REVIEWS

N. Nikolov, M. Panchovska and Zl. Kolarov. ECONOMIC ANALYSIS IN RHEUMATOLOGY

Summary. Diseases of the musculoskeletal system cause a growing interest among the general medical community and society due to their wide distribution, the risk of disability, significant advances in science and clinical medicine and pharmaceutical science and industry, and last but not least – the high cost of their treatment. Increased life expectancy combined with a number of environmental factors and individual, social and genetic peculiarities of different nations brought to the fore previously neglected diseases such as osteoarthritis and osteoporosis. According to the evaluation of the World Health Organization (WHO) in 2003 musculoskeletal disorders are the most common cause of disability, limiting an individual's ability to perform daily tasks and to participate in public life and employment. Nearly a quarter of Europeans suffer from some form of arthritis and musculoskeletal diseases (Eurobarometer 2003). Therefore, the WHO declared the years 2000 to 2010 the decade of rheumatic diseases. The logical question was asked: How much do diagnosis, treatment and rehabilitation of rheumatic diseases cost to the society? Interest to pharmacoeconomic analysis dates from the 70s and experienced rapid progress in recent years. In connection with the enormous social and financial importance of rheumatologic diseases governments and health ministries in many countries around the world and in Europe funded major studies on this topic. This review focuses on economic and clinical aspects of rheumatic diseases and analyzes the results of studies in this field carried out in recent years.

Key words: pharmacoeconomic analysis, rheumatic diseases, treatment costs

R. Shumnalieva and Zl. Kolarov. EPIGENESIS IN RHEUMATOLOGY

Summary. Over the last decade great endeavors are being made to study the etiopathogenetic mechanisms of rheumatic diseases at molecular level. It is believed that their appearance is a result from the interaction between genetic, hormonal, immune and environmental factors. The relationship between the etiological factors is made through mechanisms of epigenetic regulation that affect gene expression. In turn, epigenetic regulation is also a subject of influence of environmental factors. Clarifying these mechanisms is the subject of current and future studies, the results of which will likely provide new therapeutic options for these diseases.

Key words: epigenetic regulation, rheumatic diseases

V. Sarafian. TOLL-LIKE RECEPTORS IN RHEUMATOLOGY – WHAT WE KNOW, WHAT WE DO NOT KNOW AND WHAT WE HOPE FOR

Summary. Toll-like receptors (TLRs) are basic receptors involved in cell signaling in innate immunity. Their exogenous ligands are conserved motifs common for multiple pathogens. The endogenous ligands result from inflammatory processes. TLRs are localized mostly on cells of the innate immune system. There is evidence for implication of TLRs in the pathogenesis of rheumatoid diseases. In autoimmune diseases like SLE, rheumatoid arthritis, systemic sclerosis immune tolerance is disrupted and chronic inflammation is initiated through TLR-mediated pathways. Psoriatic arthritis and gout are also TLR-dependent diseases, as inflammation generates endogenous ligands. Their binding to TLRs activates an intracellular signal cascade, production of adhesion molecules, proinflammatory cytokines, chemokines and IFN-α. The secreted mediators break the immune tolerance and cause an autoimmune disease. Blocking of TLRs by

oligonucleotide inhibitors is a promising approach for control of the subtle molecular mechanisms in the pathogenesis of rheumatoid diseases.

Key words: TLRs, SLE, rheumatoid arthritis, oligonucleotide inhibitors

N. Stoilov, R. Rashkov and R. Stoilov. ANTIPHOSPHOLIPID SYNDROME – HISTORICAL DATA, ETIOLOGY AND PATHOGENESIS

Summary. Antiphospholipid syndrome is an autoimmune disease characterized by circulating antibodies against different phospholipids and their co-protein factors. The base manifestation of antiphospholipid syndrome is thrombosis. This process involves the endothelial cells, monocytes, platelets, and complement. Endothelial cells and monocytes can be activated by antibodies against β2GPI. Many autoimmune diseases in rheumatologycal practice including. RA and SLE API are characterized by accelerated atherosclerosis and therefore an increased risk of cardiovascular disease and mortality. As an immune-mediated process macrophages are included in its pathogenesis, which are transformed into foam cells, T cells, autoantibodies, autoantigens, which are usually components of the vessel wall, cholesterol particles and cytokines secreted by the cells presented in atherosclerotic plaques such as IL-1, IL-2, IL-6, IL-8, IL-12, IL-10, TNF, INFγ and platelet growth factor.

Key words: antiphospholipid syndrome, trombosis, pathogenesis

S. Monov and R. Rashkov. GOLIMUMAB (SIMPONI) IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Summary. Golimumab (Simponi) is a fully human monoclonal IgG1k antibody with pronounced affinity to human TNF-α. The GO-RAISE study examined the effectiveness and safety of Golimumab in 356 patients with ankylosing spondylitis (AS), aged over 18 years, for a period of 24 weeks and an extension of up to two years. The results of the GO-RAISE have demonstrated rapid initial and prolonged (104 weeks) effects of the drug in regard to disease activity, functional status and quality of life of patients. Golimumab (Simpomi) has a good safety profile in AS.

Key words: ankylosing spondylitis, tumor necrosis factor-alpha, golimumab

I. Sheytanov, R. Rashkov and Tsv. Petranova. CIMZIA – A NEW RELIABLE ALTERNATIVE THERAPY OF RHEUMATOID ARTHRITIS

Summary. Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease. The significant incidence of RA, its long duration and serious damages, that are caused in the functions of the musculoskeletal system with resulting consequences, determine its medical and social significance. The main goal of rheumatoid arthritis treatment is to achieve low disease activity and, ideally, complete remission. In recent years, significant progress has been made in the treatment of this disease through the development and implentation of TNF-α inhibitors in clinical practice. The combination of these medicines with methotrexate (MTX) gives the best therapeutic results with a good safety profile. The focus of this review is aimed at Cimzia (certolizumab pegol). The presented two large multicenter clinical trials evaluate the therapeutic efficacy and safety profile of certolizumab pegol in patients with active RA. It is concluded that Cimzia is a reliable therapeutic alternative to other TNF-α antagonists in the treatment of this severe chronic disease.

Key words: rheumatoid arthritis, Cimzia

ORIGINAL ARTICLES

I. Gruev and A. Toncheva. SUB-CLINICAL ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Summary. In patients with rheumatoid arthritis (RA), increased cardiovascular morbidity and mortality have been observed. Carotid ultrasound is a well-known screening method for diagnosing sub-clinical atherosclerosis and, therefore, an increased cardiovascular risk. Our study showed that 80 RA patients had significantly higher values of intima-media thickness (IMT), compared with 72 sex and age matched hypertensive controls (0.099 cm vs 0.084 cm for the left carotid artery and 0.098 cm vs 0.083 cm for the right carotid artery). Age, disease history, number of affected joints and levels of uric acid, CRP and HDL-cholesterol have been found to be risk factors for sub-clinical atherosclerosis among our group of RA patients. Having in mind that the SCORE system does not assess most of these risk factors, we totally agree with Mary Roman, that RA patients, like diabetics, should be considered to be at high cardiovascular risk.
Key words: rheumatoid arthritis, atherosclerosis, cardiovascular risk factors

Sv. Dimitrov, T. Shivacheva and Vl. Kadinov. OUR EXPERIENCE WITH ADALIMUMAB IN THE TREATMENT OF PATIENTS WITH INFLAMMATORY JOINT DISEASES

Summary. Treatment of inflammatory joint diseases has been gaining serious advances in recent years due to the introduction of biological agents in rheumatological practice. The aim of the study was to evaluate the efficacy and safety of adalimumab in the treatment of patients with inflammatory joint diseases for a period of one year. The study involved 64 patients: 20 patients with ankylosing spondylitis, 24 patients with rheumatoid arthritis and 20 patients with psoriatic arthritis. The duration of the disease was of at least one year. On baseline, in Month 1, 3, 6 and 12, evaluations of the total number of painful and and swollen joints, the duration of early morning stiffness (in minutes), visual analogue scale (VAS), DAS28 and BASDAI were performed. Adalimumab was subcutaneously administered at a dose of 40 mg twice per month. The obtained data were analyzed by using the individual analyses and Student's t-test. Clinical and laboratory improvement was registered in the end of the first month of treatment with adalimumab in all patients ($p < 0.05$). DAS28 (in patients with rheumatoid arthritis) revealed statistically significant reduction in the end of the first month of treatment and remained low during the whole period ($p < 0.01$). The same dynamics was observed for BASDAI (in patients with ankylosing spondylitis). No serious adverse effects were registered during the period of treatment with adalimumab. Adalimumab is very well tolerated and highly efficious in the treatment of patients with inflammatory joint diseases.
Key words: inflammatory joint diseases, adalimumab, efficacy, safety

R. Stoilov, M. Ivanova, N. Stoilov and S. Marincheva. COST ANALYSIS OF THE TREATMENT OF RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS WITH SYNTHETIC AND BIOLOGIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS FOR 2010 IN BULGARIA

Summary. Early diagnosis and early aggressive treatment of rheumatoid arthritis (RA) are among the major factors for delaying the rate of bone-tendon destructions and, respectively, of invalidism. Such observations have also been reported in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Regarding this, great hopes are reposed in disease-modifying antirheumatic drugs (DMARDs) and, particularly, in biologic

agents. The aim of this study was to determine and evaluate the utilization of synthetic and biologic DMARDs in the treatment of RA, AS and PsA for 2010 in Bulgaria. For 2010, an increase of the number of RA treatments with synthetic DMARDs was registered, predominantly attributed to treatments with leflunomide (Arava). This fact can be explained by the consensus achieved by the members of the Bulgarian Society for Rheumatology that a biologic agent is to be included in the treatment of RA, only after a lack of response to methotrexate and leflunomide. In 2010, expenditures for biologic DMARDs were 5 times higher compared with these for the preceding 2009. This increase was attributed mostly to RA and AS treatments. The lack of sufficiently effective synthetic medicinal products (NSAIDs and DMARDs) for the treatment of AS, has stimulated the use of biologic agents. Despite the increased utilization of biologic agents in the treatment of inflammatory joint diseases in Bulgaria, the proportion of their users is too small, compared with the average 12% in the other EU countries. In our country, 0.42% of the RA patients and 0.40% of the AS patients are on TNF-α blockers. This indicates that the access to expensive and highly effective treatments with biologic DMARDs is very limited in Bulgaria. The reimbursement policy of the health insurance system is the key to improving the access to biologic agent treatment. The reimbursement of only 75% of the cost of this treatment is still far beyond patient affordability. The proportion of patients treated with synthetic DMARDs is still too low. Of course, reimbursement of synthetic DMARDs is of importance, but it has no such heaviness as this of biologic agents. Rheumatologist’s opinion and patient's compliance are of greater importance.
Key words: rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, treatment access

C O N T E N T S

REVIEWS

ORIGINAL ARTICLES