L. Sapundzhiev and S. Lambova. CURRENT VIEWS ON THE ROLE OF VISCOSUPPLEMENTATION IN OSTEOARTHRITIS WITH DIFFERENT LOCALIZATIONS

Summary. Hyaluronic acid (HA) is a major component of articular cartilage and synovial fluid. It is responsible for synovial fluid viscosity, contributes to joint lubrication, buffers load transmission across articular surfaces, imparts antinociceptive, anti-inflammatory, chondroprotective properties. In osteoarthritis (OA), the molecular weight and concentration of HA in synovial fluid are diminished and it disturbs the homeostasis of the affected joints. The treatment with exogenous HA for OA has been termed viscosupplementation. Therapeutic properties of HA depend on the elastoviscosity of the different therapeutic products. Anti-inflammatory and chondroprotective effects are characteristic of low molecular weight preparations (500-700 kDa) and occur later after administration. Predominant effects of high molecular weight HA (6000-14 000 kDa) are lubrication and antinociception, which are with earlier manifestation. Intraarticular administration of HA is safe, without systemic effects. The incidence of local adverse reactions is low and they are usually mild and transient. Pseudoseptic arthritis is a rarely described adverse event. Treatment with HA as a disease-modifying agent is a part of EULAR and ACR guidelines for the treatment of knee OA. In EULAR guidelines for the treatment of hip OA, therapy with HA is defined as a method with good symptomatic effect and probable disease-modifying effect. The absence of well-defined inclusion criteria for the appropriate patients and randomized clinical trials is underlined. In the recent years, treatment with HA in patients with OA of ankle, shoulder, first carpometacarpal and temporomandibular joint has shown to be both effective and safe, and determination of inclusion criteria for this treatment and the optimal therapeutic schemes have to be established in future randomized clinical trials.

Key words: hyaluronic acid, osteoarthritis

V. Reshkova and R. Rashkov. NEW ASPECTS IN THE TREATMENT OF FIBROMYALGIA

Summary. Fibromyalgia (FM) is characterized by chronic diffuse muscle pain lasting for a minimum of three months, pain at mechanical pressure in at least 11 of the 18 specified tender points in the tendons, muscles, general fatigue, sleep and functional disorders. Fibromyalgia is a widely spread disease among different age groups (30-50). This syndrome affects women and men in an approximate ratio of 20:1. There are no available epidemiological data for the spreading of the syndrome in Bulgaria. FM syndrome has no specific ethnic predisposition either. There are a huge number of etiopathogenetic hypotheses trying to explain the FM. The most important factor aiming to ameliorate the condition in patients with FM is focused on: influencing positively the adaptation and quality of life; adequate treatment of chronic pain, sleep disorder, depression; elaboration of proper strategy and individual approach to each one patient. The treatment of FM patients is carried out with medicines of different groups – antidepressants, antiepileptic drugs, analgesics, soporifics, growth hormone, amino acids etc.

Key words: fibromyalgia, trigger points, treatment

Zl. Kolarov and R. Rashkov. PAIN TREATMENT IN OSTEOARTHRITIS WITH CONVENTIONAL DRUGS

Summary. Viewed are the main aspects in the treatment of osteoarthritis and the most commonly used for the time being considered conventional, preparations for relieving the pain – nonsteroidal anti-inflammatory agents, COX-2 inhibitors, opioids.

Key words: osteoarthritis, pain, nonsteroidal anti-inflammatory agents, COX-2 inhibitors, opioids

S. Marincheva, R. Rashkov and Zl. Kolarov. AUTOINFLAMMATORY SYNDROMES. PART II: GENERAL PRINCIPLES IN THE PATHOGENESIS OF Autoinflammatory syndromes

Summary. Autoinflammatory syndromes (AIS) are diseases typically presented with recurrent episodes of systemic inflammation not classified as infectious, autoimmune, allergic and immunodeficient diseases. A dysfunction of innate immune response is fundamental for AIS with or without further deterioration of the adaptive immunity. The understanding of AIS pathogenic mechanisms requires profound knowledge on the physiology of the innate immune system (IIS). While in acquired immunity B- and T-lymphocytes utilize antigen receptors (such as immunoglobulins and T-cell receptors) to recognize non-self, the key to innate immune system recognition of "dangerous" molecules are the pattern recognition receptors. Receptors’ stimulation triggers different intracellular signaling pathway activation, which in the case of IIS, conducts an inflammatory response, phagocytosis, or apoptosis. Despite of the significant advances in the detection of pathogenic mechanisms, many questions remained unanswered. Can we set a precise borderline between
autoimmune diseases and autoinflammatory syndromes? Why adaptive immunity is not always activated in the presence of invading microbes and is there a connection between infections and AIS presentations? Why irrespective to the existence of different gene defects there is significant clinical overlap between AIS? The following review will summarize the data available up to date.

**Key words:** autoinflammatory syndromes, innate immune system, pattern recognition receptors

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**ORIGINAL ARTICLES**

I. Gruev and A. Toncheva. **SERUM URIC ACID: A MARKER OF DEVELOPMENT OF SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH INFLAMMATORY JOINT DISEASES**

**Summary.** The association between gout and hypertension, diabetes, renal and cardiovascular diseases had been known since 19th century. But in the 50-60-ies of the 20th century this correlation had been rediscovered. Since then, a number of epidemiological surveys has proved the association between the levels of serum uric acid (SUA) and large number of cardiovascular diseases, such as hypertension, metabolic syndrome, coronary artery disease, cerebrovascular disease, vascular dementia, preeclampsia and renal diseases. Despite of that, the role of SUA as an independent cardiovascular risk factor has still been questioned. The aim of our study was to search for a correlation between the presence of subclinical atherosclerosis (defined as carotid intima-media thickness above 0.9 mm or presence of plaque) and traditional (hypertension, diabetes, dyslipidemia and smoking) and also nontraditional (SUA and inflammatory markers – CRP and SR) risk factors. 105 patients with inflammatory rheumatic diseases (IRD) – 80 with rheumatoid arthritis, 18 with psoriatic arthritis and 7 with ankylosing spondylitis, and a control group of 72 hypertensive patients were investigated. The traditional and nontraditional (CRP, SR and SUA) risk factors were measured in all the patients. Also a carotid sonography of both common carotid arteries was performed. A vascular transfuser 3-12 MHz of Philips Envisor HD machine was used. Our results showed that in patients with IRD, the increased levels of SUA were associated with increased risk of development of atherosclerosis. Our conclusion fully corresponds with the conclusion made by Panoulas et al. in 2007, that SUA is an independent predictor of cardiovascular diseases in patients with rheumatoid arthritis.

**Key words:** uric acid, inflammatory joint diseases, subclinical atherosclerosis

K. Nikolov, E. Bozhikova and M. Baleva. **FAMILIAL ANTIPHOSPHOLIPID SYNDROME**

**Summary.** There are not many reports about familial antiphospholipid syndrome (APS). We observed 33 members from 14 families. 92,3% of them had positive anticardiolipin antibodies. The most frequent skin symptom for APS was livedo reticularis (73%), and the rarest – Burger’s disease (3%). Other symptoms were: spontaneous abortions and fetal death (30%), pulmonary embolism (18%), headache (15%); 15% of the patients had heterozygous factor V Leiden, 6% of them were treated with contraceptives, 25% were tobacco smokers, 3 had lupus and 1 – juvenile arthritis. These data pose the problem of the necessity of determination of antiphospholipid antibodies and some genetical prothrombotic mutations among the family members of patients with APS.

**Key words:** familial antiphospholipid syndrome

D. Tonev, S. Radeva and A. Toncheva. **NON-PHARMACOLOGICAL TREATMENT OF SUBACUTE AND CHRONIC LOW BACK PAIN WITHOUT RADICULOPATHY: ACUPUNCTURE VERSUS PHYSIOTHERAPY**

**Summary.** The evolution of non-specific acute low back pain into subacute and chronic one reflects the problems and sometimes helplessness of medical therapy. Recently, the interest in data for clinical efficacy and cost-effectiveness of alternative methods of treatment has been growing. The aim of the present research is to find out prospectively the extent of improvement of pain intensity and lumbar spine motion in patients with subacute and chronic low back pain without radiculopathy after implementation of classic acupuncture + manual massage (B group, n = 24) versus physiotherapy (electrotherapy with ultrasound and low frequency magnetic field) + the same manual massage (A group, n = 24). In both groups, the course of treatment was daily implemented within 10 working days. The intensity of pain was assessed by VAS (100 mm) and the change of lumbar mobility (cm) was assessed by modified Schober test at admission, after the end of procedures, at 3th month, and at 12th month. The results showed greater effectiveness of application of acupuncture (B group) versus physiotherapy (A group) (significant decrease of pain intensity – p < 0.01 and increase of lumbar motion) after the end of treatment and 3th months later while at 12th month there was no difference (p > 0.01) between both groups. Findings support the suggestion for incorporation of clas-
sic true/verum acupuncture in European Guidelines for non-pharmacological treatment of low back pain without radiculopathy.

Key words: non-specific low back pain, subacute, chronic, acupuncture, physiotherapy, massage

D. Kalinova. MYOSITIS-SPECIFIC AUTOANTIBODIES AND INCREASED IFN-γ SECRETION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Summary. Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune diseases. Various antibodies have a significant role in the pathogenesis of these diseases. The role of the main immunoregulatory cells – T helper cells – is discussed as an important factor in autoimmune response in IIM. Dis-balance of Th1/Th2 cells and secreted cytokines are immunoregulatory disturbances, which participate in the pathogenesis of systemic lupus erythematosus and IIM. The aim of this study was to determine the prevalence of myositis specific antibodies and myositis associated antibodies, as well as to establish the role of IFN-γ and IL-10, underlying cytokines, secreted of Th1 and Th2 cells, in the pathogenesis of IIM. Nineteen patients (18 women and 1 man) and thirteen healthy controls were enrolled in this study. The immunological profile was evaluated with immunoblot analysis and ELISA method. Levels of IL-10 and IFN-γ cytokines in the serum were defined with ELISA method. MSA and MAA were found in 25% of patients with IIM, analysed by immunoblot. Respectively: anti-Jo-1 – 12.5%, anti-Mi-2 – 6.25%, anti-PM/Scl – 6.25%. Jo-1 antigen was proven also with alternative ELISA method. Increased levels of IFN-γ and IL-10 were found in four patients with IIM (three with dermatomyositis and one with polymyositis) compared with healthy controls, where as in two of them there were found MSA in the serum, respectively anti-Jo-1 and anti-Mi-2. According to activity of the disease, three patients with increased levels of IFN-γ were with inactive disease, fourth patient was with active polymyositis. Increased levels of IL-10 were not found in patients with IIM. We found connection between MSA and IFN-γ in the pathogenesis of IIM. We supposed that increased levels of IFN-γ are result of predominating Th1 cells in patients with inactive diseases. Probably the patients were studied in an inactive stage when cell-mediated immunity and respectively Th1 cells prevailed.

Key words: pathogenesis, autoantibodies, myositis-specific, IFN-γ

V. Reshkova, R. Rashkov, Zl. Kolarov and P. Bekyarova. EFFECT OF THE SPECIFIC MECHANISM OF ACTION OF TRAZODONE (TRITTICO) AS AN INDEPENDENT REPRESENTATIVE OF SARI GROUP IN PATIENTS WITH FIBROMYALGIA

Summary. There are no available epidemiological data for the incidence of fibromyalgia (FM) in Bulgaria. There are a huge number of etiopathogenetic hypotheses trying to explain FM. The most frequently used medicines for treatment of FM are antidepressants. Trazodone (Trittico) is a representative from the group of Serotonin Antagonist and Reuptake Inhibitors (SARI). Presently, there are no data or clinical studies of Trazodone effects in patients with FM. The scope of the present clinical study is to precisely evaluate the effect of Trazodone on the enhancement of pain threshold, the improvement of sleep and chronic fatigue, as well as the remaining symptoms in patients with FM. In the Clinic of Rheumatology, a 3-month clinical study with 150 mg/day Trittico took place, with a purpose to evaluate the treatment effect in 22 FM patients of mean age 44 years. During the clinical study, the pain in 18 specified tender points was evaluated. The study covered the changes of pain threshold in the trigger points by dolorimetry (kg/cm²) using the Fisher dolorimeter, and evaluation of the accompanying clinical complaints.

Key words: fibromyalgia, SARI, Trazodone

CASE REPORTS

V. Peycheva, L. Marinchev and R. Rashkov. THERAPEUTIC PROBLEM IN A PATIENT WITH PROGRESSIVE SYSTEMIC SCLEROSIS AND TUBERCULOSIS

Summary. In a 53-year-old Caucasian woman with proven in 1987 PSS due to the aggressive course of the disease, 25 consecutive pulse therapies with methylprednisolone 1.0.o. and cyclophosphamide 1.o. were performed. In May 2009, there was established hematogenically disseminated tuberculosis with involvement of the lung. The patient has a significant therapeutic problem due to the impossibility of implementation of cun- prenil because of an allergic reaction, and of methotrexate – due to severe bilateral pneumofibrosis and overlaying specific infection of the lung. An alternative possibility in this case is treatment with imuran. Currently, the patient is held in a third consecutive 15-day course with penicillin 20 million i.v. as a disease modifying therapy.

Key words: progressive systemic sclerosis, tuberculosis, penicillin
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