VIP RELEASE FROM SMALL INTESTINE AND MEMBRANE CURRENT RESPONESES IN MYENTERIC NEURONS IN RESPONSE TO ACRTYLCHOLINE

Hiroyuki KIMURA

Department of Pharmacology,
Faculty of Veterinary Medicine,
Hokkaido University, Sapporo 060, Japan

1. The aim of this study is to identify the types of cholinergic receptors in relation to the release of vasoactive intestinal polypeptide (VIP) from isolated blood-perfused small intestine, isolated myenteric plexus-, and submucosal plexus-containing preparations in the dog. Furthermore, current response to acetylcholine (ACh) was examined in myenteric neurons isolated from rat small intestine using a patch-clamp technique.

2. In isolated blood-perfused small intestine, ACh caused dose-dependent increases of blood flow and the plasma VIP level.

3. Increases in blood flow and VIP release in response to ACh were partially inhibited by hexamethonium (C_6) alone and abolished by a combination of C_6 with atropine.

4. KCl and veratridine elicited VIP releases from the myenteric plexus, which were abolished by the removal of Ca^{2+} and by tetrodotoxin, respectively.

5. VIP release evoked by ACh from the myenteric plexus was partially inhibited by C_6 alone and abolished by C_6 plus atropine. Pirenzepine, a selective M_1 receptor antagonist, also inhibited ACh-induced VIP release.

6. Dimethylphenylpiperazinium (DMPP) slightly induced VIP release from the myenteric plexus. This effect was completely antagonized by C_6.

7. Although the secretagogue-evoked VIP release from the submucosal plexus was less than that from the myenteric plexus, sensitivity to antagonists was not different between the plexuses.

8. ACh evoked inward currents in myenteric neurons, which generated Na currents in response to depolarizing pulses. These inward currents were inhibited by C_6 and atropine in a dose-dependent manner. The inhibitory effect of C_6 was greater than that of atropine. DMPP also caused inward currents, which were inhibited by C_6 but not by atropine.

9. It is suggested that ACh caused VIP release mainly via muscarinic activation and partially via nicotinic activation in canine small intestine, and that the ACh-induced current in the myenteric neurons of rat small intestine is due to both nicotinic and muscarinic receptor activations.