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TRANSCUTANEOUS INFLUENCE OF LASER RADIATION ON THE OXYGEN SATURATION OF VENOUS BLOOD

The work is devoted to the determination of the external transcutaneous laser radiation effect on the relative concentration of oxyhemoglobin in venous blood. It is shown that transcutaneous laser irradiation of biological blood-filled tissue changes the venous blood oxygen saturation value only if a certain level of laser-stimulated photodissociation of oxyhemoglobin in arterial blood is reached (more than 6% decrease of the arterial blood oxygen saturation value). From our point of view, this process is not a direct laser-stimulated photodissociation of oxyhemoglobin in venous blood, because the dissociation curve is situated in the region with high values of partial oxygen pressure. The decrease in the relative concentration of oxyhemoglobin in venous blood is most likely related to compensatory mechanisms of hypoxia in peripheral tissues, accounting for the recombination of oxyhemoglobin molecules during their passage from the point of irradiation to the point of oxygen extraction by cells.

K e y w o r d s: oxyhemoglobin, venous saturation, photodissociation, laser irradiation, arterial saturation.

1. Introduction

Aerobic metabolism of cells is primary in mechanism of providing mammalian tissues with energy. Tissue oxygenation plays an important role in the efficiency of many biochemical reactions. Factors that can affect the delivery and content of oxygen in tissues are of considerable interest, and one of such factors is the irradiation of tissues with electromagnetic waves in the optical interval. Photodissociation of oxyhemoglobin (HbO_2) has been known for over 50 years, starting from work [1], but all the mechanisms of both the release of oxygen and changes in its consumption by cells have not been studied yet. In recent decades, low-level laser therapy, which uses external laser transcutaneous irradiation leading to photodissociation of oxyhemoglobin, has become widespread for the treatment of a number of diseases [2, 3].

The relative concentrations of oxyhemoglobin in arterial and venous bloods (the values of the arterial (SaO_2) and venous (SvO_2) oxygen saturation) are two main parameters used to assess the process of oxygen delivery and to control the oxygen extraction by tissues. These two parameters are important for the analysis of oxygen circulation over the whole body. The value of oxygen extraction from arterial

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blood is an indicator of the adequacy of local tissue perfusion. Its determination is necessary for the early diagnosis of microcirculatory dysfunction, in particular, in sepsis and cardiogenic shock. Thus, a continuous monitoring of both SaO_2, which is currently the "gold standard", and SvO_2 is relevant for the hemodynamic and perfusion control under clinical conditions [4].

Hemodynamic parameters such as the blood pressure, heart rate, diuresis, and blood gas composition, which are usually applied to assess organ and tissue perfusion, can be normal despite tissue hypoxia, which does not exclude an imbalance between the total need for oxygen and its delivery. A reduction in either the volumetric blood flow through the tissue (ischemia) or in the oxygen content in the arterial blood (hypoxia) form the tissue oxygen deficiency. One of the first compensatory mechanisms aimed at eliminating the tissue oxygen deficiency is an enhancement of its extraction from the arterial blood, which leads to an inevitable decrease of the oxygen content in the venous blood [5–8].

The value of the venous blood oxygen saturation is an important indicator of oxygen exchange in tissues and a criterion for the adequacy of oxygen delivery to the tissue. The SvO_2 parameter reflects the balance between the oxygen delivery and its consumption by tissues. The oxygen delivery depends on the cardiac output, arterial blood oxygen saturation, and hemoglobin concentration. The degree of oxygen extraction is determined by the ratio between the oxygen consumption and delivery, and, usually, its normal valiue is about 25%. Under normal conditions, the oxygen consumption does not depend on the oxygen delivery, because tissues can compensate their need by increasing the degree of oxygen extraction. When the compensatory mechanism is exhausted, the oxygen consumption becomes dependent on the delivery. In this case, the anaerobic metabolism is engaged, and the lactate level begins to grow.

The oxygen delivery and consumption depend on the load on physiological organs (systems) and on their clinical condition. In a healthy person, the anaerobic metabolism usually emerges, when SvO_2 falls below 40–50%. In patients with heart failure, the degree of oxygen extraction is increased at rest, and they can live with SvO_2-values in this low-value interval without visible manifestations of hypoxia due to adaptive mechanisms (the shift of the oxyhemoglobin dissociation curve toward higher partial oxygen pressures and the adaptation of the peripheral microcirculatory bed) [9].

Our previous studies were focused on the determination of the dependence of the oxyhemoglobin photodissociation efficiency on various parameters. In particular, it was found that the action spectra have maxima near 525, 605, and 850 nm [10].

The aim of our work is to determine the effect of the external transcutaneous laser radiation on the relative concentration of oxyhemoglobin in the venous bloods. This will allow us to assess the effect of oxyhemoglobin photodissociation on the efficiency of oxygen extraction from the blood, i.e., the oxygen consumption by tissues. For out studies, we selected the wavelengths at which the maximum effect of the laser radiation was observed (525 and 605 nm).

2. Materials and Methods

2.1. Experimental setup

In the experiment, we recorded photoplethysmogram signals at two wavelengths: in the red (660 nm) and near-infrared (940 nm) intervals with the sampling rate $f_1 = 348$ Hz. A pulse oximeter finger sensor was applied in which transmitted light is used to reduce the distance of light passage through the tissue. The sensor was assembled on the basis of a standard pulse-oximetric pair of LEDs with emission wavelengths of 660 and 940 nm and a silicon photodiode BPW34 (OSRAM). The sensor operation control and the data collection and transmission were provided by a measuring unit connected to a personal computer (PC), which processed information, displaying it on the monitor screen, and stored the signal trend on the hard disk.

The measuring unit included input and output paths and a microcontroller, which governed the operation of both paths and provided two-way information exchange with the PC. The hardware design of the measuring unit allowed eight signals to be registered independently.

The microcontroller governed the sequence of power supply to the LEDs and the photodiode sampling, ensured the continuity of measurement data by storing them in the internal memory of the unit during the periods when the PC interrupted the exchange. It was a microprocessor unit, which included a micro-

processor, RAM, ROM, decoder, timer, quartz-stabilized clock generator, and input-output ports. The input path of the measuring unit consisted of amplifiers with signal source matching circuits, an input switch, a signal sample and storage device (SSD), and a 16-bit ADC. The input path worked with channel separation in time. The sensor sampling rate was $f_1 = 348$ Hz. The output path included a 10-bit DAC, pulse shapers, and output signal switches.

The operating mode of the measuring unit was set by special software. The software shell allowed the operator to set the required operating parameters using the PC: the number of LEDs and photodiodes, the sequence of switching on the output signals (LED glow), and the selection of the setting mode for the gain of input signals and the amplitude of output pulses (the automatic and manual modes). The selected signals from all sensor channels were displayed on the monitor screen in real time. The data from all channels were registered in *.log-files in ASCII codes and stored on the hard disk. To control the operation mode of the LEDs, the dependence of the radiation power of LEDs on their supply current was measured. The measurements were carried out using an IMO-2N meter (a meter of laser radiation with average power and energy). The obtained results were averaged by linearly approximating several measurement series using the least squares method. In the future, the radiation power will be controlled by measuring the voltage drop across the reference (calibrated) resistor in the LED supply circuit.

2.2. Data measurements and processing

For each external radiation wavelength, from 15 to 20 signal recordings were made according to the following scheme: 30 s without radiation, 30 s with radiation on, and 30 s without radiation. For each recording, the average values of local arterial blood saturation SaO_2 were calculated within the intervals without and with radiation, as well as the change of SaO_2 under the influence of radiation, which was afterward averaged over the number of recordings. Errors were calculated using t-tables for the probability $p = 0.95$.

From the registered photoplethysmograms, the linear regression and correlation coefficients of the signals in the red and infrared channels were determined with the discreteness $1/f_1 = 0.00287$ s. The signal quality was evaluated by the changes in the pairwise correlation coefficient: if there were sharp jumps and the coefficient fell below 0.95, the record was excluded from further analysis. The linear regression coefficient has the same physical meaning as the ratio between the signal modulation coefficients at two wavelengths, but it allows the value of the arterial blood saturation SaO_2 to be determined within a time period shorter than the cardiac cycle duration. The values of SaO_2 were calculated with the same discreteness $1/f_1$, and the curve behavior made it possible to control the signal quality. Below, the average values of SaO_2 are shown as the experimental results.

To determine the venous saturation value, we used a method based on the modulation of optical signals from natural human respiratory rhythms. This approach is based on the fact that the modulation of the relative concentrations of oxidized and reduced hemoglobins with the respiratory rate mainly takes place in the venous component of the vascular system [11–17].

To calculate the venous saturation values, the Fourier transform of the signals was performed (using the Hahn window method) in order to obtain their amplitude-frequency spectra. The latter were used to determine the frequency of the respiratory rhythm maximum, and a narrow-band Fourier filter with a center at the found frequency and a bandwidth that allows only respiratory oscillations to be distinguished was applied to the photoplethysmographic signal. Fourier filtering was performed with regard for the constant component of the signal. The respiratory oscillations identified for two wavelengths were used to determine the ratio between the respiratory rhythm modulation coefficients, which was applied to calculate the value of the venous blood oxygen saturations SvO_2 [18].

Eight volunteers aged from 25 to 54 years participated in the studies. The power level of applied radiation corresponded to that is used in low-intensity laser therapy and is safe for humans; the radiation was non-invasive. The schematic diagram of the relative ents of the sensor and the external radiation source are exhibited in Fig. 1.

3. Results

If the irradiation power is low at both examined wavelengths, a change in the value of the arterial blood

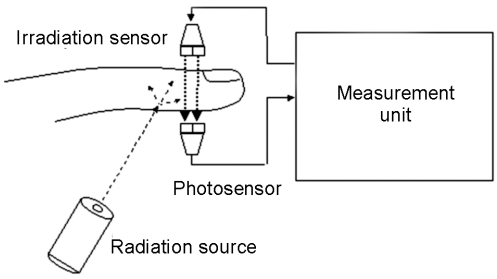

Fig. 1. Schematic diagram of irradiation procedure

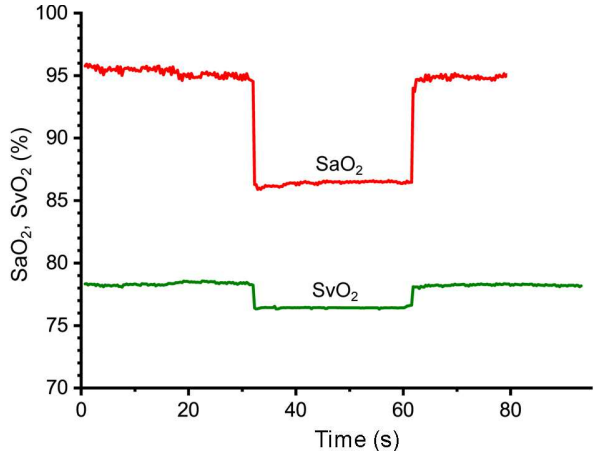

Fig. 2. Changes in the arterial, SaO_2, and venous, SvO_2, blood oxygen saturation values at the irradiation of a finger (the 1st phalanx) with laser radiation with a wavelength of 525 nm

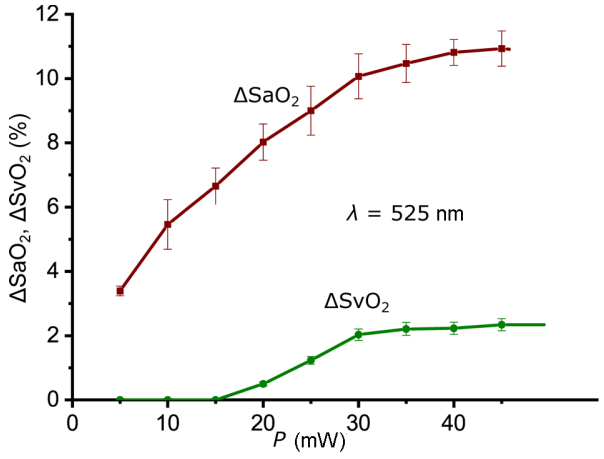

Fig. 3. The dependences of the magnitudes of the ΔSaO_2 and ΔSvO_2 drops on the irradiation power at irradiation of the 1st phalanx of the finger at a wavelength of 525 nm

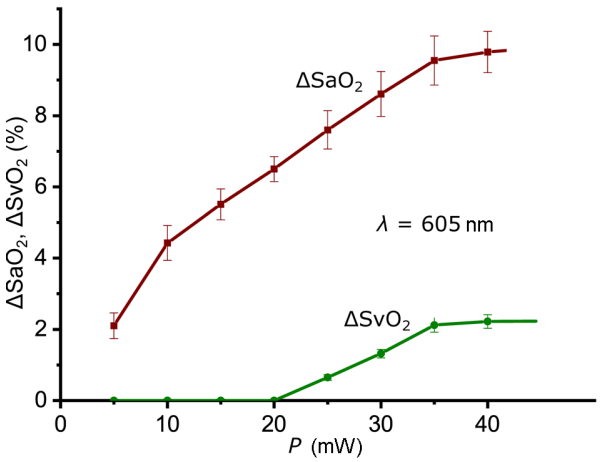

Fig. 4. The dependences of the magnitudes of the ΔSaO_2 and ΔSvO_2 drops on the irradiation power at irradiation of the 1st phalanx of the finger at a wavelength of 605 nm

oxygen saturation is clearly observed against the unchanged background of the venous blood oxygen saturation. Only at laser radiation powers that provided a decrease of more than 8% in the arterial blood oxygen saturation, there appeared a change in the venous saturation. In Fig. 2, an example of experimental data is illustrated, where simultaneous changes in the oxygen saturations of arterial and venous bloods were observed.

In Fig. 3, the dependences of a decrease in the arterial (ΔSaO_2) and venous (ΔSvO_2) blood saturations on the power of irradiation with a wavelength of 525 nm are shown. The average values of SaO_2 and SvO_2 without irradiation have a certain variability for a series of experiments with different powers (95.4 ± 0.4SD% and 78.6 ± 0.33SD%, respectively). The value of SvO_2 begins to change at an external irradiation power of 15 mW; it occurs at the moment, when the change of the SaO_2 value becomes larger than 6%.

Figure 4 demonstrates the dependences of the decrease in arterial (ΔSaO_2) and venous (ΔSvO_2) blood oxygen saturations on the power of irradiation at a wavelength of 605 nm. The average values of SaO_2 and SvO_2 without irradiation were 95.8 ± 0.4SD% and 78.5 ± 0.28SD%, respectively. At this wavelength, the value of SvO_2 begins to change at an external irradiation power exceeding 20 mW, at the moment, when the change in the SaO_2 value also becomes larger than 6%.

Since the interaction of optical radiation with blood hemoglobins is a single-photon process, in Fig. 5, for a better understanding and a comparison of the course of processes at different wavelengths, we show the dependences of the venous blood oxygen saturation change on the photon flux with various wavelengths. Note that at a wavelength of 525 nm, the process reaches saturation at a lower flux value.

4. Discussion

The relative concentration of oxyhemoglobin in the venous blood can change via two mechanisms. First, this is the direct photodissociation of oxyhemoglobin in the venous blood. Second, this is a consequence of a reduction in the arterial blood saturation value and the action of compensatory mechanisms.

According to [19], the mechanism of photodissociation of the heme-ligand complex in the arterial blood can be described as follows. Light absorption triggers the photolysis of a diatomic ligand and the spin transition in the iron(II) atom, which initiates conformational changes in the protein. The photolysis and cross-spin transition reactions occur simultaneously on a femtosecond time scale. Coherent oscillations of the bond distance with an amplitude of about 1 Å are observed. These nuclear motions induce a pronounced geometric reorganization, which makes the dissociation irreversible. At the first reaction stage, vibrations that break the symmetry and lead to the transfer of an electron from the porphyrin to the iron dominate. Then the wave packet becomes weaker to a triplet set within about 75 fs , and, to a quintet set, within about 430 fs. The results clarify the central role of nuclear vibrations in the emergence of ultrafast photodynamics of organometallic complexes [19].

In our opinion, this mechanism does not work for the venous blood, because the O_2 molecule is partially replaced by a CO_2 molecule and, accordingly, the dissociation curve shifts toward higher values of the partial oxygen pressure. The decrease in the venous saturation occurs most likely due to the action of compensatory mechanisms of oxygen consumption by peripheral cells, which compensate the lack of oxygen in the arterial blood by its larger extraction from oxyhemoglobin. It should also be taken into account that if the changes of the arterial blood saturation value are small, the recombination of oxyhemoglobin molecules will occur on the way from the irradiation point to the point of oxygen extraction by the cells.

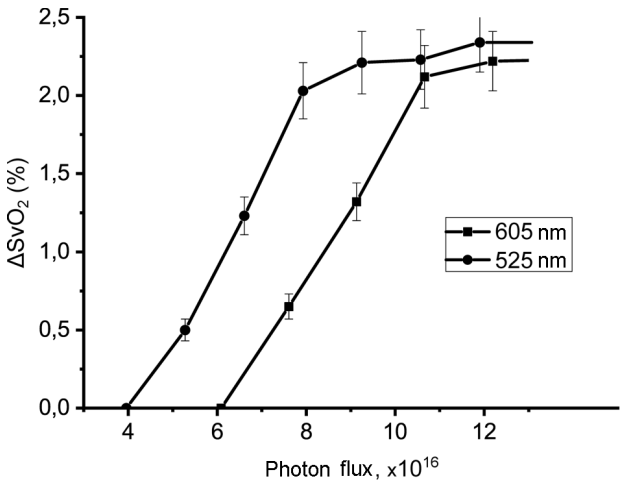

Fig. 5. The dependences of the magnitudes of the ΔSvO_2 drop on the photon flux for various irradiation wavelengths

5. Conclusions

To summarize, we have shown that, under the transcutaneous laser irradiation of biological blood-filled tissue, a change in the venous blood oxygen saturation value is observed, only when a certain level of laser-stimulated photodissociation of oxyhemoglobin is reached in the arterial blood (a reduction of more than 6% in the arterial blood oxygen saturation). In our opinion, this process is not a direct laser-stimulated photodissociation of oxyhemoglobin in the venous blood, because the dissociation curve is in the region of high oxygen partial pressure values. The decrease in the relative concentration of oxyhemoglobin in the venous blood is most likely associated with compensatory mechanisms of hypoxia in peripheral tissues with regard for the recombination of oxyhemoglobin molecules on the way from the irradiation point to the point of oxygen extraction by the cells.

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ТРАНСКУТАНТНИЙ ВПЛИВ ЛАЗЕРНОГО ВИПРОМІНЮВАННЯ НА ВЕЛИЧИНУ САТУРАЦІЇ ВЕНОЗНОЇ КРОВІ КИСНЕМ

Робота присвячена визначенню впливу зовнішнього черезшкірного лазерного випромінювання на відносну концентрацію оксигемоглобіну в венозній крові. Показано, що при черезшкірному лазерному опромінюванні біологічної кровонаповненної тканини зміна величини сатурації венозної крові киснем спостерігається тільки при досягненні певного рівня лазерностимульованої фотодисоціації оксигемоглобіну в артеріальній крові (зменшення величини сатурації артеріальної крові киснем більш ніж на 6%). На нашу думку, цей процес не є безпосередньою лазерностимульованою фотодисоціацією оксигемоглобіну в венозній крові, оскільки крива дисоціації знаходиться в області високих значень парціального тиску кисню. Зменшення відносної концентрації оксигемоглобіну у венозній крові скоріш за все пов'язано з компенсаторними механізмами гіпоксії периферичних тканин з врахуванням рекомбінації молекул оксигемоглобіну на шляху від точки опромінювання до точки екстракції кисню клітинами.

Ключові слова: оксигемоглобін, венозна сатурація, фотодисоціація, лазер, артеріальна сатурація.