EFFECT OF HYPERBARIC OXYGEN THERAPY ON ERYTHROPOIESIS IN THE RECOVERY PERIOD AFTER HEMORRHAGIC COLLAPSE

É. N. Barkova and A. V. Petrov

UDC 616-005.1-085.835.3-07:616.155.1-007.1-076.5

Hyperbaric oxygenation (2 atm O_2, 40 min) accelerates the restoration of the normal cell count and hemoglobin concentration in the peripheral blood of albino rats after acute blood loss (2.8% of body weight). In the bone marrow, coupled with increased proliferative activity of erythroblasts and normoblasts, intensive maturation of hemoglobin-containing forms was observed. The maximal level of plasma erythropoietic activity of the anemized animals was found on the first and tenth days after blood loss. The serum possessed erythropoiesis-inhibiting properties on the 15th day. It is postulated that hyperbaric oxygenation after acute blood loss potentiates the stimulation of erythropoiesis induced by erythropoietin.

KEY WORDS: acute blood loss, hemorrhagic collapse, erythropoiesis, erythropoietin, hyperbaric oxygen therapy.

Data in the literature on the effect of a raised oxygen pressure on erythropoiesis are very contradictory and they are concerned chiefly with responses of the blood system in the intact organism [1, 4, 7-9, 13, 14, 19]. Interest in this problem has increased in connection with the use of hyperbaric oxygenation in the prevention and treatment of terminal states [5, 12, 20]. The beneficial effect of hyperbaric oxygen therapy on the energy metabolism of the body after acute anemization [10] suggests that there is a metabolic aspect in the mechanism of the therapeutic action of hyperbaric oxygen [11]. Data on the effect of hyperbaric oxygen therapy in the recovery period after hemorrhagic collapse deal only with changes in the peripheral blood [6].

The dynamics of serum erythropoietic activity was investigated parallel with that of bone-marrow erythropoiesis and also the intensity of restoration of erythrocytes, hemoglobin, and reticulocytes in the peripheral blood during hyperbaric oxygen therapy after hemorrhagic collapse.

EXPERIMENTAL METHOD

Experiments were carried out on 120 male albino rats weighing 200-220 g. Acute hemorrhagic collapse was produced by repeated withdrawal of small volumes of blood from the right jugular vein (2.8% of the body weight in 30 min). Hyperbaric oxygen was administered in a 90-liter pressure chamber under a pressure of 2 atm of medical oxygen for 40 min, with absorption of carbon dioxide and water vapor. Compression and decompression were carried out at the rate of 0.4 atm/min. The animals were investigated hematologically 1, 3, 5, 7, 10, 15, 20, and 25 days after bleeding. The erythrocyte and reticulocyte counts and hemoglobin concentration in the peripheral blood were determined by the usual methods. Erythropoietic activity was estimated from myelograms and partial erythroblastograms. The serum erythropoietic activity was tested by determination of the stathmokinetic index [15] and the increase in the reticulocyte count in polycythemic albino rats with reduced erythropoiesis [18].

Department of Pathological Physiology and Central Research Laboratory, Voronezh Medical Institute. Department of Pathological Physiology, Tyumen' Medical Institute. (Presented by Academician V. N. Chernigovskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 81, No. 2, pp. 156-158, February, 1976. Original article submitted March 17, 1975.

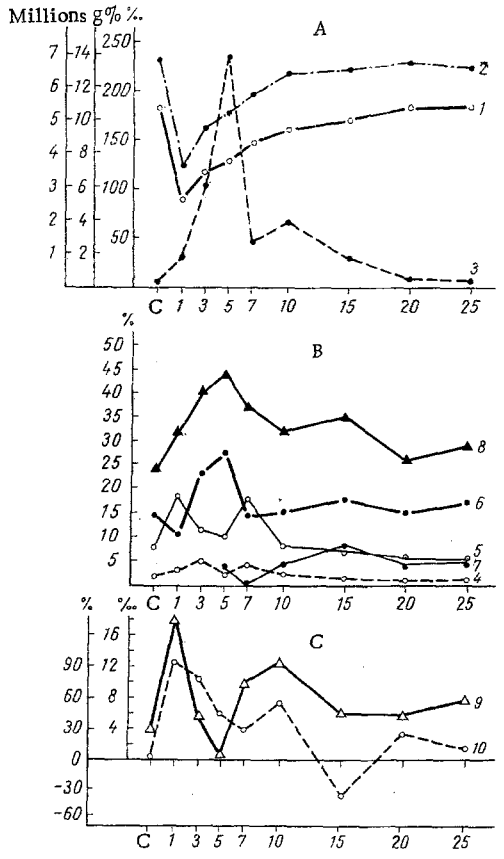

Fig. 1. Dynamics of indices of peripheral blood (A), erythroblastograms (B), and erythropoietic activity (C) in recovery period after hemorrhagic collapse during hyperbaric oxygen therapy. Abscissa, time after bleeding (in days); C) control; 1) erythrocyte count (in millions); 2) Hemoglobin concentration (in g %); 3) reticulocyte count (in ‰); 4) erythroblasts; 5) basophilic normoblasts; 6) polychromatophilic normoblasts; 7) oxyphilic normoblasts; 8) total number of erythroblasts and normoblasts; 9) serum erythropoietic activity (based on increase in reticulocyte count in polycythemic albino rats); 10) serum erythropoietic activity expressed as deviation of stathmokinetic index from control, in % (zero line shows control erythropoietin content).

EXPERIMENTAL RESULTS

The erythrocyte count in the peripheral blood 24 h after bleeding was reduced by 50% ($P < 0.01$), evidence of severe anemia (Fig. 1). On the third day the erythrocyte and hemoglobin levels started to rise ($P < 0.01$) and reached their initial levels by the 15th day after anemization. The reticulocyte count increased 24 h after bleeding ($P < 0.01$) and reached a maximum on the fifth day. This index then gradually returned to normal.

The myelograms showed that during the first three days after blood loss and hyperbaric oxygen therapy the total number of erythroblasts and normoblasts in the hematopoietic tissue increased considerably ($P < 0.01$). The partial erythroblastograms revealed more rapid proliferation of erythroblasts and basophilic normoblasts on the first, third, and seventh days. On the fifth day, polychromatophilic forms greatly predominated ($P < 0.05$). The hyperplastic response of the erythroid cells was biphasic in character: The first phase lasted from the first to the tenth, the second from the 11th to the 20th days after anemization. Strong stimulation of erythropoiesis in the first phase took place on account of increased mitotic activity of the erythroid cells and their precursors, combined with intensification of hemoglobin synthesis. The increase in number of the erythroid cells in the second phase was chiefly on account of polychromatophilic forms.

The intensity of erythropoiesis correlated with the dynamics of activity of the humoral factors controlling it. Tests of the serum on polycythemic and intact animals gave similar results. On the 15th day, when the main parameters of erythropoiesis were back at their initial level, the serum, while preserving the normal level of erythropoietic activity, acquired inhibitory properties (it lowered the stathmokinetic index of erythroblasts and normoblasts in the intact recipients, $P < 0.01$).

As a result of the combined action of two extremal factors (massive blood loss and hyperbaric oxygen therapy), the inhibitory effect of the increased oxygen pressure on erythropoiesis, a regular feature of the intact organism, was thus cancelled out. The beneficial effect of hyperbaric oxygen therapy on cortical metabolism and electrical activity found in analogous experiments [10, 11] suggests normalization of central nervous influences on the functions of the systems responsible for maintaining the oxygen supply to the body and, in particular, erythropoiesis [17]. Increased production of erythropoietin must be regarded as a mechanism of compensation for acute oxygen deficiency. The plasma erythropoietin level is known to depend not only on the intensity of erythropoietin formation, but also on the degree of its utilization by the hematopoietic tissue and also on its destruction and elimination from the body [16]. Intensive erythropoiesis in the bone marrow coupled with the rapid normalization of the erythrocyte and hemoglobin levels in the peripheral blood during the 15 days after massive blood loss proves the efficiency of erythropoietin utilization by hematopoietic tissue. The special character of the dynamics of humoral factors of erythropoiesis can possibly be attributed to excessive erythropoietin in response to massive blood loss, which would terminate in death of all the animals in the course of 1 h in the absence of hyperbaric oxygen therapy.

Considering correlation between the metabolism of hematopoietic tissue and the degree of erythropoietin utilization [2, 3] it can be concluded that hyperbaric oxygen therapy after acute anemization potentiates the stimulation of erythropoiesis induced by erythropoietin.

LITERATURE CITED

1. B. V. Aretinskii, Pat. Fiziol., No. 6, 8 (1956).
2. É. N. Barkova, Byull. Éksperim. Biol. Med., No. 6, 15 (1972).
3. É. N. Barkova and V. A. Makhnev, Éksper. Khir., No. 6, 61 (1973).
4. I. S. Breslav, O. V. Klestova, O. I. Moiseeva, and A. M. Shmeleva, Byull. Éksperim. Biol. Med., No. 3, 39 (1968).
5. V. I. Burakovskii and L. A. Bokeriya in: The Use of Oxygen under Increased Pressure in Medicine [in Russian], Moscow (1971), pp. 28-30.
6. Z. I. Burtseva, in: Hemorrhagic Collapse and Hyperbaric Oxygen Therapy [in Russian], No. 1, Voronezh (1969), p. 73.
7. V. P. Dudarev, Pat. Fiziol., No. 3, 39 (1974).
8. A. G. Zhironkin, Oxygen. Its Physiological and Toxic Action [in Russian], Leningrad (1972).
9. E. A. Ladynina, V. V. Kostyukov, and I. L. Mikhailova, Pat. Fiziol., No. 1, 65 (1974).
10. A. N. Leonov and M. E. Akulenko, Pat. Fiziol., No. 5, 50 (1973).
11. A. N. Leonov, in: Hemorrhagic Collapse and Hyperbaric Oxygen Therapy [in Russian], No. 1, Voronezh (1969), p. 7.
12. B. V. Petrovskii and S. N. Efuni, in: The Use of Oxygen under Increased Pressure in Medicine [in Russian], Moscow (1971), p. 6.
13. Ya. G. Uzhanskii, Physiological Mechanisms of Blood Regeneration [in Russian], Moscow (1968).
14. N. A. Fedorov and M. G. Kakhetelidze, Erythropoietin [in Russian], Moscow (1973), p. 25.
15. B. V. Farber, Klin. Med., No. 1, 46 (1948).
16. V. N. Chernigovskii, S. Yu. Shekhter, and A. Ya. Yaroshevskii, The Regulation of Erythropoiesis [in Russian], Leningrad (1967).
17. V. N. Chernigovskii and A. Ya. Yaroshevskii, Aspects of the Nervous Regulation of the Blood System [in Russian], Moscow (1953).
18. L. O. Jacobson, E. Goldwasser, and C. W. Gurney, in: Ciba Foundation Symposium on Haemopoiesis, London (1960), p. 423.
19. E. B. Thorling and A. J. Erslev, Blood, 31, 332 (1968).
20. C. Vacca, Riv. Med. Aeronaut. Spas., 20, 430 (1966).