COMPARATIVE ANALYSIS OF THE LEUKOCYTE REACTION TO CLINICAL AND EXPERIMENTAL TRANSFUSIONS OF POLYGLUCIN

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We have studied the action of the synthetic blood substitute polyglucin on hemopoiesis from patients' records and from animal experiments.

After transfusions of substances analogous to polyglucin [2, 5, 9] a leukopenic reaction has been observed to develop in the peripheral blood during the first few days. In the accessible literature we found no information concerning changes in the leukocyte count at later periods.

EXPERIMENTAL METHOD

The experimental part of the investigation was conducted on 172 rabbits and 4 dogs. Polyglucin was given intravenously in doses of 20 ml/kg and 2 ml/kg respectively to two groups of animals. The total leukocyte count and the leukocyte formula of the peripheral blood were estimated in the rabbits and dogs after 5, 15, 30, and 120 minutes, and thereafter on alternate days until the 25th day.

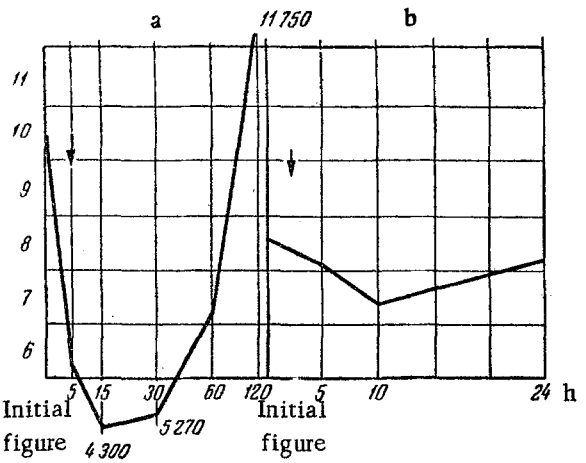

Fig. 1. Leukopenic phase of the leukocyte reaction to polyglucin transfusion. Mean statistical data. a) Experiments on healthy rabbits; b) after giving polyglucin transfusions to patients with malignant disease. —Moment of transfusion. Along the axis of abscissas—time of investigation (in minutes); along the axis of ordinates—number of leukocytes (in thousands).

The clinical material comprised 172 patients with malignant neoplasms, 90 with burns, 74 with osteomyelitis, 40 with peptic ulceration, and 4 with cirrhosis of the liver, who were given polyglucin transfusions. The dose of polyglucin given at each transfusion was 500 ml, and each patient received one transfusion.

For the sake of clarity, the figures showing the composition of the leukocytes in the patients are collected together from the case records to correspond to the times mentioned above for the experimental part of the work.

The numerical data obtained for the leukocyte count and formula were treated mathematically at the Central Mechanical Computer Station of the Central Statistical Directorate of the Council of Ministers of the USSR.

EXPERIMENTAL RESULTS

After receiving intravenous transfusions of polyglucin without compensatory withdrawal of blood, all the animals developed leukopenia irrespective of the dose given. The fall in the leukocyte count of the peripheral blood of the dogs receiving 20 ml/kg of the preparation, and rabbits receiving 2 ml/kg, was observed within a few minutes after transfusion (Fig. 1a).

It may be seen from Fig. 1 that 5 minutes after transfusion the leukocyte count of the rabbits fell by 39.6% ($P^* < 0.001$), and the maximal fall was observed at the 15th minute after transfusion of polyglucin – 54.2% ($P < 0.001$) of the initial leukocyte count. In absolute figures, the number of leukocytes fell on the average from 10,650 to 4,300 in rabbits and from 9,750 to 5,050 in dogs.

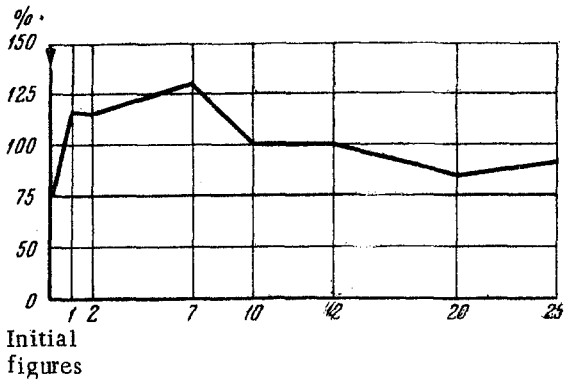

Fig. 2. Leukocyte reaction to the transfusion of polyglucin in rabbits. Mean statistical data. – Moment of transfusion. Along the axis of abscissas – days of investigation; along the axis of ordinates – variation from initial level in %.

The leukopenia was accompanied by definite changes in the leukocyte formula of the peripheral blood: in rabbits the polymorphonuclear forms fell from 31 to 11.5% ($P < 0.05$) after 30 minutes, and in some animals the complete disappearance of stab cells was observed. The number of lymphocytes increased relatively to 77.8% ($P < 0.001$) from the initial figure of 53.9%. The greatest change was seen in the eosinophil count. In all the experiments aneosinophilia developed immediately after the polyglucin transfusion, and it lasted until the end of the observations. The fluctuations in the number of monocytes and basophils followed a parallel course to the changes in the total leukocyte count.

Twenty four hours after transfusion of the preparation, the leukopenia was replaced by leukocytosis.

A similar reaction to polyglucin developed in the human subjects. In the group of cancer patients, 5 minutes after transfusion the number of leukocytes fell by 7% (see Fig. 1b), and after 10 minutes by 15.2% ($P < 0.05$), or in absolute figures from 8,600 to 7,300. The numbers of polynuclears and eosinophils were reduced at the same time. When the patients were investigated 24 hours after transfusion, the leukocyte count corresponded to its original level.

The less marked leukopenia in the patients was evidently associated with the decrease in their general ability to react as a result of the pathological process.

In order to elucidate the mechanism of the development of leukopenia, in special experiments [7] we studied the distribution of the leukocytes in the blood of various parts of the vascular system in rabbits after receiving polyglucin. It was shown that the development of leukopenia in the peripheral blood of these animals took place parallel with an increasing leukocytosis in the blood passing to the liver and lungs. There seems to be no doubt that the leukopenic reaction developing after polyglucin transfusion is brought about by redistribution. This reaction is not specific for the particular blood substitute we have studied; it develops, as many references in the literature show [1, 4, 8], after administration of several other substances, both those closely resembling polyglucin in their chemical structure and those of protein origin.

According to our observations, the leukopenic reaction was accompanied by an increase in the activity of free histamine and of serotonin in the recipients' blood.

*P is the probability of the difference. A probability of not less than 95% ($P < 0.05$) is considered to be statistically significant.

The second phase of the leukocyte reaction to polyglucin transfusion was that of leukocytosis. In the first day the leukocyte count in the peripheral blood of the rabbits rose by 41.2% ($P < 0.01$). The highest leukocytosis, exceeding the initial figure by 51.8% ($P < 0.001$) was observed on the 7th day after transfusion of the preparation (Fig. 2). The increase in the leukocyte count in the first 5 days was accompanied by a considerable lymphocytosis. A slight leukocytosis persisted until the end of the period of observation, i.e., for 25 days.

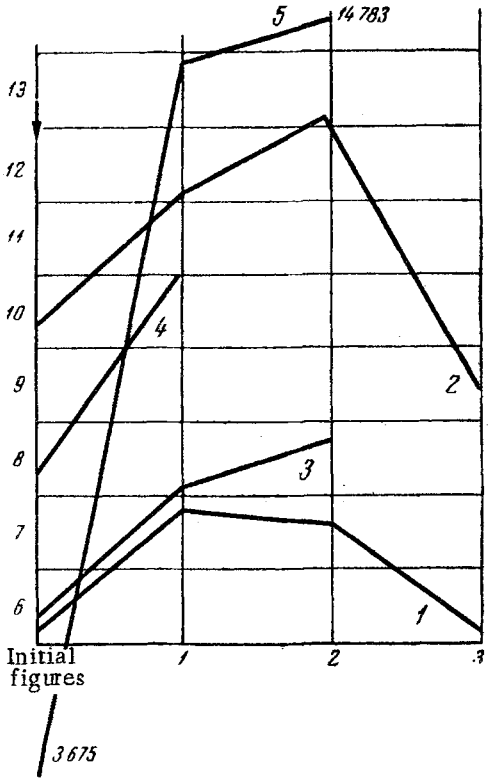

Fig. 3. Leukocyte reaction to polyglucin transfusion in patients with cancer (1), burns (2), peptic ulceration (3), osteomyelities (4), and parenchymatous hepatitis (5). Mean statistical data. —Moment of transfusion. Along the axis of abscissas—time of investigation (in weeks); along the axis of ordinates—number of leukocytes (in thousands).

During the period of greatest development of the leukocytosis, the bone marrow of the animals showed activation of the leukoblastic series, with increased mitotic activity of the cells and accelerated maturation of the granulocytes [6].

It is interesting that all the patients observed, notwithstanding the difference in their diseases, also showed a marked leukocytosis (Fig. 3).

In the patients with malignant neoplasms, the leukocyte count increased during the first week after transfusion by 29.9% (P 0.001), and rose by a further 26.2% above the initial values (P 0.001) during the second week. A persistent leukocytosis of similar degree also developed in the patients with burns, namely, by 17.7% (P 0.05) over the initial level during the first week and by 28.6 % (P 0.001) during the second week. In absolute figures, the corresponding leukocyte counts were 12,000 and 13,200 (Fig. 3).

Patients with peptic ulceration, osteomyelitis, and cirrhosis of the liver were no exception to the general rule so far as the development of a hyperleukocytic reaction to polyglucin transfusion was concerned. In the last mentioned group of patients the leukocyte count increased fourfold (see Fig. 3).

In all the patients the development of leukocytosis was accompanied by regeneratory changes in the leukocyte formula: the number of neutrophils rose and a marked nuclear shift to the left was observed.

A comparative analysis of our results thus shows that the leukocyte reaction to polyglucin transfusion is identical in man and experimental animals, and occurs regularly as two phases. The first phase of the leukocyte reaction is one of leukopenia, which is observed during the hours immediately after transfusion, and which is independent of the volume of polyglucin given. The second phase – leukocytosis – appears 24 hours after polyglucin transfusion and persists for 2 weeks. The differential leukocyte count is characterized in the first phase by a relative lymphocytosis and aneosinophilia; and in the second phase by an increase in the absolute number of neutrophils and a nuclear shift to the left.

SUMMARY

A study was made of the leukocytic response to polyglucine transfusion. Experiments were performed on 176 animals and 380 case-histories were analyzed. A transitory leukopenia occurred soon after the administration of the preparation, alternated later by a stable leukocytosis. Regular leukographic changes were demonstrable in each phase.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
