Medical Sciences

Knee Osteoarthritis and Viscosupplementation: The Evolving Treatment Trend

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Osteoarthritis is one of the most common degenerative joint diseases especially among elderly population. Deeper understanding of the pathophysiology of the nature of the disease helped the scientist to come up with new treatment options and trends.

Osteoarthritis is a very common progressive chronic degenerative joint disease with the main pathology being destruction of joint cartilage, inflammation of the synovial membrane or sclerosis of the underlying bone. The main goal in treatment is pain reduction and halting the disease progression. The viscosupplementation therapy has been in use during the last decade, and helps the patients with both pain reduction and halting the disease progression by different mechanisms such as inducing endogenous hyaluronic acid production, inflammation suppression and reduction of the degradation of the cartilage. This study is a review study on the safety and efficacy of viscosupplementation therapy and a brief literature review in this field.

Although intraarticular injection of viscosupplementations has showed safety and efficacy especially through 26 weeks of the initiation of treatment, but controversy in regard of using this system is still questionable. Despite of controversy, it can delay the surgical intervention in knee osteoarthritis and can be considered as a good alternative for long-term therapy and for pain reduction and joint function improvement.

Osteoarthritis | Viscosupplementation | Hyaluronic Acid

Introduction
Osteoarthritis (OA) is the most common degenerative joint disease which is characterized by the loss of cartilage and decreased friction surface between joints and affects middle age to the elderly. The progressive loss of cartilage is the main cause of pain which leads to disability. The main goal in OA treatment is pain reduction, functional and mobility and life quality improvement. Conservative treatment including non-steroidal anti-inflammatory drugs (NSAIDs) and other pain reducing and analgesic medications are the first line treatment options but considering the comorbidities in patients especially the older populations raise concern about these commonly prescribed medications and question the safety and efficacy of them. This led to initiating the intraarticular injections therapies which can be a safe treatment option. (1)

Discussion
Osteoarthritis is a very common progressive chronic degenerative joint disease which results from destruction of joint cartilage, inflammation of the synovial membrane or sclerosis of the underlying bone. (2) Synovial fluid consists of polysaccharides, glucosamine, glucuronic and hyaluronic acid. Being a weight bearing joint, knee joint is mostly affected with degenerative changes. The patients can experience various symptoms such as swelling, pain, joint stiffness or being unable to perform daily activities based on the progression of the degeneration of the joint. (3) As per the literature, knee OA has an incidence rate of 10% in men and 13% in women over the age of 60 years. (4) There are several different etiologies such as genetics, age, obesity, mechanical injury, misalignments of the bones, hormonal factors and etc. (5) The featured characteristics for OA are movement limitation, crepitus, joint effusion and pain and inflammation.

There are two goals in treating OA patients in today’s practice: 1. Reduction of the pain and improving the joint mobility. 2. Decreasing the disease progression. (6) The traditional treatment for OA includes analgesics, corticosteroid injection, physical therapy, Nonsteroidal anti-inflammation drugs (NSAIDs) and weight reduction. (7) Although in case of conservative traditional treatment failure joint arthrodesis is considered the gold standard treatment but the reduction of the patient’s functional quality made the clinicians to search for new alternative treatments. (8) During the 80s, viscosupplementation therapy such as intraarticular injection of hyaluronic acid (HA) has been used widely for the treatment of knee OA in some countries including Brazil (9, 10) but it was approved by FDA in US in 1997. (11) In 2008 the Osteoarthritis Research Society International added intraarticular hyaluronic acid injection to the beneficial treatment options for the knee and hip OA. (12) Synovial fluid consists of polysaccharides, glucosamine, glucuronic and hyaluronic acid. The pathophysiology of OA includes the reduction of hyaluronic acid concentration and thus decreased viscosity and lubrication and shock absorption of the joint. (13) Hyaluronic acid inhibits inflammatory mediators and cartilage degeneration and consequently reduction in cartilage degradation and increased cartilaginous matrix production. (14) The viscosupplementation therapy has different mechanisms such as endogenous hyaluronic acid production, suppression of the inflammation and degradation of the cartilage. (15, 16) There are chemically modified hyaluronic acid compounds with higher molecular and longer half-life and thus increased effectiveness. (17, 18) One of the new chemically modified compounds is Arthrum HCS (40mg of hyaluronic acid and 40mg chondroitin sulfate). Chondroitin sulfate connects to high molecular weight monomers and the compound plays a viscoelastic role and can interact with the surrounding tissue, and thus leads to protection of the cartilage. Also chondroitin sulfate inhibits the extracellular proteases, stimulates proteoglycan production, and inhibits cartilage cytokine production thus causes apoptosis of articular chondrocytes in connective tissues. (19) Delaying the surgical procedures as far as possible is one of the ultimate goals in OA treatment which can be achieved by supplementing the synovial fluid with viscosupplementations in order to protecting the cartilage. (20, 21)

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The clear indication for viscosupplementation is still unclear but hyaluronic acid injections should be considered in patients who did not respond to the traditional therapy or patients who hasn’t tolerated the treatment well, or has side effects, patients who are not candidates for total knee replacement. (22, 23)

There are several studies and clinical trials in this area. The Chevalier et al. is one of the first clinical trials which is a multicenter double blind randomized clinical trial of 253 patients. The study was finalized after 26 weeks. The study group was divided to two arms: placebo and high molecular weight compound (Hylan G-F 20). The safety and efficacy of the treatment arm was statistically significant. (24)

One of the other important studies is the Raynauld et al. which includes 255 patients in two different arms, placebo and treatment groups. Patients were evaluated after a one year period and the results revealed significant clinical improvements in the treatment arm. (25)

The Amelia project is a multicenter clinical trial which evaluated 306 patients during a time period of one year. Patients were divided to two arms, placebo and treatment. The treatment arm received four cycles of intra-articular hyaluronic acid injections. The safety and efficacy of the treatment was proven by the improvement in symptoms. (26)

Bannuru et al. published a meta-analysis in regard of intra articular injection of hyaluronic acid injection and evaluation of pain management over 6 months. This study showed the peak effectiveness at 8 weeks, and residual effectiveness until 24 weeks. The results of the study revealed greater efficacy from other analgesics. (27)

Intra articular corticosteroids are another method of treatment which helps in the short term reduction of pain and joint mobility. (28) The long term benefits of the corticosteroid use is still questionable. Although few but there are clinical trials which compare the effectiveness of corticosteroids and hyaluronic acid intra articular injections. Ray et al. compared the duration of effectiveness of the viscosupplementation and the nonsteroidal anti-inflammatory drugs and corticosteroid injections. The study result manifested the longer pain relief with viscosupplementation than corticosteroid group (approximately 26 weeks) especially when it is administered in the early stages of the OA. (29)

Comparing the duration of effectiveness of corticosteroids and hyaluronic acid injection, hyaluronic acid is superior in pain relief duration, with corticosteroid administration every 2 months and hyaluronic acid injection every 3 months. (30)

The Leopod study compared one hundred patients with OA in two groups, Hylan G-F 20 and corticosteroids. The results of the study revealed no significant difference between the two groups but more significant response in women than men. The gender related difference in treatment groups will need more investigation. (31) The Jones et al. was a prospective randomized clinical trial which compared the patients who received corticosteroids with patients who received hyaluronic acid after 6 months of follow up and revealed more pain relief in the hyaluronic acid arm. (32)

The Leardini et al. studied forty patients in two different groups of hyaluronic acid and corticosteroid arms, with the pain relief after two months follow up which revealed statistical significance in the hyaluronic acid group. (33)

Dahlberg et al. studied 28 patients over a one year period with no difference in pain relief or functional activity in the treatment group. (34) Dougados et al. studied 110 patients in two arms, 55 treatments and 55 control group. At seven weeks follow up, the visual analog pain scale was significantly different in the treatment group. The efficacy of the treatment was assessed also at one year follow up which revealed statistical significance in the treatment arm. (35)

The Henderson et al. included 91 patients in two arms, 45 treatment and 46 control. The patients were followed five months after the injection of hyaluronic acid but the results were not significant difference between two groups. (36) The Listrat et al. included 36 patients in two arms, 19 treatment and 17 control patients. During the one year follow up there was no significant difference between the two groups but the quality of life was superior in the treatment group. (22) Another study is the Puhi et al. which included 95 patients in the treatment group and 100 patients in control group. At 14 weeks follow up the visual analog pain scale was less than the control group and there was significant difference between the two groups. (37)

Implementing the guidelines to clinical practice, in order to apply recommendations in the clinical settings will help the physicians to visualize the patient flow. (38) There are some studies including Altman et al, Kirchner and Marshall studies which questions the outcomes of intra articular injection effects. (39) The extra cellular matrix protein matrilin-3 has an important role in chondrocyte differentiation and function. Therefore immobilized matrilin-3 on biopolymers, as hyaluronan can be a new therapeutic method which needs more investigation. (40)

Conclusion
Worldwide 20% of population is affected by OA, which can cause movement abnormalities and 25% has limitations in their daily life activities. (As listed before) Although intra articular injection of viscosupplementations has been showed safety and efficacy through 26 weeks, controversy in regard of using intraarticular hyaluronic acid injection still remains as uncertain. The uncertainty is likely secondary to inconsistency with guidelines and literature. (As listed before) But overall, intra articular injection of hyaluronic acid can delay the surgical intervention in knee osteoarthritis and can be considered for long term therapy and also for pain reduction and joint function improvement.


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