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Rheumatoid Arthritis and Gastroduodenal Damage (Retrospective Analysis)

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Authors' contributions

This work was carried out in collaboration between all authors. Author NKT designed the study, wrote the protocol, performed data collection; wrote the initial manuscript and revisions. Author BSA performed the literature review, data analysis and processing, manuscript writing, edition and revisions. Author MSK helped with the writing of the manuscript. Author IRM helped with the statistical analysis. Author MVS edited the manuscript and revisions. All authors read and approved the final manuscript.

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ABSTRACT

Background: Assessment of progress and process in Rheumatoid Arthritis (RA) and Gastroduodenal Damage (GDD) control at the population level is increasingly important. Rheumatoid arthritis is an autoimmune disease of unknown etiology. We aimed to investigate coherence between RA and pathology of Gastroduodenal Zone (GDZ) and shown development of GDZ pathology cause of use Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) for treating RA.

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Methods: The work focused on identifying, among patients newly presenting with undifferentiated inflammatory synovitis, factors that best discriminated between those who were and those who were not at high risk for persistent and/or erosive disease—this being the appropriate current paradigm the disease construct “rheumatoid arthritis” and “gastroduodenal damage” [1,2,3]. In this article, it based on a retrospective analysis of case histories of patients with RA, data research pathology GDD to the extent of disease activity, duration of history and the failure of the joints, as well as the characteristics of ongoing pharmacotherapy.
Results: The results show that the pathology GDD in RA patients are often, in every fifth patient is a concomitant disease, and every tenth - is manifested in the form of clinical symptoms, the main causes of gastroduodenal lesions are viscera, long-term course of the disease and the frequent use of NSAIDs and corticosteroids. Among the patients 567 were women (90.7%), men - 58 (9.3%), i.e. in a ratio of 9.8: 1.0.
Conclusion: This new retrospective analysis shown that the pathology of Gastroduodenal Zone (GDZ) in patients with RA is quite common; every third patient has the symptoms of GDZ. Moreover, the main causes of gastroduodenal damage during RA are visceral, a long-term course of the disease, and the frequent use of NSAIDs and glucocorticosteroids (GCs).

Keywords: Rheumatoid arthritis; gastroduodenal damage; gastroduodenal zone; non-steroidal anti-inflammatory drugs; glucocorticosteroids.

1. INTRODUCTION

According to modern concepts, Rheumatoid Arthritis (RA) is a chronic, systemic, unknown etiology, autoimmune disease that primarily affects the joints. It characterized by symmetrical erosive arthritis (synovitis) and a wide range of extra-articular manifestations. Approximately 0.5% of the adult population worldwide suffers from RA. The functional disability that results from progressive joint destruction is associated with substantial cost, significant morbidity and premature mortality [1,2,3,4,5,6]. And also the joints synovial membrane is damaged, its continued hyperplasia and rapid increase in synovial tissue, accompanied by progressive destruction of cartilage and bone tissue. As a result, patients are developed disability and even reducing life expectancy [7].

The prevalence of patients with RA reaches 1% and the economic loss of society is comparable to those of coronary heart disease [7,8] there are 2-3 times more women with RA than men. The disease can begin in any period of life, but most often it strikes people of working age [9,10]. In the absence of the effective therapy, the lifespan is decreased 3 years for women and 7 years for men [11,12]. During the natural process of RA, and even while making the standard therapy, 60-90% of patients lose their ability to work and 1/3 become disabled after 20 years of disease commencement [13].

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are widely used for the treatment of RA. NSAIDs show a number of undesirable side reactions in addition to the positive effect in patients with RA. Among the most common side effects of NSAIDs are gastropathy. According to some authors the incidence of this (with gastropathy) complication in patients with RA is up to 15-60% [12,13]. The development of gastroduodenal side-effects of NSAIDs is fraught with dangerous complications such as gastrointestinal bleeding, perforation of the stomach ulcers, etc. [14,15,16]. In the development of gastroduodenal complications when using NSAIDs in RA is important the presence of risk factors such as older age, the presence of pathology of the gastroduodenal zone, the combined use of two NSAIDs or NSAIDs with glucocorticosteroids or with other drugs [14,17,5,18]. Therefore, to ensure safe and effective pharmacotherapy of RA it is important to assess the risk of gastroduodenal complications from used NSAIDs.

Gastroduodenal damage was diagnosed with endoscopic, X-ray examinations and basis of patients’ complaint. Patients have complained to pain where localized epigastric region is. Moreover, Helicobacter Pylori was determined in the blood with using Enzymoimmunoassay (EIA).

2. MATERIALS AND METHODS OF THE STUDY

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There was held a retrospective analysis of 625 case histories of patients with RA (aged 16-90) who were treated at the Rheumatology Department of Tashkent Medical Academy (TMA) from 2012 to 2014. In addition, functional health status of patients was differentiated. According to process of disease under the clinical data we separated 2 groups: Slowly progressing and quickly progressing RA (70.3% and 29.7% respectively). Furthermore, immunological analysis (serodiagnostic assay) has shown two major groups: Seropositive (61.4%) and seronegative (39.6%). As a matter of fact, patients were divided into 3 groups according to the presence of disease in upper abdomen: The first group - RA patients without concomitant pathology of GDZ; second - patients with concomitant pathology of GDZ; third group - RA patients with symptomatic damage of GDZ [18,6]. The state of the gastroduodenal zone was assessed taking into account the duration of the anamnesis, the degree of disease activity, functional insufficiency of the joints, forms of the disease, patient's age and underlying disease pharmacotherapy. Statistical analysis was performed using a set of packet EXEL.

3. RESULTS

Conducted retrospective analysis of medical records of patients with RA who were treated in the department of rheumatology of III clinic in Tashkent Medical Academy in the period from 2012 to 2014 illustrates that during this period, 625 patients were treated with a diagnosis of RA. Among the patients 567 were women (90.7%), men - 58 (9.3%), i.e. in a ratio of 9.8: 1.0, which is consistent with literature data. A careful analysis of the medical records revealed that 33.3% of patients with RA. They had signs of destruction of GDZ in the form of complaints, such as heartburn, belching, loss of weight, gravity in epigastric zone and objective clinical signs. At the same time, the diagnosis as a comorbidity of GDZ diagnosed in only 9.3% of patients, i.e. in half of patients with signs of GDZ damage (Fig. 1).

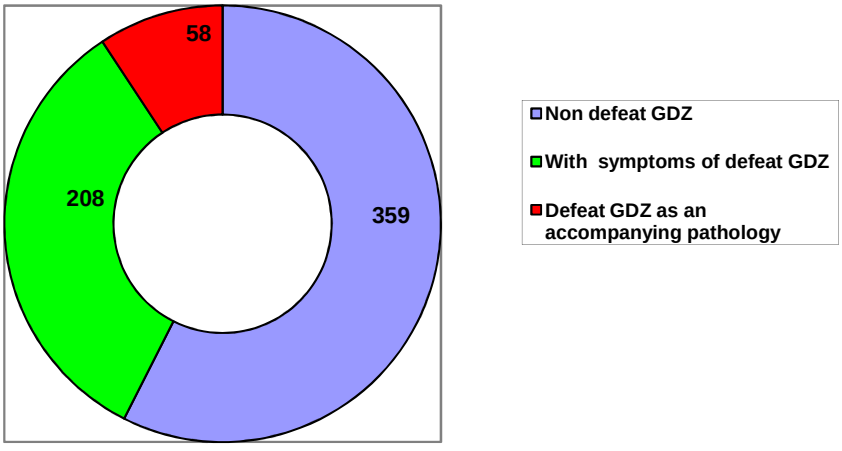

Fig. 1. The specific ratio of RA patients with and without disease pathology of GDZ

Thus, it is evident that the damage of GDZ in RA is a frequent phenomenon and occurs almost in every second patient. Furthermore, among patients with signs of damage of GDZ, 33.3% had complaints. Only 9.3% of patients were diagnosed with concomitant disease of GDZ. Therefore, in general, almost every third patient has symptoms of GDZ damage and a place associated disease GDZ, then every tenth is diagnosed with comorbidity. However, it remains unknown whether they had the symptoms of RA associated GDD or visceral form of RA. In addition, we should remember that NSAIDs and GCS, commonly used in RA treatment, may also cause the formation of these symptoms.

From the analysis it is evident that the disorder of GDZ in RA is a frequent phenomenon. Moreover, almost every third patient has symptoms of gastroduodenal zone damage, and then every tenth is diagnosed with comorbidity. However, it remains unknown whether they had the symptoms of RA associated GDZ damage or visceral form of RA.

The analysis of the dynamics of occurrence of RA with GDZ damage in the structure of all patients with this disease was held in the period from 2012 to 2014. The results are shown in Fig. 2.

The proportion of RA patients with symptoms of GDZ damage and comorbidities of GDZ fluctuated from 31.5% to 37.9% and from 5.5% to 12.9% respectively in the structure. In the Fig. 2 the highest share took place in 2012. Overall, the results of this study authors considered relatively equal proportion of RA patients with GDZ pathology in the structure of RA patients in the analyzed period.

As mentioned above, the genesis of occurrence identified during the analysis of the damages of GDZ in patients with RA, require further focused study. In this regard, the variants of RA process depending on the presence or absence of symptoms of GDZ disorder were studied. As can be seen from the data presented in Fig. 3, the proportion of patients with articular-visceral form of RA in the group with the GDZ damage was 16.7% higher than the group without pathology of GDZ.

Therefore, among RA patients with GDZ pathology there are relatively more patients with articular-visceral form of the RA. The ratio between the joint and the joint-visceral form of RA in the group of patients without GDZ pathology is 3.5: 1.0, while in the group of patients with GDZ pathology it is 1.6: 1.0, respectively. These data suggest that the GDZ pathology identified in the process of retrospective study may be a manifestation of the underlying disease, caused by a primary lesion of connective tissue stroma of GDZ.

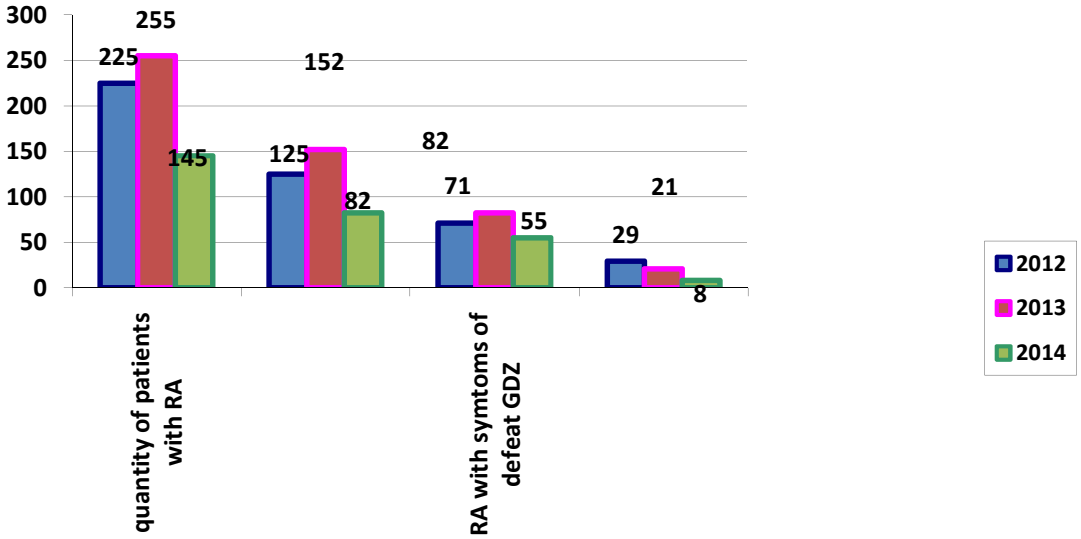

Fig. 2. Incidence of patients with RA and its combination with GDZ for the years 2012 - 2014

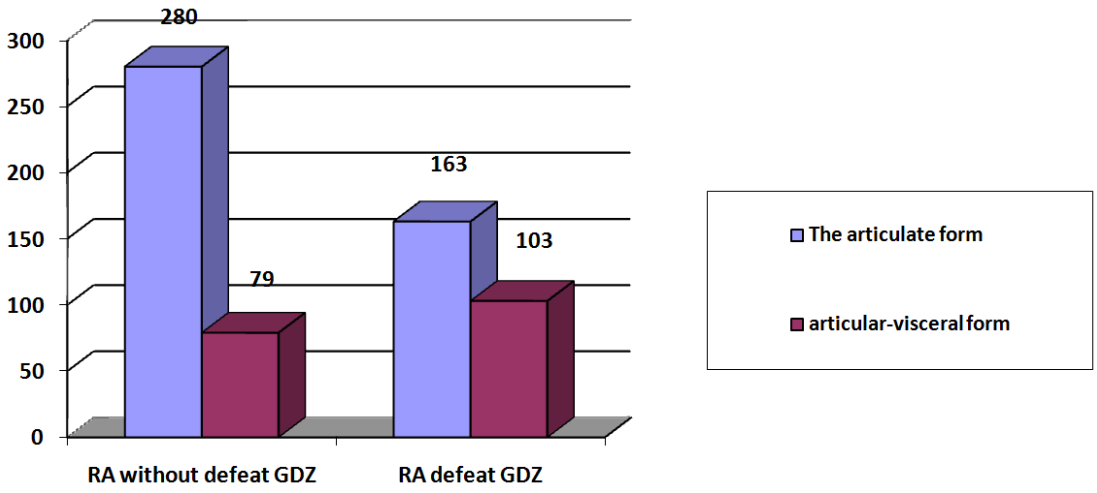

Fig. 3. Relative density joint and joint-visceral forms RA in patients with and without GDZ pathology

To confirm this hypothesis, the degree of severity of RA and the severity of functional impairment of joints, depending on the presence or absence of GDZ lesions were analyzed. The results of this analysis were presented in Table 1.

Table 1. The division of patients with RA depending on the activity (%)

The degree of activity	The degree of activity of RA	
	RA without gastropathy	RA with gastropathy
I	12,8	9,4
II	66	67,7
III	21,2	22,9

As can be seen from the data, the severity of RA in both compared groups of RA patients was predominantly presented by II and III degree of activity. The proportion of patients with degree II and III of RA is 90.6% in the group of patients with GDZ pathology and 87.2% in the group without GDZ pathology.

Almost a similar pattern can be observed in the degree of functional failure of joints (Table 2).

Therefore, the degree of severity illness and joints functional failure, both of groups were comparable. From the above it becomes obvious that the genesis of the emergence of GDZ destruction in RA cannot be explained only by the damage of the connective tissue of this area (visceral damage), and that dictates need to find other reasons.

As mentioned above, one of the leading causes of injury of GDZ under development and progression of RA is a destruction of the mucosa layer of GDZ by medications used for treatment of this disease.

Table 2. The division of patients with RA depending on the degree of functional failure of joints (%)

The DFFJ	The degree of functional failure of joints	
	RA without gastropathy	RA with gastropathy
0	9,5	4,1
I	25,9	25,9
II	57,9	58,3
III	6,7	11,7

Thus, the structure of medications used for patients with RA and their share depending on the presence or absence of GDZ pathology has been studied.

The results of this analysis are presented in the Table 3.

As can be seen from the data presented, the highest share in the structure of RA pharmacotherapy is occupied by NSAIDs, which in the groups of patients with the GDZ pathology and without it is 41% and 39.3%, respectively. However, the ratio of injection and oral dosage forms was similar in both groups and it was 1.4: 1.0 and 1.3: 1.0.

Table 3. The structure of the medications and the proportion of NSAIDs and glucocorticosteroids in the pharmacotherapy of RA

Medications	The dosage form	Total number (abs)		The share in the structure of treatment (%)	
		RA	RA+gastropathy	RA	RA+gastropathy
GCS	Injection	498	225	19,2	23,2
	Pill	231	98	8,9	10,1
	Total	729	323	28,1	33,3
NSAIDs	Injection	593	224	22,9	23
	Pill	424	175	16,4	18
	Total	1017	399	39,3	41
IPP		573	239	22,1	24,6
Basic means		272	111	10,5	1,1
Total		2591	972	100	100

Glucocorticosteroids were ranked in the second structure of pharmacotherapy and patients without pathology of GDZ are 28.1% and in the group of patients with GDZ pathology are 33.3%. The ratio of injections to oral forms was 2.2: 1.0 and 2.3: 1.0. Consequently, in both groups within pharmacotherapy were equally often used NSAIDs and glucocorticosteroids.

The share of basic drugs (symptom-modifying antirheumatic drugs (SMARD) and disease-modifying antirheumatic drugs (DMARD)) in patients without gastroduodenal pathology was 10.5%, while in the group with GDZ pathology was only 1.1%.

Drugs aimed to protect GDZ took less weight in the pharmacotherapy of patients without GDZ disease and reached 22.1%, and in RA patients with GDZ pathology was 24.6% (Table 3).

As can be seen from the results, drugs used in the pharmacotherapy in both groups were applied in comparable proportions, although the prevalence proportion of GCS in patients with pathology of GDZ can be observed. In addition, in the group of patients with GDZ pathology is noticeable; there is not enough proportion of antisecretory action of drugs.

Thus, the analysis of pharmacotherapy of RA depending on the presence of pathology of GDZ suggests that the structure of medicines and their specific weight of the compared groups do not differ significantly. That's why, the role of drug therapy in the genesis of GDZ damage identified during the analysis cannot be regarded as proven, but also we cannot refute it. Possibly, the drug aggression in the genesis of the identified GDZ pathologies acquires importance considering the length of treatment of RA patients. To clarify this issue, a focused analysis of case histories of patients with RA depending on the length of history was conducted. The results of this analysis are presented in Figs. 4. A and B.

As can be seen from the data, in the group of RA patients without GDZ pathology specific weight of patients with a case history of a year was 1.7% and in the group of patients with GDZ pathology was 3%. When disease duration is from 1 to 5 years, RA patients without GDZ pathology made dominance (35.9% and 25.9%, respectively). By increasing the longevity of anamnesis, of the specific weight of patients with GDZ pathology prevailed over the group of patients without GDZ disease. Thus, the number of patients with a longevity history of 5-10 years, 10-15 years and over 15 years in the group of patients without GDZ disease was 25.9%, 17.5% and 18.9%, and in the group with GDZ pathology was 27.1%, 19.9% and 24.1%, respectively. That is, the number of RA patients with GDZ pathology increases with the duration of the disease, which is quite reasonable, since RA patients have to take drugs for a long time, causing damage to the gastric mucosa.

In analyzing the distribution of patients with and without GDZ disease by age categories (Fig. 5.) the results were revealed: a significant difference in the age aspect of the study groups of patients with and without gastropathy was not revealed.

Thus, a retrospective study showed that the GDZ pathology is found in 33.3% of patients with RA, which to some extent agrees with the literature data. At the same time, it was impossible to identify a clear relationship between the degree of severity of RA, functional failure of joints, the age aspect of RA patients, and the presence of

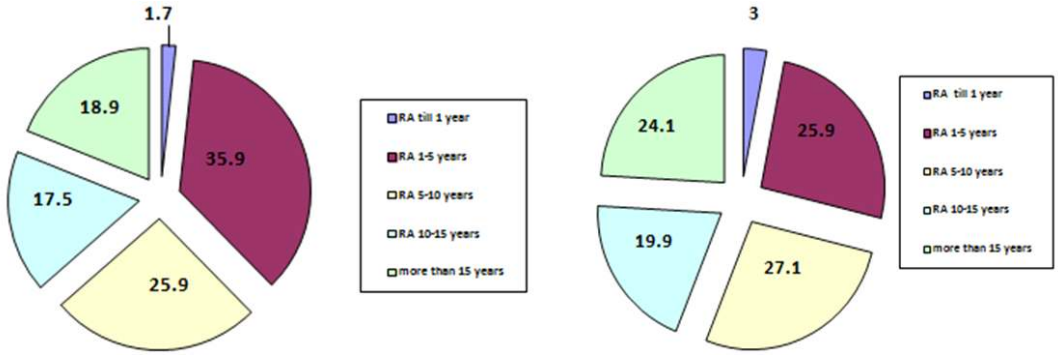

Fig. 4. The division of patients with RA depending on the length of history without GDZ pathology (A) and with GDZ pathology (B)

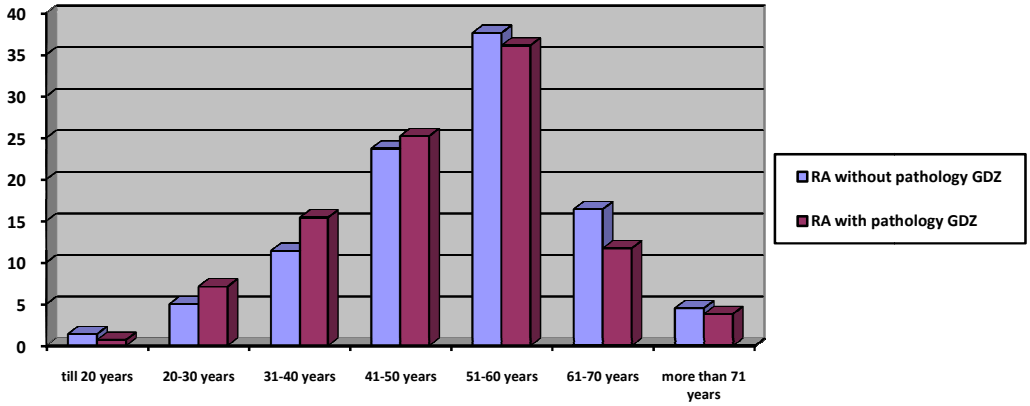

Fig. 5. The division of RA patients by age groups

damage of GDZ. It should be pointed out that exact relation between duration of RA, its clinical form and frequency of pathology GDZ was observed.

4. DISCUSSION

Administration of NSAIDs and GCs in the current study induced gastric ulceration and deep erosions with shedding of the superficial epithelial cells. According to mechanism of ulcerogenic effects of NSAIDs and GCs the gastric mucosa is congested and oxyntic cells are vacuolated [19]. The ulcerogenic gastrointestinal side effects of the NSAIDs are among the more serious complications in patients taking these drugs [20]. The latter authors added that prostaglandin deficiency plays a critical role in the pathogenesis of NSAID induced gastric injury. Suppression of prostaglandin synthesis is associated with reduction of gastric mucosal blood flow, disturbance of microcirculation, decrease in mucus secretion, lipid peroxidation, and neutrophil activation, which are involved in the pathogenesis of gastrointestinal mucosal disorders. Furthermore, the development of the gastroduodenal zone disorders induced by NSAIDs and GCs may also be mediated through generation of oxygen free radicals [21,19,20,22,23]. On the other hand, we should notice effects of NSAIDs and GCs in the treatment of patients with RA. GCs have been employed extensively for the treatment of RA and other autoimmune and systemic inflammatory disorders.

5. CONCLUSION

The main factors contribute to determine that the pathology of GDZ in patients with RA is quite common; every third patient has the symptoms of GDZ. Secondly, the main causes of gastroduodenal damage during RA are visceral, a long-term course of the disease, and the frequent use of NSAIDs and GCs.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Altman RD. Semin. Rheum Arthritis. 1990;(Suppl)19(2):1-5.
2. Brooks PM. American Journal. Med. 1998;104(3A):9-13.
3. Silverstein FE. Dig. Dis. Sci. 1998;43:447-458.
4. Amirjanova VN, Koylubaeva GM, Goryachev DV, et al. The cost of rheumatoid arthritis in clinical practice. Journal of South Kazakhstan Medical Academy. 2006;1(C).
5. Structure and dynamics of rheumatic diseases according hospitalization therapeutic department of the medical center. Zholdin BK, Berkinbaev SF, Talipova I Zh, Herald of the South Kazakhstan Medical Academy. 2006;1:28.
6. Erdes Sh, Lesnyak OM, Melnikova LV, et al. Efficacy and tolerability of two doses of Melox (meloxicam) at rheumatoid arthritis and osteoarthrosis. Russian Medical Journal. 2004;12(6 –C):1-4.
7. Balabanov RM, Rheumatoid arthritis. In the book. Rheumatic diseases. Edited VA. Nasonova NV. Bunchuk. - Moscow Medicine. 1997;S257:294.
8. Balabanov RM, Kashevarov RY, Olyunin YA. Antidestructive effect of leflunomide in early rheumatoid arthritis. Therapeutic Archives. 2006;6:5-10.
9. Balabanov RM. Rheumatoid arthritis with systemic manifestations. Dissertation MD. M. 1990;57.
10. Brundtland GH. Speech at the opening of the WHO Scientific Group on the damage caused by musculoskeletal disorders (The Bone and Joint Decade 2000-2010 13 January 2000 Geneva). Scientific Practical Rheumatology. 2001;1C:5-7.
11. Immunological features of rheumatoid arthritis in patients infected with hepatitis B, C and crioglobulinaemia. Therapeutic Archives. 2004;11S:74-77.
12. Karateev AE, Nasonov EL. Non-ulcer dyspepsia, NSAID associated with: The possibility of using antacids//scientific-practical. Rheumatology. 2003;2C:28-30.
13. Karateev AE, Nasonova VA. Assessing the impact of glucocorticoids and NSAIDs on the development of erosive and ulcerative lesions of the gastrointestinal tract in patients with rheumatic diseases// Therapeutic Archives. 1999;2S:26-30.
14. Nasonov EL. Therapeutic Archives. 2001;5:57-61.
15. Nasonov EL. Pharmacotherapy rheumatoid arthritis with position of demonstrative medicine. New Recommendations. Breast cancer. Tom. 2002;10(6-C):1-11.
16. Nasonov EL, Karateev AE. Clin. Med. 2000;3:4-10.
17. Nasonov EL, Svetkova ES, Tov NL. Therapeutic Archives. 1998;5:8-14.
18. Sheptulin AA. Clinical Medicine. 1999;2: 12-17.
19. Hafstrom I, Albertsson K, Boonen A, et al. Remission achieved after 2 years treatment with low-dose prednisolone in addition to disease-modifying anti-rheumatic drugs in early rheumatoid arthritis is associated with reduced joint destruction still present after 4 years: An open 2-year continuation study. Ann Rheum Dis. 2009;68:508:13.
20. Capell HA, Madhok R, Hunter JA, et al. Lack of radiological and clinical benefit over two years of low dose prednisolone for rheumatoid arthritis: Results of a randomized controlled trial. Ann Rheum Dis. 2004;63:797-803.

21. Kavanaugh A, Alvin F. Wells. Benefits and risks of low-dose glucocorticoid treatment in the patient with rheumatoid arthritis. Rheumatology; 2014. DOI:10.1093.
22. Choy EH, Smith CM, Farewell V, et al. Factorial randomized controlled trial of glucocorticoids and combination disease modifying drugs in early rheumatoid arthritis. Ann Rheum Dis 2008;67:656-63.
23. Myles AB, Schiller LF, Glass D, Daly JR. Single daily dose corticosteroid treatment. Ann Rheum Dis. 1976;35:73-6.

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