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TISSUE OXYGENATION MEASUREMENT IN PATIENTS WITH SEPSIS COMPARED TO THE LACTATE LEVELS AND HEMODYNAMICAL MONITORING

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Abstract

Near-infrared spectroscopy (NIRS) is a noninvasive method for measuring tissue oxygenation. The method allows for monitoring tissue perfusion in shock by revealing tissue hemoglobin oxygen saturation (StO_2). The current study aims to compare tissue oxygenation levels with hemodynamical monitoring and lactate levels in patients in severe shock. Study encompasses 19 patients treated in intensive care unit (ICU) at Alexandrovska University Hospital. Ten of the patients cover the criteria for severe sepsis, the remaining nine patients have no data for septic condition. In both groups of patients tissue oxygenation levels measured with INVIOS monitor, mean arterial pressure (MAP), oxygen saturation in mixed venous blood (SvO_2) and lactate levels within 72 h of intensive care unit admission are compared. The patients with severe sepsis have significantly lower levels of StO_2 in comparison with patients without sepsis. Tissue oxygenation levels correspond to the mean arterial pressure levels, oxygen saturation in mixed venous blood. StO_2 levels in the current study do not correlate significantly with the lactate levels in patients with sepsis. Near-infrared spectroscopy as StO_2 levels correlate with the hemodynamical monitoring in patients with severe sepsis, but do not correlate significantly with the severity of the disease. This data might indicate that tissue oxygenation monitoring has clinical significance in patients with sepsis. Further profound studies are necessary for assessing the role of tissue oxygenation monitoring in the early phase of resuscitation in septic patients.

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Introduction. Severe sepsis accounts for the great number of hospitalizations in intensive care unit (ICU) structure worldwide [1]. According to the statistics in USA more than 500 000 are in emergency units and more than 750 000 annually [2]. The aetiology and clinical manifestations of sepsis remain heterogenous, while the pathophysiology includes impaired response regulation of the host, inflammatory and coagulation cascades activation, tissue hypoxia, cell dysfunction, organ dysfunction and in lack of intervening, eventually death.

Biological questions and contradictions remain but it is proven that early identification and timely supportive treatment in combination with antibiotic therapy and control of the source of infection are connected with better outcome. Therefore current international consensus guidelines for resuscitation of patients with severe sepsis or septic shock recommend aggressive actions, based on the invasive monitoring [3]. Unfortunately invasive monitoring is not always possible and this is a barrier for performing the resuscitation protocols. Noninvasive methods for monitoring would be helpful for guiding early resuscitation in sepsis.

Tissue hypoxia should be recognized as soon as possible [4,5]. Several indicators for tissue hypoxia are most popular in the clinical practice. These represent lactate concentration, pH, oxygen supply (DO_2), oxygen consumption (VO_2) and mixed venous oxygen saturation (SVO_2) [6]. These indices are connected with invasive monitoring or constant blood samples.

One possibility for noninvasive tissue hypoxia measurement is Near-infrared spectroscopy (NIRS), which was first described in 1977 as a method for oxygen level measurement in muscles and other tissues in vivo. NIRS uses computational analysis of infrared spectrum 700–2500 nm for determining hemoglobin oxygenation in tissues. The technique is based on the principle that abortion of light by oxyhemoglobin, deoxyhemoglobin and myoglobin differs in different infrared waves [2]. This technique allows quick, noninvasive and continuous measurement of local tissue oxygen saturation (StO_2) [7].

In several animal models with hemorrhagic shock StO_2 correlated well with invasive DO_2 measurements [8,9], as early hemorrhagic shock is not connected with global changes in the regional DO_2. StO_2 changes during septic shock are not completely clarified as the global oxygen consumption usually increases, similar to DO_2, especially in patients with adequate resuscitation. The current study measures StO_2 in patients with severe sepsis and in patients non-qualifying for the criteria for sepsis and compares them with hemodynamical monitoring.

The working hypothesis proposed is that the StO_2 in patients with severe sepsis is connected with the severity of the disease and correlates with the hemodynamical monitoring.

Materials and methods. The study includes patients hospitalized at the ICU of Alexandrovska University Hospital. The study is prospective and cohort. Patients with severe sepsis are included after obtaining informed consent from the relatives or a legal representative.

Inclusion criteria are:

- Patients > 18 years old;
- Patients diagnosed with severe sepsis and at least one episode of hypotension, defined as systolic arterial pressure (SAP) < 90 mmHg;
- Patients having at least one organ dysfunction, positive results from microbiology;
- Two of the four following physiological indexes:
  - Leucocytes $> 12\,000$ mm^3 or < 4000 mm^3
  - Body temperature < 36 or $> 38\,^\circ$C
  - Tachycardia > 90/min
  - Tachypnea > 20/min

Patients are divided into two groups: Group A ($n = 10$) – patients covering the criteria for severe sepsis and group B ($n = 9$) – patients without severe sepsis.

All patients are followed up three consecutive days, with the following parameters being assessed three or more times:

- Tissue oxygenation: StO_2;
- Oxygen saturation in mixed venous blood: SvO_2;
- Systolic, diastolic and mean arterial pressure;
- Serum lactate;
- Hemoglobin;
- Arterial blood gases.

Tissue oxygenation measurement is performed by the method of reflected infrared spectroscopy (NIRS – near infrared spectroscopy) with the aid of INVOS monitor. NIRS sensors are placed on the thenar eminence of the thumb and the backside of the forearm. StO_2 is calculated by measuring the attenuation of light in the following wave lengths – 680, 720, 760, and 800 nm. At these length waves light penetrates into the tissues and is absorbed according to the oxygen saturation in different tissues. Light that is not absorbed returns as optical signal and is converted in the 720 nm scale secondary attenuated value representing the ratio of oxygenated hemoglobin to total hemoglobin: StO_2 [10].

All tissue oxygenation measurements are performed within one hour of laboratory and other instrumental tests. Medical staff performing the study is blinded to the StO_2 values. In patients without severe sepsis after obtaining informed consent from the patient or relatives, tissue oxygenation is measured with NIRS method as well as lactate level and venous blood hemoglobin values.

Statistical analysis. For the purposes of statistical analysis SPSS11 for Mac (SPSS Inc., Chicago, IL) is used. For all continually monitored parameters are calculated values, 95% confident interval and reference range separately and in groups. Digital values are compared with Mann–Whitney U test and categorical values with Fisher test. Pearson correlation coefficient is used and results are presented as R and p values. For statistical significance $p < 0.05$ is accepted.

Results. Physiological data of the patients are shown in Table 1.

In patients with severe sepsis the results in mean arterial pressure (MAP), diastolic arterial pressure (DAP), systolic arterial pressure (SAP) and mixed venous oxygen saturation (SvO_2) correspond to the tissue oxygenation (StO_2) values, which suggests that tissue oxygenation measurement has significance in monitoring sepsis similar to hemodynamical parameters.

For all patients APACHE II (Acute Physiology And Chronic Health Evaluation II) scale is calculated within 24 h of enrollment in the study, which is similar for all patients: 19 ± 5 (standard deviation) points. Male/female distribution in group A is 6/4 and in group B is 6/3. Mean age in group A is 62 ± 11 yrs and in group B is 62 ± 12 yrs.

In patients from group A mean arterial pressure (MAH) is lower while lactate level is higher as compared to patients in group B. In group A patients tissue oxygenation presented as StO_2 is significantly lower in comparison with patients in group B.

Aetiology of sepsis, vasopressors use, hospitalisation duration and stay in ICU, as well as mechanical ventilation duration are shown in Table 2. No statistically

Table 1

Physiological data of the patients

	Systolic arterial pressure (mmHg)	Diastolic arterial pressure (mmHg)	Mean arterial pressure (mmHg)	Mixed venous oxygen saturation (SvO_2)	Tissue oxygenation (StO_2%)	p values
Day 1	120 (47)	60 (15)	65 (15)	55 (15)	75 (15)	$p < 0.05$
Day 2	117 (53)	55 (13)	57 (13)	53 (16)	76 (17.2)	$p < 0.05$
Day 3	130 (42)	52 (14)	56 (9)	50 (18)	83 (7)	$p < 0.05$

T a b l e 2

Characteristics of patients with severe sepsis

Characteristics of the patients	N
Lethal cases	4
Sepsis aethiology	
Intraabdominal infection	6
Pneumonia	2
Clostridium difficile colitis	1
Soft tissues infection	1
Microorganism	
Gram-negative	1
Gram-positive	4
Anaerobes	1
Fungi	3
Unknown	1
Vasopressors	
None	5
Dopamine	1
Norepinephrine	2
Hospital stay	31.8 ± 21.9 (14–18)
ICU stay	15.1 ± 14.7 (4–52)
Days on mechanical ventilation	14.1 ± 15.4 (2–52)

significant difference in the StO_2 values is evident between patients with and without vasopressor therapy.

There is no significant correlation between lactate values ($R = 0.13$), basic excess (BE) ($R = 0.14$) and the tissue oxygenation values (StO_2) in patients with severe sepsis. The values are shown in Table 3.

Table 4 presents lactate values, tissue oxygenation and mean arterial pressure values in patients from group B. The table demonstrates higher values of tissue oxygenation in group B patients as compared to group A, as well as lower lactate and higher mean arterial pressure levels in group B as compared to group A.

T a b l e 3

Lactate levels, basic excess and tissue oxygenation in severe sepsis patients – group A

Day	Lactate (mEq/l)	Basic excess (BE)	Tissue oxygenation (StO_2)	p values
Day 1	6.2 (2.1)	−2.4 (3.2)	75 (15)	$p < 0.01$
Day 2	5.9 (3.2)	−2.3 (3.4)	76 (17.2)	$p < 0.05$
Day 3	4.7 (2.9)	−2.5 (2.9)	83 (7)	$p < 0.01$

Table 4

Lactate values, mean arterial pressure and tissue oxygenation in patients without sepsis – group B

Day	Lactate (mEq/l)	Mean arterial pressure (mmHg)	Tissue oxygenation (StO_2)	p values
Day 1	0.1 (2.1)	75 (5)	85 (13)	$p < 0.05$
Day 2	0.3 (3.2)	60 (12)	81 (17)	$p < 0.05$
Day 3	0.2 (2.9)	59 (10)	82 (16)	$p < 0.05$

Discussion. The differences observed in the serum lactate concentrations and mean arterial pressure between patients in group A and group B are in concordance with the expected results, in regard to the alterations associated with the septic condition. Tissue oxygenation levels are higher in patients without sepsis. PAREZNIK et al. [11] examine the level of deoxygenation of the thumb muscle during severe ischemia in patients with sepsis and septic shock. The authors observe that StO_2 decreases during severe ischemia after initial hemodynamical stabilization and this decrease is lower in patients with septic shock as compared to patients with severe sepsis and localized infection. Similarly CRETEUR et al. [12] observe that tissue oxygenation (StO_2) is lower in patients with sepsis as compared to patients without sepsis in ICU.

In the current study the values of tissue oxygenation correlate with the values of central venous oxygenation in patients with sepsis. Similar results are published by TORTORIELLO et al. [13] in pediatric patients after cardiac surgery – cerebral oxygenation measurement through NIRS methodology corresponds with the invasive measurements of central venous oxygenation.

Similar results suggest potential use of tissue oxygenation as a method for monitoring resuscitation in patients with severe sepsis which are nonstable and at risk for applying invasive monitoring techniques.

PODBREGAR and MOŽINA [14] study the relation between tissue oxygenation and central venous oxygenation in patients with severe left sided heart failure with or without severe sepsis and septic shock. In patients with data for sepsis and septic shock there is lack of correlation between tissue oxygenation and central venous oxygenation values. Possible explanations for this phenomenon are as follows: firstly tissue oxygenation measured in peripheral tissues is a sum of hemoglobin saturation in small vessels both arterial and venous while central venous saturation measures saturation in mixed venous blood. And secondly tissue oxygenation measurement stops at $StO_2 < 70\%$.

The current study has several limitations: the results obtained for haemodynamical monitoring are from noninvasive measurement. The patients with sepsis are not in the early phase of resuscitation which probably explains the lack of correlation with lactate values. The study includes patients mainly above middle age and does not encompass young patients.

Conclusion. Measuring tissue oxygenation through NIRS technique is still in its early stage. The studies are focused on determining the role of tissue oxygenation as monitoring and guiding resuscitation in early phases of sepsis. In patients with severe trauma, tissue oxygenation values during the first hours after emergency department admission are significantly predictive regarding the risk of lethal outcome and multiorgan insufficiency development [15]. Using tissue oxygenation monitoring as noninvasive easily applied method in a larger group of patients is a matter of further studies.

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