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Review Article

Investigation of the Effect of Nonsteroidal Anti-Inflammatory Drugs on the Motor Activity of the Stomach and Duodenum

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Summary

Investigation of the influence of non-steroidal anti-inflammatory drugs on the motor activity of the stomach and duodenum. The effect of non-steroidal anti-inflammatory drugs on the electromotor activity of smooth muscle of the stomach and duodenum in normal rats and in the simulation of gastric and duodenal ulcer was investigated. It is shown that cyclooxygenase blockers increase the electromotor activity of the gastroduodenal complex and accelerate the repair processes in the area of gastric ulcers.

Keywords: Duodenum; Non-steroidal anti-inflammatory drugs; Stomach

Nonsteroidal anti-inflammatory drugs (ketorolac, ketoprofen, celecoxib) are selective inhibitors of cyclooxygenase-2 (COX-2) [1,2]. COX-2 is induced in response to the inflammatory process, which leads to the synthesis and accumulation of inflammatory prostanoids (in particular, Prostaglandin E2), which, in turn, causes inflammation, swelling and pain syndrome. Prostaglandins increase the sensation of pain by initiating inflammation of the tissue at the site of its damage, therefore, along with the anti-inflammatory effect, these drugs have a pronounced analgesic effect [3,4]. Celecoxib does not inhibit COX-1, therefore, it does not affect prostanoids synthesized due to the activation of COX-1, and, due to this, does not interfere with the development of processes associated with the action of COX-1 in tissues (ulcerative lesions of the stomach and duodenum, perforations, obstruction, lack of inhibition of COX-2-dependent aggregation platelet activity).

The purpose of this study is to identify the possible influence of ketorolac, ketoprofen and celecoxib on the motor function of the stomach and duodenum.

Research methodology. The experiments were carried out on 24 Wistar rats weighing 200-250 g. Previously, for 10 days, the rats were administered ketoprofen at a dose of 0.5 mg / kg intramuscularly, ketorolac – 0.4 mg / kg intramuscularly and celecoxib at a dose of 1.5 mg / kg through a probe and 2.5 mg / kg intramuscularly. On the 10th day of the experiment, laparotomy was performed under gentle conditions and the electromotor activity of the stomach and duodenum was recorded. The control group consisted of 7 experimental animals of comparable body weight who were injected with saline solution. Electromyography (EMG) of the antral and fundal parts of the stomach and ascending duodenum was recorded using silver electrodes with a contact surface area of 1.5-2.0 mm2 using a Nihon Kohen electromyograph (Japan). Statistical analysis was carried out by the Mann-Whitney small sample method at $p < 0.05$

Results.

Ketorolac

The fundal part of the stomach. The background frequency of slow-wave activity was 7.4±0.8 v min, the amplitude was 0.21 ± 0.05 mV. The slow-wave activity of the fundal part of the

stomach increases slightly against the background of ketorolac administration: the frequency is up to 8.1 ± 0.8 per minute (9.4%, p 0.05) and the amplitude is up to 0.28 ± 0.03 mV (33%, p 0.05). Therefore, the introduction of ketorolac stimulates the slow-wave activity of the fundal part of the stomach. Antral part of the stomach. Background EMA of smooth muscles of the antrum of the stomach is represented by frequency and amplitude characteristics. The frequency of slow waves of EMA was 5.6 ± 1.9 v min, the amplitude was 0.18 ± 0.05 mV. The introduction of ketorolac practically does not change the frequency of slow waves of the antrum of the stomach (5.7 ± 0.7 per minute), the amplitude increases to 0.8 ± 0.1 mV (350%, $p < 0.05$). Consequently, the administration of ketorolac increases the amplitude component of the EMA of the antrum of the stomach. Duodenum. The background frequency of slow waves of the duodenal EMA was 18.5 ± 0.9 v min, the amplitude was 0.23 ± 0.03 mV. The introduction of ketorolac slightly increases the electromotor activity: the frequency increases to 21.6 ± 2.3 per minute (16.8%. P 0.05), the amplitude is up to 0.47± 0.05 mV (104.3%, $p< 0.001$). Thus, ketorolac stimulates the electromotor activity of the fundal part of the stomach and duodenum and increases the amplitude of the slow waves of the antral part of the EMA.

Ketoprofen

The fundal part of the stomach. The introduction of ketoprofen leads to an increase in the frequency and amplitude of slow waves of EMA: frequency up to 8.0 ± 0.9 v min (8.1%, p 0.05), amplitude - up to 0.62 ± 0.07 mV (195%, $p < 0.001$). Consequently, the administration of ketoprofen stimulates the slow-wave activity of the fundal part of the stomach. Antral part of the stomach. The introduction of ketoprofen leads to an increase in the frequency and amplitude of slow-wave activity of smooth muscle EMA: the frequency increases to 6.5 ± 0.7 per minute (16%, p 0.05), the amplitude - to 0.72± 0.09 mV (by 300%, $p < 0.001$). That is, the introduction of ketoprofen increases the amplitude-frequency characteristics of the EMA of the antral part of the stomach somewhat more than the fundal one. Duodenum. The introduction of ketoprofen slightly reduces the frequency of slow waves of EMA – up to 16.2 ± 2.3 per minute (less by 11.8%, p 0.05) and increases the amplitude – up to 0.54 ± 0.07 mV (more by 134.8%, $p < 0.001$). Thus, ketoprofen changes the chrono-inotropic relationship in the contractile activity of the duodenum by increasing the amplitude of the local response.

Celecoxib

The fundal part of the stomach. The slow-wave activity of the fundal part of the stomach against the background of the administration of celecoxib at a dose of 1.5 mg / kg was: the frequency was 7.4 ± 1.1 per minute, and the amplitude was 0.62± 0.08 mV (199.9%, $p < 0.01$). Against the background of the administration of celecoxib at a dose of 2.5 mg / kg, the frequency of slow waves of the fundal gastric EMA increased to 16.0± 2.5 per minute (117.5%, $p<0.01$), the amplitude decreased to 0.5± 0.05 mV (-19.3%, $p< 0.05$). Thus, the administration of celecoxib dose-dependently stimulates the frequency component of the slow-wave activity of the fundal part of the stomach. Antral part of the stomach. The administration of celecoxib at a dose of 1.5 mg / kg slightly increases the frequency of slow waves of EMA of the antrum of the stomach to 6.3 ± 1.2 per minute (12.5%, p 0.05), the amplitude to 0.43 ± 0.06 mV (138.8%, $p < 0.001$). Against the background of the administration of celecoxib at a dose of 2.5 mg / kg, the frequency of slow waves of EMA of the antrum of the stomach increased to 11.8 ± 1.5 per minute (87.3%, $p < 0.05$), the amplitude - to 0.82 ± 0.13 mV (90.7%, $p < 0.05$). Thus, the administration of celecoxib dose-dependently increases the amplitude-frequency characteristics of slow waves of EMA of the antrum of the stomach.

Duodenum. The administration of celecoxib at a dose of 2.5 mg / kg increases the frequency of slow waves of EMA to 27.0 ± 3.3 per minute (50.3%, $p < 0.05$) and the amplitude to 0.7± 0.08 mV (204.3%, $p < 0.001$). In 66% of observations, spike activity appears with a frequency of 0.75 ± 0.05 and an amplitude of 1.7 ± 0.3 mV. Thus, celecoxib enhances and increases slow-wave electromotor activity and promotes the appearance of spike activity, enhancing the motility of the duodenum as a whole.

Thus, the electromotor activity of the fundal part of the stomach changes slightly under the influence of ketorolac, and with the introduction of ketoprofen and celecoxib, the amplitude characteristics of slow waves reflecting depolarization processes are mainly subject to changes. The antral part of the stomach reacts to the administration of NSAIDs unidirectionally: the frequency and amplitude of slow EMG waves increases. The response of the duodenum to the introduction of ketorolac was an increase in frequency, and to the introduction of ketoprofen - an increase in the amplitude of slow waves, to the introduction of celecoxib – an increase in slow-wave and spike activity. That is, the most pronounced reaction of the duodenum is noted on the introduction of celecoxib. Thus, the introduction of nonsteroidal anti-inflammatory drugs that inhibit the synthesis of prostaglandins leads to an increase in the electrical activity of the smooth muscle tissue of the stomach and duodenum, moreover, an increase in the amplitude-frequency characteristics of the EMA of the stomach and duodenum against the background of the action of celecoxib is dose-dependent.

Conclusion

It has been shown that ketorolac stimulates the electromotor activity of the fundal stomach and duodenum and increases the amplitude of slow waves of the antral EMA, whereas ketoprofen changes the chrono-inotropic relationships in the contractile activity of the duodenum. When analyzing the effect of celecoxib on the motor function of the stomach and duodenum, it was shown that the administration of the drug dose-dependently stimulates the frequency component of the slow-wave activity of the fundal stomach; the introduction of celecoxib dose-dependently increases

the amplitude-frequency characteristics of slow waves of the EMA of the antral stomach and enhances and increases slow-wave electromotor activity and promotes the appearance of spike activity of the smooth muscles of the duodenum. Thus, the introduction of nonsteroidal anti-inflammatory drugs that inhibit the synthesis of prostaglandins leads to an increase in the electrical activity of the smooth muscle tissue of the stomach and duodenum, moreover, an increase in the amplitude-frequency characteristics of the EMA of the stomach and duodenum against the background of the action of celecoxib is dose-dependent

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