EFFECT OF BRADYKININ ON PLATELET AGGREGATION

R. A. Markosyan and A. V. Suvorov

UDC 612.111.7.014.46:577.175.853

The effect of bradykinin on ADP-induced aggregation of blood platelets was investigated in rabbits. Bradykinin reduced the degree of aggregation; maximal inhibition of aggregation was observed with the use of bradykinin in a concentration of 10-100 ng/ml. Higher concentrations of bradykinin were less effective. An essential condition for inhibition was a period of preincubation of bradykinin with the platelets. Inhibition of aggregation by bradykinin also was observed on canine platelets.

KEY WORDS: platelets; aggregation; bradykinin.

Despite a very intensive study of the mechanisms of regulation of the dynamic properties of platelets, such as aggregation, adhesion, viscous metamorphosis, etc. [6, 7], many aspects of this problem still remain unresolved.

The pathways for the supply of energy and the role of cyclic nucleotides [6], activity of thrombosthenin, an analog of smooth muscle protein [5], and intracellular prostaglandins [8] have been discussed as the key components determining the functional properties of platelets.

On the basis of evidence showing the extremely high biological activity of kinins, resulting in dilatation of the smooth muscle of the blood vessel wall and a decrease in the viscosity of blood [1-3], the writers postulated that bradykinin (an active kinin in human and animal blood) may affect the dynamic functions of the platelets, and in the investigation described below the action of bradykinin on aggregation of platelets was accordingly studied.

EXPERIMENTAL METHODS

Platelet-enriched plasma (PEP) obtained from citrated (9:1) rabbit and canine blood, was used. Aggregation of the platelets was determined by the method in [4].

ADP (from Reanal) in a final concentration of 1-10 μM was used to induce aggregation.

Synthetic bradykinin was made available by Doctor of Biological Sciences Professor M. I. Titov, Director of the Laboratory of Peptide Synthesis, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR.

The scheme of the experiments was as follows: control) 800 μl PEP + 20 μl physiological saline + incubation at 37°C with mixing + 40 μl ADP; experiment) 800 μl PEP + 20 μl bradykinin solution + incubation at 37°C with mixing + 40 μl ADP.

EXPERIMENTAL RESULTS AND DISCUSSION

Experiments on PEP from rabbit blood (300,000-360,000 platelets per μl) showed that the degree of aggregation induced by ADP was less in PEP incubated with bradykinin than in PEP incubated with physiological saline. The doses of bradykinin used (final concentration 5 to 10,000 ng/ml PEP) did not cause platelet aggregation.

An essential condition for inhibition of ADP-induced aggregation by bradykinin was a period of preincubation of the PEP with bradykinin (3-15 min); if bradykinin and ADP were added simultaneously to the platelets, the degree of induced aggregation remained unchanged.

Group for the Study of Mechanisms of Thrombosis, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Sciences of the USSR E. I. Chazov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 8, pp. 139-141, August, 1979. Original article submitted February 27, 1978.

 0007-4888/79/8808-0826$07.50

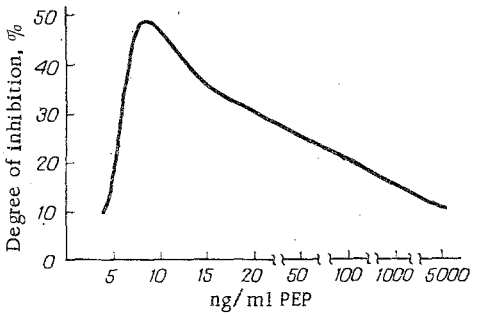

Fig. 1. Degree of inhibition of platelet aggregation plotted against bradykinin concentration. Abscissa, bradykinin concentration in ng/ml PEP; ordinate, degree of inhibition, in %.

The results of the experiments to determine the optimal preincubation time showed that there is no definite fixed period for samples of PEP obtained from different animals. In most experiments the optimal duration of preincubation was 5-10 min.

The results of an experiment to determine the effect of bradykinin concentration on the degree of ADP-induced platelet aggregation are given in Fig. 1. They show that maximal inhibition of aggregation was obtained by bradykinin in a concentration of 10-20 ng/ml . If the dose of bradykinin added was increased, the effectiveness was reduced.

This illustration reflects a general tendency recorded in most experiments (including those to study induction of aggregation by ADP in different concentrations). However, it must be pointed out that the degree of inhibition of platelet aggregation induced by bradykinin varied considerably in experiments on PEP from different rabbits.

The results can be summarized in the conclusion that the greatest effect was observed when bradykinin was added to the sample in concentrations of 10 to 100 ng/ml.

The high variability of the effect of bradykinin (dependence on concentration, preincubation time), in the writers' view, may indicate differences in the functional state of the platelets or variation in kinase activity in the blood of different animals.

The effect of a decrease in the degree of ADP-induced aggregation under the influence of bradykinin also was observed in tests of platelets from canine blood.

It can thus be concluded from the results that bradykinin, the active agent of the kinin system, in physiological concentrations can influence aggregation of platelets.

LITERATURE CITED

1. O. A. Gomazkov, Kardiologiya, No. 7, 130 (1973).
2. A. A. Nekrasova, L. A. Laniberg, and I. M. Kutyrina, Kardiologiya, No. 10, 18 (1973).
3. T. S. Paskhina, in: The Molecular Basis of Pathology [in Russian], Moscow (1966), pp. 123-178.
4. G. V. R. Born, J. Physiol. (London), 162, 67P (1962).
5. J. L. Daniel and R. S. Aldelstein, Biochemistry (Washington), 15, 2370 (1976).
6. P. L. Haslam, in: Biochemistry and Pharmacology of Platelets, Amsterdam (1975), pp. 121-144.
7. E. F. Luscher and P. Massini, in: Biochemistry and Pharmacology of Platelets, Amsterdam (1975), pp. 5-22.
8. J. B. Smith, C. M. Ingerman, and M. S. Silver, in: Biochemistry and Pharmacology of Platelets, Amsterdam (1975), pp. 53-64.