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CLINICAL PHARMACOLOGICAL APPROACH TO THE USE OF NONSTEROIDAL DRUGS IN CHILDREN

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Abstract:

The article discusses the mechanisms of action, various effects of nonsteroidal anti-inflammatory drugs, a consensus view on the risks of developing induced damage to the upper and lower gastrointestinal tract, as well as ways to overcome them. Drugs with relatively little side effect on the gastrointestinal tract are characterized.

Keywords: children, nonsteroidal anti-inflammatory drugs, complications, gastrointestinal toxicity, propionic acid derivatives.

INTRODUCTION

It is now obvious that non-steroidal anti-inflammatory drugs (NSAIDs) are widely used by specialists in various fields of medicine. They are used in traditional pediatric practice, rheumatology, cardiology, neurology, and oncology [1]. The unique action of NSAIDs is that, on the one hand, they have an anti-inflammatory, analgesic and antipyretic effect, and on the other hand, they are characterized by relative safety, with an equivalent risk of side effects on the mucous membrane of the esophagus, stomach, duodenum, as well as the small and large intestine, i.e. the entire gastrointestinal tract (GIT). There is evidence that the degree of risk in each individual patient is different. It depends on the dose of the drug, concomitant use of other drugs and is little associated with the dosage form of the NSAID and the route of its administration [2]. This is why the peak of scientific research and maximum clinical attention is focused on problematic issues of gastrointestinal toxicity of NSAIDs, the possibilities of prevention and treatment of such conditions [3, 4].

MATERIALS AND METHODS

In the list of pathological processes developing in the upper and lower sections of the gastrointestinal tract, special attention should be paid to ulcers with clinical symptoms or complications (bleeding, perforation, peritonitis), as a result of the formation of which the risk of death increases. At the same time, the relative prevalence of serious side effects from the designated anatomical and physiological sections of the gastrointestinal tract is similar in nature and is 60 and 40%, respectively [5]. Based on the results of laboratory studies with high diagnostic potential (study of leukocytes of coprofiltrates labeled with indium, determination of fecal calprotectin, erythrocytes and albumin labeled with chromium) and the method of capsule enteroscopy, it was established that long-term use of NSAIDs can negatively affect the architecture of intestinal mucosa cells, forming enteropathy, diaphragm-like strictures of the small intestine, membrane disease, and various forms of colitis [5]. The severity of NSAID-induced side effects from the proximal gastrointestinal tract has not been fully clarified, but the presented evidence of intestinal complications makes us think about optimizing the duration of anti-inflammatory therapy and the possibility of its flexible individualization.

RESULTS AND DISCUSSION

According to available literature data, potentially life-threatening complications develop annually in approximately 1–4% of patients taking NSAIDs [6–12]. It is noteworthy that the onset of undesirable side effects is most likely at the beginning of treatment; however, and this is significant, the threat of functional or structural damage to the gastrointestinal mucosa persists throughout the entire period of therapy. At various times, studies have been published in which the authors have shown that approximately 2% of patients with rheumatoid arthritis are hospitalized annually due to serious gastrointestinal toxic effects of NSAIDs, of which 0.2% are fatal. On this basis, 107,000 hospitalizations and 16,500 deaths are predicted annually in the USA due to dangerous NSAID-induced complications from the gastrointestinal tract [13]. New evidence from a statistical analysis of the Spanish National Health System suggests that the mortality rate associated with long-term use of NSAIDs is 15.3 cases per 100,000 people, which is much lower than in the USA [14].

Currently, the predictors of NSAID-induced gastrointestinal complications can confidently include such patient characteristics as genetic predisposition, the presence of underlying gastrointestinal pathology (history of peptic ulcer, previously observed

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complications of the digestive system caused by taking NSAIDs). In addition, the risk of an ulcerogenic effect increases with the parallel use of antiplatelet agents, glucocorticoids and anticoagulants, the simultaneous administration of several NSAIDs, a prolonged course of therapy, and an increase in the daily dose of the drug [15–17]. Currently, it is considered proven that a history of peptic ulcer and/or ulcer complications carries a 3–5-fold increase in the risk of developing NSAID-induced gastrointestinal complications [18]. A negative influence of the age factor has also been noted: the risk increases by approximately 4% per year [13]. In addition, there is a stable tendency towards the formation of pathology not only of the digestive tract, but also of other functional systems of the body, which leads to a significant increase in the risk of adverse drug reactions and drug interactions. For example, it is reported that out of 17 thousand patients taking NSAIDs in connection with a chronic inflammatory disease of the musculoskeletal system, 60% of patients had a high risk of developing NSAID-induced gastrointestinal complications; for every fourth, a high risk of combined damage to the gastrointestinal tract and cardiovascular system was determined [19, 20].

It should also be remembered that all classes of NSAIDs are characterized by dose-dependent side effects on the gastrointestinal tract, and this dependence is linear [13]. Meta-analyses of the results of clinical studies and observational observations have shown that of all non-selective NSAIDs, the safest for the gastrointestinal tract are ibuprofen, etodolac and nabumetone [18, 30, 31], while NSAIDs such as indomethacin, piroxicam and ketorolac with pronounced enterohepatic circulation and a significant half-life have serious side effects on the gastrointestinal tract [32].

Attempts to reduce the risks of adverse effects of NSAIDs on the gastrointestinal tract should begin with an assessment of the need to use NSAIDs to relieve acute and chronic pain. The likelihood of gastrointestinal complications can be mitigated by influencing risk factors and compensated for by prescribing additional therapy. The risk can be reduced by using the minimum effective dose of NSAIDs for the shortest possible time. Of all NSAIDs, it is recommended to choose drugs with relatively little side effect on the gastrointestinal tract, such as coxibs and some non-selective NSAIDs (ibuprofen) [22]. Combinations of NSAIDs with other drugs, including low-dose acetylsalicylic acid, the use of other antiplatelet agents and anticoagulants should be avoided. Among the modifiable risk factors, eradication of Helicobacter pylori should be considered, as this measure has been shown to reduce the incidence of peptic ulcers in patients initiating NSAID treatment. It is important to note that the protective effect of H. pylori eradication does not extend to patients with a history of ulceration [33–35].

It is appropriate to emphasize that currently in real medical practice the prevailing tendency is to prescribe antisecretory drugs (proton pump inhibitors, H2-receptor blockers, antacids), the use of which should be started as early as possible, literally with the first dose of NSAIDs. According to experts, proton pump inhibitors are able to reduce the incidence of endoscopically diagnosed peptic ulcers associated with the use of NSAIDs by 90% [36–38]. At the same time, H2-receptor antagonists also reduce the risk of ulcer formation in the duodenum, but do not affect the incidence of gastric ulcers [36]. There is no doubt that clinicians should use only those NSAIDs that meet the basic requirements for this group of drugs. This is why NSAIDs with proven high efficacy and favorable safety profile are of interest and practical significance.

CONCLUSION

Thus, NSAIDs have a variety of positive effects, but there is no "best" NSAID. Before prescribing an NSAID to a patient who requires long-term treatment, the physician must take into account all risk factors for the development of gastrointestinal complications. Relatively recently, new genetic methods for studying drug metabolism depending on the functional state of human genes (genome) have been proposed. On this basis, it is possible to justify the prescription of an optimal drug for the treatment of a certain nosology in a specific child with the possibility of predicting adverse drug effects. In the future, a thorough analysis of the accumulated data will allow more accurate use of these methods in real clinical practice.

REFERENCES

1. Jacobsen R. B., Phillips B. B. Reducing clinically significant gastrointestinal toxicity associated with nonsteroidal anti-inflammatory drugs. Ann. Pharmacother. 2014; 38:1469–1481.
2. Yeomans N. D. A clinical approach to management of patients with non-steroidal anti-inflammatory gastropathy. Ital. J. Gastroenterol. Hepatol. 2019; 31:89–92.
3. Canadian Coordinating Office for Health Technology Assessment. Gastroduodenal ulcers associated with the use of nonsteroidal anti-inflammatory drugs: a systematic review of preventive pharmacological interventions. Ottawa. 2013. Report no. 38.79 p.
4. Barskova V. G. Letter from the editor. Modern rheumatology. 2011; 2:82–83.
5. Southey E. R., Soareus-Weiser K., Kieijnen J. Systematic review and meta-analysis of the

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Available Online at: https://www.scholarexpress.net
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clinical safety and tolerability of ibuprofen compared with paracetamol in pediatric pain and fever. Curr. Med. Res. Opin. 2019; 25(9):2207–2222.