

Viscosupplement Use for Osteoarthritis

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ABSTRACT

Although viscosupplement has been recommended for osteoarthritis for a sometime recent findings does not support is positive action in most of the cases. Therefore, we have to be very careful in using this treatment for osteoarthritis.

Key words: Viscosupplement, osteoarthritis.

Hunter stated that osteoarthritis is a clinical problem and gave several recommendations. In this study, a 67-year-old woman, as well as a friend at her golf club, with right-knee osteoarthritis is referred by her primary care physician for treatment of her knee pain. Different treatments are discussed for these two patients with osteoarthritis (1).

The patient has had intermittent pain for 9 years, which has been relieved with infrequent use of naproxen. A friend at her golf club received a hyaluronate injection and had sustained relief of her knee pain for 6 months. The patient inquires whether this form of therapy may be appropriate for her. The specialist recommends weight loss and exercise and counsels the patient about the appropriate use of viscosupplements.

Approximately 46 million people in the United States, or 10%–12% of the adult population, have symptomatic osteoarthritis (2-4). Recent estimates suggest that knee osteoarthritis affects approximately 250 million people worldwide (5). Osteoarthritis was the fastest increasing major health condition with disability in 2010, which reflects a 64% increase during the period from 1990 to 2010. A majority of people with osteoarthritis (64%) are of working age (15–64 years), and 11% of the workforce comprises people with osteoarthritis (5,6).

Typically, knee pain limits activity and impairs the quality of life. The risk of mobility disability (defined as the need for help while walking or climbing stairs) attributable to knee osteoarthritis alone is greater than that associated with any other medical condition in people 65 years of age or older (7,8).

The pathogenesis of osteoarthritis is perhaps best understood as excessive mechanical stress applied in the context of systemic susceptibility (9). Susceptibility may be increased in part by genetic factors (a family history increases the risk), older age, ethnic background, nutritional factors (vitamin D or K deficiency), and female sex (10).

The pathogenesis of osteoarthritis is characterized by progressive cartilage loss, subchondral bone remodeling, osteophyte formation, and synovial inflammation.

Hyaluronate is a naturally occurring component of the cartilage and the synovial fluid. It is a polysaccharide composed of continuously repeating molecular sequences of β -D-glucuronic acid and β -D-N-acetylglucosamine, with a molecular mass in normal synovial fluid ranging from 6500 to 10,900 kDa (11).

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Within the normal adult knee, there is approximately 2 mL of synovial fluid, with a hyaluronate concentration of 2.5–4.0 mg/mL (12). Hyaluronate is responsible for the rheologic properties of synovial fluid, enabling it to act as a lubricant or shock absorber, depending on the forces exerted on it (13).

In osteoarthritis, synovial hyaluronate is depolymerized (molecular mass, 2700 to – kDa (11) and cleared at higher rates than normal (14).

In a normal joint, the average intrasynovial half-life of hyaluronate is approximately 20 h (12). In an inflamed joint, this half-life is decreased to 11–12 hours. These changes reduce the viscoelasticity of the synovial fluid. Exogenous intraarticular hyaluronate is available as a treatment for the symptoms of knee osteoarthritis. The injected polymers range in size from 100 to 10,000 kDa. The therapeutic goal of administration of intraarticular hyaluronate is to provide and maintain intraarticular lubrication, which increases the viscoelastic properties of the synovial fluid (15); this form of therapy is therefore sometimes termed “viscosupplementation.” It is also claimed that hyaluronate exerts antiinflammatory, analgesic, and possibly chondroprotective effects on the articular cartilage and joint synovium (12). The clinical benefits of treatment with intraarticular hyaluronate, which may persist well beyond the intraarticular residence time of the product, have been suggested to be caused by the reestablishment of joint homeostasis as a result of an increase in the endogenous production of hyaluronate that persists long after the exogenous injected material has left the joint (14).

Despite numerous trials and meta-analyses, the efficacy of hyaluronate-related agents in patients with knee osteoarthritis remains debated and uncertain. Comprehensive management of osteoarthritis should always include a combination of treatment options that are directed toward the common goal of alleviating pain and improving function (16,17).

The recommended hierarchy of management should consist of nonpharmacologic methods first (such as weight loss, exercise, braces, and assistive devices such as canes), then analgesic medications, including nonsteroidal antiinflammatory drugs (NSAIDs), and finally surgery (18–20).

The use of local therapy for osteoarthritis management has inherent appeal because it may mitigate some of the serious concerns regarding the side effects associated with systemic therapies, including gastrointestinal bleeding and myocardial infarction. Local therapies include topical agents, such as topical NSAIDs and capsaicin, as well as intraarticular glucocorticoids and intraarticular hyaluronate.

The currently available evidence suggests that viscosupplementation may be as effective as NSAIDs and results in fewer systemic adverse events; in comparison with intraarticular glucocorticoids, it has a delayed onset of effects and a longer-lasting benefit (21).

The hyaluronates are approved by the Food and Drug Administration (FDA) as class III medical devices for persons with osteoarthritis of the knee whose condition has not responded adequately to conservative nonpharmacologic treatment and simple analgesics.

Different hyaluronate formulations are available worldwide, from a low-molecular-mass preparation (range 500–730 kDa) to more recent intermediate-molecular-mass formulations (range 800–2000 kDa) and even cross-linked, high-molecular-mass formulations (mean 6000 kDa), including hylans, nonanimal-derived hyaluronate, and others (22). There is no reliable evidence of the superiority of any one brand of viscosupplement to other brands. There is no clear evidence supporting any specific clinical criteria to select patients who will most likely benefit from hyaluronate injections. This treatment is contraindicated in persons with known hypersensitivity to hyaluronate products, women who are pregnant or nursing, pediatric patients, patients with bacteremia, or patients with infections in or around the target knee, although these recommendations are not necessarily based on reports of adverse events.

Intraarticular injections should always be performed under sterile conditions; the aseptic technique must be followed to avoid joint infection. Aspiration of any effusion before injection is highly recommended to prevent dilution of the injected hyaluronate.

Typically, the most pronounced improvement is expected from 5 to 13 weeks after injection (23) with some residual effect still present at 24 weeks (24). It is reasonable to follow up at 6 months after the procedure to determine the next suitable steps for management.

For patients whose condition does not respond, it is important to continue treatment with nonpharmacologic methods and analgesics and, if necessary, to consider the next steps; these may include treatment with tramadol, duloxetine, or opioids, as well as joint replacement.

One study suggests that a lack of response to an initial course of intraarticular hyaluronate does not necessarily mean that a repeat course will not be effective (25). The FDA has approved repeat courses of intraarticular hyaluronate; however, many insurance plans require at least a 6-month interval between treatments.

Minor side effects include pain at the injection site, local joint pain and swelling, and local skin reactions (26). Pseudoseptic reactions, which are characterized by inflammation and swelling of the joint that are not caused by infection, can be severe and may require further medical treatment. These reactions usually occur after sensitization with the second or third injection of a series or with a repeat treatment course. True joint infections have also been reported, but these appear to be rare (27). Some forms of hyaluronate may cause these adverse effects more frequently than others. A meta-analysis of adverse events showed that the frequency of flares of pain and swelling was higher after intraarticular injections of high-molecular-mass hyaluronate than after injections of the standard form of intraarticular hyaluronate (28).

The actual overall efficacy of intraarticular hyaluronate, if any, is an area of ongoing uncertainty. A summary of the current conflicting literature would suggest that hyaluronate has, at best, a small treatment benefit. The supportive meta-analyses consistently show this small effect (23, 29-31), whereas the negative reviews highlight the absence of a definite difference from placebo, the heterogeneity of the published literature, and the potential for publication bias (32,33,28).

Although there are some data suggesting that younger patients and patients with less-severe disease may have greater benefit from this treatment than do older patients and those with more advanced disease (13,30), further evidence is required to support this claim.

The effect of intraarticular hyaluronate on the structural progression of osteoarthritis, especially after repeat administration over longer intervals, remains an open question, with some pilot evidence suggesting positive effects (34,35).

Jubb et al (34) conducted a secondary analysis after adjusting for baseline differences in the width of the joint space and found a protective effect in the subgroup of persons with milder disease.

A magnetic resonance imaging study by Wang et al (35) provided evidence suggesting a beneficial effect on knee cartilage, although it was a small study involving 78 patients and the results were based on an analysis that included only participants who completed the trial, in which there was a dropout rate of approximately 30% and a higher rate of surgical intervention in the hylan G-F 20 group.

At present, these studies are best described as suggestive of an effect, but the results are in need of replication before any conclusive clinical recommendations can be made.

The current consensus is not to advocate for the use of hyaluronate (18,36). At present, the management of osteoarthritis is best characterized as palliative, with numerous missed opportunities for more beneficial intervention (16) and typical clinical practice that does not reflect guideline recommendations (37-41). The treatment of osteoarthritis is not unique in this regard (42).

Consistent with the contradictory meta-analyses, available guidelines also have conflicting recommendations, despite being based on the same research evidence. The 2010 Osteoarthritis Research Society International (OARSI) guidelines recommended intraarticular hyaluronate as potentially useful in patients with knee or hip osteoarthritis, with a modest effect size for pain relief (19). A more recent update of the evidence from the OARSI suggested that the data from the more rigorous trials did not show a significant difference between the effect of hyaluronate and that of placebo; as a result, it was not recommended for the treatment of either knee or multiple-joint osteoarthritis (43). In the American Academy of Orthopaedic Surgeons clinical practice guideline, it was determined that the evidence was inconclusive and a recommendation could not be made for or against the use of intraarticular hyaluronate (36).

The current evidence base would not advocate the use of intraarticular hyaluronate for the management of knee osteoarthritis. Similarly, although there are some data suggesting a benefit of high-molecular-mass products compared with low-molecular-mass preparations, the data are inconsistent. For the case in question, this patient was counseled to lose weight, undertake a strengthening exercise program, and avoid the use of intraarticular hyaluronate.

Are there any narrower therapeutic indications for which the use of intraarticular hyaluronate may be justified? At this point in time, there is no sufficient evidence to indicate that younger patients with less severe disease, or other patient subgroups, have a more favorable outcome.

This study shows that should be limited to the use of viscosupplementation in knee osteoarthritis because the exact benefits have not been demonstrated.

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