RETRACTION OF THE BLOOD CLOT AND ITS MODIFICATION BY CERTAIN HEMOSTATIC AGENTS

I. É. Akopov and V. M. Yadrova

UDC 615.771.5-092:612.115

The determination of the retractile properties of the blood clot was first discussed 150 years ago [18], but the physiological role of this phenomenon has not yet been adequately studied. Meanwhile the retraction indices are of great interest to the clinician [16].

Several authors [4,6,17] have suggested that the retraction of the blood clot has no essential influence on hemostasis. Others [1,2,8], however, consider that this process promotes hemostasis.

According to the "physiological ligature" theory of Fonio [15], the blood clot, as it retracts, draws the edges of the blood vessel together like a purse string and narrows its lumen. In this connection it is assumed that to strengthen hemostasis it is more rational to use hemostatic agents which increase retraction of the clot. However, the basis of this theory must be considered as inadequate. Critical remarks have been made by several authors [3,7,10].

Few investigations have been made of the effect of pharmacological substances on the process of clot retraction [9,11,12,13].

The authors have attempted to establish the normal course of retraction of the blood clot and then to examine the influence of various hemostatic agents on this process.

EXPERIMENTAL METHOD

The investigations were carried out with the aid of I. É. Akopov's hemoretractometer [5]. Blood (2 ml) was poured into the ampule of the retractometer. After the blood had clotted, the ampule was placed inside the cylinder. To study the dynamics of retraction, the volume of expressed serum was recorded every 10 min during the first hour, and thereafter at the end of the 2nd, 3rd, and 24th hour.

Experiments were carried out on 120 dogs. Blood was taken from the great saphenous or femoral vein. The following hemostatic agents were studied: infusion of lagochilus (10 dogs), yarrow (15), stinging nettle (8), peppery waterwort (10), a decoction of the bark of the black haw (13), and vikasol (a vitamin K preparation) (6 dogs). The preparations were injected intravenously in doses of 5 ml of a 10% infusion or decoction per kilogram body weight. Vikasol was injected intramuscularly for 6 days in a dose of 0.5 mg/kg daily. Blood was taken for investigation 30, 60, and 120 min after the injection (in the experiments with vikasol after the 6th day of its administration). For control purposes, 10 dogs received an intravenous injection of physiological saline (5 ml/kg body weight).

Besides the experiments on animals, others were carried out in vitro. The preparations were added in a dose of 0.1 ml to 2 ml of blood, which was approximately the same as their possible concentration in the animal's blood. The action of lagochilus (30 experiments), yarrow (20), nettle (23), black haw (20), and physiological saline (26) was studied.

EXPERIMENTAL RESULTS

The retraction index, i.e., the ratio between the volume of serum expressed in 24 h and the initial blood volume, had a mean value in these experiments of 0.49, in agreement with data in the literature [3,4,11]. The fastest rate of retraction was observed in the first hour. For example, the volume of serum expelled in the first 10 mın was 0.8%, in 20 min 6%, in 30 min 15%, in 40 min 26%, in 50 min 36%, and in 60 min 44% of the 24-h volume. The speed of retraction then fell slightly. The volume of serum expelled in 2 h was 70%, and in 3 h 84% of the total volume of serum expressed in 24 h. These results led the authors, like others [9,16], to conclude that the retraction of the clot is largely complete in the first 3 h. Consequently, there is no need to continue observations on retraction

Department of Pharmacology, Red Army Kuban Medical Institute, Krasnodar. (Presented by Active Member of the Academy of Medical Sciences of the USSR V. V. Parin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 62, No. 8, pp. 64-67, August, 1966. Original article submitted December 21, 1964.

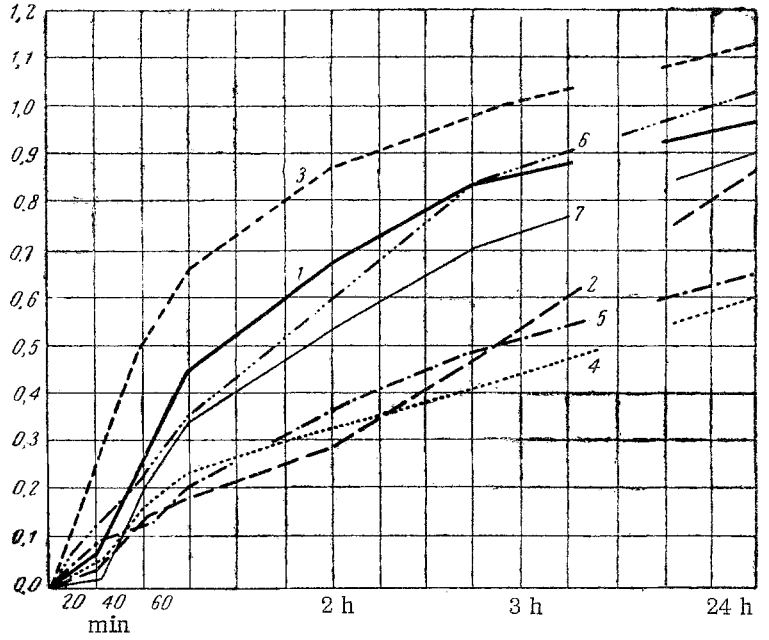

Fig. 1. Changes in retraction of the blood clot for 2 h after injection of hemostatic preparations into animals: 1) normal; 2) lagochilus; 3) yarrow; 4) nettle; 5) peppery waterwort; 6) black haw; 7) vikasol.

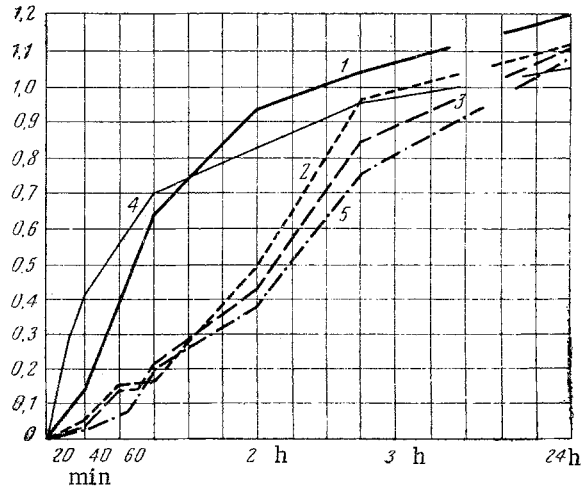

Fig. 2. Changes in retraction of the blood clot under the influence of hemostatic preparations in vitro: 1) lagochilus; 2) nettle; 3) yarrow; 4) black haw; 5) sodium chloride.

for 24 h, as is usually done, more especially because the 24-h test does not reflect the dynamics of the process and the sample used is contaminated by products of fibrinolysis [8].

The most marked changes in retraction under the influence of hemostatic preparations were observed 2 h after injection of the preparations into the animals (Fig. 1).

Infusion of lagochilus reduced by more than 50% the retractile power of the blood clot, especially in the first 2 h of the observations ($P < 0.001$). After 24 h, the difference from normal in the clot retraction was slightly reduced, but the retraction index was still low (0.42). Stronger inhibition still of retraction was produced by the infusions of nettle and peppery waterwort. The retraction index after administration of these preparations was 0.3 and 0.32, respectively ($P < 0.01$). The inhibitory effect of vikasol on the clot retraction was rather less, although still significant ($P < 0.05$), especially in the first 3 h of the observations. The retraction index after administration of vikasol was 0.45.

Unlike the other preparations, infusion of yarrow increased the retractile properties of the clot throughout the period of observation ($P < 0.05$). The retraction index following administration of yarrow was 0.56.

Decoction of black haw bark and physiological saline had no significant effect on the speed or magnitude of the retraction ($P > 0.4$).

Burstein [14], Quick [18], and others consider that clot retraction is an important factor in the development of thromboses and emboli. In Quick's opinion, to prevent venous thrombosis, it is desirable to lower the contractile power of the blood clot. He states that "substances which diminish or slow retraction of the clot could be valuable in the prophylaxis of thrombosis." If this conclusion is correct, the use of hemostatic agents such as lagochilus, peppery waterwort, nettle, or vikasol is best, because by slowing the clot retraction these preparations present a lower risk with respect to the development of thrombosis in the patient.

By comparing the speed of retraction of the blood clot with the speed of clotting of the blood, no regular relationship could be established between these processes. For example, lagochilus, yarrow, and black haw bark almost doubled the speed of clotting of the blood, whereas lagochilus slowed and yarrow stimulated retraction of the blood clot.

The results of the experiments in vitro are given in Fig. 2. Infusion of lagochilus and decoction of black haw, when added directly to the blood, speeded clot retraction twice or three times. This was especially clear in the first 2 h of observation. For example, the volume of serum expressed in 1 h was 53-67%, in 2 h 76-82%, and in 3 h 86-90% of the volume expressed in 24 h. Yarrow and nettle had no effect on the course of retraction in the conditions of the experiments in vitro.

The results of these experiments showed that the character of the influence of hemostatic preparations on the retraction of the blood clot differs if they are injected into animals and if they are added to the blood in vitro. For example, infusion of lagochilus, which slows retraction when injected into animals, clearly accelerated this process when added to blood in experiments in vitro. Infusion of yarrow, on the other hand, which stimulated retraction of the blood clot when injected into animals, had no such action when added directly to blood. The changes in clot retraction following administration of the hemostatic preparations evidently cannot be explained by their direct influence on the blood.

Hence, the process of retraction of the blood clot was largely complete in the first 3 h after coagulation of the blood.

Parenteral administration of hemostatic agents to animals differed in its action on the retractile properties of the blood clot: some inhibited retraction (lagochilus, nettle, peppery waterwort, vikasol), while others stimulated (yarrow), and a third group had no effect on this process (black haw bark).

The addition of hemostatic substances to the blood in the conditions of experiments in vitro may have a different action on the clot retraction from their administration to the living organism.

The processes of retraction of the clot and clotting of the blood do not always proceed along parallel lines.

LITERATURE CITED

1. A. M. Abezgauz, Hemorrhagic Diseases in Children [in Russian], Leningrad (1963), p. 51.
2. N. I. Averina, Abstracts of Proceedings of a Scientific Session of the Kirghiz Medical Institute to Celebrate the Institute's 15th Anniversay [in Russian], Frunze (1954), p. 63.
3. I. É. Akopov, Byull. éksp. biol., 5, 49 (1954).
4. I. É. Akopov, Byull, éksp. biol., 5, 75 (1955).
5. I. É. Akopov, Lab. Delo, 12, 44 (1963).
6. A. A. Bagdasarov, Ch. S. Guseinov, G. A. Chernov, et al., Sov. Med., 4, 17 (1960).
7. N. S. Dzhavadyan, Byull. éksp. biol., 12, 29 (1952).
8. M. A. Kotovshchikova and B. I. Kuznik, Lab. Delo, 5, 6 (1962).
9. N. P. Kochetkova, Klin. Med., 19, 4, 59 (1941).
10. A. A. Markosyan, The Nervous Regulation of Blood Clotting [in Russian], Moscow (1960), p. 127.
11. N. Rozhanskii, Russk. fiziol. Zh., 8, 1-2, 19 (1925).
12. D. L. Rubinshtein and M. P. Petrova, Byull. éksp. biol., 23, 6, 434 (1947).
13. I. A. Troitskii and M. V. Kudryashov, Transactions of the All-Union Institute of Experimental Veterinary Medicine, Vol. 15 [in Russian], Moscow (1940), p. 184.
14. M. Burstein, La coagulation du sang, Paris (1949).
15. A. Fonio, Schweiz. med. Wschr., 51, 146 (1921).
16. J. Jürgens and F. K. Beller, Klinische Methoden der Blutgerinnungsanalyse, Stuttgart (1959), p. 317.
17. A. Quick, Surg. Cynec. Obstet., 91, 226 (1950).
18. C. T. Thackrah, An Enquiry into the Nature and Properties of the Blood as Existent in Health and Disease, London (1819).