Methotrexate; a trustworthy answer to an inflammatory response in osteoarthritis

Dear Editor,

Osteoarthritis (OA), the most prevalent arthritis, represents a leading functional impairment and disability challenge for health-care systems. The catabolism and anabolism disproportion, resulting in joint damage in OA, is created by interaction of numerous mechanisms, including aging, mechanical overload, genetic background, inflammation, and synovitis.[1] Therefore, there is a vast diversity in the management plan and therapeutic regimens. However, most of the treatments are entirely pain-relieving, and, unexpectedly, they can modify disease progression and clinical course. Based on non inflammatory synovial fluid ; OA is considered wrongly as noninflammatory arthritis.[2]

Indeed, findings of the presence of inflammatory mediators such as prostaglandins, cytokines, and chemokines in OA in recent years bring up that OA should be noticed as serious as RA from the point of view of disability rates, morbidity, and costs.

Methotrexate (MTX) is a traditional disease modifying antirheumatic drug (DMARD) for the treatment of many autoimmune diseases, most popular in the management of RA. It belongs to the group with rather long half-life and especially postdrug effect.[3] Anti-inflammatory effects of MTX by suppressing neutrophils, lymphocytes, macrophages, dendritic cells, and monocytes through adenosine release lead to reduce cytokine including TNF-α and IL-6.[4]

The first study about using MTX in OA is a 2-month open-label study in the setting of erosive OA of hand; 10 mg weekly MTX in 21 patients was prescribed, which showed a significant improvement in pain scores.[5] In 2011, 30 patients with knee OA were treated with oral MTX and showed an analgesic effect. 43% of participants achieved 30% reduction in visual analog scale score and OsteoArthritis Research society International (OARSI) criteria.[6] Recently, in a randomized trial, OA patients who received oral MTX (initial dosage 7.5 mg/weekly to be raised to 15 mg during the 1st month) had significantly less pain and improved quality of life besides better functional status after 6 months.[7]

Subcutaneous (SC) MTX injection, in patients with normal renal function with a range of 7.5–25 mg weekly, is clinically superior to orally administered MTX.[8] SC MTX, especially with weekly doses of ≥15 mg, results in higher bioavailability compared to oral root.[4]

Based on our experiences in a pilot study on more than 100 patients, injection of SC MTX can be effective in control of pain. As we know, adverse effects of Non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids limit their use in the elderly; thereafter, finding new safer and more efficacious treatments has great value and helps control substantial burden on health-care systems globally.

Practical protocols based on our experiences on MTX off-label using during more than 10 years are suggested as follows:

1. Weekly SC injections of 10–20 mg (considering body weight) for 3 weeks, continuing with 10 mg monthly SC injections for more 3 months
2. Monthly SC injection of 10–20 mg sandwiched by hydroxychloroquine 200 mg daily or sulfasalazine 500 mg once or twice daily
3. Monthly SC injection of 10–20 mg sandwiched by weekly "oral" 7.5–10 mg MTX for 3 months.

In the first and last protocol, MTX can be repeated if needed according to patients' response.

We are open to receiving reader's complementary comments.

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Conflicts of interest

There are no conflicts of interest.

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