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Original Research Article

# Ideal Mean Arterial Pressure Target in Septic Shock: The Hunt Goes On!

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## Abstract

The objective of this study was to evaluate the effects of two different mean arterial blood pressure (MAP) targets in septic shock. Sepsis is a syndrome is caused by a dysregulated inflammatory response to bacterial infections. We carried out a prospective observational study enrolling patients admitted to the ICU with sepsis from 01/01/2017to 01/03/2018. Both the medical and surgical units of the ICU were included. This study was conducted at Apollo Health City, Critical Care Medicine, Hyderabad, India after obtaining permission from the hospital ethics committee. A total of 100 members were included in this study, had septic shock. These were divided in to two groups aiming at increasing mean arterial pressure from 65mmHg to 80mmHg in older patients. MAP at the end of resuscitation was 57.32 ± 13.69 mmHg (mean ± SD) and 78.45 ± 17.23 mmHg respectively, for low-MAP and high-MAP groups. The high-MAP group had a more positive fluid balance. MAP below 65 mm Hg was shown to be associated with highest mortality during the first 48 hours of septic shock. The longer the time spent below MAP 65 mmHg, the higher the risk of mortality, acute kidney and myocardial injury. The MAP target of around 75–85 mmHg may reduce the incidence of acute kidney injury (AKI) in patients with chronic hypertension. The perfusion pressure is highly heterogenous not only between different patient but also in the same patient between different organs and different periods of septic shock. Hence the MAP target needs to be individualized according to patient requirements.

**Keywords:** Mean arterial pressure, Sepsis, Outcome, Chronic diseases, Adults.



## INTRODUCTION

Sepsis is a syndrome is caused by a dysregulated inflammatory response to bacterial infections. Among the major risks is end-organ damage consequent to hypoperfusion and cellular/metabolic dysfunction, especially renal and myocardial injury. Since hypotension worsens tissue perfusion, it seems likely that some organ injury can be prevented by maintaining a suitable arterial pressure.

Preventing hypotension is therefore a crucial component of sepsis management. The Society of Critical Care Medicine's Surviving Sepsis Guidelines suggest initially maintaining mean arterial pressure (MAP) > 65mmHg followed by monitoring via multiple hemodynamic parameters to an endpoint of tissue perfusion. However, as emphasized by the Surviving Sepsis Campaign guidelines, for patients with atherosclerosis or previous hypertension, a higher blood-pressure target may be better. Systolic blood pressure of 100 mmHg or less is a component of the quick Sequential Organ Failure Assessment score (qSOFA) which helps identify adult patients with suspected infections who are more likely to have poor outcomes typical of sepsis. The evidence for clearly defining blood pressure targets in septic patients is currently contentious and weak.

This study was aimed at increasing mean arterial pressure from 65mmHg to 80mmHg in older patients with sepsis and to evaluate the outcome in sepsis patients of intensive care unit.

## MATERIALS & METHODS

We carried out a prospective observational study enrolling patients admitted to the ICU with sepsis from 01/01/2017to 01/03/2018. Both the medical and surgical units of the ICU were included. This study was conducted at Apollo Health City, Critical Care Medicine, Hyderabad, India after obtaining permission

from the hospital ethics committee. A total of 100 members were included in this study, had septic shock that was refractory to fluid resuscitation, treated with vasopressors (norepinephrine or epinephrine) at a minimum infusion rate of 0.1 μg per kilogram per minute, and were evaluated within 6 hours after the initiation of vasopressors. Fluid resuscitation was performed with norepinephrine administered as a first-line vasopressor.

The use of diuretics, nonsteroidal antiinflammatory drugs, the use of iodinated contrast agents unless necessary for imaging, and the use of nephrotoxic antibiotics unless judged necessary by the attending physician were excluded.

Renal-replacement therapy was initiated if at least one of the following criteria was present: anuria, hyperkalemia with electrocardiographic changes, pure metabolic acidosis with a pH of less than 7.2, or a blood urea nitrogen level of more than 84 mg per deciliter (30 mmol per liter) or a creatinine level of more than 5.65 mgper deciliter (499 μmol per liter).

After enrolment, patients were assigned to vasopressor treatment that was adjusted to maintain a mean arterial pressure of 80 to 85 mm Hg (high-target group) or 65 to 70 mm Hg (low-target group). The target mean arterial pressure was to be maintained for a maximum of 5 days or until the patient was weaned from vasopressor support; after that, the target pressure was determined by the attending physician.

From all the patients after taking written consent form, the history and the critical illness parameters, surgical status, pre-existing diseases, haemodynamic parameters and vasopressor used in therapy were analysed. These patients were monitored every day until 90 days of study inclusion period.

## RESULTS

This study was conducted at Apollo health city, Hyderabad. A total of 100 patients were allotted to two target groups with low and high blood pressure of 65 and 85mmHg. In all patients were Simplified Acute Physiology Score (SAPS) II and Sequential Organ Failure Assessment (SOFA) score, serum lactate levels, and norepinephrine/ infusion rates were measured, indicating patients were critically ill. The base line parameters were given in Table-1.

**Table-1: Base line parameters of the study**

| Parameter | Low MAP | High MAP |
|---|---|---|
| Number | 50 | 50 |
| Age | 58.56±18.25 | 57.29±17 |
| Sex (male/female) | 28/22 | 27/23 |
| Simplified Acute Physiology Score (SAPS) | 58.12±10.21 | 56.98±13.29 |
| Sequential Organ Failure Assessment score (SOFA) | 10.5±2.8 | 10.4±3.1 |
| **Recent surgical history —** | | |
| Elective | 2 | 3 |
| Emergency | 7 | 8 |
| Pre existing diseases | | |
| Ischemic heart disease | 4 | 3 |
| Chronic heart failure | 6 | 6 |
| Chronic obstructive pulmonary disease | 9 | 6 |
| Chronic kidney disease | 3 | 4 |
| Chronic kidney disease requiring long-term dialysis | 4 | 5 |
| Liver cirrhosis | 2 | 3 |
| Diabetes | 7 | 10 |
| Cancer or autoimmune disease | 5 | 4 |
| Chronic arterial hypertension | 10 | 9 |
| **Haemodynamic parameters** | | |
| Mean arterial pressure — mm Hg | 68±17 | 70±15 |
| Heart rate — beats/min | 98±10.2 | 102±13.5 |
| Arterial pH | 7.3±0.2 | 7.4±0.18 |
| Serum lactate level — mmol/liter | 4.2±1.3 | 3.8±1.2 |
| Fluid therapy before inclusion — ml | 3259±826 | 3196±965 |
| **Vasoactive drug infusions at randomization — no. (%)** | | |
| Norepinephrine | 15 | 16 |
| Epinephrine | 5 | 5 |
| Median vasopressor dose at randomization — μg/kg/min (IQR) | | |
| Norepinephrine | 0.38 | 0.42 |
| Epinephrine | 0.25 | 0.28 |
| Mechanical ventilation — no. (%) | 21 | 19 |
| Pao2:Fio2 ratio — mm Hg | 200 | 202 |

**Table-2: Outcome of study**

| Parameter | Low MAP | High MAP |
|---|---|---|
| Duration of catecholamine infusion — days | 4 | 5 |
| Primary outcome: death at day 30 — no. (%) | 17 | 18 |
| **Secondary outcomes — no./total no. (%)** | | |
| Death at day 90 | 21 | 23 |
| Survival at day 30 without organ support‡ | 30 | 30 |
| Doubling of plasma creatinine | 41 | 42 |
| No chronic hypertension | 19 | 17 |
| Chronic hypertension | 22 | 25 |
| Renal-replacement therapy from day 1 to day 7 | 33 | 35 |
| No chronic hypertension | 16 | 24 |
| Chronic hypertension | 17 | 11 |
| **Adverse effects** | | |
| Acute myocardial infarction | 3 | 5 |
| Atrial fibrillation | 1 | 5 |
| Ventricular fibrillation | 3 | 4 |
| Ischemia | 1 | 1 |
| Bleeding | 10 | 2 |
| Others | 20 | 24 |

## DISCUSSION

Septic shock is essentially characterized by reduced tissue perfusion due to distributive shock as a consequence of infection. One of the essential components in its management is restoration of tissue perfusion [1]. To achieve this goal, one of the first steps is fluid resuscitation followed by the use of vasopressors, if required, in order to maintain tissue perfusion pressure. As perfusion of the vital organs cannot be gauged directly, one of the most commonly used surrogates is the mean arterial pressure (MAP), as it can be measured easily [2].

The blood pressure value that should be targeted during the management of septic shock is an important clinical issue. The mean arterial pressure (MAP) is one of the first variables that is monitored in these patients, and manipulation with vasopressor agents is relatively easy [3]. Prolonged hypotension, defined as a MAP of less than 60 to 65 mm Hg, is associated with poor outcome [4, 5].

The Surviving Sepsis Guidelines recommend that a MAP of 65 mmHg should be the initial target and vasopressors should be used if this target is not met after adequate fluid resuscitation (generally 30 mL/kg body weight) [1]. These recommendations are based on some evidence that MAP <60–65 mmHg is associated with poor outcomes [4, 5].

A study in an animal model suggests that while targeting a lower MAP was associated with a higher risk of acute kidney injury, a higher MAP target resulted in increased net positive fluid balance and vasopressor load during resuscitation [6]. The patients with uncontrolled hypertension may have higher autoregulatory thresholds and thus a need to maintain a higher MAP, While a higher MAP may be required for adequate organ perfusion, the use of vasopressors to achieve it is also associated with detrimental effects such as increased risk of arrhythmias and even increased mortality, especially when there is an abrupt and sustained increase in MAP [7].

Targeting a mean arterial pressure of 80 to 85 mm Hg, as compared with 65 to 70 mm Hg, in patients with septic shock undergoing resuscitation did not result in significant differences in mortality at either 28 or 90 days [8].

In a study at 28 days, there was no significant between-group difference in mortality, with deaths reported in 142 of 388 patients in the high-target group (36.6%) and 132 of 388 patients in the low-target group (34.0%). There was also no significant difference in mortality at 90 days, with 170 deaths (43.8%) and 164 deaths (42.3%), respectively. The occurrence of serious adverse events did not differ significantly between the two groups (74 events (19.1%) and 69 events (17.8%), respectively. However, the incidence of newly diagnosed atrial fibrillation was higher in the high-target group than in the low-target group. Among patients with chronic hypertension, those in the high-target group required less renal-replacement therapy than did those in the low-target group, but such therapy was not associated with a difference in mortality [9]. In our study also 17 members in low MAP and 18 patients in high MAP were died at 30 day which is in accordance to the above study. The adverse observed in this study were in according to the Asfar study.

Kato and Pinsky *et al.*, [10] review examines the available evidence for targeting a specific mean arterial pressure (MAP) in sepsis resuscitation. The clinical data suggest that targeting an MAP of 65–70 mmHg in patients with septic shock who do not have chronic hypertension is a reasonable first approximation. Whereas in patients with chronic hypertension, targeting a higher MAP of 80–85 mmHg minimizes renal injury, but it comes with increased risk

of arrhythmias. Importantly, MAP alone should not be used as a surrogate of organ perfusion pressure, especially under conditions in which intracranial, intra-abdominal or tissue pressures may be elevated. Organ-specific perfusion pressure targets include 50–70 mmHg for the brain based on trauma brain injury as a surrogate for sepsis, 65 mmHg for renal perfusion and >50 mmHg for hepato-splanchnic flow. Even at the same MAP, organs and regions within organs may have different perfusion pressure and pressure–flow relationships. Thus, once this initial MAP target is achieved, MAP should be titrated up or down based on the measures of organ function and tissue perfusion. Our results were also in agreement with these results.

The adverse observed in this study were in according to the Asfar study. Hence the study concludes that Mean Arterial Pressure is a surrogate and not the organ perfusion pressure. In fact organ perfusion pressure is highly heterogenous not only between different patient but also in the same patient between different organs and different periods of septic shock. There is no "one-size fits all" when it comes to optimal MAP for septic shock.

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