

THERAPEUTIC EFFECT OF TRANSFUSION WITH  
UV-IRRADIATED PLASMA IN OBSTRUCTIVE JAUNDICE

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UDC 616.36-008.51-085.382.015.2:615.831.4

KEY WORDS: liver; jaundice; ultraviolet light; blood plasma; treatment

Autotransfusion of UV-irradiated blood is used in medical practice. The bactericidal and antitoxic effects, intensification of the oxygen transport function, and stimulation of the nonspecific resistance of the recipient, observed when this method is used, have led to its successful application for the treatment of several diseases: cardiovascular and gastrointestinal diseases, anemias of varied genesis, suppurative and septic states, toxemias of pregnancy, etc. [3, 10, 13, 15].

The mechanisms of the action of irradiated blood on the body have not been adequately studied. There are only sporadic data on changes in particular biochemical and clinical parameters of patients' blood in the period immediately after reinfusion of the irradiated blood. The use of different types of sources of UV light, of different exposures and different wavelengths makes determination of the relationship between dose of irradiation and therapeutic effect difficult. Theoretical ideas on the main biological acceptors of the energy of UV irradiation, on the complex photochemical and free-radical processes initiated by exposure to this agent are only now beginning to be formulated [6, 8, 14]. Some workers have shown that during the action of UV light on the blood the principal photochemical processes develop in the blood serum [1, 12].

The blood bilirubin is known to have increased sensitivity to UV radiation and to be decomposed by it. This property of bilirubin lies at the basis of the phototherapy of icterus neonatorum by whole-body UV irradiation [6]. On the basis of these views the possibility of photodestruction of bilirubin can be predicted not only as a result of the direct action of UV light, but also under the influence of stable photo-oxidation products formed under these circumstances in the plasma.

In connection with the facts described above it was decided to study the clinical and biochemical effects of transfusion of UV-irradiated plasma, obtained from blood donors, in diseases of the liver complicated by jaundice.

#### EXPERIMENTAL METHOD

The dose of UV-irradiation of plasma (UVIP) was established in experiments on a model of obstructive jaundice of two weeks' duration on 30 noninbred rats of both sexes weighing 150-200 g. Obstructive jaundice was produced by ligation of the common bile duct at its point of entry into the small intestine. Autologous plasma was irradiated with UV light with a wavelength of 253.7 nm and in a dose of 108-216 J/m<sup>2</sup> in a volume of 0.1 ml/100 g body weight of the experimental animal, followed by reinfusion, in order to obtain a therapeutic effect. As the most important biochemical parameters of cholestasis, we studied the content of alkaline phosphatase (AP), of bilirubin with the aid of Lachema Biotest kits of reagents (Czechoslovakia), triglycerides, nonesterified fatty acids (NEFA), cholesterol by Ikles' method [11], and lipid peroxidation (LPO) activity by a chemiluminescence method [9]. A biomicroscopic study was made of the mesenteric microcirculation with morphometry

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Central Postgraduate Medical Institute, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. N. Orekhovich.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 101, No. 3, pp. 282-284, March, 1986. Original article submitted April 19, 1985.

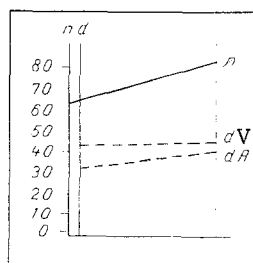


Fig. 1. Trend of parameters of the micro-circulatory bed in rats with obstructive jaundice during treatment with irradiated plasma: n) index of density of vascular network (in per cent), dA) diameter of arterioles (in  $\mu$ ), dV) diameter of venules (in  $\mu$ ).

of the parameters of the functioning bed, and also light-optical and electron-microscopic investigations of the liver in rats with two weeks' old jaundice before treatment with UVIP and 7 days after treatment. UVIP also was used to treat 20 patients (5 men and 15 women) aged from 28 to 73 years, admitted to hospital with the diagnosis of obstructive jaundice. Treatment was given with plasma obtained from donors of the same blood group, irradiated with UV radiation (wavelength 253.7 nm, dose 109-216 J/m<sup>2</sup>, in a volume of 1 mg/kg body weight, injected by intravenous drip. The state of the patients' liver function was assessed by biochemical tests of the blood and radioisotope liver scanning using <sup>131</sup>I-labeled bromsulfan.\* The control group consisted of patients treated by traditional method. Parameters of the acid-base balance also were investigated both in patients and in experimental animals by the micro-Astrup method. All the numerical results were subjected to statistical analysis by Student's t test.

#### EXPERIMENTAL RESULTS

After injection of irradiated plasma into rats with 2-week-old jaundice a therapeutic effect was observed after 1 week. Comparison of the biochemical parameters of the blood of animals of this group and of untreated animals with 3-week-old jaundice revealed normalization of the bilirubin level and cholesterol and NEFA concentrations, a decrease in AP activity and the triglyceride concentration, and an increase in the coefficient of cholesterol esterification. The time course of these parameters demonstrated an improvement of the liver function. Parameters of the blood acid-base balance showed a tendency toward normalization under the influence of UVIP.

Biomicroscopic investigation of the mesenteric microcirculation of rats with obstructive jaundice showed absence of a harmful action of UVIP in the chosen dose. Meanwhile, during the 40 min after injection of the irradiated plasma, adaptive reactions of the microvessels developed, leading to the improvement of the circulation in the splanchnic basin (Fig. 1). As Fig. 1 shows, after injection of the irradiated plasma an increase in the number of functioning microvessels and dilatation of arterioles, accompanied by constriction of the venular section, were observed, leading to acceleration of the blood flow and disappearance of erythrocyte aggregation in the postcapillary bed.

Morphological investigations of the liver showed dilatation of the sinusoids and disappearance of the phenomena of stasis observed in rats with untreated obstructive jaundice under the influence of UVIP.

The experimental results demonstrated the possibility of using UVIP, under the conditions described above, for the treatment of patients with jaundice of varied genesis. Treatment was given in the pre- and postoperative period to patients with jaundice of varied genesis and with marked hepatic failure (choledocholithiasis, chronic hepatitis, cirrhosis). The duration of jaundice in these patients varied from 1 week to 2 months. Treatment was given under the control of LPO activity in the capillary blood, determined by a chemiluminescence micromethod, of the blood biochemical parameters, and the results of radioisotope scanning of the liver before and after treatment.

\*Soviet bromsulfthalein analog.

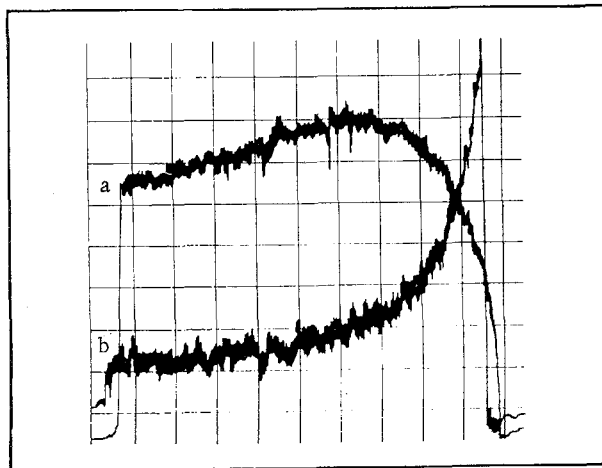


Fig. 2. Radionuclide liver scan with  $^{131}\text{I}$ -Normal liver scan (a) and blood clearance (b).

In all patients an improvement of the general state, a gradual reduction of the intensity of the jaundice of the skin, sclerae, and mucous membranes, and disappearance of the pruritis were observed clinically on the 3rd-7th days after a single injection of irradiated plasma. Investigation of the blood biochemical parameters showed a significant fall in the bilirubin level (total from  $126.74 \pm 20.52$  to  $58.15 \pm 11.29$   $\mu\text{moles}$ , direct from  $88.08 \pm 15.39$  to  $47.04 \pm 16.42$   $\mu\text{moles}$ ), AP activity (from  $56.0 \pm 7.62$  to  $46.88 \pm 0.55$  IU/liter), and transaminase activity (from  $49.12 \pm 10.33$  to  $40.6 \pm 5.15$  activity units), a fall in concentrations of cholesterol (from  $9.75 \pm 0.806$  to  $7.48 \pm 0.59$  mmol/liter), triglycerides (from  $2.82 \pm 0.33$  to  $2.41 \pm 0.4$  mmol/liter), and lipoproteins (from  $9.8 \pm 1.43$  to  $6.7 \pm 1.05$  mmol/liter) an increase in the coefficient of cholesterol esterification (from 0.25 to 0.53), normalization of the parameters of the blood acid-base balance, and a fall in the concentration of hydroperoxides in the blood (from  $0.18 \pm 0.04$  to  $0.12 \pm 0.01$  relative unit/5  $\mu\text{l}$  of blood).

Radionuclide liver scanning on the patients revealed restoration of the secretory and excretory function of the liver. It will be clear from Fig. 2 that 7 days after injection of irradiated plasma the patient's liver scan and blood clearance were indistinguishable from those of a normal person.

A single injection of irradiated plasma, incidentally, has a prolonged action and gives rise to a stable effect which lasts 2-3 months, as was confirmed by the results of repeated liver function tests.

Data in the literature are evidence that in mechanical jaundice energy metabolism in the liver is disturbed, with a resulting deficiency of high-energy compounds. This situation is based on uncoupling of respiration and oxidative phosphorylation in the mitochondria as the result of damage to their membrane by products of free-radical oxidation of NEFA of phospholipids [4, 7, 16]. An increase in the intensity of LPO leads to exclusion of oxygen and the energy substrate from enzymic oxidation [2].

In the electron-microscopic studies after administration of UVIP the degree of destruction of the mitochondria was reduced and their regeneration potentiated in the liver of rats with 3-week-old jaundice.

The therapeutic effect of UVIP may be associated with normalization of oxidation-reduction processes, lying at the basis of the energy supply of the liver, with a fall in the level of nonenzymic free-radical oxidation, and with potentiation of microsomal oxidation.

During the clinical use of UVIP, a fall in the level of LPO products was observed after one week in the patients' plasma. Meanwhile a positive trend of the biochemical parameters of the blood was observed, reflecting the state of the liver function, and this was confirmed by the results of radioisotope scanning. Normalization of the state of the liver function may perhaps be brought about by intensification of microsomal oxidation, a change in the membrane permeability of the cellular structures of the liver, and an improvement of the microcirculation in the organ.

This suggested method of treatment of patients with jaundice of varied genesis is thus a pathogenetically based and technically simple method which gives a marked and prolonged therapeutic effect.

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## EFFECT OF ENKEPHALINS ON FUNCTION OF CALCIUM-REGULATING ENDOCRINE GLANDS IN SHOCK

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UDC 616-001.36-07:[616.441+616.447]  
-008.6-02:615.357:577.175.859

KEY WORDS: shock, Leu-enkephalins, calcium-regulating glands

One of the distinctive features of dysfunction of the endocrine system in various critical states is disturbance of the activity of calcium-regulating endocrine glands [2, 4, 12, 15]. The writers showed previously that increased activity of the C-cells of the thyroid gland and biphasic changes in parathyroid gland function are observed in traumatic, cardiogenic, and burn shock. The hypocalcemia thus arising greatly aggravates the course of the pathological process and is an unfavorable prognostic sign in shock [4, 5, 10, 11]. These disturbances are evidently based not only on specific factors (disturbances of the peripheral circulation, tissue hypoxia, toxemia), but also on nonspecific mechanisms (a powerful post-aggressive response to extremal stimulation). It can be postulated that measures aimed at preventing stress will lead to improvement of the activity of the parathyroid glands and of the C cells of the thyroid gland in shock. Data have been obtained to show a marked anti-stress effect of enkephalins and endorphins, which are endogenous opioid peptides [7, 8],

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Laboratory of Pathophysiology, Siberian Branch, All-Union Cardiology Scientific Center, Academy of Medical Sciences of the USSR, Tomsk. (Presented by Academician of the Academy of Medical Sciences of the USSR R. S. Karpov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 101, No. 3, pp. 284-287, March, 1986. Original article submitted March 25, 1985.