The problems of selection of adequate therapy for comorbid patients with rheumatoid arthritis

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Introduction

Rheumatoid arthritis (RA) is an immunoinflammatory rheumatic disease characterized by chronic erosive arthritis and systemic damage to internal organs, leading to early disability and reduced life expectancy in patients. Comorbid conditions in RA worsen the course and prognosis of the disease itself, the quality of life of patients and affect the choice of treatment tactics. Also, the presence of several comorbid diseases in a patient often leads to forced polypharmacy, which in itself negatively affects life expectancy.

Purpose of the study

To study the structure and frequency of comorbid pathology in patients with RA, its impact on the ongoing basic therapy.

Materials and Methods

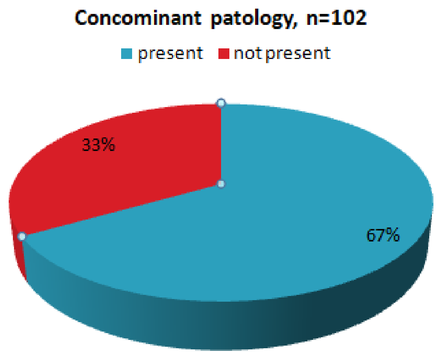
We examined 102 patients with RA (of which 67% were women) who received treatment in the cardio-rheumatology department of the University Hospital "Semey Medical University“ (Semey, Kazakhstan) and on an outpatient basis in the city's polyclinics from January 2022 to February 2023. Mean age 48.9±0.48 years, mean duration of illness 51.5±4.16 months.
The 2010 ACR/EULAR classification criteria were used to verify the diagnosis. Modified classification of RA according to Steinbroker for X-ray stage and DAS 28 index (the score of disease activity for 28 joints in modifications using ESR and CRP) were used. All subjects, upon admission to the clinic and in some cases in dynamics, underwent clinical and laboratory examinations (ECG, general blood and urine tests, AST, ALT, total protein, lipid profile, urea, creatinine, uric acid, alkaline phosphatase, blood glucose, RF, ACCP).
Clinical characteristics of patients see in the table 1.
Patients received: methodoject at an average dose of 15.4±4.8 mg/week – 48%, leflunomide 20 mg/week - 22.5%, sulfasalazine 1000 mg/day - 14.7%, combined therapy - 16.8%.

Table 1. Clinical characteristics of patients, n= 102

Sign	Characteristic	Frequency, n (%)
Stage of the disease	Very early stage	**0**
	Early stage	29 (28.4)
	Expanded stage	**48 (47.1)**
	Late stage	25 (24.5)
Form of the disease	Systemic manifestations	**74 (72.6)**
	Without systemic manifestations	28 (27.4)
X-ray stage	I	2 (3,9)
	II	**50 (49)**
	III	**42 (41.2)**
	IV	6 (5,9)
Disease activity	1	2 (2)
	2	**49 (48)**
	3	**51 (50,0)**
DAS Index (average value)		**5,23**
Immunological characteristic	ACCP- positive	**77 (75.5)**
	ACCP- negative	21 (7,5)
	not detected	4 (3.9)
	RF – positive	**68 (66.5)**
	RF - negative	18 (17.6)
	not detected	16 (15.7)
Complications	yes	**53 (52)**
	no	**49(48)**

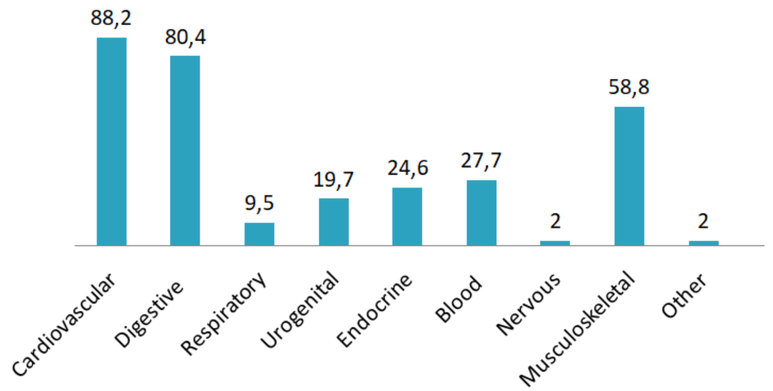
Results and disscussions

According to the results of the study, it was found that concomitant pathology was observed in 66.7% of patients, and 25% of patients had more than one disease, which generally corresponds to the literature data. (Pic.1)
When assessing the clinical and demographic characteristics of patients, it was revealed that patients with comorbid conditions are older in age, among them there were more women, however, according to all clinical, laboratory and radiological characteristics, at the time of the start of the study, there were no statistically significant differences with the group of RA patients without concomitant pathology.



Picture 1. The frequency of comorbidities in patients with RA (n=102)

Most often, patients had lesions of the cardiovascular system, gastrointestinal tract and musculoskeletal system. (Pic.2)



Picture 2. Damage to different systems in patients with RA (n=68)

Arterial hypertension (57.9%), endocrine pathology (thyroid diseases and diabetes mellitus 48% and 28.4%, respectively), osteoarthritis (51.9%), chronic pyelonephritis (48%), and ulcerative lesions of the gastrointestinal tract (GIT) (38.2%), liver pathology (28.4%) were prevailed. (Tabl.2)
As is known, the presence of chronic inflammation in the gastrointestinal tract, primarily erosive or ulcerative lesions, is a deterrent in the appointment of symptomatic and basic therapy in patients with RA and requires timely treatment. However, more than half of patients with a history of gastrointestinal pathology did not receive adequate therapy.
Osteoarthritis (OA) was detected in 51.9% of RA patients, mainly in patients older than 45 years. In 70% of patients, OA developed 1–5 years after the onset of RA and was of a secondary nature. In 4.6% of cases, RA was combined with gouty arthritis.
Chronic inflammatory diseases of the urinary tract, exacerbations of which create a problem in the selection of basic therapy, were recorded in 48% of patients with RA.

Table 2. The structure of comorbid pathology in patients with RA, n=68

Система	Нозология	Частота встречаемости n (%)
Cardiovascular system	IHD, including:	**55,8**
	Heart attack I-II FC	16,4
	Heart attack III-IV FC	**83,6**
	Myocardial infarction (anamnesis)	35,6
	Arterial hypertension (total)	**57.9**
	I	10
	II	17,6
	III	**30,3**
Digestive system	Chronic gastritis / peptic ulcer of the stomach and duodenum	**38.2**
	Chronic cholecystitis	14,2
	Chronic pancreatitis	4,7
	Liver pathology	28.4
Respiratory system	COPD	7,2
	Asthma	2,3
Endocrine system	Diabetes2 type	**28.4**
	Autoimmune thyroiditis	18.7
	Goite	**30.1**
Musculosceletal system	Osteoarthritis	51.9
	Gout	4.6
Urogenetal system	Chronic pyelonephritis	48
Blood system	Anemia	27,7
Other		14,2

After a year of observation of patients in the group with concomitant diseases, the clinical response to treatment was significantly lower compared to patients without concomitant pathology: DAS28 were 2.03 ± 0.14 points compared with 2.52±0.16 points, respectively ($p<0.05$). Incidence of side effects was significantly higher in patients with concomitant diseases (60.2% and 48.6%, respectively, $p<0.05$), although in terms of the number of patients with complications requiring BT discontinuation, groups with the presence and absence of comorbid conditions did not differ significantly (25.5% and 19.3%, respectively). Significant differences between groups were observed regarding complications from the gastrointestinal tract. Thus, dyspeptic syndrome and an increase in the level of transaminases were observed almost twice as often in the presence of concomitant pathology. In both groups, there was a trend towards a more frequent development of side effects when using combination therapy (32.5% in the presence of concomitant pathology and 29.4% in its absence), the least common complications occurred during treatment with leflunomide (14.8% and 12. 5% respectively)

Conclusion

The presence of concomitant pathology in patients with RA is associated with a lower clinical efficacy of BT, and therefore, this category of patients needs careful dynamic (every 3 months) monitoring of the course of the disease and timely correction of treatment. In patients with comorbid conditions, side effects develop with a significantly higher frequency when using basic drugs, in particular, complications from the gastrointestinal tract occur twice as often. The incidence of serious side effects is generally higher with combined BT. Thus, the ongoing therapy should not only lead to a decrease in the activity or achieve remission of rheumatoid arthritis, but also help to improve the clinical and laboratory parameters of the concomitant disease at the same time. In real practice, this dictates the need for joint monitoring of such patients by a primary care physician, a rheumatologist, and other narrow specialists.

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