EFFECT OF THE SALIVARY GLANDS ON INTENSITY OF KININ PRODUCTION IN BLOOD PLASMA

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Kinins are formed in the body as a product of the functioning of the kallikrein–kinin system (KKS) of the blood and tissues, the activity of which is determined by the intensity of kinin formation [1, 3, 6, 7]. Administration of kallikrein preparations obtained from the digestive glands gives rise to marked activation of the KKS of blood plasma [8]. This enzyme is present in large quantities in the digestive glands [10]. The salivary glands, in which kallikrein is present in the active form [9], are particularly interesting.

The object of this investigation was to study the state of the blood KKS in rats after removal of the parotid and submandibular glands.

EXPERIMENTAL METHODS

Experiments were carried out on 210 noninbred male albino rats weighing 80-120 g. The control group consisted of 24 of these animals, the parotid glands were removed from 90 rats, and the submandibular glands from 92. The level of activity of the blood KKS in the rats was investigated 7, 14, 21, 28, and 35 days after removal of the salivary glands. Control rats were tested at the same time as the experimental animals. The level of activity of the blood KKS was estimated as the plasma concentrations of kininogen [4], prekallikrein [2], and activity of kallikrein [5] and its inhibitors [2]. Active plasma kinins were investigated in a separate series of experiments at the same times after removal of the glands [5]. Blood

TABLE 1. Time Course of Components of Blood KKS after Removal of Parotid Salivary Gland in Rats (M ± m)

Time, days	Components of KKS			
	kallikrein, μg/ml plasma	kininogen, μg/ml plasma	prekallikrein, μmoles/ml·h BAEE	kallikrein inhibitos, units
7	1,03±0,15	4,71±0,49	212,75±7,36	1,33±0,70
	(*n* = 8)	(*n* = 7)	(*n* = 7)	(*n* = 8)
P	<0,001	<0,001	<0,001	>0,5
14	1,35±0,24	6,68±0,46	244,48±26,40	1,47±0,04
	(*n* = 7)	(*n* = 9)	(*n* = 9)	(*n* = 9)
P	<0,001	<0,001	<0,01	<0,05
21	0,12±0,04	1,90±0,24	137,25±14,63	1,06±0,04
	(*n* = 8)	(*n* = 7)	(*n* = 7)	(*n* = 8)
P	<0,001	<0,01	>0,5	<0,05
28	0,47±0,10	3,53±0,28	142,85±16,53	1,32±0,01
	(*n* = 7)	(*n* = 7)	(*n* = 7)	(*n* = 7)
P	>0,5	<0,5	>0,5	<0,5
35	3,14±0,29	5,27±1,67	149,25±0,83	1,34±0,11
	(*n* = 6)	(*n* = 6)	(*n* = 6)	(*n* = 6)
P	<0,001	<0,05	<0,5	>0,5
Control	0,39±0,03	2,97±0,18	140,22±5,79	1,31±0,06
	(*n* = 12)	(*n* = 12)	(*n* = 12)	(*n* = 12)

Legend. Here and in Table 2: P) significance of differences compared with control, BAEE) N-benzoyl-L-arginine ethyl ester hydrochloride.

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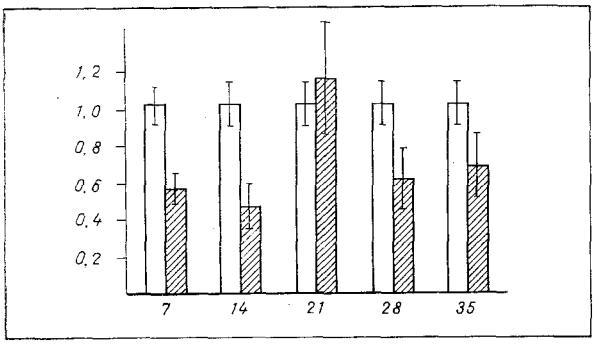

Fig. 1

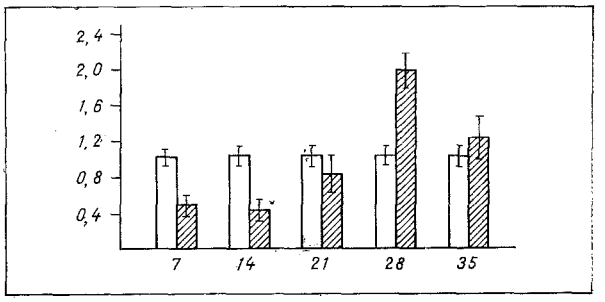

Fig. 2

Fig. 1. Dynamics of active blood plasma kinins after removal of parotid salivary glands in rats. Unshaded columns — control, shaded — experiment. Abscissa) time after operation (in days); ordinate) bradykinin concentration (in ng/ml).

Fig. 2. Dynamics of active blood plasma kinins after removal of submandibular salivary glands in rats. Legend as to Fig. 1.

for testing was taken from the inferior vena cava. The numerical results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Removal of the parotid salivary glands caused significant changes in activity of the blood plasma KKS (Table 1).

On the 7th and 14th days the prekallikrein concentration increased significantly by 51.4% ($P < 0.001$) and 74.2% ($P < 0.01$). The kininogen concentration showed significant changes, being increased significantly on the 7th day and by 125.2% on the 14th day ($P < 0.001$). Increased activity of kallikrein inhibitors also was observed on the 14th day.

Accumulation of prekallikrein in the plasma and an increase in activity of the kallikrein inhibitors reflected a decrease in the intensity of kinin formation in the blood plasma on the 7th and 14th days after removal of the parotid salivary glands. This is confirmed by a fall in the level of active kinins in the blood. For instance, on the 7th day after the operation the concentration of active kinins in the plasma was 45.4% below the control ($P < 0.05$) and 53.9% lower on the 14th day ($P < 0.01$; Fig. 1). The increase in total kallikrein activity observed under these circumstances was evidently due to an increase in the content of prekallikrein, which makes an important contribution to total kallikrein activity [5]. On the 21st day the levels of all components of the KKS fell below those for the preceding period

TABLE 2. Time Course of Components of Blood KKS after Removal of Submandibilar Salivary Gland in Rats (M ± m)

Time, days	Components of KKS			
	kallikrein, μg/ml plasma	kininogen, μg/ml plasma	prekallikrein, μmoles/ml·h BAEE	kallikrein inhibitors, units
7	1,02±0,17	3,30±0,35	139,60±26,70	1,16±0,07
	($n = 8$)	($n = 8$)	($n = 8$)	($n = 8$)
P	<0,01	<0,5	>0,5	<0,5
14	1,55±0,12	4,11±0,54	161,20±11,30	1,17±0,13
	($n = 6$)	($n = 6$)	($n = 6$)	($n = 6$)
P	<0,001	<0,05	<0,05	<0,5
21	0,47±0,16	4,91±0,56	165,10±8,29	1,79±0,06
	($n = 8$)	($n = 7$)	($n = 7$)	($n = 8$)
P	<0,05	<0,01	<0,05	<0,001
28	0,39±0,04	3,19±0,33	155,20±10,20	1,42±0,14
	($n = 7$)	($n = 7$)	($n = 7$)	($n = 7$)
P	>0,5	>0,5	<0,5	>0,5
35	2,12±0,34	7,90±0,35	158,50±12,80	1,44±0,11
	($n = 6$)	($n = 6$)	($n = 6$)	($n = 6$)
P	<0,001	<0,01	<0,5	>0,5
Control	0,39±0,03	2,97±0,18	140,22±5,79	1,37±0,06
	($n = 12$)	($n = 12$)	($n = 12$)	($n = 12$)

with the exception of the active kinins. The prekallikrein concentration fell under these circumstances to the control values, whereas activity of kallikrein and its inhibitors and the kininogen level were lower than in intact animals. These changes in the components of the KKS were accompanied by normalization of the active kinin concentration in the blood plasma.

In the next period of the investigation a second wave of an increase in the concentrations of these components of the KKS was observed, so that their values exceeded the controls on the 29th day and kallikrein activity and the kininogen concentration were significantly increased by the 35th day. These changes, like those observed on the 7th-14th day, were accompanied by a fall in the active kinin level.

Investigation of the state of the blood plasma KKS in the animals after removal of the submandibular salivary glands revealed changes in its activity similar to those found after removal of the parotid glands. For instance, on the 14th day after operation an increase in the prekallikrein and kininogen concentrations was observed in the animals (Table 2), reflecting a decrease in the intensity of formation of active kinins, the concentration of which was below the control as early as on the 7th day after the operation (Fig. 2); on the 14th day it was down to 0.33 ± 0.13 ng/ml, which was 64.6% below the control level (1.02 ± 0.11 ng/ml; $P < 0.001$).

At subsequent times of the investigation the concentrations of active kinins in the blood rose to the control level, on the 28th day they were 2.1 times higher than the control, and on the 35th day they had returned to their basal level.

Removal of the large salivary glands in animals was thus accompanied by significant changes in the rate of kinin formation in the blood plasma.

These experiments suggest that the salivary glands and their endocrine function, especially the production of biologically active substances and, in particular, of kallikrein, play an essential role in maintaining the functional state of the blood plasma KKS.

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