

EXPERIMENTAL STUDY OF THE EFFECT OF NEOMYCIN
ON THE COCHLEAR CIRCULATION

B. S. Ivanov

UDC 615.332(Neomycinum).015.4.[612.858.4.612.13

Acute experiments were carried out on anesthetized cats to study the cochlear circulation after intravenous injection of neomycin solution (10,000-15,000 units/kg body weight). The response of the vascular system was recorded by rheocochleography. Features indicating an increase in the blood volume of the cochlear system and interference with the drainage of blood from it were recorded for a considerable time. The systemic arterial pressure showed only slight and transient changes, so that the hemodynamic changes observed in the cochlea must be attributed to the action of neomycin on the vascular system of this organ.

Antibiotics of the neomycin group have a broad spectrum of antimicrobial action but their use is limited by their toxic manifestations. It is reported in the literature that neuritis of the auditory nerves, amounting in some cases to their degeneration, may develop during treatment by these substances [1, 2, 6].

A number of investigations have been made of the ototoxicity of antibiotics on the neomycin group [3, 4] with the discovery of inhibition of auditory function, histological changes in various parts of the auditory system, and an increased concentration of the antibiotic in the lymph of the ear.

The mechanism of action of neomycin on the organ of hearing has not yet been finally established. The causes of the increased concentration of the antibiotic in the liquid media of the labyrinth have not been determined. No information is available on the effect of the antibiotic on the cochlear vascular system.

Acute experiments were carried out to study the cochlear circulation in 13 cats weighing from 2.5 to 4 kg under chloralose (0.04 g/kg) and urethane (0.6 g/kg) anesthesia and artificial respiration. The method of rheocochleography was used to record the effect [5].

EXPERIMENTAL METHOD

Neomycin solution was injected intravenously into the animals in a dose of 10,000-15,000 units/kg body weight. This dose of the antibiotic at a single injection was chosen because it is close to the therapeutic dose, in agreement with the latest data in the literature [4].

The rheocochleograms (RCG) were recorded by means of the RG-1-01 rheographic attachment and a type ÉÉChS-1 two-channel electroencephalograph, the second channel of which recorded the ECG (standard lead II). The arterial pressure was recorded simultaneously in the common carotid artery by a mercury manometer. The RCG was recorded before and 1 min after the injection of neomycin and every 5 min thereafter. The total duration of the investigation was from 60 min to 2.5 h. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

In response to intravenous injection of neomycin an increase was observed in the amplitude of the rheographic wave on the average by 49% ($P < 0.001$) not later than the 5th minute. In five experiments this

E.N.T. Clinic, Semipalatinsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. F. Tur.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 1, pp. 63-65, January, 1973. Original article submitted August 3, 1971.

© 1973 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.

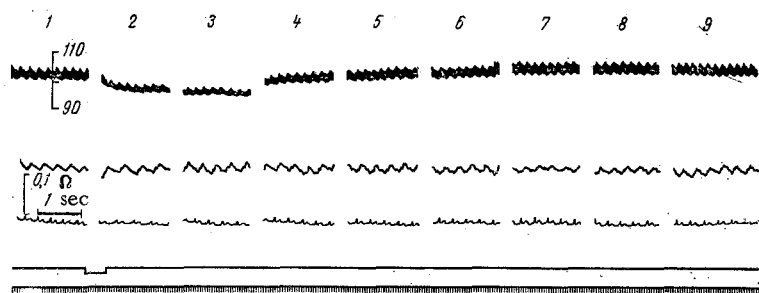


Fig. 1. Dynamics of changes in rheocochleogram and systemic arterial pressure after intravenous injection of neomycin into a cat. From top to bottom: systemic arterial pressure, rheocochleogram, ECG in standard lead II, marker of injection of neomycin, time marker. 1) initial data (before injection of neomycin); 2-9) 1, 5, 10, 15, 20, 30, 40, and 60 min respectively after injection of neomycin.

TABLE 1. Mean Data for Arterial Pressure and RCG Indices in Percentages of Initial Level With Standard Error of the Means

Number of experiments	Systemic arterial pressure	RCG index				Rheographic index
		<i>H</i>	α	β	<i>T</i>	
13 <i>P</i>	$-18 \pm 0.8\%$ <0.001	$+49 \pm 0.6\%$ <0.001	$-5 \pm 3.7\%$ >0.05	$+14 \pm 6.1\%$ 0.03	$+13 \pm 3.5\%$ 0.001	$+66 \pm 11.3\%$ <0.001

increase was 25-33%, in four experiments 50-66%, and in two experiments 100-128%. In one case a bi-phasic response was recorded (the amplitude first increased by 25% and then fell by 50%) and in one case the animal died 20 min after injection of the antibiotic.

Only twice (60th and 70th minutes) did the amplitude reach its initial level. In the other cases (nine of thirteen) the increase in this index was observed for a period of 1 h or longer. The maximal effect was recorded at the 5th minute (eight experiments) and at the 15th-30th minute (four experiments). In four experiments there was a brief (1-3 min) period of spasm of the cochlear vessels immediately after the injection of neomycin.

The increase in amplitude of the rheographic wave is primarily an index of the blood filling of the cochlear vessels. The intensity of the blood filling in this region was also characterized by the rheographic index which increased, as the measurement showed, on the average by 66%.

The anacrotic phase of the rheographic wave increased only slightly (difference not statistically significant). In nine cases this phase showed no change, in three it increased by 26-33%, and in one it fell by 28%. These indices, accompanied by a marked increase in the amplitude of the wave, reflect the high degree of elasticity of the cochlear vessels.

The catacrotic phase showed more substantial changes: it increased on the average by 14% ($P=0.03$), indicating interference with the outflow of blood from the region studied [7]. Other features confirmed this conclusion: in six cases the apex of the rheogram was rounded (in half of them into a "plateau"), in three cases a dicrotic wave appeared and moved toward the apex as the recording progressed; in five experiments a venous wave appeared on the RCG. Whereas, as was mentioned above, in some cases there was a gradual decrease in the amplitude of the rheographic wave to or very close to the initial values, the changes in the RCG characterizing the obstructed outflow of blood were stable and prolonged (over 2.5 h) everywhere. This observation agrees with results obtained by other workers [8, 9], who found that antibiotics of the neomycin group accumulate in the inner ear because of interference with their elimination.

The duration of the rheographic wave increased moderately, on the average by 13% ($P=0.001$). In three cases it increased by 7-10%, in five cases by 14-16%, and in the rest by between 28 and 33%. The waves were regular in character (Fig. 1).

The systemic arterial pressure is an important factor determining the intensity of the circulation in the inner ear. In the present experiments it fell very slightly at the 1st-2nd minute after injection of the neomycin and returned to its initial level at the 10th-12th minute. It can accordingly be postulated that the hemodynamic changes observed in these experiments were the result of the action of neomycin on the cochlear vascular system.

The results of these tests are given in Table 1.

It can be concluded from the results of these experiments that neomycin, if injected parenterally, lowers the tone and increases the blood filling of the cochlear vessels for a long time.

The outflow of blood from the cochlea is obstructed and this may evidently account for the high concentration of the antibiotic in its liquid media.

LITERATURE CITED

1. E. A. Govorovich, *Klin. Med.*, No. 9, 28 (1963).
2. A. E. Luts, in: *Proceedings of the Third Inter-republican Conference of Otorhinolaryngologists of Latvia, Lithuania, and Estonia* [in Russian], Riga (1969), p. 62.
3. V. S. Muraveiskaya, *Disturbance of Hearing and Histological Changes in the Organ of Corti of Guinea Pigs after Administration of Antibiotics of the Neomycin Group and Monomycin*. Author's Abstract of Candidate's Dissertation, Moscow (1964).
4. M. S. Pluzhnikov and T. I. Teplitskaya, *Vestn. Otorinolar.*, No. 1, 52 (1971).
5. V. A. Romanov, *Byull. Ékserpim. Biol. i Med.*, No. 3, 120 (1971).
6. V. A. Shorin, *Complications Produced by Antibiotics* [in Russian], Moscow (1958).
7. Kh. Kh. Yarullin, *Clinical Rheoencephalography* [in Russian], Leningrad (1967).
8. J.-P. Brun, H. Stupp, F. Lagler, et al., *Arch. Klin. Exp. Ohr. Nas. Kehl. Heilk.*, 196, 177 (1970).
9. H. F. Stupp, *Acta Oto-Laryng. (Stockholm)*, 78, 269 (1970).