metrium is an important prognostic parameter. As follows from our data, the patients with mild virilization and transformation of the type of menstrual disturbances, which probably reflects desensitization of the endometrium to hormonal stimulation, have the highest risk of severe endometrial pathologies.

Thus, complex examination of women with menstrual disturbances provides new insights into pathogenesis of gynecological disorders and allows one to develop new strategy of the treatment of these disorders.

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Biological and Clinical Effects of Violet and Blue Light

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Biological and clinical effects of violet and blue light are described. Effect of photohemotherapy is evaluated in 31 patients with chronic arterial insufficiency of the lower extremities caused by atherosclerosis.

Key Words: *violet light; blue light; photohemotherapy*

Violet and blue light (VL and BL) are an electromagnetic irradiation with wavelength ranging within 380-440 and 440-495 nm, respectively.

Although the energy of VL and BL photons is much lower than that of γ-, x-, and UV-radiation, VL and BL exert strong biological effects due to numerous photoreceptors occurring in biological objects. One of them, riboflavin, is an integral part of the most important enzymes. It is a constituent of flavin nucleotides, prosthetic groups of dehydrogenases which absorb BL (450 nm). The final electron acceptor for the flavin-dependent dehydrogenases is the VL absorbing cytochrome system: cytochrome *b* (429 nm), cytochrome *c* (418 nm), cytochrome c_1 (415 nm), and cytochrome *a* (429 nm). The absorption of VL is due to iron-porphyrin prosthetic groups. Thus, the energy of VL and BL is absorbed by the energy-synthesizing system.

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The second group of VL and BL-absorbing compounds includes all forms and derivatives of hemoglobin and bilirubin. Thus, blood, which is extremely rich with these compounds, intensely absorbs BL and VL in the so-called Soret band.

The third large group of BL- and VL-absorbing substances is presented by carotenoids whose functions remain poorly understood. For instance, carotenoids of heart homogenate absorb at 450 nm, carotene at 440 nm, and neurosporine at 416 and 470 nm.

Studies of the biological effects VL and BL on various organisms (tadpoles, frogs, salamander embryos, fly larvae, trout eggs, piglets, etc.) have demonstrated their pronounced ability to stimulate metabolism, growth, and development [3,4]. It has been established that VL induces the maximum activation of vital processes accompanied by more perfect metamorphosis [2].

Damaging effects of BL on cell cultures have been noted. For instance, Schoroeter [19] observed accumulation of chromosome aberrations in cultured

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human lymphocytes irradiated with high doses of BL. Parshad [17] showed that antioxidants added to the culture medium prevent chromosome aberration in cultured mouse cells irradiated with BL. Thus, the BL-induced damage to DNA is mediated through generation of reactive oxygen species. Singlet oxygen, a potent cytotoxic agent, is generated in the photodynamic reaction where the role of photosensitizer is played by riboflavin [21].

Bilirubin in the presence of BL (450 nm) induces photohemolysis of erythrocytes, photodegradation of biopolymers, and damage to DNA [8,16,22].

Uroporphyrin is an active VL acceptor (405 nm). Lim [14] showed that VL-irradiation of uroporphyrin-containing blood plasma rises the total hemolytic activity of the complement and stimulates chemotaxis of blood phagocytes. This mechanism also underlies complex damage occurring in patients with erythropoietic protoporphyria induced by light containing porphyrin band.

Blue light was first applied for medical purposes more than 100 years ago, when its potent analgesic effect in contusions and neuralgias and healing effect in trophic ulcers and purulent wounds, as well as its ability to resolve joint transudates, were demonstrated. Potent antibacterial effect of BL allowed for its use in the treatment of chronic gonorrhea and even tertiary syphilis [1].

The antibacterial and antiviral effects of BL can be enhanced by introducing a dye-photosensitizer, for example, methylene blue, into the system. The treatment of eczema herpeticum, a disease characterized by 20% mortality, with a combination of BL with methylene blue is a striking example. The affected skin treated with methylene blue is irradiated with VL and BL (400-490 nm). The light energy is absorbed by the dye and transferred to oxygen. The latter transforms into singlet oxygen and attack virus herpes simplex [18]. Even simple external irradiation with BL provides satisfactory results in the treatment of pustular disease [15].

Hager [9] showed that irradiation of the body surface with the light within 340-440 nm stimulates the immune system in cancer patients. Therefore, VL and BL irradiation can be recommend for cancer patients scheduled for radiation therapy and for patients with ulcers, wounds, and skin metastases. Experiments on *nude* mice showed that VL and UV irradiation of the body surface prevented the development of malignant tumors induced by short-wavelength UV rays [5].

In 1958, Cremer [6] found that BL (450-490 nm) converts bilirubin into photobilirubin by turning one pyrrole ring over the C=C bond. Photobilirubin is a polar, water soluble, nontoxic substance that is excreted into the bile without conjugation. Irradiation of the body surface gained wide acceptance in the treatment of neonatal hyperbilirubinemia. The radiant emittance in the BL range should 5-6 times exceed that of solar irradiation, the duration of irradiation being several hours per day. Some complications of phototherapy are described: photohemolysis, bronze coloration of the skin, retinopathy, diarrhea, and decreased intestinal transit time. Indirect effects of BL irradiation on the neuroendocrine system and biological rhythms are also possible [7,12,20,23].

Good clinical results were obtained when BL was applied for the treatment of the Crigler—Najjar syndrome, congenital nonostructive nonhemolytic jaundice resulting from reduced activity of bilirubin glucuronosyl transferase [10].

In patients with alcohol cirrhosis, phototherapy with BL promoted bilirubin transport from the skin pool into gallbladder and stimulated the production of bile acids, the liver function being unchanged [11].

MATERIALS AND METHODS

Both VL and BL only slightly penetrate through the skin and tissues, being assumed to exert their effects by acting on the blood passing through skin vessels. In 1986, Kost and co-workers first applied BL for irradiation of the blood in patients with essential hypertension and angina pectoris [13] and observed a positive clinical effect accompanied by a decrease in plasma cholesterol and low density lipoproteins.

This approach was used by us for patients with chronic arterial insufficiency of lower extremities caused by atherosclerosis.

Blood (200 ml) was drawn from the ulnar vein into a sterile vial with a conservant and then reinfused to the patient at a rate of 60 drops per min. The blood was irradiated in the plastic tube of the blood transfusion system using fluorescent lamp emitting light within 420-480 nm with the maximum at 435 nm and 0.16 W/cm^2 power density. Blood samples were taken before and immediately after the procedure (from the other hand). The treatment consisted of 5-6 procedures on the other day.

Photohemotherapy with BL was applied in 31 patients (12 women and 19 men) aged 42-78 years in whom drug therapy was ineffective.

RESULTS

In all patients, pronounced changes in the composition and properties of the blood were noted immediately after infusion of irradiated blood. These changes were as follows: a 16% decrease in blood viscosity with a high shear stress; a 10-20% decrease

in the plasma viscosity; a drop of hematocrit by 3-8 vol.%; a drop of blood hemoglobin by 10-20%; pH shift toward acidosis. In the venous blood, Pco_2 decreased, while Po_2 rose, and 60-70% of hemoglobin was saturated with O_2; the concentration of sodium and calcium ions dropped, while the content of potassium ions increased. Activity of plasma creatine phosphokinase rose and attained 200-300% in patients with severe ischemia of the legs. Plasma triglyceride content decreased by 50-70%. Aggregation ability of platelets was enhanced, and the size of aggregates increased.

Thus, infusion of a small portion of autologous blood (about 5% of the circulating volume) irradiated with VL produced marked shifts of the homeostasis. Of particular interest is a considerable hemodilution resulting in a drop of blood viscosity. Venous blood becomes more oxygenated due to a shift in oxydissociation, or a block of microcirculation, or reduced oxygen utilization in tissues. These changes are apparently transient and do not manifest themselves clinically.

It should be noted that there were no differences between irradiated and nonirradiated blood. No changes in viscosity, coloration, platelet activity were noted, and no photohemolysis occurred. However, in irradiated blood some nonidentified bioactive substances appear, which modulate homeostasis.

Clinical studies demonstrated that in 14 out of 28 patients with stage II of the disease the pain-free walking distance increased by 50-120% after the first procedure and in others such improvement was observed after 2-3 procedures. The pain-free walking distance increased from 168±23 to 589±48 m during the treatment. All patients felt much better and reported a surge of cheerfulness and strength.

Night pains in the affected legs disappeared in 3 patients with stage III; the pain-free walking distance in this group increased 2- to 3-fold. Remission in this group lasted 1-3 months. Eighteen patients with stage II were followed up for 2 years. In 12 of them the duration of remission was about one year, after that the treatment was repeated; in 4 of these patients remission lasted for 1.5 years and in two patients for 2 years.

Laboratory tests revealed that the blood viscosity decreased by 15-20% by the end of treatment. Since according to the Hageman's law the volume of blood is inversely proportional to its viscosity, it can be assumed that this mechanism underlies the observed clinical improvement.

The published data summarized above and our observations should call clinicians' attention to the study of VL and BL potentials in combating various diseases.

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