SEROTONIN AND 5-HYDROXYINDOLEACETATE IN ACUTE RENAL ISCHEMIA

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Similar changes in the serotonin level were found in the ischemic and contralateral kidneys of rabbits during the development of acute renal ischemia (up to 24 h). The serotonin concentration in the tissues studied fell during the first 15 min of ischemia and then showed a tendency to rise, to reach a maximum in the ischemic kidney after 60 min and in the contralateral kidney after 3 h of ischemia. Later the serotonin concentration in the tissues fell again, more especially in the ischemic kidney. The blood serotonin level rose a little after ischemia for 60 min. The increase in the 5-hydroxyindoleacetate concentration in the urine coincided in time with a period of decrease in the tissue serotonin concentration.

KEY WORDS: serotonin; 5-hydroxyindoleacetate; acute renal ischema.

Biogenic amines [2, 4, 13, 15], especially serotonin, which has a marked effect on intracellular processes [1, 3, 11], may play an important role in the pathogenesis of metabolic disturbances in tissues deprived of their blood supply.

This paper describes the results of an investigation of serotonin metabolism in acute renal ischemia.

EXPERIMENTAL METHOD

The left renal artery was ligated in dogs for various times (15 min to 24 h). The serotonin concentration was determined in the ischemic and contralateral kidneys and in the blood [5]. The concentration of the end product of serotonin metabolism, 5-hydroxyindoleacetate (5-HIA), in the urine was determined by a method based on the reaction with nitrosonaphthol [17], in the writers' micromodification, by means of which this metabolite can be determined in 1.2 ml urine. Total protein (by Lowry's method) also was determined. For each period of ischemia, animals undergoing laparotomy under general anesthesia were used as the control. Five control and 5 experimental rabbits were investigated at each time.

EXPERIMENTAL RESULTS AND DISCUSSION

The results given in Table 1 show that the serotonin level in both kidneys fell during the first 15 min of ischemia to 76.5% in the ischemic kidney and 61.1% in the contralateral kidney of the control values. This could be a compensatory factor when the blood supply to the tissues was disturbed, for serotonin can uncouple oxidative phosphorylation [8, 9]. A tendency later was observed for the serotonin concentration in the kidneys of the experimental animals to rise. The maximum increase in the serotonin level in the ischemic kidney was observed after 60 min, and in the contralateral kidney after 3 h of ischemia. This was evidently due to the liberation of serotonin from intracellular complexes under the influence of stress [6]. The greater accumulation of serotonin in the ischemic kidney after 30 and 60 min of ischemia was possibly the result of reduced ability of the platelets to take up serotonin under anaerobic conditions [14]. Later the serotonin level in the kidneys fell, more especially in the ischemic kidney.

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TABLE 1. Serotonin Concentration in Kidney Tissues (in μg/g) and Blood (in μg/ml) and 5-Hydroxyindoleacetate Concentration in Urine (in μg/ml) of Rabbits (M ± m)

Periods of ischemia (in h)	Serotonin concentration				
	ischemic kidney			contralateral kidney	
	control	expt.	P	expt.	P
1/4	157,7±3,7	119,9±6,8	0,002	95,8±5,2	0,001
1/2	52,6±4,5	95,1±3,0	0,001	80,3±2,9	0,001
3/4	61,0±1,3	41,6±1,5	0,001	71,6±1,1	0,001
1	69,6±1,4	175,8±1,8	0,001	110,8±6,8	0,001
3	130,0±3,9	121,7±2,0	0,001	290,5±2,8	0,001
6	152,2±3,8	84,3±3,0	0,001	204,2±6,3	0,001
18	168,1±1,4	58,2±0,6	0,001	171,5±4,4	0,05
24	169,8±3,6	44,8±3,6	0,001	142,5±1,4	0,001

Table 1 (continued)

Periods of ischemia (in h)	Serotonin concentration			Concentration of 5-HIA in urine	
	blood				
	control	expt.	P	control	expt.
1/4	4,7±0,5	4,6±0,4	0,5	—	—
1/2	3,1±0,7	2,1±0,6	0,2	—	—
3/4	3,0±0,6	2,1±0,3	0,02	—	—
1	2,9±0,4	3,3±0,3	0,02	6,5±0,7	5,1±0,4
3	4,1±0,4	3,4±0,5	0,5	5,9±0,6	7,9±0,6
6	4,3±0,6	3,8±0,5	0,5	5,9±0,3	9,2±0,6
18	5,0±0,6	4,6±0,7	0,5	5,5±0,2	9,9±0,4
24	4,7±0,7	4,7±0,2	0,5	6,0±0,2	6,3±0,3

The importance of serotonin in the development of adaptation to ischemia may be attributed to its ability to accelerate metabolic processes in vivo [3, 12, 16] and also its ability to participate in the mechanism of the postaggressive liberation of catecholamines from the adrenals [10, 11].

The small increase in the serotonin concentration in the blood after ischemia for 60 min coincided in time with the onset of the so-called "critical period" [7] in the ischemic kidney, as a result of the development of irreversible changes in the tissue. Liberation of serotonin in the blood stream may also take place from other organs, especially the intestine, in response to the accumulation of toxic factors in the blood. The subsequent fall in the blood serotonin level correlated with a decrease in its concentration in the tissues studied and could be connected with stimulation of its metabolism in the liver, kidneys, and certain other structures. This is shown by the increase in 5-HIA in the urine, which began after 3 h of ischemia and reached a maximum after 18 h. Toward the end of the experiment 5-HIA level was almost back to the control figures.

It is interesting to note that changes in the serotonin concentration in the ischemic and contralateral kidneys were in the same direction. This may due to changes in the general hemodynamics in the postaggressive period, when vasoconstriction develops [16, 17].

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