



TREATMENT OF NSAID-INDUCED GASTROPATHY WITH REBAGIT

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| Article history: | Abstract: |
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| <p>Received: November 11th 2023 Accepted: December 11th 2023 Published: January 14th 2024</p> | <p>More than 30 million people in the world take NSAIDs daily, and in 2/3 of cases - without a doctor's prescription or supervision. One of the most common negative manifestations associated with the use of this group of drugs is gastropathy induced by taking NSAIDs (NSAID gastropathy), which is characterized by the occurrence of erosions and ulcers of the mucous membrane (MU) of the stomach and duodenum. Of the reviewers, 8/11% are men and 65/89% are women. Women are 8 times more susceptible to the development of NSAID-induced gastropathy than men (Table 1). The average age of men was 57 years, and for women 46 years. The quality of life in patients in the control group, before the start of treatment (standard treatment - without rebait), the coefficient was equal to 32.4. After completing a 6-week course of treatment, this figure decreased to 31.8. When analyzing the study data, it was revealed that patients suffering from rheumatoid arthritis and complications of NSAID-induced gastropathy, the risk of blood loss was on average 2.9%. Particularly important is the attachment of patients to the course of treatment for gastrointestinal diseases, in particular NSAID-induced gastropathy, which contributed to effective treatment, which is reflected in the MARS questionnaire.</p> |
| <p>Keywords: NSAID-induced gastropathy, drug Rebagit , GERD-Q; DAS-28; EQ-5D and MARS, and Charlson score , risk of bleeding, annual mortality rate, Helicobacter pylori</p> | |

RELEVANCE

More than 30 million people in the world take NSAIDs daily, and in 2/3 of cases - without a doctor's prescription or supervision. An annual increase in the number of hospitalizations and deaths associated with complications of NSAIDs has been reported. therapy, the economic costs of their treatment increase. Thus, up to 60% of hospitalized patients with gastric bleeding indicate previous use of NSAIDs. Through the efforts of doctors, patients, government and public figures, the World Decade of Osteoarticular Diseases was organized in January 2000 in Geneva (The Bone and Joint Decade 2000-2010), designed to draw public attention to this problem. In the Tokyo Manifesto of April 19, 2002, rheumatologists set the goal of "reducing the burden of bone and joint pathology on society" and expanded research in this area.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications worldwide. However, their use is associated with a number of side effects [1]. One of the most common negative manifestations associated with the use of this group of drugs is gastropathy induced by taking NSAIDs (NSAID gastropathy), which is characterized by the occurrence of erosions and ulcers of the mucous membrane (MU) of the stomach and duodenum [2].

In a study by J. Kim et al . (2014) included 479 patients who required long-term use of NSAIDs in standard

doses. During the randomization process, group 1 received rebamipide at a dose of 100 mg 3 times a day, while group 2 received misoprostol 200 mcg 3 times a day. Both drugs were used for 12 weeks . The incidence of NSAID-induced gastric ulcers was similar in both groups and was 20.3% with rebamipide versus 21.9% with misoprostol , but the incidence and severity of gastrointestinal side effects was lower in the group of patients taking rebamipide (19, 4% versus 27.1%). It is also important that in the misoprostol group , patients refused to continue therapy almost 2 times more often [3]. Similar data were obtained in Korea. The incidence of ulcers was 4.5% in the rebamipide group and 4.4% in the misoprostol group [4].

According to Western authors, gastric or duodenal ulcers are detected in 10-15% of patients regularly taking NSAIDs, and gastrointestinal tract or perforation can develop in 1-1.5% of cases within a year [5, 6, 7, 8].

PURPOSE OF THE STUDY : To study the features of treatment of NSAID-induced gastropathy when adding the drug Rebagit to standard treatment, as well as the use and study of the role of GERD-Q questionnaires; DAS-28; EQ-5D and MARS, and Charlson scales .

THE PURPOSE OF THE STUDY: To study the features of NSAID-induced gastropathy treatment when adding



the drug Rebagit to standard treatment, as well as the use and study of the role of the GERD-Q; DAS-28; EQ-5D and MARS questionnaires, and the Charlson scale.

MATERIALS AND METHODS:

The study was conducted during the period from December 2020 to December 2022 on the basis of the Regional Multidisciplinary Medical Center, in the Department of Rheumatology in the Khorezm region. The study analyzed 73 reviewers who were hospitalized or treated as outpatients during the time period from December 2020 to December 2022. Of the reviewers, 8/11% are men and 65/89% are women. Women are 8 times more susceptible to the development of NSAID-induced gastropathy than men (Table 1). The average age of men was 57 years, and for women 46 years. The study included patients of both sexes over 18 years of age who were hospitalized or undergoing outpatient treatment in the rheumatology department of a regional multidisciplinary medical center. Patients with treatment adherence were recruited for the study and assessed using the MARS . The study included patients with gastritis, ischemic heart disease, and rheumatoid diseases. The study widely used: social and hygienic, sanitary and statistical, clinical, and laboratory methods.

RESULTS AND DISCUSSIONS

Informed consent was signed by all patients prior to study procedures. The study was conducted in accordance with the standards of good clinical practice and the principles of the Declaration of Helsinki. The study protocol was approved by the local ethics committee. The initial dose of 300 mg/day was chosen by the examining physician, following the instructions for use of the drug. The active treatment period lasted 12 weeks. Dose titration was performed at 4-week intervals based on assessment of clinical status and laboratory data. If necessary, the dose may be reduced or the drug may be temporarily discontinued. During the entire study period, all patients were surveyed using the following questionnaires: GERD - Q ; DAS -28; EQ -5 D and MARS surveys, and the Charlson scale was also used . Safety parameters were assessed - physical examination, vital signs, laboratory data and incidence of adverse events were assessed. The results were generated using the Microsoft software package office Excel 2020.

The study analyzed 73 reviewers who were hospitalized or treated as outpatients during the time period from December 2020 to December 2022 . Of the reviewers, 8/11% are men and 65/89% are women. Women are 8

times more susceptible to the development of NSAID-induced gastropathy than men (Table 1). The average age of men was 57 years, and for women 46 years. 52/(72%) patients were referred from the clinic, 5/(7%) of them were referred for preventive purposes, and the remaining 16/(21%) were referred from other private clinics. Of these, 8 (11%) patients were admitted to the intensive care unit. During their inpatient stay, patients were treated with groups of medications in accordance with standards.

The target dose of the drug Rebagit is 300 mg per day. The target dose is achieved within 7 days.

Table No. 1

Clinical and demographic characteristics of the groups

| Options | General group (n =27) |
|--|------------------------|
| Gender male/female, n | 2 1 (78)/ 6 (22) |
| Age, Me (IQR), years | 67.0 [5 7 ; 46] |
| BMI, kg/m ² | 27.2 |
| Smoking | 11% (7 ;1) |
| Arterial hypertension, n | 53 / 7 2.6% |
| IHD n | 30 / 41% |
| Chronic kidney disease stages 1–3, n (%) | 20 (27.4) |
| Diabetes mellitus, n (%) | 17 (23.3%) |

When reviewers were grouped by age group, the following findings were obtained; 7/9.6% of them were in the age group of 18-30 years, and this group had the smallest number of patients; 23/31.5% were in the 31-45 age group; 34/46.7% were in the age group of 46-60 years, and in this group the number of patients is the highest; and the age group of 61-75 years included 9/12.2%; and only in the age group 76-90 years were there no patients.

When studying the type of activity of the reviewers, it was revealed that the majority of them were unemployed 52/71% and also pensioners 11/15%, and the lowest figure was among teachers, only one reviewer.

When reviewers were grouped by disability group, it was found that 37/50.6% were Group 3 disabled, 27/37% were Group 2 disabled, and 9/12.4% were Group 1 disabled, which is a high rate of disability.

In patients, the average value of the Charlson index was $1.9 \approx 2$. Based on this index, the annual mortality rate on average was 6%, while the highest annual mortality rate was 13%, which is a high indicator. The majority of patients who had the highest annual mortality rates were women in the age group



46-60 years (8/72%). They also had a high risk of bleeding. In addition, a relationship was found between the annual mortality rate and the DAS -28 scale; the higher the Charlson index and the annual mortality rate, the higher the DAS -28 scores .

In a study, the risk of bleeding in patients with NSAID-induced gastropathy The following data emerged. Of all 73 patients, 22/30% have an average risk of bleeding, and 38/52% have a low risk of bleeding. These same patients belong to both sexes, but it is worth emphasizing that all males belong to this group, and representatives of both sexes belong to the age group

of 18-30 years and 30-45 years. There are no patients at risk of bleeding. High risk of bleeding in 30/41% of patients, all of them female. This indicator determines female gender as one of the main and significant risk factors for bleeding in NSAID-induced gastropathy . When grouping patients into age groups of 18-30 years, 31-45 years, 46-60 years, 61-75 years and 75-90 years, it is clear that the high risk of bleeding for this disease occurs mainly in older women who have passed the period postmenopausal , in the following percentages: 22/73.3% in the age group 45-60 years; 8/26.65V age group 61-75 years.

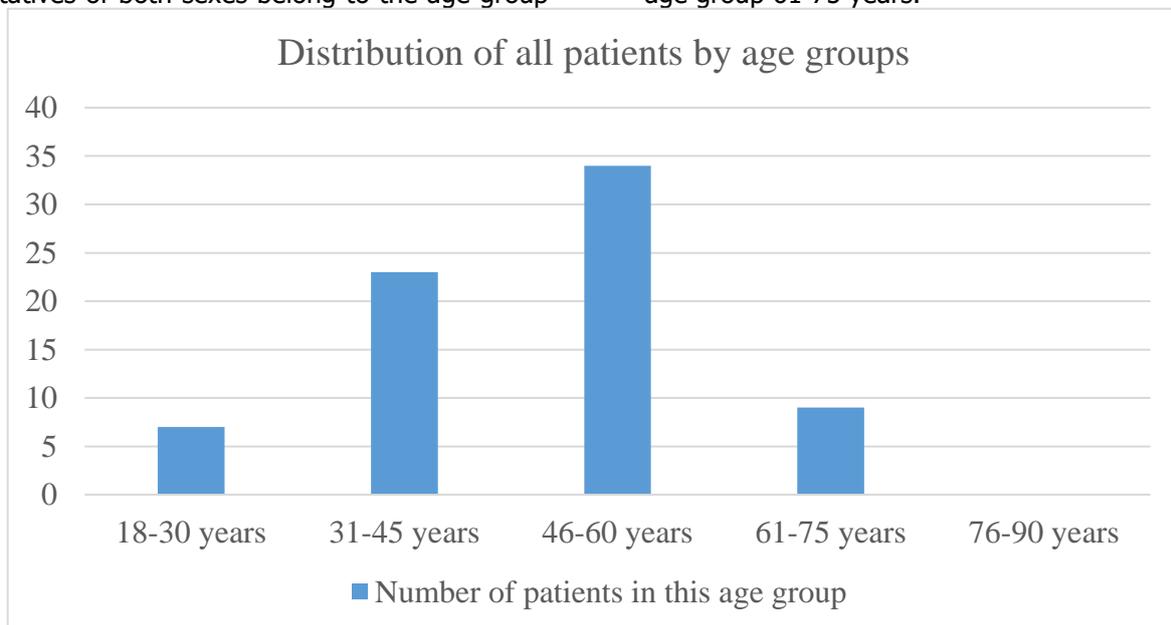


Figure No. 1

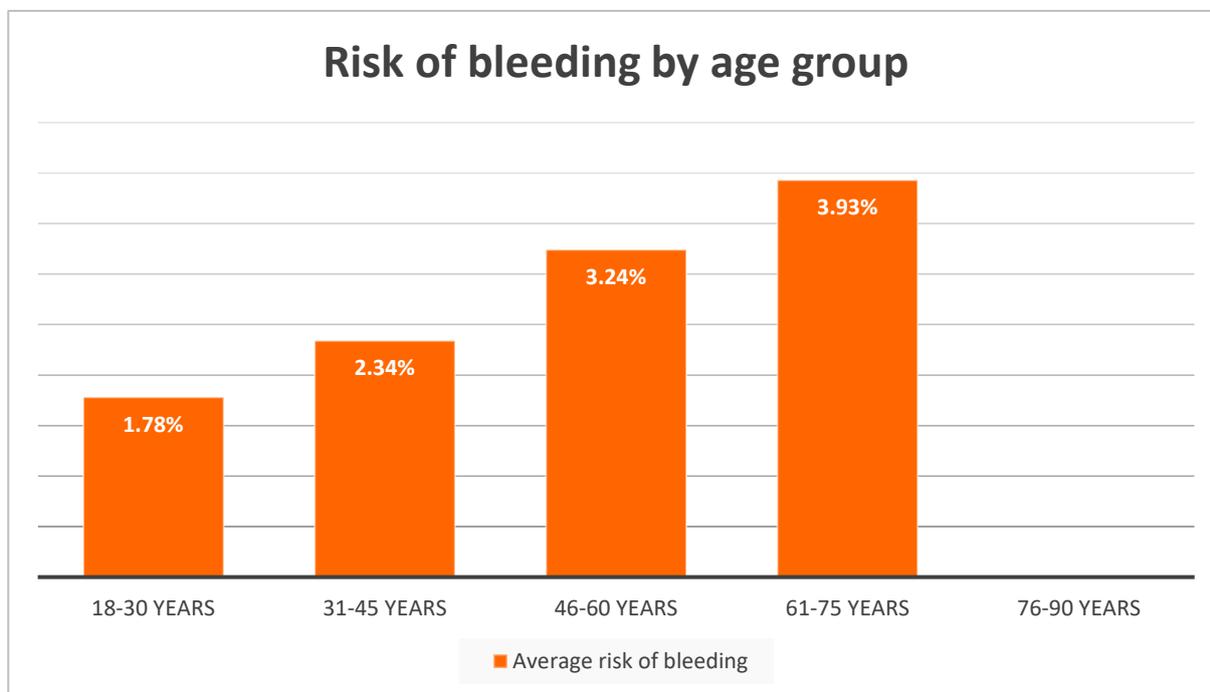


Figure No. 2

Patients who were at high risk of bleeding had low hemoglobin levels, ranging from 64 to 92 g/L.

These same patients with a high risk of bleeding had a low level of red blood cells per 1 ml of blood. The average red blood cell count was 2.88 million per ml, while the highest was 3.8 million per ml and the lowest was 2.2 million per ml, well below the normal range of 4.5-5.5 million per ml.

When studying concomitant diseases, patients with an average and high risk of bleeding had a concomitant disease of NSAID-induced gastropathy due to rheumatoid arthritis.

When studying the duration of the disease of rheumatoid arthritis, it was found that the average duration of the disease was 7.2 years, and the shortest value was 1-2 years and these patients had the lowest risk of bleeding, respectively, these patients had risk factors and clinical manifestations associated with the risk bleeding and rheumatoid arthritis were much closer to normal, in contrast to other reviewers in patients whose duration of NSAID gastropathy was much longer and the highest rate was 18 years. These same patients had the highest risks of bleeding and other related indicators.

Laboratory tests of patients' blood revealed that in those patients who took drugs from the group - proton pump inhibitors (PPIs), which are designed to slow down the release of HCl in the stomach, their total amount was 63/86%. The average duration of use of these drugs

was 2 years, while the highest point was 5-6 years, and accounted for 12/20% of the total number of reviewers taking this drug. The same 12/20% of reviewers had a low magnesium level in blood tests; its average value was 0.6-0.65 mmol/l, and for calcium the average value was 1.8 mmol/l, the lowest value was 1.2 mmol/l. And only 4/7% of patients took these medications daily, and the remaining 59/93% only when dyspeptic complaints intensified.

When studying the use of a group of drugs for the treatment of ulcerative colitis to reduce discomfort and pain, 68/93% of patients took them. The average duration of admission was 9 years, while the highest duration was 29-31 years. When studying the tactics of taking drugs, it was revealed that all patients took selective drugs for the treatment of nonspecific ulcerative colitis. But there were also those who simultaneously took selective and non-selective ones - which are another risk factor with an average degree of impact, which in turn contributed to the development and exacerbation of NSAID-induced gastropathy.

All patients who take GCS drugs also take antihypertensive drugs and antiplatelet agents, as they have high blood pressure, thereby increasing the risk of developing LES gastropathy.

When studying risk factors and the degree of their influence on the development and progression of NSAID-induced gastropathy, the following data were obtained.



HIGH IMPACT RISK FACTORS:

Age mainly becomes a significant risk factor in men after 60 years of age, and in women after 55 years of age. About 20/28% of patients have this risk factor, in

particular due to the high ratio of reviewers 17/85% of them are female;

Female gender is also a risk factor for NSAID-induced gastropathy and 65/85% of reviewers are women who are of senile age.

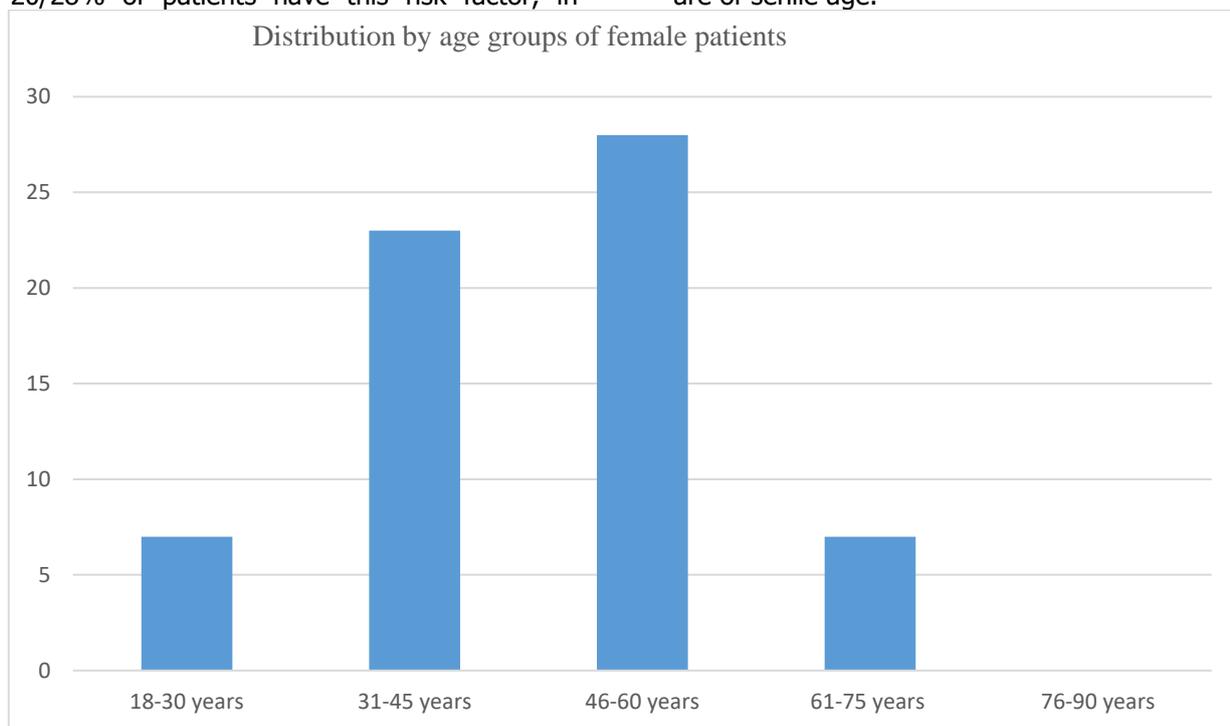


Figure No. 3

The presence of peptic ulcers, particularly in the gastrointestinal tract, is one of the main risk factors. 15/20% of patients have peptic ulcers in the gastrointestinal tract in varying degrees of severity, and an interesting fact is that 6 out of 7 patients, which is 86%, belong to the age group of 18-30 years, which in turn is not at risk for age had peptic ulcers in the gastrointestinal tract in varying degrees of severity. These data show the degree of influence of this factor on the development of NSAID-induced gastropathy .

MEDICATIONS TAKEN

Taking drugs from non-selective groups of NSAIDs to reduce discomfort and pain is also a risk factor with a moderate impact. As evidence, 58/79% of patients who, in addition to taking selective NSAID drugs, also took non-selective NSAID drugs had a high risk of exacerbation of NSAID-induced gastropathy and its other risks;

In addition, another important factor when taking NSAID drugs is the correct dosage. Almost all patients increased the dose of the drug, which is a risk factor with an average degree of impact, which contributed to the prolongation of the effect of NSAID drugs on the mucous membrane of the gastrointestinal tract;

Long-term use of NSAIDs for more than 6 months is a risk factor with a moderate impact. All reviewers had been taking NSAID medications for more than 6 months, and the average duration of use was 8-9 years, and the highest duration of use was 29-30 years, which is much longer, and they had the highest risk and progression of NSAID-induced gastropathy ; Combining drugs from the NSAID group and glucocorticosteroids in the treatment of NSAID-induced gastropathy also has its side effects in the form of aggravation of the disease. According to data, 59/80% of patients take combined treatment with NSAIDs and glucocorticoids, which in turn affects the extent of risk factors. Based on all these data, we can draw an ironclad conclusion that the correct choice, dosage and adequate course of treatment of NSAID drugs has an important place both in the treatment and in not aggravating gastrointestinal diseases.

The drugs that patients took on a long-term basis, these drugs included the standards of treatment for the following groups

GASTROENTEROLOGICAL STANDARD DRUGS.

As can be seen, all patients took gastroenterological standard drugs. The highest intake rate among patients



was the drugs Creon and omeprazole (69 and 67 patients), and the lowest intake was the drug bismuth tripotassium (16 patients).

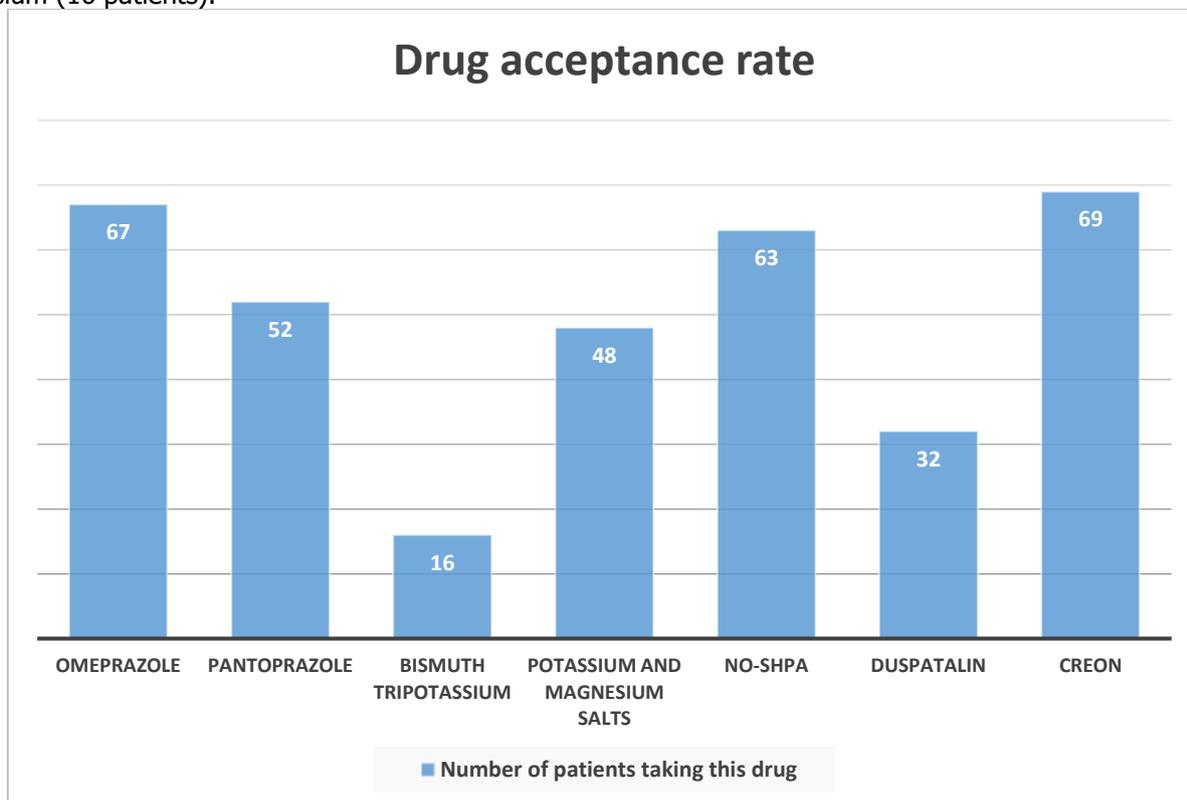


Figure No. 4

RHEUMATOLOGICAL STANDARD DRUGS.

All patients took gastroenterological standard drugs. The highest intake rates among patients were the drugs methotrixant and methylprednidazole (59 and 51 patients), and the least taken drugs were paracetamol and asperin (2 patients). It is worth noting that the use of selective NSAIDs among patients is observed in small quantities:

Nimesulide 12 / 17%

Enterocoxib 16 / 22%

Tenoxicam 3/4%

Meloxicam 5/7%

It is interesting that all patients take selective NSAID drugs, but 58/79% of patients also take non-selective NSAID drugs, thereby increasing corrosion in the stomach, increasing the risk of bleeding and the development of gastrointestinal ulcers.

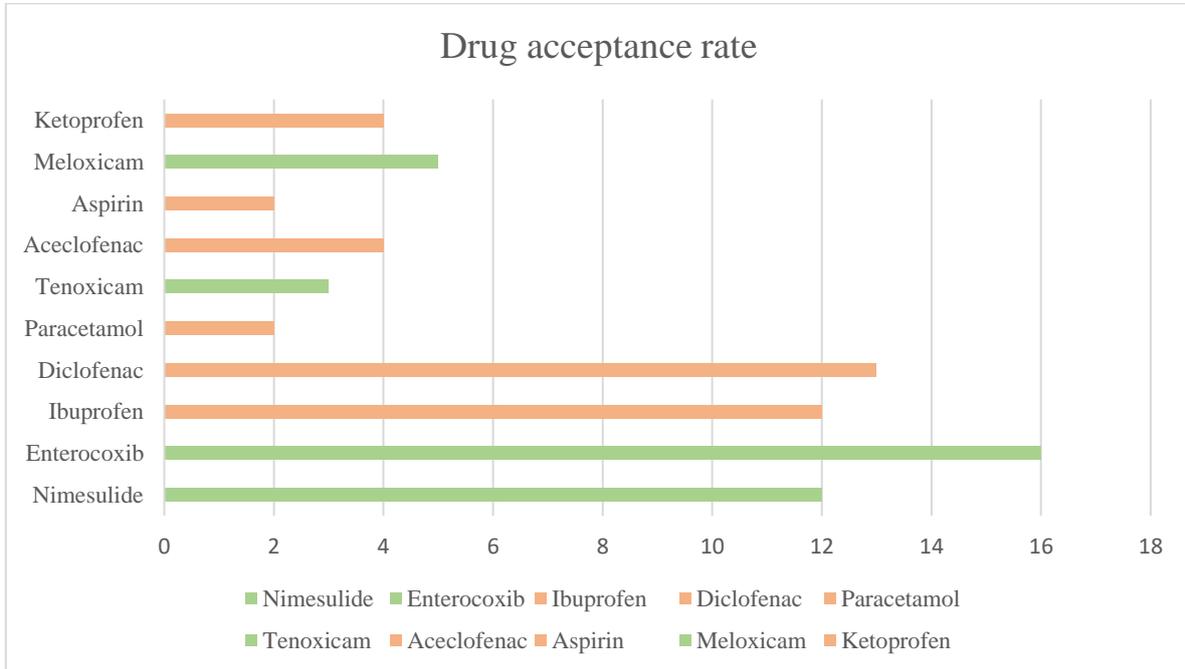


Figure No. 5

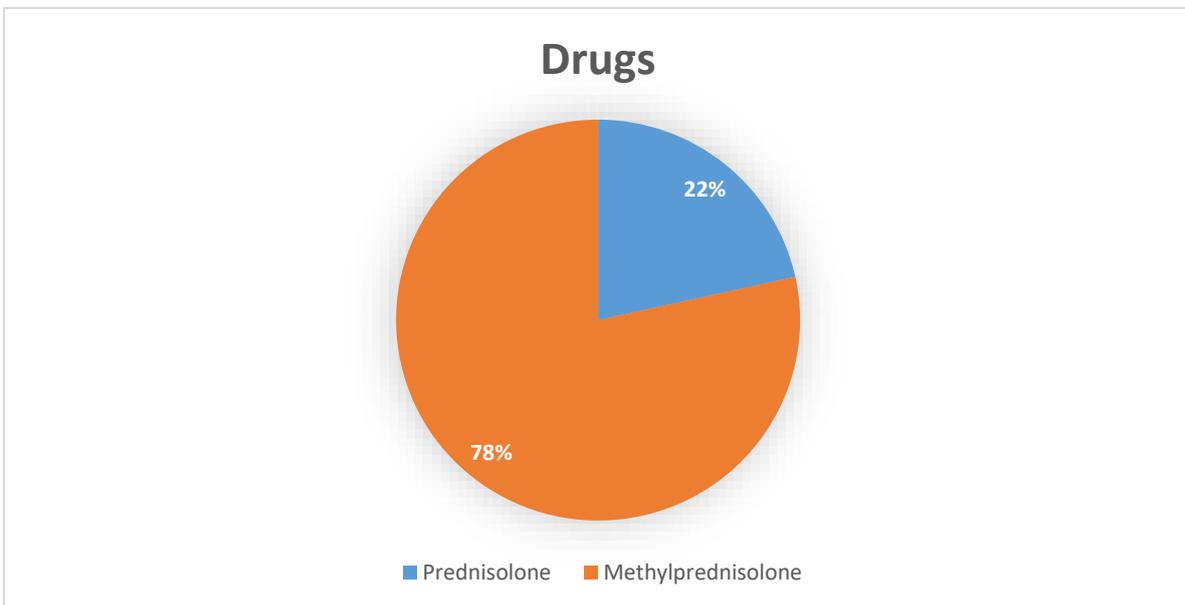


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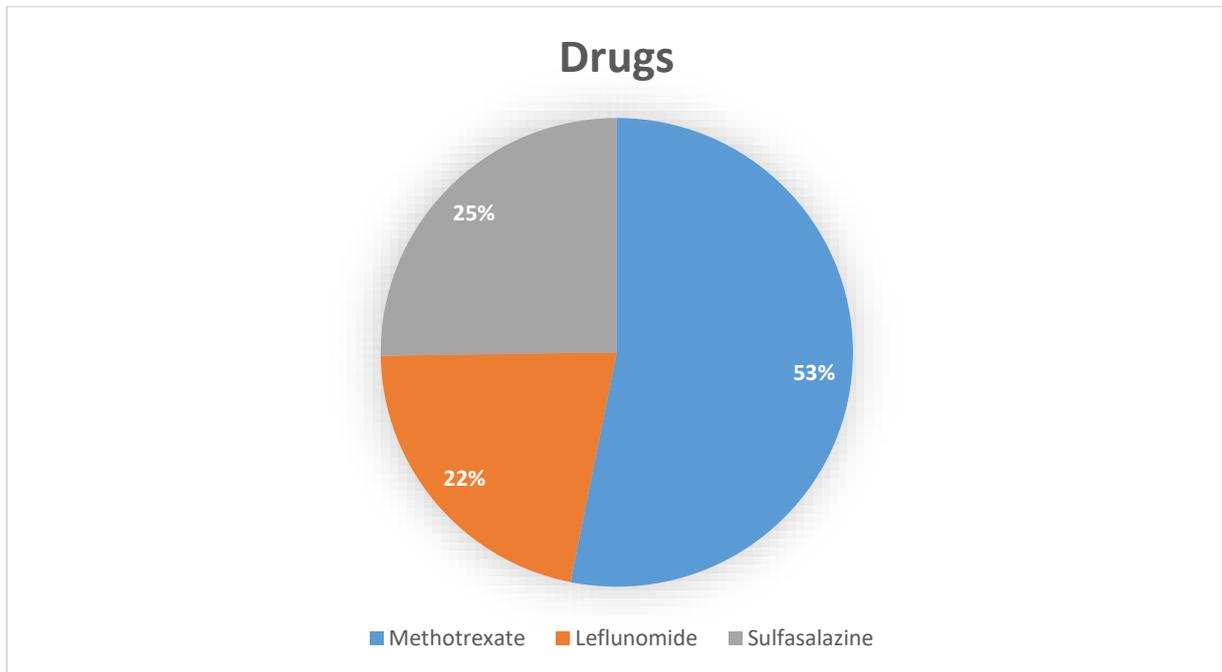


Figure No. 7

CARDIOLOGICAL STANDARD DRUGS.

Almost all patients took cardiac standard drugs. The highest rates of use among patients were beta-blockers and ACE inhibitors (53 and 35 patients), and the least taken drugs were SGLT2 inhibitors and anticoagulants

(12 and 9 patients). About 9/12% are forced to take anticoagulants, and 18/24% are forced to take antiplatelet agents , which in turn greatly increases the risk of bleeding.

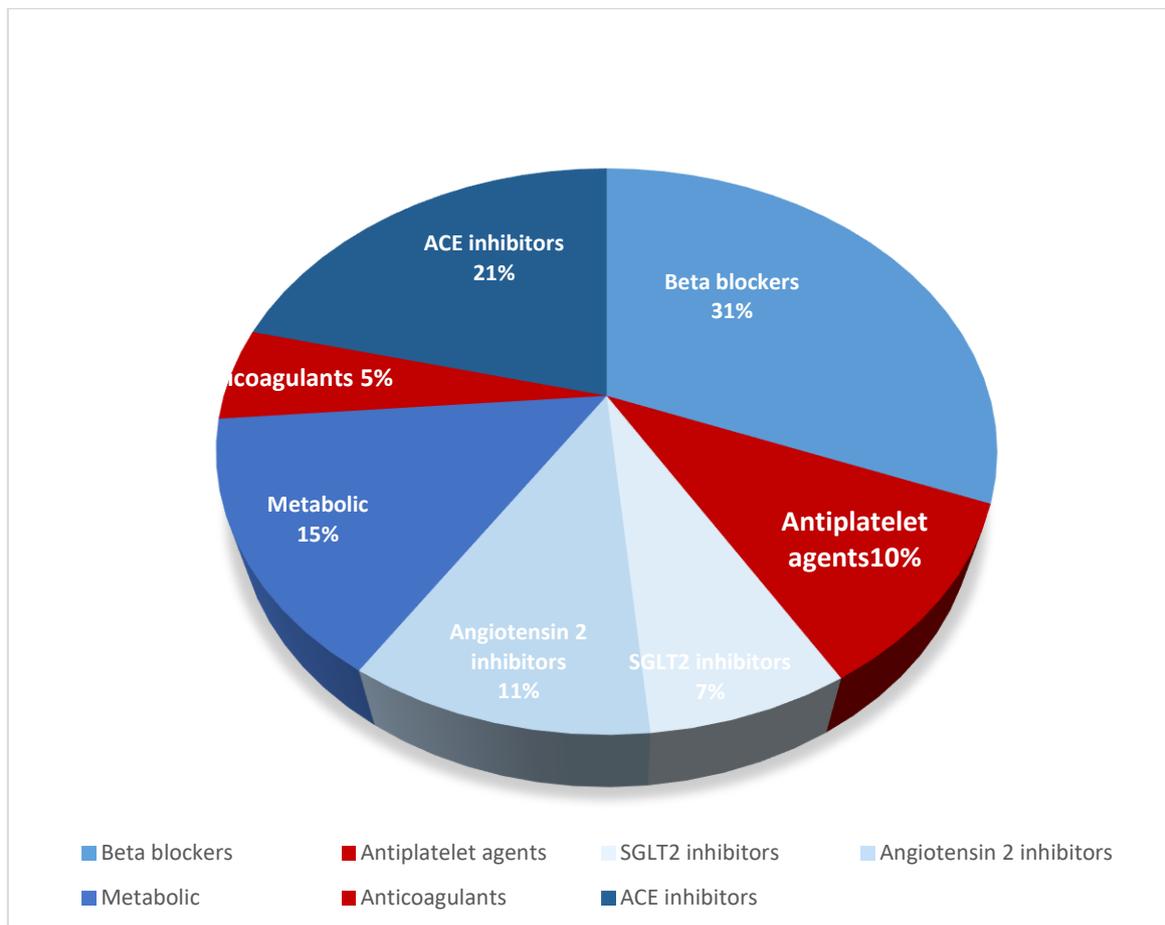


Figure No. 8

LOW IMPACT RISK FACTORS:

The presence of a history of coronary heart disease also increases the risk of development and progression of NSAID-induced gastropathy. The study found that 25/34% of patients have coronary artery disease in its various stages. Of these, 21/84% of patients have high scores (5-6 points) on the Charlson scale, and they also have the highest annual mortality rates of all patients (12-13%).

HELICOBACTER INFECTION PYLORI

At the moment, there is no comprehensive data on the contribution of Helicobacter pylori infection to ulcerogenesis in patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) for a long time. Accordingly, the role of Helicobacter pylori in preventing this pathology is not well defined.

NSAIDs and proton pump inhibitors (PPIs) should be used at therapeutic dosages; Study data in the main and control groups should be comparable.

The role of Helicobacter pylori infection and its contribution to the pathogenesis of gastropathy is not

completely clear. There are a number of studies showing that the interaction between Helicobacter pylori and non-steroidal anti-inflammatory drugs in the development of ulcers can be synergistic, additive, independent or antagonistic.

At the same time, in a meta-analysis by JQ Huang, the use of NSAIDs and Helicobacter pylori infection were identified as independent risk factors for the development of ulcers, which in combination act together. Presence of Helicobacter pylori increased the risk of developing ulcers in patients taking NSAIDs by 3 times (the prevalence of erosive and ulcerative changes in patients with HP infection was 53% and 21% in patients without HP). These data indicate that some patients with Helicobacter pylori are prone to the development of erosive and ulcerative complications when using NSAIDs or that NSAIDs may aggravate complications in individuals with Hp-induced ulcers.

There are several clinical factors that increase the risk of serious upper gastrointestinal complications in individuals taking NSAIDs: age, concomitant treatment



with anticoagulants and corticosteroids, a previous history of peptic ulcer disease, use of high-dose NSAIDs. Most NSAIDs are organic acids, and in aqueous dilution the pH of NSAIDs is higher than that of the parietal cell hydrochloric acid, so NSAIDs move into mucosal cells according to a pH gradient. Thus, in addition to the lack of prostaglandin, NSAIDs damage the gastric lining by hyperacidity .

Stopping NSAIDs and reducing the dose of NSAIDs is often not possible in patients with rheumatoid arthritis; in addition, many of them receive high doses of NSAIDs in combination with corticosteroids, which leads to an increased risk of gastroduodenal ulcers . Many of the studies on the use of NSAIDs have been conducted on patients with rheumatoid arthritis ; however, unfortunately, there are no data on other drugs. In addition, some immunosuppressants are likely to interact with Helicobacter pylori , so, according to AS Taha , the use of sulfasalazine increases the risk of stomach ulcers.

Thus, reducing the risk of developing erosive and ulcerative changes in the gastroduodenal zone after Helicobacter eradication pylori is more clearly noted in patients just starting to take NSAIDs compared to those already receiving NSAID therapy. Helicobacter eradication pylori and the prevention of complications of gastropathy should be as individual as possible based on recently obtained data.

DRINKING ALCOHOL

Ethanol has a special place in the development and production of NSAID-induced gastropathy . All male reviewers consumed alcoholic beverages in different amounts and at different times. Among female reviewers, this figure was 4/6%. Alcohol not only contributes to the development of ulcerative diseases in the gastrointestinal tract and increases the risk of bleeding, which is one of the main causes of NSAID-

induced gastropathy , it develops cardiovascular diseases in a specific form such as coronary artery disease with a further increase in the index on the Charlson scale and an increase in the annual mortality rate, but also develops chronic renal failure.

TREATMENT OF NSAID-INDUCED GASTROPATHY WITH THE ADDITION OF THE DRUG REBAGIT TO THE STANDARD TREATMENT .

Assessment of the condition of patients in the main and study groups

During the study, patients were divided into two groups: The main group included 30 patients, and the control group included 43 patients. The first group included patients who received standard treatment with the addition of rebagit (rebapimid) to the treatment. The second group included patients who received only standard treatment, without the drug Rebagit (rebapimid).

The standard treatment of NSAID-induced gastropathy included the following drugs: The treatment algorithm for NSAID- associated gastropathy primarily decides on the possibility of discontinuing aspirin and other non-selective NSAIDs, or replacing them with selective COX 2 inhibitors;

4. PPI therapy in double doses;
5. Eradication therapy - standard treatment regimens aimed at the complete destruction of Helicobacter pylori in the gastric mucosa in order to provide favorable conditions for the healing of ulcers and other damage to the mucosa;
6. Adding a drug to standard treatment - Rebagit .

In patients of these groups, indicators of quality of life and the condition of patients before treatment and after treatment were examined and compared.

The following data were obtained during the study of the main group.

Table No. 2

General characteristics of patients by groups

| Indicators | 1st group | | 2nd group | |
|---------------------------|-----------|-----|-----------|-----|
| Floor: | | | | |
| women | 24 | 80% | 41 | 95% |
| men | 6 | 20% | 2 | 5% |
| Age: | | | | |
| under 50 years old | 12 | 40% | 21 | 48% |
| over 50 years old | 18 | 60% | 22 | 52% |



| | | | | |
|---------------------------------------|----|-------|----|---------|
| Duration of disease, years | | | | |
| >5 years | 17 | 56.6% | 26 | 61% |
| <5 years | 13 | 43.3% | 17 | 39% |
| Immunological characteristics: | | | | |
| seropositive RA | 26 | 86% | 34 | 79% |
| seronegative RA | 4 | 14% | 9 | 21% |
| DAS28 activity: | | | | |
| low (<3.2) | 1 | 3% | 10 | 23% |
| average (3.2–5.1) | 6 | 20% | 13 | thirty% |
| high (>5.1) | 23 | 77% | 20 | 47% |
| X-ray stage: | | | | |
| I | 0 | 0% | 1 | 4.3% |
| II | 13 | 43.3% | 9 | 21% |
| III | 14 | 46.6% | 28 | 65% |
| IV | 3 | 10% | 5 | 11.7% |
| Functional class: | | | | |
| I | 1 | 3% | 0 | 0% |
| II | 22 | 73.3% | 29 | 67% |
| III | 6 | 20% | 13 | thirty |
| IV | 1 | 3.3% | 1 | 3% |

Before treatment, 12/40% of patients had unrestricted movement, and 18/60% had partially limited movement. After treatment, movement became unrestricted in 16/54% of patients, which shows a 25% improvement in movement in patients with limited movement. There were no patients on the pastel regimen.

When studying the degree of self-care, it was revealed that before treatment, 2/7% of patients were not able to eat and put on their shoes on their own. After treatment, this figure dropped to 1/3% of the patient. About 15/50% of patients had partial limitation of self-care. After treatment, this figure was 12/40%.

When examining the degree of discomfort, it was revealed that before treatment, 4/13.3% experienced a high level of discomfort and pain. After treatment, the same figure dropped to 1/3% of patients, which greatly improved their standard of living. 16/54% of patients had a low level of discomfort. After treatment, this figure decreased to 10/33.3%. 3/10% of patients had

severe fear and deep depression. After treatment, this indicator was absent in patients, which reduced the risk of disease progression and greatly improved their standard of living.

When studying the control group, the following data were obtained. The results were more modest compared to the main group. Before treatment, 18/45% of patients had unrestricted movement, and 25/55% had partially limited movement. After treatment, movement became unrestricted in 21/48% of patients, which shows a 15% improvement in movement in patients with limited movement. There were no patients on the pastel regimen.

When studying the degree of self-care, it was revealed that before treatment, 3/7% of patients were not able to eat and put on their shoes on their own. After treatment, this figure dropped to 2/5% of the patient. About 19/44% of patients had partial limitation of self-care. After treatment, this figure was 17/40%. When examining the degree of discomfort, it was found that



before treatment, 3/7% experienced a high level of

| Patients' condition | Before treatment | | After 6 weeks of treatment | | After treatment | |
|---|------------------|------|----------------------------|------|-----------------|------|
| | n | % | n | % | n | % |
| Movement | | | | | | |
| Unlimited | 13 | 0.43 | 15 | 0.50 | 17 | 0.57 |
| Partially limited | 17 | 0.57 | 15 | 0.50 | 13 | 0.43 |
| In bed rest | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 |
| Self-service | | | | | | |
| Unlimited | 14 | 0.47 | 15 | 0.50 | 16 | 0.53 |
| Partially limited | 15 | 0.50 | 14 | 0.47 | 13 | 0.43 |
| Unable to put on shoes and wash himself | 1 | 0.03 | 1 | 0.03 | 1 | 0.03 |
| Daily routine | | | | | | |
| Unlimited | 14 | 0.47 | 15 | 0.50 | 16 | 0.53 |
| Partially limited | 15 | 0.50 | 14 | 0.47 | 13 | 0.43 |
| Unable to carry out daily activities | 1 | 0.03 | 1 | 0.03 | 1 | 0.03 |
| Pain and discomfort | | | | | | |
| No | 8 | 0.27 | 9 | 0.30 | 14 | 0.47 |
| Eat | 20 | 0.67 | 19 | 0.63 | 15 | 0.50 |
| Severe pain and discomfort | 2 | 0.07 | 2 | 0.07 | 1 | 0.03 |
| Anxiety and depression | | | | | | |
| No | 7 | 0.23 | 12 | 0.40 | 16 | 0.53 |
| Eat | 22 | 0.73 | 18 | 0.60 | 14 | 0.47 |
| Severe fear and depression | 1 | 0.03 | 0 | 0.00 | 0 | 0.00 |

discomfort and pain.

After treatment, the same figure dropped to 2/5% of patients, which greatly improved their standard of living. 19/44% of patients had a low level of discomfort. After treatment, this figure dropped to 16/37%. 4/9% of patients had severe fear and deep depression. After treatment, this figure was present in 2/5% of patients, which reduced the risk of disease progression and greatly improved their standard of living.

When examining the degree of discomfort, it was found that before treatment, 3/7% experienced a high level of discomfort and pain. After treatment, the same figure dropped to 2/5% of patients, which greatly improved their standard of living. 19/44% of patients had a low level of discomfort. After treatment, this figure dropped to 16/37%.



4/9% of patients had severe fear and deep depression. After treatment, this figure was present in 2/5% of patients, which reduced the risk of disease progression and greatly improved their standard of living. When studying the quality of life and its changes during the study, the following data were obtained.

The EQ-5D questionnaire index is the main value in measuring quality of life. Thus, the quality of life in patients of the main group, before the start of treatment (standard treatment + rebagitis), the coefficient was equal to 19.8. After completing a 6-week course of treatment, this figure decreased to 17.6. It can be seen that the coefficient decreased by 2.2 points or 11%. The quality of life index of patients at the end of treatment decreased from the initial 19.8 points to 14.8 points. The coefficient decreased by 5 points or 25%.

The quality of life in patients in the control group, before the start of treatment (standard treatment - without rebagitis), the coefficient was equal to 32.4. After completing a 6-week course of treatment, this figure decreased to 31.8. It can be seen that the coefficient decreased by 0.6 points or 2%. The quality of life index of patients at the end of treatment decreased from the initial 32.4 points to 30.6 points. The coefficient decreased by 1.8 points or 5.56%.

As can be seen from the results, in the main group, which also took the drug Rebagit along with standard treatment, the improvement in quality of life was 4.5 times greater than in the control group.

Within the main group, patients were divided into two groups:

1) The first group, where patients took 100 mg of Rebagit 3 times a day for 10 weeks (18/60%).

2) The second group, where patients took 100 mg of Rebagit 3 times a day, but for 3-5 weeks (12/40%). After 12 weeks of treatment, the incidence of gastric and duodenal ulcers and the influence of other risk factors were two times lower in patients of the first group who took drug Rebagit for 12 weeks at a dose of 300 mg per day, compared to the second group, where treatment lasted only 3-5 weeks.

Undesirable drug reactions leading to withdrawal of the drug Rebagit appeared from the 50-58th day, which explains the high tolerance of the body to this drug.

The results of clinical studies carried out from the standpoint of evidence-based medicine substantiate the conclusion that the drug Rebagit is a highly effective and safe remedy for the prevention and treatment of NSAID-induced gastropathy. It is advisable to use the drug during short-term use of NSAIDs, as there is a risk of developing induced gastropathy. Prescribing Rebagit is also advisable for apparently healthy individuals when treated with NSAIDs. Taking Rebagit is also indicated for patients who require long-term use of NSAIDs. As previously demonstrated, the drug Rebagit, when taken

prophylactically, significantly reduces the risk of developing NSAID-induced gastropathy. After all, the drug Rebagit can and should be prescribed not only as a treatment for NSAID-induced gastropathy, but also for the prevention of the disease if the patient has risk factors. The drug showed the most effective when dosed 3 times a day, 100 mg. The full course of treatment lasted 3-5 weeks, but it turned out that the best effect was achieved with an 8-10 week course of treatment.

All data obtained allow us to conclude that Rebagita is safe and highly effective in the prevention and treatment of NSAID-induced gastropathy.

PREVENTION OF NSAID-INDUCED GASTROPATHY

The preventive algorithm for NSAID-induced gastropathy mainly depends on the NSAID drug received, the risk of "erosive ulcerative" lesions of the duodenum and stomach in the patient.

If patients do not have risk factors for NSAID-induced gastropathy, the least ulcerogenic non-selective NSAIDs such as Ibuprofen and others are prescribed, and if possible, not in the full dose, but in the minimum effective dose per day.

At moderate risk, when the patient has a couple of risk factors, and in these cases, PPI drugs.

In the presence of a large number of factors, a high risk of developing NSAID-induced gastropathy, the simultaneous use of aspirin, corticosteroids or anticoagulants is prescribed a combination of PPI drugs and COX-2 inhibitors.

Before prescribing NSAIDs, patients should be screened for the presence of Helicobacter infection. pylori. In the presence of many risk factors and anamnestic complications of ulcerative lesions, the risk of NSAID-induced gastropathy is very high. In this case, preference should be given to the use of selective COX-2 drugs in combination with PPIs and the use of NSAIDs should be avoided.

No less importance in the prevention of NSAID-induced gastropathy has correct use of NSAID drugs themselves, as well as the use of selective NSAIDs, and the exclusion of modifiable risk factors,

Consequently, an adequate assessment of the risk factors for NSAID-induced gastropathy, creating, if necessary, a cover in the form of prescribing a PPI, choosing the optimal NSAID drug for a given patient, GCS and the drug Rebagit reduce the risk of such lesions and prevent the development of serious complications.

Nowadays, in the treatment and prevention of erosive and ulcerative lesions when taking NSAIDs, drugs of the following groups are mainly used:

- proton pump inhibitors (PPIs);
- synthetic prostaglandin analogues;
- histamine H2 receptor blockers.



After conducting many randomized and multicenter studies (OMNIUM, ASTRONAUT), it was concluded that the most effective means for the treatment and prevention of NSAID-induced gastropathy are PPI drugs.

First of all, the process of treating NSAID-induced gastropathy requires solving the issue of the possibility of banning the use of non-selective PVPs and replacing them with other alternative drugs.

If a Helicobacteri infection is detected pylori eradication therapy is carried out in reviewers .

Nowadays, a set of measures has been created that can increase the effectiveness of standard triple therapy - this

Taking PPI drugs twice a day in an increased dose - double the standard dose;

Increasing the duration of triple therapy to two weeks;

Addition of tripotassium bismuth dicitrate at a dose of 240 mg 2 times a day, to standard triple therapy;

Addition of Saccharomyces probiotic boulardii (enterol 250 mg 2 times a day) to standard triple therapy.

The current option for the first line of " Eradication " therapy if the patient has intolerance to penicillin is the classic four-component scheme: based on tripotassium bismuth dicitrate - 120 mg 4 times a day, with a combination of metronidazole - 3 times a day, 500 mg, with a PPI - 2 times a day in a standard dose, tetracycline 4 times a day, 500 mg, for 10 days.

If standard triple therapy " Quadrotherapy " with tripotassium bismuth is ineffective dicitrate is also used as the main second-line treatment regimen.

Quad therapy without bismuth preparations includes: Amoxicillin - 2 times a day, 1000 mg; Praton pump inhibitors - 2 times a day in standard dosage ; Metronidazole - 2 times a day, 500 mg and Clarithromycin - 2 times a day, 500 mg.

These two alternative options for " Eradication " therapy are also used in cases of resistance of Helicobacteri strains pylori to Clarithromycin .

Third-line therapy is based on determining the individual sensitivity of Helicobacteri pylori to antibiotics.

CONCLUSIONS:

1. When analyzing the study data, it was revealed that patients suffering from rheumatoid arthritis and complications of NSAID-induced gastropathy , the risk of blood loss was on average 2.9%.

2. A comorbid condition with NSAID-induced gastropathy worsens the course of the disease, its prognosis, as well as the quality of life of patients. This is proven by the fact that all patients who had high risk factors received a high negative score in the EQ-5d questionnaire. And the use of the drug Rebagit in these patients improved their quality of life. Over a 12-week course of treatment, patients' discomfort and pain

decreased from 67% to 50% ($p < 0.05$) according to the EQ-5d questionnaire.

3. In patients with rheumatoid arthritis, the use of the Charlson index to determine the comorbid condition is not targeted, since all patients with a high risk factor have a low Charlson index and a high risk of bleeding.

4. When the drug Rebagit was added to the standard treatment, patients' dyspeptic complaints significantly decreased compared to those who did not take the drug Rebagit . You can also see a decrease in GERD-Q scores from 15 points to 7, with a 12-week course of treatment.

5. Particularly important is the attachment of patients to the course of treatment for gastrointestinal diseases, in particular NSAID-induced gastropathy , which contributed to effective treatment, which is reflected in the MARS questionnaire.

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