Research Article

The evaluation of effectiveness of pharmaceutical correction of the physiological stomach function with the use of information technologies

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ABSTRACT

Aim: The paper describes the potential use of the drug "trimebutine" in children. It presents the results of the research of its effectiveness in teenagers at the moment of exacerbation of chronic gastritis with regard to an accelerated motor-evacuation function of the stomach. **Materials and Methods:** In the course of the study, such methods as a clinic anamnestic survey, an observational supersonic scanning of abdominal space with examining the gallbladder function, and a supersonic scanning of stomach with examining its motor-emptying function are used. The study has been conducted regarding the voluntary informed consent of the patients. The design of the study is aligned with accordance to the Helsinki Declaration of the World Medical Association and has been approved on the meeting of the local ethics committee. **Results:** The results presented in the current study, verify that trimebutine ("trimedate") is a regulator of a motor function of gastrointestinal tract and possesses a significant pain-alleviating effect, caused by its unspecific effect on all the types of opiate receptors. **Conclusion:** Nevertheless, it should be noted that the effect of the discussed drug on the children of other age groups as well as the children with a normal or slower emptying function of stomach needs further researching.

KEY WORDS: Children, Stomach diseases, Trimebutine

INTRODUCTION

The most common symptom of gastrointestinal disorders in kids and teenagers is an abdominal pain. The complaints of a stomach pain are common for all age groups. A large number of epidemiological studies confirm that 25–40% of children and teenagers may have an abdominal pain. Understanding of the mechanisms underlying the pain syndrome can partially help in finding its causes and choosing the way of its regulation.[1] It is known that the occurrence of pain is connected with the activation of nociceptors (being in the muscular wall of a hollow viscus, in the capsules of the parenchymal organs, and the mesogaster and peritoneal lining of the back wall of the abdominal space), the ectasia, the stress of the hollow organ wall, and the muscle actions. The gastrointestinal mucosa does not have nociceptive receptors, so its damage does not cause pain. Signals from the intestinal tract are transmitted along the afferent fiber through the spinal ganglion and reach the anterior brain regions, wherein the post-central gyrus, the pain is felt. All of the above make to pay special attention to the motor gastrointestinal disorders including the emptying peristaltic function of the stomach and the antroduodenal joint. The stomach emptying process is the most complex process, which is under the efferent influence of central nervous system (by means of the vagus and sympathetic nerves), the volume and nature of the food getting into the stomach, and the work of the smooth muscular fiber, whose activity is controlled by the own intramural nervous interplacement. Nowadays, in the pharmaceutical market, there is a great number of drugs influencing the motor function of gastrointestinal tract (GIT) to one degree or another and managing the pain symptoms, but they are mostly spasmolytics, having no positive influence on the emptying function of GIT that can change in the exacerbation period of chronic gastritis in children. The drug trimebutine ("trimedat") stands alone, it is

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an opiate agonist, having a modulating action on the motion of GIT and a pain-relieving effect, connected with a non-specific effect on all the classes of peripheral opiate receptors: μ, κ, and δ.[2]

In GIT, there are all the three types of opiate receptors, which are both in the smooth muscle cells of the GIT and in the enteric nervous system. In the smooth muscle, the opiate receptors are present in the circumferential layer;[3] in the enteric nervous system, they are located in the ganglion cells of the myenteric and submucous plexi of the small bowel and on the intramural nerve fiber.[4] It is known, opioid peptides intensify contractions in a small bowel, having an effect right on the opiate receptors of the circumferential smooth muscles.[5,6]

The induction of the constant segmenting contractions and the suppression of the propulsive peristalsis results in the delay of the stomach contents moving along the intestine.[7,8] The local contractions of GIT segments are connected with a myogenic mechanism, while the coordination of adjacent GIT segments is connected with the regulating influence of the enteric nervous system. The enteric nervous system of a small bowel is responsible for the irradiation of the migrating myoelectric complex (MMC), which provides a propulsive coordinated peristalsis and the transition of the stomach contents in the period when the digestion does not take place.[9] It is well known that opioid peptides intensify contractions in a small bowel, having an effect right on the opiate receptors of the circumferential smooth muscles.

With regard to the fact that endogenous opioid peptides suppress the release of excitatory and inhibitory neurotransmitters in the enteric nervous system, and the opiate receptors are located practically on all the neurons of the enteric nervous system, the impact of the opioid peptides and the opiate agonists on the motility of the GIT depends on the prevalence of the excitatory or inhibitory influences. That is why, the effect of the opioid peptides or their agonists in the enteric nervous system is modulating in the regulation of the propulsive motility.

The drug is certified for use in a child treatment. However, most of the medical works devoted to its study, concern the patients over the age of 18 years old. Thus, in 1989, Grandjouan *et al*. carried out a comparative clinical trial of the metoclopramide and trimebutine effect on the small bowel motility in 15 non-patient volunteers. The received results show that the above-mentioned drugs intensified the motility of the small bowel. Besides, trimebutine induced an extraordinary phase of the ambulant motor system, while metoclopramide caused a motor index without forcing an extraordinary phase of the MMC.[10]

The effect of the trimebutine on the motility of GIT has been studied in 20 patients having a gastric ulcer. The patients were divided into two groups. The first group (10 patients) took proton-pump inhibitors (PPI) and the second group (10 patients) took trimebutine in conjunction with PPI for 8 weeks. The patients who took trimebutine have shown a better motor and emptying function of the stomach, while the patients who took only PPI have shown no change in this parameter.[11]

The opiate peptides of all the types are found both on the peripheral endings of the primary afferent neurons and in the intervertebral ganglions. The peripheral action of endogenic opioid peptides and opiate agonists can take place by effecting the peripheral endings of the primary afferent neurons (for instance, by diluting substance P) or inhibiting the carrying of pain impulses along the peripheral nerves and intervertebral ganglions. Morphine, trimebutine, and fedotozin effectively reduce the splanchnesthetic sensibility due to their impact on the level of an intervertebral ganglion.[12,13] It is obvious that trimebutine and its metabolite non-trimebutine block the sodium channels on the cell membrane of neurons of an intervertebral ganglion (Chevalier *et al*.; Roman *et al*.).[14,15]

The above-mentioned randomized clinical study by Zhong *et al*., which involves 129 patients with a functional dyspepsia coexisting with diarrhea-dominant irritable bowel syndrome, highlights the effectiveness of trimebutine in managing an abdominal pain.[16]

The meta-analysis by Poynard *et al*., including 23 researches, has shown that antispasmodic therapy is more effective than placebo in managing an abdominal pain in patients, having an irritable bowel syndrome.[17-19] In the course of the meta-analysis, six drugs have been analyzed. They are cimetropium bromide – 5 researches; hyoscine butylbromide – 4 researches; mebebeverine – 5 researches; otilonium bromide – 4 researches; pinaverium bromide – 2 researches; and trimebutine – 4 researches. In total, the data from 1888 patients have been analyzed, among them, there are 945 patients, who took one of the drugs, compared with the rest of the mentioned patients who took placebo. The patients, taking placebo, admitted a pain relief in 41% of cases, in comparison with these data, the patients taking a spasmolytic and admitting a pain relief have accounted for 53% ($P < 0.001$).

As a rule, the study of the motor function of GIT and its connection with the pain symptoms lasts for a long period of time, as the motor peristaltic functioning of the internals is prolonged in time. That is why, the diagnostic process can be optimized with the use of a number of informative technologies. In particular,

it can be carried out with the use of the programs of pattern recognition and automatic calculation of a number of characteristics.[20-24]

The aim of our research is to appreciate the efficiency of the trimebutine correction of the motor disorders and pain symptoms in teenagers at the moment of exacerbation of their chronic gastritis.

MATERIALS AND METHODS

A group of children aged between 16 and 18, having chronic gastritis, has been examined. In the course of the study, such methods as a clinic anamnestic survey, an observational supersonic scanning of abdominal space with examining the gall bladder function, and a supersonic scanning of stomach with examining its motor-emptying function are used. The study has been conducted regarding the voluntary informed consent of the patients. The design of the study is aligned with accordance to the Helsinki Declaration of the World Medical Association and has been approved on the meeting of the local ethics committee.

To examine the emptying function of the stomach of A. Yu. Kizerskey (a patient №. 2297183) by the method of Terentyeva, the cross-sectional area of the organ filled with a contrast agent is calculated automatically with the use of an image recognition software (the certificate of registration number is №. 201617820, the authors are Terentyeva *et al*.). It significantly accelerates the study process. The received data are compared with the standard ratio of the given age group.

RESULTS

The preliminary examination allows selecting a group of children with an accelerated motor-emptying function of stomach (26 children). The children are divided into two subgroups by the stratification randomization method. The first group has a standard treatment in the exacerbation phase (12 patients) and the target group (besides, a standard treatment) takes "trimedate" regarding their age (14 patients). Before the start of the treatment, the children of these two groups complain of colicky pains in the epigastric region in the fasted state or 2 h later after a meal (26 children – 100%), sickliness (8 children – 30.8%), and liability to obstipation (a defecation by a sheep type, rare defecation in small portions) – 11 children (42.3%). Eight children show dyskinesia changes in a gallbladder, 2 children (26.9%) have an accelerated emptying of stomach, and five children have a slow emptying of stomach (71.42%). All the children complain of colicky pains in the right subcostal area after meals or physical activities.

After prescribing them "trimedate" for 2 weeks, the target group shows the following dynamics of the clinical symptoms and the motor-emptying function of stomach. In the course of treatment, we observe the improvement of all the parameters. Besides, the dynamics of changes in the target group taking "trimedate" is authentically higher ($P < 0.05$). The abdominal pains are regulated in 14 cases (100%), while in the control group, only 7 patients (58.3%) stop complaining of the pains. The sickness and the spastic dyskinesia of the large bowel totally disappear. The normalization of emptying a stomach is observed in 11 children (78.6%), taking "trimedate," as for the control group, the normalization is observed only in 6 children (50%).

CONCLUSION

Thus, the results presented in the current study, verify that trimebutine ("trimedate") is a regulator of a motor function of GIT and possesses a significant pain-alleviating effect, caused by its unspecific effect on all the types of opiate receptors. The modulating effect of trimebutine on the motility of GIT and its pain-relieving effect allow using it in children aged between 15 and 18 with an accelerated emptying function of stomach in the gastritis inflammation phase. Nevertheless, it should be noted that the effect of the discussed drug on the children of other age groups as well as the children with a normal or slower emptying function of stomach needs further researching.

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