ERYTHROPOIETIC PROPERTIES OF PLASMA AND CHANGES

IN THE BLOOD COMPOSITION IN EXPERIMENTAL HYDRONEPHROSIS

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An increase in the erythropoietic activity of the plasma and the development of erythrocytosis were observed in unilateral experimental hydronephrosis. The results indicate that the kidneys play a role in the formation of the erythropoietic properties of the plasma and in the development of erythrocytosis in the experimental animals.

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The connection between some diseases of the kidneys and changes in the blood composition, including erythrocytosis, is now well known [1, 3, 4, 10, 17]. However, the mechanism of this connection remains uncertain.

Considerable attention is now being paid to the study of humoral stimulators of hematopoiesis, the erythropietins (hemopoietins) first discovered by Carnot and Deflandre in 1906 [8]. The most probable place of their formation is the kidney [6, 12, 13, 16]. Accordingly, several investigators [3, 4, 10, 17] have attached great importance to an increased content of erythropoietins excreted by the kidneys in the development of polycythemia. However, data indicating a link between renal erythrocytosis and the erythropoietic activity of the plasma are based mainly on isolated observations.

The development of erythrocytosis and the increase in erythropoietic activity of the plasma after constriction of the renal artery were observed under experimental conditions by Fisher and co-workers [9] and by Kachanova [2].

The object of this investigation was to study the erythropoietic properties of the plasma, the composition of the peripheral blood, the state of medullary hematopoiesis, and their mutual relations in experimental hydronephrosis during which the development of erythrocytosis is observed [15, 18].

EXPERIMENTAL METHOD

Experiments were carried out on 30 male rabbits weighing 2-3 kg. Hydronephrosis was produced by double ligation of the left ureter 2.5-3 cm below the renal pelvis. The operation was carried out under nembutal anesthesia (30-35 mg/kg, intravenously), and 8 rabbits underwent a control laparotomy, under nembutal anesthesia, without ligation of the ureter.

The erythropoietic properties of the plasma were studied 24 h and at various later times (from 56 to 90 days) after production of hydronephrosis. Plasma was obtained from blood taken from the heart. Extracts were made from the plasma by the method of Borsook and co-workers [7]. The erythropoietic properties were studied by calculating the mitotic activity of the bone marrow in a liquid culture by Lajtha's method as modified by Shekhter [5]. The results were assessed by means of the statmokinetic index (the number of mitoses per thousand normoblasts capable of mitotic division).

The composition of the peripheral blood (hemoglobin, erythrocytes, hematocrit) was investigated every 5-6 days.

TABLE 1. Comparison of Mean Hemoglobin Concentration, Erythrocyte Count, and Hematocrit Index in Mice (M±m)

Indices of peripheral blood	Animals investigated		P
	exptl.	control	
Hemoglobin (in g %)	13,0±0,36	11,0±0,33	<0,01
Erythrocyte (in millions/mm³)	5,70±0,18	4,39±0,04	<0,01
Hematocrit index	40±0,7	34±0,7	<0,01

The state of medullary hematopoiesis (number of myelokaryocytes, percentage of normoblasts) was studied in 28 of the 30 rabbits. The bone marrow was obtained by puncture of the femoral epiphysis.

EXPERIMENTAL RESULTS

The plasma in all 11 rabbits 24 h after ligation of the left ureter was erythropoietically active, the activity of 10 of them being high (from +90 to +280 conventional units).

The mean content of erythropoietins in this group of animals was +127±19 units, much higher than in the control group (+50±21 units; P < 0.02).

In the late stages (from 56 to 90 days) after production of unilateral hydronephrosis, the presence of erythropoietins in the plasma was detected in 13 of the 18 rabbits. The mean indices of erythropoietic activity (+123±18 units) also were much higher than in the control group (+66±12 units; P < 0.01).

The erythropoietic properties of the plasma of 9 rabbits were investigated periodically (after 24 h and at various later times after ligation of the ureter). In 4 cases the activity of the plasma was reduced, in 3 it was increased, and in 2 it was essentially unchanged. However, the mean content of erythropoietins was high both 24 h (+132 units) and also at later times (+121 units) after the production of unilateral hydronephrosis.

The hemoglobin concentration, erythrocyte count, and hematocrit index in the animals of the experimental group were higher than in the control group (Table 1).

Erythrocytosis (6 million erythrocytes or more) was present in 8 of the 19 animals (42%), while 2 showed moderate anemia. The erythrocytosis developed 35-65 days after ligation of the ureter.

With respect to medullary hematopoiesis, hyperplasia of the erythroid series (over 30% of normoblasts) was found in 4 of the 16 rabbits, and erythrocytosis was present also in three of them. In the other cases of erythrocytosis, hyperplasia of the erythroid series was absent in the bone marrow.

In most experimental animals (9 of 12) the thickness of the renal parenchyma of the hydronephrotic kidney varied from 3 to 12 mm, and was much less than normal (from 15 to 20 mm). It is interesting to note that in 4 of the 8 rabbits with well developed erythrocytosis, the thickness of the renal parenchyma of the hydronephrotic kidney differed only slightly from normal, varying from 12 to 20 mm. This can evidently be explained by the fact that in three of them a loose ligature was applied to the left ureter, and some drainage of urine took place, so that atrophy of the renal tissue was absent. At the same time, all these animals exhibited the highest erythropoietic activity of the plasma and the highest erythrocytosis in the circulating blood.

These results indicate that the degree of hydronephrotic pressure plays an important role in the development of erythrocytosis, as other workers have previously demonstrated [18].

At the same time, a marked increase in erythropoietic activity of the plasma was observed in animals with unilateral hydronephrosis compared with the controls, both in the early (24 h) and late periods after the operation.

The increase in erythropoietic activity of the plasma was evidently connected with ischemia of the renal tissue, the presence of which has been demonstrated in experimental hydronephrosis by several investigators [11, 14, 18]. In turn, the presence of an increased content of erythropoietins in the plasma was evidently an important factor in the development of the erythrocytosis. It is important to note the regular appearance of these substances in the plasma in the early stages after production of unilateral hydronephrosis. Subsequently, in several cases the plasma erythropoietic activity was observed to diminish, and inhibitory properties actually developed, possibly explaining the transient character of the erythrocytosis or its absence in some cases. High erythropoietic activity of the plasma in experimental hydronephrosis indicates participation of the kidneys in the liberation of erythropoietic substances.

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