EULAR Recommendations for the Management of Rheumatic Diseases: 2007 Updates

The EULAR Standing Committee on International Clinical Studies, including Therapeutic Trials (ESCISIT) regularly establishes and publishes evidence-based recommendations for the management of rheumatic disorders, as well as recommendation for conducting/reporting clinical trials. Each of these recommendations is developed by a combined approach involving both review of available research evidence and expert consensus; incorporation of a third type of evidence – patient opinion – is now undertaken for management recommendations. The recommendations are reviewed and updated as required to remain current with changes in technology and research advances. At this year's EULAR congress in Barcelona, several new and revised recommendations were announced.

EULAR Recommendations for Vasculitis

Systemic Vasculitis

Patients with primary systemic vasculitis should be treated in collaboration with expert centers. Patients with antibody associated systemic vasculitis (AAV) should be categorized according to European Vasculitis Study Group recommendations. A combination of cyclophosphamide (IV or oral) and glucocorticoids should be used to induce remission of generalized or severe AAV; methotrexate and glucocorticoids may be used for remission induction of localized or early systemic AAV. In severe disease, plasma exchange will improve renal survival. Azathioprine or methotrexate is appropriate for maintenance of remission.

Primary Small Vessel Vasculitis

Long term regular follow-up is recommended for patients with prior exposure to cyclophosphamide, and with persistent unexplained hematuria.

Large/Giant Vessel Arteritis

High dose glucocorticoids should be used to induce remission. Visual symptoms of giant cell arteritis should be treated with a short course of high dose IV glucocorticoids. Patients with giant cell arteritis, with previous cardiac, visual or ischemic symptoms should be treated with low-dose aspirin.

EULAR Recommendations for the Management of Behçet's Disease

Recommendations on vascular disease, neurological and gastrointestinal involvement are based mainly on expert opinion due to a lack of controlled evidence.

Eye Disease

Azathioprine and systemic corticosteroids should be included in the treatment regimen for patients with inflammatory eye disease affecting the posterior segment. Severe eye disease is most appropriately treated with either cyclosporine A or infliximab combined with azathioprine and corticosteroids.

Vascular Disease

Immunosuppressive agents (eg, corticosteroids, azathioprine, cyclophosphamide, cyclosporine) are recommended for the management of acute deep vein thrombosis. For the management of both pulmonary and peripheral arterial aneurysms,

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cyclophosphamide and corticosteroids are recommended. There are no controlled data on, or evidence of benefit from uncontrolled experience with, anticoagulants, anti-platelet or anti-fibrinolytic agents in the management of deep vein thrombosis or for the use of anticoagulation for the arterial lesions of Behçet's disease (BD).

Gastrointestinal Involvement

There is no evidence-based treatment that can be recommended for the management of gastrointestinal involvement of BD. Agents such as sulfasalazine, corticosteroids, azathioprine, TNF antagonists, or thalidomide should be tried first, before proceeding with surgery, except in emergencies.

Central Nervous System (CNS) Involvement

Corticosteroids, interferon-alpha, azathioprine, cyclophosphamide, methotrexate, and TNF antagonists may be appropriate for parenchymal involvement. For dural sinus thrombosis corticosteroids are recommended. Cyclosporine should only be used in patients with CNS involvement if necessary for treatment of intraocular inflammation.

Skin and Mucosa

Mucocutaneous involvement should be treated according to the dominant or co-dominant lesions present. Topical measures (ie, local steroids) should be the first-line of treatment for isolated oral and genital ulcers. Acne-like lesions are usually of cosmetic concern only. Thus, topical measures as used in acne vulgaris are sufficient. Colchicine should be used when the dominant lesion is genital ulcer or erythema nodosum. Leg ulcers might have different causes. For these ulcers, azathioprine, interferon-alpha and TNF antagonists may be considered in resistant cases.

EULAR Recommendations on the Management of Systemic Glucocorticoid Therapy in Rheumatic Diseases

Patient Education

The adverse effects of glucocorticoid therapy should be considered and discussed with the patient before therapy is started.

Dosing

The glucocorticoid dose depends on the underlying rheumatic disease, disease activity, risk factors and individual patient response. Comorbidities and risk factors for adverse effects should be evaluated and treated when therapy is first initiated. For prolonged treatment, the glucocorticoid dosage should be kept to a minimum and a glucocorticoid taper should be attempted in the case of remission or low disease activity.

Monitoring

Patients should be monitored for body weight, blood pressure, peripheral edema, cardiac insufficiency, serum lipids, blood and/or urine glucose, and ocular pressure depending on the individual patient's risk, glucocorticoid dose, and duration.

Patients receiving prednisone ≥7.5 mg daily for >3 months should receive supplemental calcium and vitamin D. Antiresorptive therapy with bisphosphonates to reduce the risk of glucocorticoid-induced osteoporosis should be based on risk factors, including bone mineral density.

Patients treated with glucocorticoids and concomitant NSAIDs should be given appropriate gastro-protective medication (eg, proton pump inhibitors, misoprostol).

Special Conditions

Patients on glucocorticoid therapy for >1 month, who will undergo surgery, must receive peri-operative management with adequate glucocorticoid replacement to overcome potential adrenal insufficiency. Glucocorticoids during pregnancy have no additional risk for mother and child. Children receiving glucocorticoids should be checked regularly for linear growth and considered for growth hormone replacement in the case of growth impairment.

EULAR Recommendations for the Diagnosis of Osteoarthritis of the Hand

Risk Factors

Risk factors for hand osteoarthritis (OA) include: female gender, increasing age (>40 years), menopausal status, family history, obesity, higher bone density, greater forearm muscle strength, joint laxity, prior hand injury, and occupation or recreation-related usage.

Symptoms

Typical symptoms are pain on usage and only mild morning or inactivity stiffness affecting just one or a few joints at any one time; symptoms are often intermittent and target characteristic sites (DIPJs, PIPJs, thumb-base, index and middle MCPJs).

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Humans lack uricase, the urate oxidase enzyme that converts uric acid to allantoin. When given intravenously uricase can reduce serum uric acid levels to nearly zero. There are reports of dramatic reduction in tophi using Rasburicase (a pegylated form of Aspergillus-derived uricase licensed for tumour lysis syndrome), but immunogenicity limits its repeated use. Therefore, there are current efforts to develop a less immunogenic form of mammalian uricase for repeated use in gout [Ganson NJ et al. *Arthritis Res Ther* 2006].

There are recent data from the UK showing that a minority of gout patients receive education, including dietary and other lifestyle advice and that only approximately one third are given ULT [Mikuls TR et al. *Ann Rheum Dis* 2005; Roddy et al. *Ann Rheum Dis* 2007. In press]. Of these, almost all are on allopurinol at a standard dose of 300mg/day, which is an insufficient dose for many patients, meaning that the majority of gout patients do not experience "cure" [Roddy et al]. Therefore education on the principles of long-term gout management and optimization of currently available treatments alone could have a major impact on improving the outcome of this common, painful, inflammatory arthritis.

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effective and safe vaccination against a human cytokine may be achievable [Le Buanex H et al. *Proc Natl Acad Sci USA* 2006].

A number of peptide, and peptidomimetic-based approaches (such as TCR-peptide vaccines and peptides derived from heat shock protein), and antisense oligonucleotide are currently being tested in animal models to treat inflammatory arthritis.

"We have learned, and will continue to learn, a great deal about cytokines, a remarkable class of potential disease altering agents that will play a major role in future therapeutics, and lead to more 'ad personam' treatment depending upon the subtypes of diseases and the gene status." Prof. Dayer concluded.

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Clinical Presentation

Clinical hallmarks include Heberden's and Bouchard's nodes, and/or bony enlargement with or without deformity affecting characteristic target joints (DIPJs, PIPJs, thumb-base, and index and middle MCPJs).

Associated Risks/Subsets

Patients with polyarticular OA of the hand are at increased risk of OA of the knee, hip, and other common target sites and should be assessed and examined accordingly. Recognised subsets with different risk factors, associations and outcomes (requiring different assessment and management) include IPJ (with or without nodes), thumb-base, and erosive OA.

Diagnosis

The differential diagnosis for OA of the hand is wide. The most common conditions to consider are psoriatic arthritis; rheumatoid arthritis, gout, and hemochromatosis. Radiographs provide the gold standard for morphological assessment of OA of the hand. Blood tests are not required for diagnosis but may be required to exclude co-existent disease.

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Dr. Gossec commented, "Measuring joint space width, in particular in the semi-flexed knee, has been shown to be the most reliable and responsive way to determine structural damage severity in knee OA trials, since overall, reliability and responsiveness were higher for JSW (in particular on semi-flexed view) than for the other scoring techniques."

Prof. Wim B. van den Berg, MD, University Hospital Nijmegen, The Netherlands, provided a glimpse into the future of OA treatment via animal model studies that are exploring novel therapeutic targets in OA. Among these are IL-1 and the role of activated macrophages and degradative enzymes such as ADAMS5 and stromelysin. Novel receptors currently being investigated include the toll like receptors (TLRs) and the receptors of advanced glycation end products. TLRs are expressed on chondrocytes and synoviocytes. When activated, they drive the degradative enzymes. Advanced glycation end products are the result of non-enzymatic glycation of proteins, such as collagen. They accumulate with age and result in pathologic stiffening of cartilage and extracellular matrix.

These ongoing investigative efforts hold promise for the development of novel drugs both for the management of pain as well as retarding the OA process.