EFFECT OF ANTIPYRETICS ON EXPERIMENTAL BRONCHOSPASM

A. I. Shevchenko

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The effect of amidopyrin, analgin, sodium salicylate, and acetylsalicylate on the development of experimental (serotonin, histamine, acetylcholine, and vagal) bronchospasm was studied in anesthetized cats and on isolated cat lungs. Of all the antipyretics investigated, only amidopyrin had any marked broncholytic properties.

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As well as receptors sensitive to acetylcholine, histamine, and tryptamine, the smooth muscle of the bronchi contains receptors sensitive to the bronchoconstrictor effect of bradykinin and blocked by amidopyrin and acetylsalicylate [1-3]. Moreover, the study of chemical mediators of inflammation has yielded definite evidence that histamine, serotonin and possibly acetylcholine exert their effects through bradykinin liberated under their influence [5-7]. On the assumption that such interaction is also concerned in the genesis of bronchoconstrictor responses, amidopyrin and other bradykinin antagonists belonging to the group of antipyretics must block the effect of histamine, serotonin, and acetylcholine (stimulation of the vagus nerves) on the bronchial smooth muscle.

The object of this investigation was to study the broncholytic activity of amidopyrin, acetylsalicylate, sodium salicylate, and analgin on serotonin, histamine, and vagal bronchospasm.

EXPERIMENTAL METHOD

Experiments were carried out on 45 cats anesthetized with urethane (1 g/kg), with natural respiration blocked by diplacin, and on 28 isolated cat lungs.

The tone of the bronchial muscle in the experiments in vivo was recorded by the Konzett–Rossler method [4]. The animal's condition during the experiment was judged from the arterial pressure in the common carotid artery. All test substances were injected intravenously. The results obtained are presented as mean values with confidence limits ($P = 0.05$).

Serotonin (50 μg/kg), histamine (25 μg/kg), and electrical stimulation of peripheral ends of the divided vagus nerve in the animal's neck with square pulses increased bronchial tone by 22.7±34, 203±37, and 196±29% respectively.

In experiments in vitro, the trachea and bronchi were perfused with Tyrode solution, aerated and warmed to 38° (the lower edges of the lungs were incised). Bronchial tone was estimated from the rate of flow of the Tyrode solution. The test substances were added directly to the solution perfusing the bronchi.

Serotonin (1×10^{-5}) and acetylcholine (1×10^{-5}) increased the bronchial tone of the isolated lungs by 32±3 and 31±8% respectively.

EXPERIMENTAL RESULTS

In experiments on the intact animal the bronchoconstrictor effect of serotonin, histamine, and vagal stimulation was prevented by amidopyrin (40 mg/kg) by 82±13, 87±10, and 91±8% respectively. The broncholytic action of amidopyrin lasted for not less than 25-30 min. The antiserotonin effect of this compound is clearly seen in Fig. 1, showing the results of one experiment with amidopyrin.

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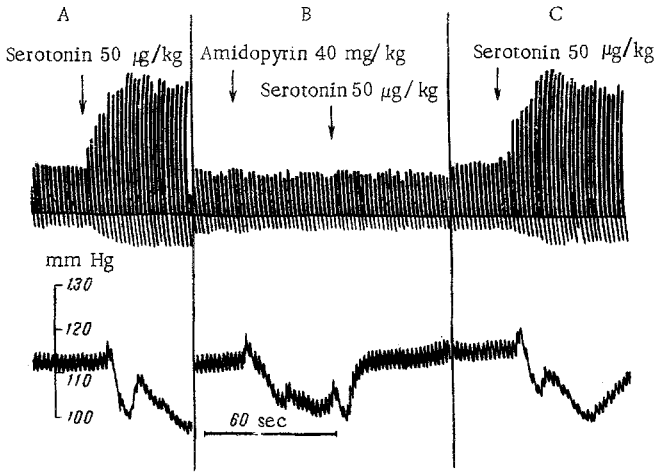

Fig. 1. Antiserotonin effect of amidopyrin. A) Response of bronchi to serotonin (50 μg/kg) under normal conditions; B) effect of amidopyrin (40 mg/kg) on response to serotonin; C) recovery of response of bronchi to serotonin (after 40 min). From top to bottom: bronchial tone with zero line; arterial pressure; time scale. Arrows indicate times of injection of test substances.

Under the influence of analgin (100 mg/kg) a slight tendency was observed for the bronchial response to serotonin only to diminish. With acetylsalicylate (40-100 mg/kg) and sodium salicylate (100 mg/kg), no broncholytic action could in general be detected on any of the experimental models of bronchospasm used.

Of all the antipyretics studied, only amidopyrin in some experiments caused slight depression of the initial bronchial tone. In some cases acetylsalicylate, however, actually increased the initial bronchial tone slightly.

In experiments on the isolated lungs, amidopyrin (4×10^{-4}) completely prevented serotonin bronchospasm and diminished acetylcholine bronchospasm by 72±11%. The initial tone in these experiments was also depressed by amidopyrin by 21±6%. Analgin (4×10^{-4}) exhibited much stronger spasmolytic properties in experiments in vitro than in those on the intact animal. The response of the bronchi to serotonin and acetylcholine was prevented by analgin to the extent of 34±7 and 31±8%. Sodium salicylate (4×10^{-4}) and acetylsalicylate (4×10^{-4}), in experiments on the isolated lungs, did not change the initial bronchial tone or the bronchoconstrictor effects of serotonin and acetylcholine.

Of all the antipyretics investigated, only amidopyrin thus showed any marked antagonism to the bronchospastic action of serotonin, histamine, and acetylcholine (stimulation of vagus nerves). However, the other antibradykinin preparation (acetylsalicylate) had no such action. This fact makes it much less probable that the effects of histamine, serotonin, and acetylcholine take place through activation of the kinin system and, in particular, of bradykinin, by these compounds.

The possibility is not ruled out that the high spasmolytic activity of amidopyrin is due to its myotropic properties, which are exhibited particularly strongly on the smooth muscle of the bronchi.

LITERATURE CITED

1. W. E. Brocklehurst and S. J. Lahiri, J. Physiol., 160, 15 (1962).
2. H. O. J. Collier and P. G. Shorley, Brit. J. Pharmacol., 15, 601 (1960).
3. H. O. J. Collier, Ann. N. Y. Acad. Sci., 104, 290 (1963).
4. H. Konzett and R. Rossler, Arch. Exp. Path. Pharmak., 195, 71 (1940).
5. G. P. Lewis, New Scientist, 16, 34 (1962).
6. G. P. Lewis, Ann. N. Y. Acad. Sci., 104, 290 (1963).
7. G. B. West, J. Pharm. Pharmacol., 14, 618 (1962).