a challenge [2-5]. In addition, rapid diagnosis is often difficult and non-documented sepsis in emergency patients has been associated with increased mortality [6]. Consequently, identifying septic patients and those who are at increased risk of death remain important challenges in emergency medicine [7-9].

Hypotension, which can be defined as a mean arterial pressure (MAP) of 70 mmHg or less, is a warning sign of cardiovascular collapse and can occur during sepsis [10]. Hypotensive patients and septic patients with non-sustained hypotension have been shown to have increased mortality in the emergency department (ED) [11,12]. In a review of six observational studies Holler et al. reported that nontraumatic ED hypotension was found between 0.4 and 1.3% of the ED admissions and was associated with a mortality of 12% [13]. The proportion of sepsis in hypotensive patients at the ED, however, is not clear.

The objective of this study was to determine in initially non-critical hypotensive adult patients the proportion of sepsis and if hypotensive septic patients had different outcome and clinical factors than non-septic hypotensive patients.
2. Methods

2.1. Design and setting

The Erasme University Hospital is a tertiary hospital located in Brussels, Belgium. The local institutional ethical committee approved this retrospective study and waived the need for informed consent. Critically ill patients at Erasme University Hospital are immediately treated in collaboration with the intensive care unit (ICU) in a shared ED/ICU care unit (i.e. the shock room) [14]. These include hemodynamically unstable patients (e.g., septic shock or severe trauma). Physicians base their decision to immediately transfer patients to the shock room on criteria such as blood pressure, heart rate, consciousness, diuresis, tissue perfusion, and apparent treatable cause of critical illness (e.g. pneumonia, tamponade, myocardial infarction, or hemorrhage). Patients that were immediately transferred to the shock room upon admission were not included in this study.

2.2. Data collection

We identified all adult patients who had at least one episode of hypotension (i.e., one measurement of systolic and diastolic non-invasive blood pressure of maximum 90 mmHg and 60 mmHg, respectively) at the ED from July 1st, 2013 to June 30th, 2014, with ED dedicated software (E-Care, Turnhout, Belgium). Patients who only had hypotension while asleep or who had a falsely hypertensive value due to equipment malfunction were not considered in this study. Patients who were immediately transferred to the shock room [14] without passing by the ED were considered as critically ill and were not studied. These patients needed immediate stabilization of an acute condition. Patients were excluded if they were readmitted during the study period, transferred to or from another hospital, or refused admission.

Included hypotensive patients (IHP) were split into three groups based on their initial evaluation and management: hypotensive non-septic infected patients (HNSIP), hypotensive septic patients (HSP), and other hypotensive patients (OHP). Patients were considered infected if the physician clinically suspected or confirmed infection (i.e., sampling of body fluids for microbial analysis and antibiotic therapy at the ED or written suspicion in the ED record). Sepsis was defined as confirmed or suspected infection with a SOFA score change (ΔSOFA) of at least 2 points as defined by the Sepsis-3 consensus [1]. The remaining patients made up the OHP group. ΔSOFA was calculated assuming patients had normal organ function before disease onset unless previous hospital records could attest to organ dysfunction (e.g. patients suffering from cirrhosis or chronic renal failure). Glasgow score was not always noted. The following estimates were established: confusion as 14/15, somnolence with confusion as 12/15, and coma as <6/15. Study outcomes consisted of ED mortality, ICU mortality, ward mortality, total in-hospital mortality, ICU length of stay (LOS), and hospital LOS. Clinical scores as well as anthropometric and clinical data were also investigated.

2.3. Analysis

Data analysis was carried out with Statistix 9.0 (Analytical Software, Tallahassee, FL, USA). The Shapiro-Wilk test was used to determine continuous variable normality. No continuous variable was normal and data were represented as medians with interquartile range (IQR: from percentiles 25 to 75) for continuous variables and counts with percentages for categorical variables. Group comparisons were done with non-parametric analysis of variance for categorical variables. There was no missing data.

3. Results

From July 1st, 2013 to June 30th, 2014, the Erasme ED admitted 45,329 patients, 423 of which were initially non-critical adult hypotensive patients (i.e., 0.93% of all patients). 40 patients were excluded because of readmission, transfer, or admission refusal. There were 136 (35.5%) septic patients, 37 (9.7%) with non-septic infection, and 210 (54.8%) with another cause of hypotension (Appendix A Fig. A.1).

HSP were more often male than HNSIP or OHP and were older than HNSIP or OHP. HSP more frequently had a history of hypertension and heart disease as well as diuretic and beta-blocker treatment than HNSIP and OHP. Angiotensin converting enzymes inhibitors (ACEI) and angiotensin II receptor antagonist (A2RA), however, were more frequently prescribed to HSP and OHP than to HNSIP. OHP had less history of chemotherapy, immunosuppressive treatment,

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A2RA: angiotensin II receptor antagonist, ACEI: angiotensin converting enzyme inhibitor, IQR: interquartile range.
and medically implanted devices (e.g., Portacath® or prosthesis) than HSP and HNSIP (Table 1).

Overall in-hospital mortality was 12.0%. Total and ward mortalities were greater in HSP than in HNSIP (20.6% vs. 5.4%, p = 0.031; 12.5% vs. 0.0%, p = 0.024, respectively) or in OHP (20.6% vs. 7.6%, p < 0.001; 12.5% vs. 1.9%, p < 0.001, respectively). Although ICU mortality did not reach statistical significance between groups, ICU LOS was longer in HSP than OHP (median(IQR): 0(0–1) days vs. 0(0–0) days, p = 0.024). Hospital LOS was greater in HSP when compared to HNSIP (median(IQR): 9(6–17) days vs. 6(1–13) days, p < 0.001) or in OHP (20.6% vs. 7.6%, p = 0.031; 12.5% vs. 5.4%, p = 0.001; 12.5% vs. 1.9%, p < 0.001, respectively). This may be due to their association with age, a known risk factor for sepsis severity and cardiovascular disease [9]. It may, however, also be due to either the chronic modification of tissue perfusion autoregulation thresholds due to hypertension or to the accentuation of organ injury in acutely hypertensive patients taking mediation that can potentiate volume depletion and decrease systemic vascular resistance. Chronically hypertensive patients are known for having moderate hypotension when developing shock [10]. A review by Leone et al. indicated that maintaining a MAP of 75 to 85 mmHg in chronically hypertensive patients with septic shock may reduce the risk of developing acute kidney injury [17]. An inadequate driving pressure in chronically hypertensive septic patients may have been one of the factors responsible for organ failure. A history of hypertension or cardiac disease in an elderly patient’s acute hemodynamic instability since these factors are associated with organ failure and death.

This retrospective, observational, monocentric study had several limitations. Clinicians did not always use the Glasgow score and the SOFA score was consequently modified. This type of limitation contributes to information bias, which is inherent to the retrospective nature of our study, and underlines the need for further prospective cohort studies. The use of a fixed threshold value for hypotension at 90/60 mmHg is also a potential limitation. A more personalized definition of blood pressure may be better, especially in chronically hypertensive patients, but determining a baseline value for blood pressure is difficult in the ED. Furthermore, this value is consistent with the SOFA score, which was used to define sepsis [1,18]. Additionally, by defining the HSP as suspected or confirmed infection, we may have included patients in the HSP who had another cause of organ dysfunction than sepsis. This study nevertheless reflects clinical practice and shows the importance of quickly identifying sepsis in hypertensive patients initially considered non-critical.

5. Conclusion

Sepsis in a prior non-critical hypertensive adult patients, when compared with other causes of hypotension, is associated with significantly higher mortality and increased LOS. Patients that present to the ED and have a MAP of 70 mmHg or less must be rigorously evaluated and have consistent follow-up.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Declaration of Competing Interest

None.

Acknowledgments

The authors would like to thank the medical and nursing teams of the Emergency and Intensive Care Departments for their help in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2019.158360.

References