Intra-articular Injection for the Management of Rheumatoid Arthritis Patients with Knee Osteoarthritis—Current Evidence and Future Prospects

Chen-Liang Chou1,2* and Yi-Tien Su3
1Department of Physical Medicine and Rehabilitation, Taipei Veteran General Hospital, Taiwan
2National Yang-Ming University, School of Medicine, Taipei, Taiwan
3Department of Physical Medicine and Rehabilitation, Far Eastern Memorial Hospital, Taiwan

Corresponding author: Yi-Tien Su, Department of Physical Medicine and Rehabilitation, Far Eastern Memorial Hospital, Taiwan, Tel: 886-903048830; E-mail: ytitiensu@gmail.com

Mini Review

Intra-articular injection of hyaluronic acid (HA) is well known to improved pain and function in patients with osteoarthritis (OA) [1,2]. As for rheumatoid arthritis (RA) patients with knee osteoarthritis, current medication for injection therapy includes steroid, hyaluronic acid, and platelet-rich plasma (PRP). In this article, we collected current studies regarding to this issue and suggest future possible research direction.

Intra-articular corticosteroid injection is long to be known as a useful adjunct therapy for the management of RA. Intra-articular injection of corticosteroid has been shown to provide clinical benefit up to 6 months and even longer [3]. From a pharmacological point of view, corticosteroid injection is able to decrease the expression of citrullinated proteins, monoclonal antibody F95, and peptidylarginine deiminase [4] in RA synovium, and the side effect is low. According to the subanalyses from the BeSt study, [4] eight-year radiographs showed similar damage in injected joints and noninjected joints. From a clinical point of view, corticosteroid injection remains a safe and cost effective way for managing RA-related OA.

Current study revealed that the hyaluronic acid (HA) molecular weight (MW) and phospholipid (PL) species in the synovial fluid vary with joint disease, as the HA concentration lower in RA and PLs higher in RA in compare with the unaffected controls. In addition, RA patients have HAMW shifted towards a lower range [5]. This study revealed the important role that lubricants play in RA patients. HA has been used for intra-articular injection in RA patients by many clinicians, and current evidence revealed that HA is beneficial in RA patients combined with knee OA up to 9 weeks when analyzing with WOMAC index, and is equally effective in stage II and III patients [6]. However, the research of optimal MW and compound of the HA is needed for the best benefit of patients.

Platelet-rich plasma (PRP) has been a popular treatment in tendinopathies and arthropathies. Current evidence showed that PRP holds some potential effects in cartilage repair and osteoarthritis [7] investigated the effect of intra-articular PRP injection in antigen-induced arthritis of knee in a porcine model and showed that PRP injection attenuate arthritis change when assessing histologically and based on the synthesis of inflammatory mediators. PRP injection may hold promise for RA patients with arthropathies; however, the relatively high cost and possible immune reaction need to be taken into consideration.

Mesenchymal stem cell showed some therapeutic potential in inflammatory diseases [8] and an ongoing study by Wang et al. revealed that intravenous injection of human umbilical MSC for patients with active RA may provide a safe, significant, and persistent clinical benefits [9,10] demonstrated a murine antigen-induced arthritis treated with intra-articular injection of MSC and showed that knee joint diameter (swelling) was significantly less in MSC treated animals compare to non-treated controls from 48 hours and the results last up to 7 days. Meanwhile, cartilage depletion, inflammatory exudates and arthritic index, which indicate disease severity, were significantly reduced in MSC-treated animals continued for 7 days. Serum concentration of tumor necrosis factor alpha also decreased to a significant level in the injection group. Intra-articular injection of MSC may reduce cartilage destruction, joint swelling, and inflammation in RA patients, but the safety and efficacy are yet to be proven.

RA is a deliberating disease. Both systemic and local approach showed benefits. Intra-articular injection of corticosteroid, hyaluronic acid, PRP, and MSC all showed some degree of positive effect. Corticosteroid and HA injection have been known for the relative low cost, safety, and efficacy. Novel therapeutic approach includes PRP and MSC injection, which all showed potential in decreasing cartilage damage and further inflammation. However, further research is needed for the safety and optimal regimen for these therapeutic approaches.

References
1. Cheng OT, Souzdalnitski D, Vrooman B, Cheng J (2012) Evidence-based knee injections for the management of arthritis. Pain Med 13: 740-753.
2. Gigante A, Callegari L (2011) The role of intra-articular hyaluronic (Sinoval) in the treatment of osteoarthritis. Rheumatol Int 31: 427-444.
3. Scherer J, Rainsford KD, Kean CA, Kean WF (2014) Pharmacology of intra-articular triamcinolone. Inflammopharmacology 22: 201-217.
4. Gvozdenovic E, Dirven L, van den Broek M, Han KH, Molenaar ET, et al. (2014) Intra articular injection with corticosteroids in patients with recent onset rheumatoid arthritis: subanalyses from the Best Study. Clin Rheumatol 33: 263-267.
5. Kosinska MK, Ludwig TE, Liebsich G, Zhang R, Siebert HC, et al. (2015) Articular Joint Lubricants during Osteoarthritis and Rheumatoid Arthritis Display Altered Levels and Molecular Species. PLoS One 10: e0125192.
6. Chou CL, Li HW, Lee SH, Tsai KL, Ling HY (2008) Effect of intra-articular injection of hyaluronic acid in rheumatoid arthritis patients with knee osteoarthritis. J Chin Med Assoc 71: 411-415.
7. Lippros S, Moeller B, Haas H, Tohidinezhad M, Steubesand N, et al. (2011) Intraarticular injection of platelet-rich plasma reduces inflammation in a pig model of rheumatoid arthritis of the knee joint. Arthritis Rheum 63: 3344-3353.
8. Newman RE, Yoo D, LeRoux MA, Danilkovitch-Miagkova A (2009) Treatment of inflammatory diseases with mesenchymal stem cells. Inflamm Allergy Drug Targets 8: 110-123.

9. Wang L, Wang L, Cong X, Liu G, Zhou J, et al. (2013) Human umbilical cord mesenchymal stem cell therapy for patients with active rheumatoid arthritis: safety and efficacy. Stem Cells Dev 22: 3192-3202.

10. Kehoe O, Cartwright A, Askari A, El Haj AI, Middleton J (2014) Intra-articular injection of mesenchymal stem cells leads to reduced inflammation and cartilage damage in murine antigen-induced arthritis. J Transl Med 12: 157.