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ALGORITHM FOR THE MANAGEMENT OF ENDOTOXIN-INDUCED HEMODYNAMIC DISORDERS

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ABSTRACT

Acute hemodynamic disorders induced by endotoxins pose a serious challenge in emergency medicine, particularly in patients with sepsis and severe inflammatory processes. These conditions are associated with vascular dysfunction, cardiac depression, and impaired organ perfusion, significantly increasing the risk of mortality.

This study introduces a novel CDR (Control Damage Resuscitation) Strategy, aimed at a step-by-step assessment and correction of hemodynamic disturbances. The necessity of an individualized therapeutic approach based on dynamic monitoring of hemodynamic parameters is emphasized. Furthermore, modern diagnostic and treatment methods for endotoxemia are discussed, highlighting their potential to enhance the effectiveness of intensive care therapy.

Key words: Hemodynamic disorders, endotoxin-induced shock, sepsis, systemic inflammatory response, hypovolemia, cardiac dysfunction, vasogenic shock, microcirculatory impairment, Control Damage Resuscitation (CDR), dynamic hemodynamic assessment, targeted hemodynamic therapy, lactate levels, venous oxygen saturation (SvO_2), capillary perfusion, total peripheral resistance (TPR), central venous pressure (CVP), mean arterial pressure (MAP), cardiac index (CI), tissue hypoxia, homeostatic intervention.

INTRODUCTION

Acute hemodynamic disorders induced by endotoxins represent one of the most challenging problems in emergency medicine. Sepsis, severe infections, and inflammatory processes lead to pronounced vascular dysfunction, reduced myocardial contractility, and impaired organ perfusion, significantly increasing the risk of mortality. In such situations, timely hemodynamic monitoring and an

appropriately selected therapeutic strategy play a crucial role in improving clinical outcomes.

Traditional approaches to correcting hemodynamic disorders often rely on standardized therapeutic protocols that do not always consider the individual characteristics of a patient's hemodynamic profile. Therefore, the CDR (**Control Damage Resuscitation**) Strategy has been developed, based on a systematic step-by-step assessment and correction of endotoxin-induced hemodynamic disturbances.

The relevance of the problem lies in the fact that, in recent years, mortality among patients with sepsis and endotoxemia has remained high. This is largely due to insufficient control of hemodynamic parameters and the delayed initiation of targeted therapy [Dellinger et al., 2012; Vincent et al., 2019]. Endotoxin-induced cardiac depression, vascular tone disturbances, and critical organ hypoperfusion require not only timely diagnosis but also a comprehensive therapeutic approach.

Research Aim. The development of medical tactical actions based on the characteristics of the pathophysiological mechanisms of hemodynamic disorders.

Materials and methods of research. The study was conducted in a prospective format and focused on investigating the pathophysiological mechanisms of hemodynamic disorders. The analysis was performed on a single group of patients with endotoxin-induced hemodynamic changes.

The study examined the following parameters:

- Hemodynamic indicators: arterial pressure, cardiac output index, total peripheral vascular resistance (TPVR), and central venous pressure (CVP) dynamics.
- Echocardiographic parameters: changes in systolic and diastolic ejection fractions, stroke volume, and myocardial contractility dynamics.
- Clinical state dynamics: stages of hemodynamic disorders and their sequential progression.

The results provided a deeper understanding of the pathophysiological mechanisms of hemodynamic disorders, as well as their dynamics and clinical significance.

Study Participants

Total number of patients: 64

- Study group: 64 patients (assessment of the pathophysiological mechanisms of hemodynamic disorders).

Inclusion Criteria

Patients meeting the following criteria were included in the study:

- Diagnosed sepsis or endotoxemia with hemodynamic disturbances.
- Presence of one or more of the following indicators:
  - Mean arterial pressure (MAP) < 65 mmHg.
  - Cardiac output index (CO) < 4 L/min.
  - Lactate level > 2 mmol/L.
- Signs of hypovolemic, hyperkinetic, or vasoplegic states.
- Dynamic changes in myocardial function confirmed by echocardiography (EchoCG).
- Alterations in central venous pressure (CVP) and total peripheral vascular resistance (TPVR).
- Age over 18 years, regardless of gender.
- Informed consent from the patient or their legal representative for study participation.

Exclusion Criteria

Patients with the following conditions were excluded from the study:

- Severe chronic heart failure (NYHA class III–IV).
- End-stage liver or kidney failure.
- Decompensated endocrine diseases (thyrotoxicosis, Addison's disease, etc.).
- Oncological and systemic autoimmune diseases.
- Conditions requiring emergency surgical intervention, preventing objective hemodynamic assessment.
- Procalcitonin blood level ≤ 0.5 ng/mL (lack of significant cellular septic response).
- Severe neuroinfections or primary central nervous system disorders.
- Pregnant and lactating women.

Research Methods

1. Hemodynamic Monitoring

Invasive methods:

- Central venous pressure (CVP).
- Venous oxygen saturation (SvO_2).

Non-invasive methods:

- Heart rate (HR).
- Mean arterial pressure (MAP).
- Cardiac output (CO) and cardiac index (CI).
- Peripheral oxygen saturation (SpO_2).
- Echocardiographic parameters (EchoCG): systolic and diastolic function dynamics.

2. Laboratory Diagnostics

Markers of inflammation and endotoxemia:

- Lactate level.
- N-terminal pro-brain natriuretic peptide (NT-proBNP).
- C-reactive protein (CRP).

Acid-base balance analysis (ABB):

- Blood pH.
- Partial pressure of carbon dioxide (pCO_2).
- Base excess (BE).
- Bicarbonates (HCO_3^-).

Complete blood count (CBC):

- Hemoglobin.
- Hematocrit.
- Leukocyte and neutrophil index.
- Platelets.

Biochemical blood analysis:

- Glucose.
- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST).
- Total protein and albumin.
- Bilirubin.

Water-electrolyte balance:

- Sodium (Na^+), potassium (K^+), chloride (Cl^-).
- Osmolarity (total blood osmotic activity).

3. Statistical Data Processing

- Data were analyzed using SPSS 26.0 software.
- Analysis of variance (ANOVA) and t-tests were used for parameter comparison.
- A significance level of $P < 0.05$ was considered statistically significant.

Discussion and Conclusion During the study, endotoxin-induced hemodynamic disorders were analyzed in a **stepwise manner**, assessing patients in states of **hypovolemic, vasogenic, microcirculatory, and cardiac hemodynamic Disorder.** The study analyzed the mechanisms and sequential progression of endotoxin-induced hemodynamic disorders. To mathematically model hemodynamic changes, the formula for calculating Mean Arterial Pressure (MAP) was used:

$$\mathbf{MAP=(SV\times TPR)+CVP}$$

where MAP (Mean Arterial Pressure) is a key indicator of tissue perfusion, reflecting the level of oxygen supply; SV (Stroke Volume) represents the volume of blood ejected per cardiac cycle, characterizing the heart's pump function; TPR (Total Peripheral Resistance) indicates vascular resistance, determining the hydrodynamic opposition in the circulatory system; and CVP (Central Venous Pressure) serves as a marker of venous return and preload.

1. Identified Parameters in Hypovolemic Hemodynamic Disorder

Parameter	**Measured Value**	**Normal Range**
Mean Arterial Pressure (MAP)	62.1 ± 4.0 mmHg	70–100 mmHg
Heart Rate (HR)	113 ± 10 bpm	60–90 bpm
Stroke Volume (SV)	3.27 ± 0.5 L/min	4.0–7.0 L/min
Cardiac Index (CI)	2.20 ± 0.3 L/min/m²	2.5–4.2 L/min/m²
Ejection Fraction (EF %)	49.5 ± 5%	55–70%
Total Peripheral Resistance (TPR)	1800 ± 200 dyn·s·cm^{-5}	900–1400 dyn·s·cm^{-5}
Central Venous Pressure (CVP)	3 ± 1 mmHg	5–10 mmHg
Lactate Level	3.9 ± 0.5 mmol/L	0.5–2.2 mmol/L
C-reactive Protein (CRP)	48 ± 8 mg/L	<10 mg/L
NT-proBNP	2500 ± 500 pg/mL	<125 pg/mL or age-related <400 pg/mL
Acid-Base Balance (pH)	7.30 ± 0.05	7.35–7.45
Venous Oxygen Saturation (SvO_2)	55 ± 10%	65–75%

Hypovolemia is characterized by a decrease in total circulating blood volume, leading to significant hemodynamic alterations. Volume depletion results in reduced stroke volume, impaired perfusion, and compensatory vasoconstriction. The primary hemodynamic change in hypovolemia is a decrease in central venous pressure (CVP), reflecting reduced venous return to the right chambers of the heart. A decline in CVP lowers ventricular filling, leading to a drop in stroke volume and MAP, which can result in shock. The development of hypovolemia is accompanied by a reduction in venous return, a decrease in CVP, and impaired ventricular filling, ultimately leading to decreased stroke volume and arterial pressure. The compensatory increase in total peripheral resistance (TPR) serves as a temporary stabilizing mechanism but does not prevent the progression of hypoxia. Prolonged tissue hypoperfusion results in capillary perfusion impairment and tissue hypoxia, which serve as predictors of multiple organ failure. The primary pathophysiological mechanisms of hypovolemic hemodynamic disorder include a decrease in CVP, a reduction in SV, and a compensatory increase in TPR to maintain MAP. However, compensatory mechanisms are limited, and prolonged hypoperfusion significantly increases the risk of multiple organ dysfunction syndrome (MODS).

2. Identified Parameters in Cardiac Hemodynamic Disorder

Parameter	**Measured Value**	**Normal Range**
MAP	45.4 ± 4.0 mmHg	70–100 mmHg
SV	1.99 ± 0.6 L/min	4.0–7.0 L/min
CI	1.35 ± 0.3 L/min/m²	2.5–4.2 L/min/m²
EF %	28.9 ± 5%	55–70%
Lactate Level	5.2 ± 0.6 mmol/L	0.5–2.2 mmol/L
SvO_2	20 ± 6%	65–75%

Cardiac hemodynamic disorder is associated with impaired myocardial pump function, leading to a decrease in stroke volume and arterial perfusion. In cardiogenic shock, even after hypovolemia is corrected, the heart remains unable to maintain an adequate cardiac output. Myocardial dysfunction results in reduced contractility, causing a severe decline in stroke volume and MAP. The increase in TPR occurs as a compensatory response due to reflex vasoconstriction aimed at preserving arterial pressure. The increase in venous return caused by impaired cardiac pump function leads to elevated right atrial pressure, contributing to venous congestion and the progression of heart failure. The combination of

decreased stroke volume and compensatory TPR elevation worsens capillary blood flow and leads to oxygen deficiency in tissues.

3. Identified Parameters in Vasogenic Hemodynamic Disorder

Parameter	Measured Value	Normal Range
Mean Arterial Pressure (MAP)	54.3 ± 5.0 mmHg	70–100 mmHg
Heart Rate (HR)	151.6 ± 15 bpm	60–90 bpm
Stroke Volume (SV)	6.06 ± 0.8 L/min	4.0–7.0 L/min
Cardiac Index (CI)	3.64±0.5 L/min/m²	2.5–4.2 L/min/m²
Ejection Fraction (EF %)	30.5 ± 6%	55–70%
Total Peripheral Resistance (TPR)	600±150 dyn·s·cm^{-5}	900–1400 dyn·s·cm^{-5}
Central Venous Pressure (CVP)	8 ± 2 mmHg	5–10 mmHg
Lactate Level	6.5 ± 0.7 mmol/L	0.5–2.2 mmol/L
C-reactive Protein (CRP)	80 ± 12 mg/L	<10 mg/L
NT-proBNP	5600 ± 700 pg/mL	<125 pg/mL or age-related <400 pg/mL
Acid-Base Balance (pH)	7.25 ± 0.06	7.35–7.45
Venous Oxygen Saturation (SvO_2)	30 ± 8%	65–75%

Vasogenic (distributive) hemodynamic disorder develops due to pathological vasodilation caused by a systemic inflammatory response. This type of disorder is characterized by a critical drop in total peripheral resistance, leading to hypotension and impaired arterial perfusion.

In vasogenic shock, cardiac output (CO) may remain elevated, but MAP continues to decline due to insufficient vascular tone. The primary pathophysiological mechanism of this disorder involves pathological vasodilation and blood redistribution, leading to an imbalance between tissue oxygen demand and actual oxygen delivery.

4.Identified Parameters in Microcirculatory Hemodynamic Disorder

Parameter	Measured Value	Normal Range
Mean Arterial Pressure (MAP)	44.9 ± 5.0 mmHg	70–100 mmHg
Heart Rate (HR)	127.9 ± 10 bpm	60–90 bpm
Stroke Volume (SV)	4.45 ± 0.7 L/min	4.0–7.0 L/min
Cardiac Index (CI)	2.41 ± 0.4 L/min/m²	2.5–4.2 L/min/m²
Ejection Fraction (EF %)	27.6 ± 5%	55–70%
Lactate Level	7.2 ± 0.8 mmol/L	0.5–2.2 mmol/L
Venous Oxygen Saturation (SvO_2)	25 ± 7%	65–75%

Microcirculatory hemodynamic disorder is characterized by critical impairment of capillary perfusion and progressive tissue hypoxia. In this condition, lactate levels increase significantly, indicating a shift toward anaerobic metabolism. A decrease in venous oxygen saturation (SvO_2) serves as an indicator of disrupted oxygen transport and utilization by tissues. The key mechanism of microcirculatory shock is capillary blood flow destabilization, which accelerates the development of multiple organ failure. This condition is also associated with acid-base imbalance and increased anaerobic metabolism, further exacerbating the pathological process.

The study findings demonstrated that endotoxin-induced hemodynamic disorders develop in a well-defined sequence of stages, each characterized by distinct pathophysiological mechanisms and compensatory responses. The hypovolemic stage is primarily associated with a reduction in stroke volume and central venous pressure. The cardiac dysfunction stage is defined by myocardial dysfunction, resulting in decreased cardiac output and compensatory TPR elevation. The vasogenic stage is characterized by a significant decrease in total peripheral resistance and arterial hypotension. The microcirculatory stage is dominated by disrupted oxygen transport and critically impaired capillary perfusion, posing a significant risk for multiple organ dysfunction.

These findings are of great importance for understanding hemodynamic disorders in endotoxin shock and sepsis and for developing effective strategies for their correction.

Conclusion. The results of the study demonstrated that each stage of hemodynamic disorder is associated with distinct pathophysiological changes:

1. In hypovolemic hemodynamic disorder, stroke volume and central venous pressure decreased, while total peripheral resistance increased compensatorily.
2. In cardiac hemodynamic disorder, stroke volume and cardiac index significantly declined, accompanied by a reflexive increase in total peripheral resistance.
3. In vasogenic hemodynamic disorder, stroke volume increased, but total peripheral resistance decreased, leading to worsening hypotension.
4. In microcirculatory hemodynamic disorder, stroke volume remained relatively stable, but capillary perfusion and oxygen transport capacity were severely impaired.

The increase in lactate levels and the decrease in venous oxygen saturation (SvO_2) across all shock stages confirmed the association of tissue hypoxia and microcirculatory disturbances with hemodynamic dysfunction.

Practical Significance. Control Damage Resuscitation (CDR) is an intensive care algorithm designed to manage endotoxin-induced hemodynamic disorders through dynamic assessment, targeted therapy, and restoration of homeostatic balance. This approach is particularly effective in shock syndromes, sepsis, and other critical pathological conditions, focusing on preserving vital organ perfusion and addressing the underlying disease.

Step 1: Pre-Diagnostic Intervention – Patient Selection Stage

Objective:

To identify patients requiring CDR while excluding those who do not meet the criteria.

Step 2: Diagnostic Intervention – Dynamic Hemodynamic Assessment

Objective:

The main goal of dynamic hemodynamic assessment is to determine the key hemodynamic determinants in the patient and develop an appropriate therapeutic strategy. This assessment is carried out in two stages:

1. Contextual Hemodynamic Assessment – Initial estimation based on clinical symptoms.
2. Integrative Hemodynamic Assessment – Confirmation of the primary determinant using instrumental and laboratory investigations.

Integrative Assessment	Contextual Assessment
↓ CVP	Hypovolemic hemodynamic disorder
↓ CO	Cardiac hemodynamic disorder
↓ TPR	Vasogenic (distributive) hemodynamic disorder
↑ Lactate & ↓ SvO_2	Capillary perfusion disorder

Step 3: Therapeutic Intervention – Targeted Hemodynamic Therapy

Objective:

To stabilize the patient by addressing the identified hemodynamic determinant.

Step 4: Homeostatic Intervention – Restoration of Homeostasis

Objective:

To re-establish internal physiological balance by correcting metabolic and systemic imbalances.

Step 5: Surgical Intervention – Elimination of the Underlying Disease

Objective:

To remove the source of infection or metabolic disorder, ensuring long-term stability and recovery.

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