PHARMACOLOGY

EFFECT OF METAMIZIL* ON CENTROGENIC CARDIAC ARRHYTHMIAS

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UDC 615.787-06 : 616.12-008.318

Metamizil (0.02-0.07 mg/kg) prevented the development of cardiac arrhythmias during electrical stimulation of the medullopontine division of the brain stem.

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The object of this investigation was to study the effectiveness of the central muscarine-like cholinolytic metamizil [1, 5] in neurogenic cardiac arrhythmias.

EXPERIMENTAL METHOD

Experiments were carried out on 16 cats anesthetized with urethane (1.1-1.2 g/kg intraperitoneally). After removal of the cerebellum access was gained to the floor of the fourth ventricle. By local stimulation (unipolar insulated electrode 30-50 μ in diameter) of the medullopontine division of the brain stem various types of cardiac arrhythmias were produced. The parameters of stimulation were as follows: 1-5 V, 60 cps, 1 msec. The localization of the stimulation was verified histologically at the end of the experiment. The method was described more fully earlier [2-4].

EXPERIMENTAL RESULTS

Most easily of all, metamizil (0.02-0.04 mg/kg) abolished the sinus bradyarrhythmia arising during stimulation of the dorsal nucleus of the vagus and the gigantocellular reticular nucleus. The sinus bradyarrhythmias developing during stimulation of the parvocellular reticular nucleus were more resistant to metamizil (0.05-0.07 mg/kg). Ventricular extrasystoles against a background of slowing of the rhythm in response to activation of neurons of the nuclei (parvocellular reticular and medial vestibular) lying next to the dorsal nucleus of the vagus were also prevented by small doses (0.03 mg/kg) of metamizil. Different forms of atrioventricular rhythm (upper, mid-, and lower nodal) were abolished by metamizil in unequal doses (0.02-0.07 mg/kg). The neurons of the dorsal nucleus of the vagus were most sensitive to metamizil (Fig. 1). In a small dose (0.02 mg/kg), metamizil prevented the development of atrioventricular rhythm, and abolished the depressor reaction or converted it into pressor. Higher doses (0.05-0.07 mg/kg) of metamizil were needed to abolish the excitability of the structures of the parvocellular reticular nucleus, stimulation of which gave rise to a mid-nodal atrioventricular rhythm (Fig. 2,1). Fractional administration of gradually increasing doses of metamizil up to a total dose of 0.07 mg/kg prevented the development of cardiac arrhythmias (Fig. 2, 3) but had no effect on the pressor vascular reaction.

The sinus bradyarrhythmias arising during stimulation of the peripheral end of the divided vagus nerve (as our observations showed) was blocked by metamizil in a dose of 0.1 mg/kg. Consequently, the transmission of nervous impulses between individual cholinergic neurons of the medullopontine division of the brain stem is blocked by smaller doses of metamizil.

The pressor vascular reactions accompanying disturbances of the cardiac rhythm and arising during activation of various morphological formations in the bulbar division of the brain stem were not suppressed

* 2-Diethylamino-1-methylethyl ester of benzylic acid (hydrochloride).

Department of Pharmacology, I. P. Pavlov First Leningrad Medical Institute (Presented by Active Member of the Academy of Medical Sciences of the USSR V. V. Zakusov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 65, No. 3, pp. 70-73, March, 1968. Original article submitted December 12, 1966.

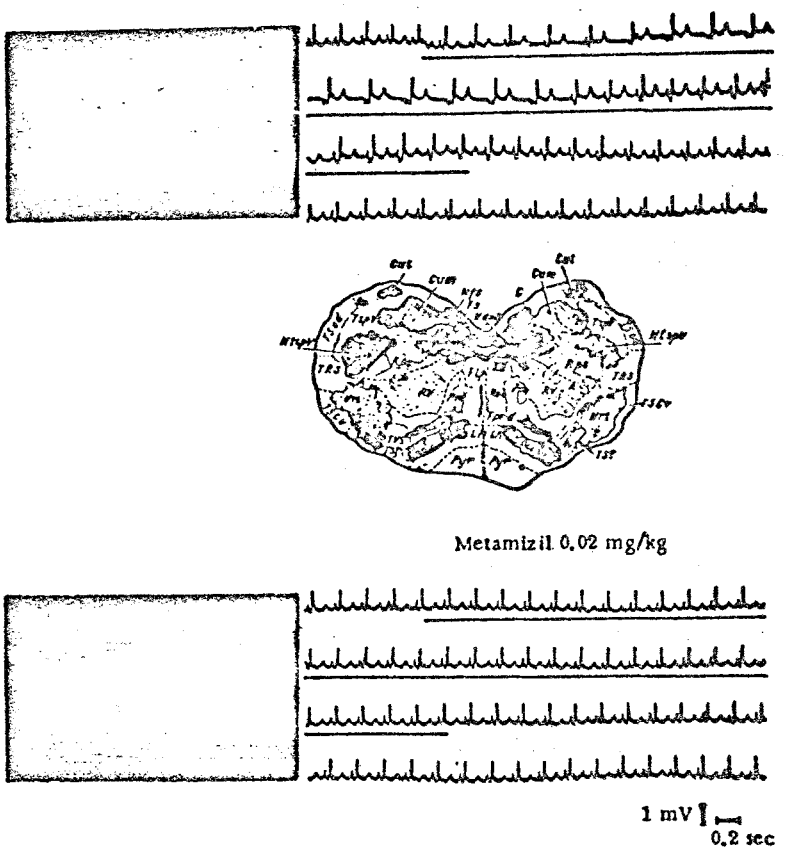

Fig. 1. Action of metamizil on development of an upper nodal atrioventricular rhythm and changes in arterial pressure produced by stimulation of the dorsal motor nucleus of the vagus nerve. Simultaneous recording of arterial pressure and ECG (lead II before, during (straight line), and after end of stimulation. 1) Initial sinus rhythm (205 contractions/min); 2) 10 min after injection of metamizil. During stimulation (straight line) the rhythm becomes slower on the average by 15 beats/min, followed by the development of an upper nodal atrioventricular rhythm (negative P wave before the ventricular QRS complex), accompanied by a depressor-pressor vascular reaction; voltage of the QRS complex and T wave is increased. Each successive line of the ECG is a direct continuation of the preceding trace.

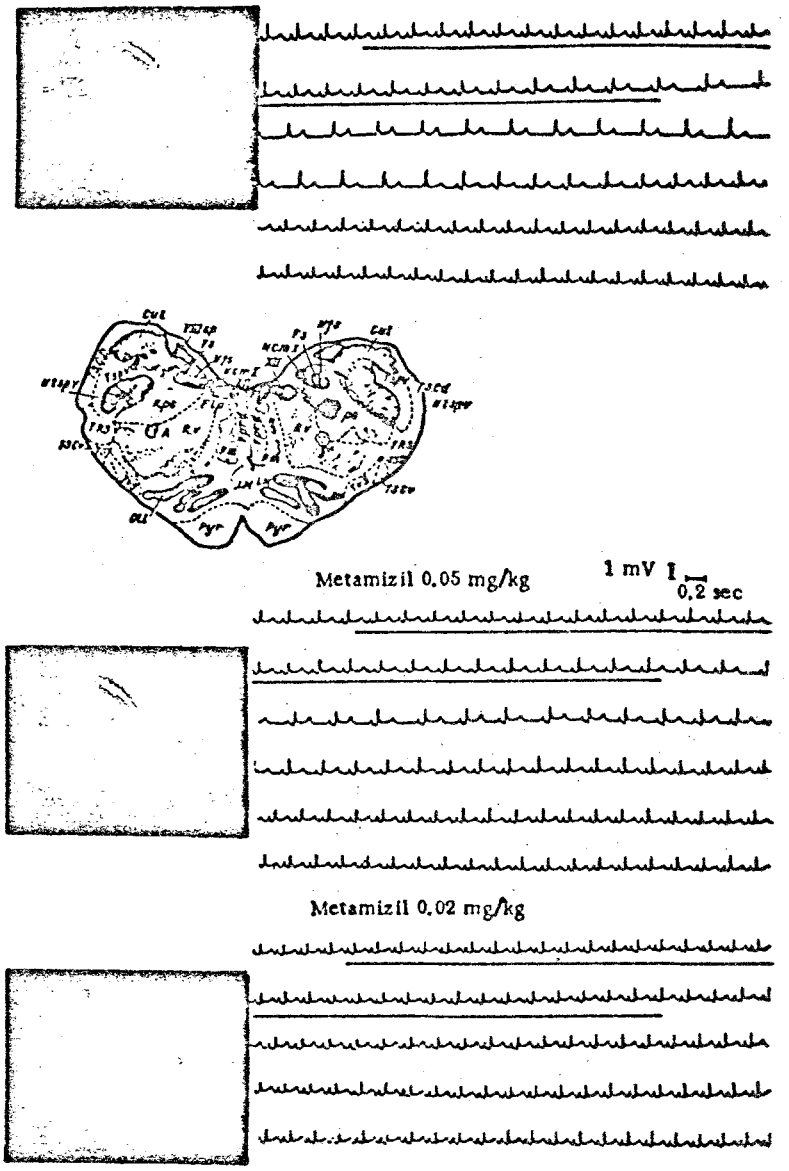

Fig. 2. Effect of increasing doses of metamizil on the development of mid-nodal atrioventricular rhythm and changes of arterial pressure arising during stimulation of the parvocellular reticular nucleus. Simultaneous recording of ECG and arterial pressure. 1) Original ECG (lead II), sinus rhythm 157 contractions/min; 2, 3) 10 min after injection of increasing doses of metamizil. During stimulation (straight line) an increasing slowing of the rhythm develops, on the average by 22 beats/min, accompanied by a pressor vascular reaction; after the end of stimulation the bradyarrhythmia is converted into a mid-nodal atrioventricular rhythm (the P wave before the QRS complex is absent); continuous tracing of ECG.

by metamizil. On the contrary, the depressor vascular reactions were inhibited by metamizil and converted into pressor. These facts show that metamizil, in the doses used, has no significant influence on effects of sympathetic nature.

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