EFFECT OF HYDROCORTISONE AND BUTADIONE ON DISTRIBUTION OF KANAMYCIN IN EXPERIMENTAL PLEURISY

Yu. S. Grosman, L. B. Gel'dner, A. A. Bykova, and É. A. Ortenberg

UDC 615.332(Canamycinum).033:616.25-002-092.9:[615.357.453-615.212.3

In rabbits with aseptic pleurisy, hydrocortisone lowers the concentration of intravenously injected kanamycin in the blood, pleural exudate, and lung tissues. Butadione increases its concentration by delaying the excretion of kanamycin with the urine.

The use of a combination of antiinflammatory and antituberculous drugs in the treatment of pulmonary tuberculosis [1-4] requires an explanation of the character of the effect of the antiinflammatory drug on the blood and tissue levels of the chemotherapeutic substance.

An investigation was therefore undertaken to determine changes in the concentration of kanamycin in the blood, lung tissues, and pleural exudate of animals with experimental pleurisy following its combined administration with hydrocortisone and butadione.

EXPERIMENTAL METHOD

Experimental pleurisy with effusion was produced in rabbits of both sexes, weighing 2.5-3.5 kg, by injecting 2 ml of 1% zinc sulfate solution into the right pleural cavity. During the next 24 h the experimental

TABLE 1. Kanamycin Concentration in Blood (in mg/ml), Pleural Exudate (in μg/g) (M ± m)

Group of animals	Time after administration			
	30 min		60 min	
	blood	exudate	blood	exudate
Control (n = 6)	210,0±23,0	58,2±6,1	94,5±5,7	88,5±6,8
Receiving hydrocortisone (n = 6)	143,5±12,9	91,0±10,5	65,5±6,6	85,3±4,7
P	<0,05	<0,05	<0,05	>0,05
Receiving butadione (n = 6)	210,2±11,3	49,5±5,4	134,0±7,2	86,9±12,8
P	>0,05	>0,05	<0,01	>0,05

Group of animals	Time after administration			
	120 min			
	blood	exudate	right lung	left lung
Control (n = 6)	43,5±9,3	85,0±4,0	25,4±3,2	17,4±5,9
Receiving hydrocortisone (n = 6)	13,4±6,5	50,0±7,3	15,0±2,8	7,4±1,7
P	<0,05	<0,01	<0,05	>0,05
Receiving butadione (n = 6)	103,4±20,1	116,1±8,4	29,4±4,2	19,2±4,5
P	<0,05	<0,05	>0,05	>0,05

Note. P given in comparison with control.

Department of Pharmacology and Central Research Laboratory, Perm' Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 70, No. 12, pp. 54-56, December, 1970. Original article submitted June 26, 1970.

TABLE 2. Excretion of Kanamycin in the Urine (M ± m)

Group of animals	Diuresis (in ml)	Kanamycin (in % of administered dose)
Control	9,3±1,8	39,9±2,1
Receiving hydrocortisone	16,3±2,9	44,7±5,1
P	>0,05	>0,5
Receiving butadione	7,4±2,0	23,4±4,9
P	>0,5	<0,05

animals received three doses of hydrocortisone (5 mg/kg, intramuscularly) or butadione (60 mg/kg, by mouth), after which the urine of the control and experimental animals was collected through a catheter and kanamycin sulfate (50 mg/kg) was injected intravenously. Samples of blood and pleural exudate were taken after 30, 60, and 120 min, after which the animals were killed, the lungs removed and homogenized, and the urine voided during the experiment was collected.

The kanamycin concentration in the samples of blood and exudate, in the lung tissue homogenate, and in the urine was determined by the agar-diffusion method (test organism Staphylococcus aureus 209-p).

EXPERIMENTAL RESULTS

The concentration of kanamycin in the pleural exudate of the control animals 30 min after administration of the antibiotic (Table 1) averaged 28% of its blood level. Later the blood kanamycin concentration fell while that in the exudate rose. As a result, after 2 h the kanamycin concentration in the exudate was twice that in the blood.

Throughout the experiment the blood kanamycin level in the rabbits receiving hydrocortisone was lowered by a statistically significant degree.

The same effect of glucocorticoids has also been observed in relation to penicillin, tetracycline [5] and monomycin [6].

The kanamycin concentration in the exudate 30 min after administration together with hydrocortisone was considerably higher than in the control, namely 63.5% of the blood level. By the end of the experiment, however, the kanamycin concentration in the exudate, just as in the lung tissue, of the experimental animals was lower than in the control.

In the rabbits receiving butadione, the blood level of kanamycin was higher than in the controls, and by the end of the investigation this difference had increased. By the end of the experiment the kanamycin concentration in the exudate also was higher than in the control, while no significant difference could be found in the kanamycin concentration in the lung tissues of the experimental and control animals. Elimination of kanamycin with the urine (Table 2) was unchanged by hydrocortisone, but it was definitely retarded by butadione.

In neither case were any significant changes observed in the diuresis.

These results demonstrate that a raised kanamycin concentration in the blood and pleural exudate following its combined administration with butadione is due to delay of its excretion in the urine (the retarding effect of butadione).

The disappearance of kanamycin from the blood and pleural exudate under the influence of hydrocortisone is probably attributable to extrarenal factors requiring special investigation.

LITERATURE CITED

1. I. I. Goncharik, Zdravookhr. Belorussii, No. 4, 22 (1968).
2. I. M. Grinval'd, Sov. Med., No. 11, 137 (1963).
3. A. V. Grishin and É. Ya. Rotenberg, in: Problems in Tuberculosis [in Russian], No. 7 (1967), p. 235.
4. V. A. Zhuravleva, Kazansk. Med. Zh., No. 1, 83 (1964).
5. B. F. Kadyrov, Antibiotiki, No. 12, 1096 (1963).
6. V. A. Shorin and B. F. Kadyrov, Med. Zh. Uzbekistana, No. 4, 29 (1966).