EFFECT OF SENSITIZATION AND ANAPHYLACTIC SHOCK ON THE PLASMA KININ SYSTEM IN GUINEA PIGS

M. S. Surovikina

UDC 616-001.36-056.3-07 : [612.124 : 547.962.4

An increase in the circulating kininogen concentration was found in guinea pigs sensitized with human serum albumin or BCG vaccine. An anaphylactic reaction, subacute in character or manifested as shock with a marked disturbance of respiration, was accompanied by an increase of 1.5-2 times in kallikrein activity and of 6-10 times in plasma kininase activity. The mean decrease in the kininogen concentration was 20-48%, but when the shock followed an acute course it fell by 73-86%. The free kinin concentration was either raised or lowered.

KEY WORDS: anaphylactic shock; kinin system.

The development of many allergic diseases is explained by increased general or local formation of free kinins. It is postulated that bradykinin, together with a slow-acting substance, plays the decisive role in the development of attacks of acute bronchospasm in bronchial asthma. Previous investigations in vitro showed 12-150-fold increase in the sensitivity of the smooth muscles of the isolated tracheo-bronchial chain in guinea pigs sensitized by noninfectious and infectious allergens, to bradykinin.

In the investigation described below the four main components of the kinin system of the blood plasma were studied in vivo during sensitization and anaphylactic shock.

EXPERIMENTAL METHOD

Twelve healthy guinea pigs and 43 guinea pigs sensitized with human serum albumin or BCG vaccine were used. Blood for testing was taken from the heart. The plasma kininogen [1], the concentration of free kinins in the blood [2], the kininase activity and the total kallikrein activity [3] were determined. In the last case, plasma previously activated by heating to 56°C in an acid medium (pH 3.0) and neutralized to pH 7.6 was treated with glass (weight of glass 500 mg, particle diameter 0.3-0.5 mm, shaking for 5 min). In this way the total activity of kallikrein, including the enzyme circulating in the active form, that contained in a complex with the inhibitor, and that existing as kallikreinogen, could be determined.

EXPERIMENTAL RESULTS AND DISCUSSION

The components of the plasma kinin system were determined 3 and 4 weeks after sensitization with human serum albumin in 16 animals, eight of which received a reacting dose of antigen (1-2 mg into the jugular vein). Tests on 27 guinea pigs vaccinated with BCG were carried out 2-5 weeks after injection of the antigen. A reacting dose of the vaccine (200 μg into the jugular vein) was given to 17 guinea pigs. In 40% of the guinea pigs of both groups the anaphylactic reaction was acute and in 60% subacute. Blood was taken 15-45 min after injection of the antigen. The results of analysis of the components of the kinin system in the healthy and sensitized guinea pigs are given in Table 1.

The plasma kinin system in guinea pigs is characterized by a higher kininogen level and by much greater kininase activity than in man or the rabbit. The sensitization process, whether with noninfectious

Department of Clinical Pathophysiology, M. F. Vladimirskii Moscow Regional Clinical Scientific-Research Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 78, No. 8, pp. 48-49, August, 1974. Original article submitted October 22, 1973.

TABLE 1. Components of the Kinin System of Guinea Pig Plasma (M ± m)

Index	Animals				
	control	sensitized with albumin		sensitized with BCG vaccine	
		before injection of reacting dose (8)	after injection of reacting dose (8)	before injection of reacting dose (10)	after injection of reacting dose (17)
Free kinins (in ng/ml blood)	2,8±0,38	2,0±0,50	8,9±1,1† (3) 1,2±0,10 (5)	2,9±0,22	9,2±1,38† (10) 1,3±0,36 (7)
Kallikrein (in μg/ml plasma)	0,95±0,19	0,55±0,10	0,93±0,22*	1,10±0,22	1,77±0,16†
Kininogen (in μg/ml plasma)	7,1±0,95	9,4±1,04*	4,9±1,0*	9,9±1,10*	7,8±0,58*
Kininases (in μg/ml plasma in 1 min)	51,0±3,80	22,3±15,4	518,0±118,0†	155,0±22,1	326,0±44,6

* $P < 0.05$.

† $P < 0.001$.

Note: Number of animals shown in parentheses.

or infectious allergen, was accompanied by an increase in the quantity of circulating kininogen. The development of both an acute and a subacute anaphylactic reaction in the animals of both groups was accompanied by activation of the kinin system, expressed as an increase of 1.5-2 times in the total kallikrein activity, with the result that the kininogen level fell on the average by 20-48%. If the course of the anaphylactic shock was acute, with severe disturbance of respiration, the kininogen concentration fell by 73-86% (from 9.4 μg/ml to 1.5-2.5 μg/ml). The changes were particularly marked in the kinin-splitting enzymes, the activity of which increased sharply. The concentration of free kinins in the blood changed variously: in some experiments there was a threefold increase in the level of these peptides, in others their concentration fell by 33-50%. The activity of the plasma kinases was evidently the factor that determined the concentration of free kinins during the anaphylactic reaction. Its excessive activity could mask the process of increased kinin formation or could even outweigh it. The results are evidence of changes in the functional state of the kinin system of the body accompanying sensitization and anaphylactic shock.

LITERATURE CITED

1. T. P. Egorova and T. S. Paskhina, Biokhimiya, 32, 354 (1967).
2. M. S. Surovikina, Byull. Éksperim. Biol. i Med., No. 5, 123 (1971).
3. M. S. Surovikina, Kardiologiya, No. 2, 119, (1973).