CME

Hyaluronic acid injections for knee osteoarthritis

Systematic review of the literature

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ABSTRACT

OBJECTIVE To determine whether viscosupplementation with intra-articular hyaluronic acid (HA) injections improves pain and function in patients with osteoarthritis (OA) in their knees.

DATA SOURCES We searched MEDLINE, Pre-MEDLINE, and Cochrane databases using the MeSH headings and key words osteoarthritis (knee) and hyaluronic acid.

STUDY SELECTION English-language case series and randomized controlled trials (RCTs) were selected. Studies with biologic, histologic, or arthroscopic outcomes were excluded.

SYNTHESIS Five case series and 13 RCTs were critically appraised. Data from three case series and three RCTs using injections of high-molecular-weight HA (Synvisc) demonstrated significant improvement in pain, activity levels, and function. The beneficial effect started as early as 12 weeks. Studies using low-molecular-weight HA had conflicting results.

CONCLUSION Viscosupplementation with high-molecular-weight HA is an effective treatment for patients with knee OA who have ongoing pain or are unable to tolerate conservative treatment or joint replacement. Viscosupplementation appears to have a slower onset of action than intra-articular steroids, but the effect seems to last longer.

RÉSUMÉ

OBJECTIF Déterminer l'efficacité d'un traitement de viscosuppléance par injection intra-articulaire d'acide hyaluronique (AH) pour procurer une amélioration fonctionnelle et un soulagement dans l'arthrose (AR) du genou.

SOURCE DES DONNÉES Une recherche a été effectuée dans les bases de données MEDLINE, Pre-MEDLINE et Cochrane à l'aide des rubriques et mots-clés MeSH osteoarthritis (knee) et hyaluronic acid.

CHOIX DES ÉTUDES Les études de cas et essais randomisés (ER) de langue anglaise ont été retenus tandis que les études d'ordre biologique, histologique ou arthroscopique ont été exclues.

SYNTHÈSE L'évaluation a porté sur cinq études de cas et 13 ER. L'injection d'AH de poids moléculaire élevé (Synvic) a procuré une amélioration fonctionnelle, une augmentation du niveau d'activité et un soulagement significatifs dans trois études de cas et trois ER. Les études qui utilisaient l'AH de faible poids moléculaire ont donné des résultats discordants.

CONCLUSION L'injection intra-articulaire d'AH de poids moléculaire élevé est un traitement efficace pour l'AR du genou accompagné de douleurs constantes ou pour les patients qui ne sont pas aptes à supporter un traitement conservateur ou l'installation d'une prothèse articulaire.

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Cet article a fait l'objet d'une évaluation externe.
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Osteoarthritis (OA), the most common form of arthritis, affects more than 10% of the population,[1] is slowly progressive, and results in severe disability in the long term. Standard nonpharmacologic treatments include patient education, self-management programs, weight loss, physical and occupational therapy, exercises, and devices that assist function.[2,3] Pharmacologic therapies are outlined in **Table 1.**[2,4] Surgical therapy includes arthroscopy and joint replacement.[1,2]

Hyaluronic acid (HA) was first used in ophthalmology for cataract surgery in the 1970s.[5,6] Intra-articular use of HA has been approved in Japan and Italy since 1987, in Canada since 1992, in most of Europe since 1995, and in the United States since 1997.[6,7] A meta-analysis of eight early randomized controlled trials (RCTs) showed that patients treated with HA were doing better than untreated patients at the end of the treatment cycle and at the end of 6 months.[8]

Despite this, viscosupplementation for treatment of OA remains controversial and perhaps underused. The primary objective of this systematic review was to determine whether HA injections improve pain and function in patients with OA in their knees. A secondary objective was to compare HA with other therapies, such as intra-articular steroids.

Osteoarthritic joints contain synovial fluid that has become less viscous and less concentrated, and has a lower molecular weight. This means that it offers less shock absorption, lubrication, and protection of joints.[8] Synovial fluid contains HA, a polysaccharide containing glucosamine and glucuronic acid.[9] The mechanism of action of HA injections is unclear, but it seems to inhibit inflammatory mediators, decrease cartilage degradation, and promote cartilage matrix synthesis.[2,7] It also insulates synovial pain fibres, thus decreasing perception of pain.[9] Effects of HA have been found to last longer than the actual compound does, suggesting that intra-articular HA stimulates synthesis of natural HA.[10]

Preparations of HA can be divided into low and high-molecular-weight (**Table 1**[2,4]). Contraindications to intra-articular HA include joint or skin infection, overlying skin disease, and allergy to chicken or eggs if using a preparation derived from rooster comb.[8,9]

Table 1. Drug therapy for osteoarthritis

Acetaminophen
Salicylates
Traditional NSAIDs
Cyclooxygenase-2 inhibitors
NSAIDS with misoprostol (Arthrotec®)
Narcotic analgesics
Glucosamine
Chondroitin sulfate
Topical therapies: capsaicin, methylsalicylate
Intra-articular glucocorticoids
Low-molecular-weight HA
• Orthovisc®
• Hyalgan®
• Artz® or Supartz®
High-molecular-weight HA
• Synvisc® (hylan G-F 20)

Data from American College of Rheumatology[2] and Ayral.[4]
HA—hyaluronic acid, NSAIDs—nonsteroidal anti-inflammatory drugs.

Data sources

Articles were obtained from MEDLINE, PreMEDLINE, and Cochrane databases from 1966 to the end of October 2002 using the MeSH terms hyaluronic acid and osteoarthritis, knee. Key words included variations of hyaluronic acid. The search was limited by clinical trials (42 trials), English language, and human studies. Additional articles were obtained by reviewing the references of selected articles. Finally, we excluded trials published before 1995 in an attempt to examine the most up-to-date methodology and outcome measures. We were left with 31 articles for critical appraisal.

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Study selection

We chose primary research trials with clinical outcome measures related to treatment with HA. Studies were excluded if primary outcome measures were histologic, biologic, or arthroscopic. We were left with 18 primary research articles: 13 RCTs and five case series. Validity and applicability of the studies were assessed using published criteria for reviewing articles on therapy.[10,11]

Synthesis

Case series. The five case series[12-16] had no control groups: two were retrospective; three were prospective (**Table 2**[12-16]). They lasted from 6 months to 2.5 years. The population profile for OA was middle-aged people, more women than men.[1]

Three trials used three injections of high-molecular-weight HA (Synvisc®). Lussier et al[13] showed that 76% of patients improved with respect to

Table 2. Recent case series of hyaluronic acid in treatment of knee osteoarthritis

STUDY	TYPE	LENGTH	NUMBER	POPULATION	EXCLUSION CRITERIA	TREATMENT*	OUTCOME MEASURES	RESULTS	COMMENTS
Lussier et al,[13] 1996	Retrospective case series	2.5 y	336: 458 knees, 1537 injections	Average age 65 with OA	NA	Three injections of Synvisc; up to four series	Pain score on ordinal scale; overall response; change in activity	76% improved in first series; 84% in second series	Average interval between courses was 8.2 mo; large study
Frizziero et al,[14] 1998	Open-label prospective case series Second investigator blinded to treatment	6 mo	40	Average age 49.5; 17 of 40 had effusion; mainly moderate OA; 13 men, 27 women	Severe concomitant disease or treatment; past intra-articular drugs; poor compliance	Five injections of Hyalgan; second series at 4-8 mo	Score on VAS for pain (rest, load); biopsy	Less synovial inflammation ($P = .001$); significantly less pain at rest and with load to 1 y; less effusion	Results to day 360
Kotz and Kolarz,[15] 1999	Open-label prospective case series	1 y	108; 73 completed	Average age 57.7; 31 men, 77 women; symptoms for >1 y; score >3.3 on VAS for pain >20 d in previous mo	NA	Five injections of Hyalgan; second series at 4-8 mo	Score on VAS for pain after exercise	68% had relief of symptoms at 4 wk; 55% maintained at 1 y	No intention-to-treat analysis
Goorman et al,[16] 2000	Prospective case series	6 mo	84; 61 completed; 110 knees	Average age 65.8; 26 men, 35 women; OA detected on x-ray examination; no benefit or intolerant of NSAIDs	Implants, infection, allergy, knee instability, marked deformity	Three injections of Synvisc	SF-36 (functional score)	Significant improvement in function ($P < .001$); no difference in general health or vitality	No intention-to-treat analysis
Evanich et al,[12] 2001	Retrospective case series	10 mo	84; 70 patients completed; 100 knees	Average age 66; 39% men, 61% women	NA	Three injections of Synvisc	Radiographs; pain score on scale of 1-10; activity level; satisfaction; hospitalization for procedures	Two thirds of knees had two thirds relief; 35% increased activity; 28% went on to surgery; no difference by age	With more severe OA, relief declined ($P < .05$) and procedures increased ($P < .05$)

NA—not applicable, NSAIDS—nonsteroidal anti-inflammatory drugs, OA—osteoarthritis, VAS—visual analogue scale.
**Type of hyaluronic acid.*

Table 3. Recent randomized controlled trials, by year, for hyaluronic acid treatment of knee osteoarthritis

STUDY	TYPE	LENGTH	N	POPULATION	COINTERVENTIONS
Adams et al,[17] 1995	Double-blind, parallel study with three arms	26 wk	32 in NSAID group, 28 in HA group, 33 received both	Patients with OA	All groups given NSAIDs 30 d earlier
Lohmander et al,[18] 1996	Double- blind, parallel	40 wk	93 treatment, 93 control	Patients with OA	NA
Wu et al,[19] 1997	Double-blind, parallel	26 wk	90 patients, 116 knees	Mild-to-moderate OA	NA
Wobig et al,[6] 1998	Triple-blind, parallel, intention to treat	26 wk	110 patients, 117 knees	Average age 62, 62% women, excluded for effusions or if erythrocyte sedimentation rate >40 or renal failure >1:160	Documented use of NSAIDs, analgesics, steroids, surgery
Altman and Moskowitz,[20] 1998	Double-blind, parallel, with three arms and intention-to-treat analysis	26 wk	495 (162 dropped out)	ACR criteria for OA, KL grade 2-3, pain score >20 mm on WOMAC, excluded women of childbearing age and those who had had HA or other IA injection in last year	Acetaminophen allowed and recorded, aspiration
Huskisson and Donnelly,[21] 1999	Double-blind, parallel	26 wk	100 (19 dropped out)	Average age 65, 67% women, KL grade 2-3, moderate-to-severe pain with walking, excluded for grade 4 x-ray results, serious illness, injection in last 3 mo	Analgesics and NSAIDs (similar use in both groups)
Payne and Petrella,[22] 2000	Double-blind, parallel	12 wk	46 (6 dropped out)	Age 57-67, unilateral OA, pain with activities of daily living, medial OA, excluded for cognitive impairment, pregnancy, avian allergy, or IA injections in last 6 mo	Acetaminophen, exercise
Brandt et al,[5] 2001	Double-blind, parallel, intention-to-treat and post-hoc analysis	27 wk	226 (175 completed), 135 analyzed in effectiveness arm	Moderate OA, KL grade 2-3, WOMAC score >12 in treated knee, WOMAC score <13 in untreated knee, excluded for recent use of steroids, IA HA in last year, comorbidity	Washout of all analgesics, acetaminophen allowed and recorded
Tamir et al,[23] 2001	Open-label, single-blind, parallel	20 wk	49 (3 dropped out)	Age 60-85, KL grade 2-4, Altman criteria for symptomatic OA, excluded for IA injections in last 6 mo, rheumatoid arthritis, infection in OA hip, allergy, >15 mL effusion aspirated	Oral agents not limited
Bunyaratavej et al,[24] 2001	Double-blind, parallel	26 wk	49 (? dropped out)	Average age 59, moderate OA, excluded for rapid OA, surgery, IA injection in last 3 mo, trauma, pregnancy, NSAIDs taken in last wk	Acetaminophen
Petrella et al,[25] 2002	Double-blind, parallel	12 wk	120 (12 dropped out)	Average age 67, KL grade 1-3, unilateral OA, excluded for taking NSAIDs not for OA, intolerance, gastrointestinal bleeding, avian allergy, IA injection in last 6 mo, taking herbal products	Acetaminophen, 2-wk washout before study
Miltner et al,[26] 2002	Single-blind, parallel	6 wk	43	Average age 67, KL grade 2-3, bilateral OA, symptoms >1 y, excluded for malalignment, instability, fracture, IA injection in last 3 mo	Acetaminophen
Raynauld et al,[27] 2002	Open-label, prospective, parallel, effectiveness trial, intention-to-treat analysis	1 y	255 (24 dropped out)	Older than 40; x-ray verified OA; ambulatory; most symptomatic knee treated; excluded for KL grade 4, tense effusion, deformity, IA injection in last 3 mo, any prior HA	NA

ACR—American College of Rheumatology, HA—hyaluronic acid, IA—intra-articular, KL—Kellgren-Lawrence (x-ray criteria grade 1-4), MODEMS—Musculoskeletal Outcomes Data Evaluation and Management System, NA—not applicable, NSAID—nonsteroidal anti-inflammatory drug, OA—osteoarthritis, VAS—visual analogue scale, WOMAC—Western Ontario and McMaster Universities index.

**Appropriate care includes NSAIDS, education, rest, ice, heat, assisting devices, physical and occupational therapy, weight loss, arthroscopy, and surgery.*

TREATMENT (TYPE OF HA)	OUTCOME MEASURES	RESULTS	COMMENTS
Synvisc high-molecular-weight preparation (6 MDa), Arms: NSAID and three aspirations, no NSAID and three HA injections, NSAID and three HA injections	Score on VAS for pain at rest, at night, and bearing weight	At wk 12, HA plus NSAID reduced pain. At wk 26, HA superior to NSAID, and HA plus NSAID superior to NSAID alone	Positive effect, NSAID plus HA superior to HA alone
Low-molecular-weight preparation (1000 kDa) in five weekly injections	Score on VAS for pain	HA same as placebo for whole group. Older patients with severe OA showed some improvement	Subgroup benefited
Five weekly injections of Artz	Symptoms, pain with daily activities	HA better than placebo up to 3 mo	Positive effect
Three injections of Synvisc, saline placebo	Score on VAS for pain with activity	At wk 12, 47% in HA group were pain free vs 8% in placebo group (P <.001). At wk 26, 39% vs 13% (P <.001). Rescue medications required by 11% in HA group and 53% in placebo group	Positive effect
Five weekly injections of Hyalgan, saline placebo, oral placebo. Arms: HA and oral placebo, saline injections and oral placebo, naproxen and subcutaneous local anesthetic	Score on VAS for pain, score on WOMAC	At wk 26, less pain walking with HA; 47.6% pain free in HA group vs 33% (P <.005) in saline and oral placebo groups, and 38.9% (P =.02) in naproxen group; Scores on WOMAC better with HA than placebo	Positive effect, high drop-out rate, HA had fewer side effects than naproxen
Five weekly injections of Hyalgan	Score on VAS for pain, score on Lequesne functional index	At 5 wk and 6 mo, less pain walking (P =.009) and (P <.005), respectively. Better knee function up to 4 mo	Positive results up to 6 mo
Suplasyn (730 kDa)	Perception of pain	HA superior to placebo	Negative response
Three injections of Orthovisc	Score on WOMAC	HA superior to placebo from wk 7-27 in effectiveness arm. No difference in intention-to-treat group	Subgroup benefit
Five weekly injections of BioHy (3 MDa)	Pain, stiffness, function, score on MODEMS	HA decreased pain and stiffness up to wk 20 (non-significant)	Negative response
Four injections of Hyalgan, saline placebo	Score on VAS for pain	HA superior to placebo	Positive effect
Three injections of Suplasyn. Arms: HA and oral placebo, HA and diclophenac with misoprostol, IA placebo and diclophenac with misoprostol, IA placebo and oral placebo	Score on VAS for pain, score on WOMAC index	HA same as NSAID for pain at rest; HA superior to placebo or NSAID for pain with activity and function	HA effect improves over time, NSAID effect unchanged after 4 weeks
Five injections of Hyalart; control was opposite knee	Score on VAS for pain, score on Lequesne functional index	HA reduced pain compared with baseline and improved peak torque on Lequesne functional index (P <.001)	Not blinded effectively with other knee as control
Three injections of Synvisc, saline placebo. Arms: appropriate care,* appropriate care and HA	Score on WOMAC	Appropriate care plus HA reduced pain in 38% vs 13% receiving appropriate care only (P = .0001); annual cost per patient receiving appropriate care plus HA for other therapy was $5 and for assisting devices was $237 compared with $16 and $305 for patients receiving appropriate care only	Positive effect; only study to look at comprehensive conservative therapy and cost effectiveness

pain and activity level. Evanich et al[12] showed that Synvisc decreased pain by two thirds in two thirds of treated knees, but pain relief decreased with severity of OA, and there was no significant difference in effect based on age. In addition to pain relief, Goorman et al[16] found that physical and social function also improved.

The two case series using five injections of 20 mg of low-molecular-weight HA (Hyalgan®), with a possible second course, showed symptom relief from week 4 to up to 1 year.[14,15] These were open-label trials and need to be interpreted with caution.

With the exception of the study by Frizziero et al,[14] none of the case series used a blind observer, which could bias results. Lack of placebo control makes data interpretation difficult. Patients might also have had difficulty recalling their initial symptoms in retrospective trials. Intention-to-treat analysis was unclear in all five case series, and cointerventions were poorly documented.

Randomized controlled trials. Most of the 13 RCTs summarized in **Table 3**[5,6,17-27] lasted from 6 to 52 weeks. Nine were parallel double-blind studies; four were not.[6,23,26,27] Physicians giving injections were blinded to outcome in only two studies,[6,24] but blinding was difficult because HA and saline appear different due to their viscosity. All RCTs used separate assessors, except one,[27] which was an effectiveness rather than an efficacy trial. Patients were not blinded to outcome in this study, nor in the two open trials.[23,26] Two RCTs might have been biased because they were funded by the Hyalgan and Orthovisc groups.[5,20] Heterogeneity of study design, population studied, length of follow up, and diverse outcomes made the data unsuitable for meta-analysis.

Three of the 13 RCTs involved three injections of Synvisc. The study by Wobig et al[6] was triple-blinded, used intention-to-treat analysis, and excluded patients with knee effusions. Synvisc was found to be superior to placebo: pain and use of rescue medication were both reduced at weeks 12 and 26. This was one of the studies with the best methodology except that it did not account for previous intra-articular injections. Synvisc was also used in an effectiveness trial comparing appropriate care with appropriate care plus Synvisc.[27] Patients taking Synvisc had significantly less pain at 1 year and lower costs per patient for other therapy or assisting devices. The third trial had three parallel treatment arms; two included use of nonsteroidal anti-inflammatory drugs (NSAIDs).[16] Unfortunately, no oral placebo was used. At week 12, all three groups had improved. Those taking HA had significantly less pain at rest than those taking NSAIDs alone (the effect continued at week 26). Combination therapy was more effective than NSAIDs alone.

The remaining RCTs all studied various low-molecular-weight preparations of HA. Other medications, such as acetaminophen, were allowed; two studies allowed anti-inflammatory drugs as well.[21,23] Most trials involved middle-aged people with OA defined radiographically as mild to moderate. Patients with knee effusions were often excluded; effusion was sometimes aspirated before intra-articular injections. Usually, patients were excluded if they had had intra-articular injections in the previous 3 to 12 months.

Most studies used visual analogue scales for pain as a primary measure. Four studies included function as a primary outcome.[21,23,25,26] Lohmander et al[18] found no difference between HA and placebo except in poststudy subgroup analysis of patients older than 60 with severe OA. Two studies found no significant differences in pain reduction in intention-to-treat analysis.[5,26] Miltner et al[26] showed that HA improved functional score, total work, peak torque, and pain compared with baseline with no change in the control knee from baseline. The study by Petrella et al indicated that HA was more effective than NSAIDs in reducing pain and improving function, and that this effect improved with time.[25] The remaining studies showed HA to be superior to placebo in decreasing pain and stiffness for up to 6 months.

Studies involving comparisons with NSAIDs are difficult to interpret. Compared with naproxen, Hyalgan injections produced similar results with fewer gastrointestinal side effects.[20] Synvisc and NSAIDs appeared similar at month 3; in combination they were better than NSAIDs alone.[17] For pain with activity and function, HA was better than NSAIDs alone.[25]

Side effects

Side effects tended to be minor; injection site pain and swelling was the most common. In two studies, the overall local adverse reaction rate with HA was 2% or 2.7% per injection.[13,27] Kotz and Kolarz[15] noted 119 adverse effects in 108 patients, the most common being back pain (16.8%), injection site reaction (11.8%), and injection site pain (6.7%). Evanich et al[12] found 15% of knees (11 patients) treated with HA had adverse reactions an average of 1.2 weeks after first injection. Two studies found injection site pain and swelling to be equal for HA and placebo.[5,21] Another trial, however, found significantly more injection site pain with HA (23%) than with placebo (13%).[20]

Gastrointestinal side effects were less common with HA (29%) than with naproxen (41%) or placebo (36%).[20] Systemic reactions were rare. One case of septic arthritis[12]; one case of cutaneous vasculitis within 1 week of injection; one case of skin peeling at week 6; and three cases of itching, cramps, or hemorrhoids were reported.[8,21]

Discussion

Results of studies of viscosupplementation with HA injections are difficult to interpret due to small patient numbers, lack of controls, cointerventions, placebo response after knee aspiration, and lack of blinding of injectors. Studies also used HA preparations that varied in molecular weight and had different schedules. High-molecular-weight HA might stimulate synovial cells to make endogenous HA to a greater extent than low-molecular-weight preparations. More head-to-head studies are needed.

Three case series and three RCTs of high-molecular-weight HA all showed positive effects on pain and function. Treatment with HA was superior to placebo for pain relief and need for rescue medication at weeks 12 and 26. In the effectiveness trial, HA lessened pain and reduced costs for other therapy and devices at 1 year.

The two case series using low-molecular-weight HA improved pain scores; improvement lasted from 4 weeks to 1 year. Several studies showed improvement in function, pain, stiffness, and range of motion that lasted from the first injection up to 6 months. Four studies,[5,8,22,23] however, showed no significant improvement in pain or proprioception in intention-to-treat analysis.

Indications for HA include pain despite other therapy, intolerance of NSAIDs, mild-to-moderate OA, no or mild effusion, no mechanical symptoms, and severe inoperable OA. Cost is an issue with treatment. Cost in Ontario without pharmacy filling fee as of May 2003 was $125 for each syringe of Synvisc or Hyalgan.

EDITOR'S KEY POINTS

- This systematic review examined five case series and 13 randomized controlled trials to determine the effectiveness of intra-articular hyaluronic acid (HA) injections for reducing osteoarthritic joint pain.
- Trials of low-molecular-weight HA produced conflicting evidence of effectiveness, although more studies demonstrated improvement.
- Trials of high-molecular-weight HA had more consistent results indicating pain relief and better functioning.
- The effects of HA appear to begin after 4 to 12 weeks and last up to a year. This contrasts with intra-articular steroid injections that act more quickly but lose effectiveness after 3 months.
- Side effects were relatively minor; the main one, local irritation, resolved spontaneously. There appears to be some rationale for combining steroid and HA injections.

POINTS DE REPÈRE DU RÉDACTEUR

- Cette revue systématique portant sur cinq études de cas et 13 essais randomisés visait à déterminer l'efficacité de l'injection intra-articulaire d'acide hyaluronique (AH) pour soulager des douleurs d'arthrose.
- Les essais portant sur l'AH de faible poids moléculaire ont donné des résultats discordants, quoiqu'une amélioration ait été notée dans la majorité des cas.
- Lorsque l'AH de poids moléculaire élevé était utilisée, un soulagement et une amélioration fonctionnelle ont été observés de façon plus régulière.
- Il semble que les effets de l'AH apparaissent au bout de 4 à 12 semaines et durent jusqu'à 1 an. En comparaison, les injections intra-articulaires de stéroïdes agissent plus vite, mais ne sont plus efficaces après 3 mois.
- Les effets indésirables ont été relativement mineur, le principal, étant une irritation locale, a disparu sans traitement. On croit qu'il serait avantageux d'associer les stéroïdes aux injections d'AH.

Hyaluronic acid or steroids?

Suggested alternatives to HA include intra-articular steroids, which can decrease acute pain and joint effusion, but are limited to three or four injections per year.[4] Several RCTs have shown good response at 1 and 4 weeks, but no effect thereafter.[28-30] In a head-to-head RCT, Jones et al[31] found that patients in the

HA group experienced less pain than those receiving intra-articular steroids at 6-month follow up; however, there was a high drop-out rate, and intention-to-treat analysis showed no statistical differences.

Intra-articular steroids and HA might be good combination therapy. Grecomoro et al[32] found that adding dexamethasone to the first of five Hyalgan injections decreased pain further after 2 months. The effect of steroids occurred earlier (at 4 to 6 weeks); the effect of HA was delayed but longer lived. Comparing HA injections with corticosteroids suggests that the former lasts longer but the latter works faster. Also, steroids might be more effective for joint effusion or other acute inflammation.

Further research is needed to determine whether viscosupplementation with HA alters the natural history of OA in human beings. We do not yet know what concomitant therapies should be offered to patients treated with HA and whether other joints, such as shoulders or hips, could benefit. Combination therapy requires further study.

Conclusion

Viscosupplementation with HA is a reasonable treatment for patients with mild-to-moderate OA of the knee who have ongoing pain or are unable to tolerate conservative treatment or joint replacement. The effect lasts longer with high-molecular-weight preparations, and patients can experience improvement in clinical outcomes for up to 1 year. Intra-articular HA appears to have a slower onset of action than intra-articular steroids but the effects seem to last longer. Patients should be warned of cost and of potential side effects, including local swelling.

Competing interests

None declared

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