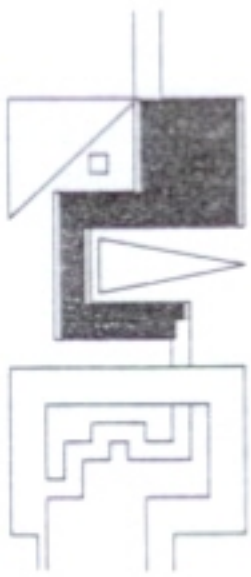

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Muscarinic M3 receptors in the human gastric smooth muscle

M3 muskarinski receptori u glatkom mišiću humanog želuca

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ABSTRACT. The aim of this study was to invetigate the role of M3 subtype of muscarinic receptors in the smooth muscles of the human gastric body. Gastric wall strips were resected from patients with gastric carcinoma and gastric or duodenal ulcers accompanied with chronic gastritis. Dose-dependent contractions of the circular and longitudinal smooth muscle preparations from gastric body were induced by acetylcholine in vitro. A specific antagonist para-fluoro-hexahydro-sila-difenidol prevented the contractions of the longitudinal smooth muscle induced by acetylcholine, but its inhibitory effect on the circular smooth muscle preparations was rather inconsistent. These findings suggest that the M3 subtype of muscarinic receptors exist in the smooth muscles of the human gastric body, and may subserve the contractions of the longitudinal smooth muscle layer.

KEY WORDS: M3 muscarinic receptors, smooth muscles, human stomach.

SAŽETAK. Cilj ovog rada bio je da se ispita postojanje i uloga M3 subtipa muskarinskih receptora u glatkim mišićima želudačnog korpusa kod čoveka. Dozno-zavisne kontrakcije preparata longitudinalnog i cirkularnog mišićnog sloja želudačnog korpusa izazivane su acetilholinom in vitro. Isečci želudačnog zida dobijeni su tokom operacije od pacijenata obolelih od karcinoma želuca i ulkusa želuca i duodenuma, praćenih hroničnim gastritisom. Specifični antagonist M3 receptora para-fluoro-heksahidro-sila-difenidol sprečio je kontrakcije longitudinalnog glatkog mišićnog sloja, dok je znatno slabije delovao na cirkularni sloj. Na osnovu dobijenih rezultata zaključeno je da se M3 muskarinski receptori mogu naći u glatkim mišićima tela želuca čoveka, i da mogu biti od značaja za kontraktilnost longitudinalnog glatkog mišića.

KLJUČNE REČI: M3 muskarinski receptori, glatki mišić, humani želudac.

A new classification of muscarinic receptors has recently been widely accepted: at least four subtypes of the muscarinic receptors were differentiated by means of selective antagonists (1, 2, 3). In the gastrointestinal smooth muscles, the predominance of the M2 subtype of muscarinic receptors has been repeatedly pointed out (4). However, the relative importance of differnt subtypes of muscarinic receptors in the gastric motility has not been elucidated yet. The aim of the present work was to study the role of the M3 subtype of muscarinic receptors in the contractility of the human gastric smooth muscles, using a specific M3 antagonist para-fluoro--hexahydro-sila-difenidol (pFHHSiD) to prevent the contractions of the smooth muscle preparations from human gastric body induced by acetylcholine in vitro.

MATERIALS AND METHODS

Gastrectomy was performed in eight patients (5 men and 3 women), aged between 45 and 69 years. Five patients had gastric cancer (adenocarcinoma, intestinal type), three patients had gastric and duodenal ulcers with chronic gastritis. Immediately after gastrectomy, a strip of the anterior gastric wall (1.5 cm wide and 2 cm long) was cut off next to the great curvature and at least 10 cm far from the the macroscopic tumor boundaries. The preparation was rinsed and immersed in Tyrode solution and transported to the laboratory.

In the laboratory, the mucosa from the strip was removed by sharp dissection. Thereafter, two segments from the full thickness of the gastric wall strip were prepared, so that the contractions of the longitudinal and circular smooth muscles could be recorded separately. A segment of the longitudinal smooth muscle was produced by cutting the strip in the direction of the longitudinal smooth muscle fibres. Some four to six cuts produced a segment of longitudinal smooth muscle of sufficent length. From the other segment, a circular muscle strip was prepared in the same manner as for the longitudinal smooth muscle strip, but the cuts were made along the length of the circular muscle fibres. The same number of cuts were similarly spaced in each of the preparations. Slight incisions were made along the longitudinal axis of both strips to interrupt muscle layers with different directions.

The smooth muscle strips were suspended in two 15 ml isolated organ baths with Tyrode solution, at 37°C and bubbled continuously with 95% O_2 and 5% CO_2. The strips were attached to an isotonic frontal writing lever and loaded with 1.5 g. The contractions were magnified about eight times. The recordings were made on a smoked drum.

The strips were allowed to equilibrate for about 45 minutes before cumulative doses of acetylcholine were added into the

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Abbreviation used in this article: pFHHSiD, para-fluoro-hexahydro-sila-difenidol