



TITLE: Viscosupplementation for Osteoarthritis of the Hip, Ankle, or Shoulder: Clinical Effectiveness

DATE: 3 May 2010

RESEARCH QUESTION:

What is the clinical effectiveness of viscosupplementation for the treatment of patients with osteoarthritis of the hip, ankle, or shoulder?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 4, 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRJ (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2005 and April 2010. No filters were applied to limit the retrieval by study type. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials (RCTs), controlled clinical trials, and observational studies.

The literature search identified three systematic reviews and eight RCTs on the clinical effectiveness of viscosupplementation (VS) for treatment of patients with osteoarthritis (OA) of the hip, ankle, or shoulder. No health technology assessments or controlled clinical trials were identified. Additional articles of potential interest are included in the appendix.

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OVERALL SUMMARY OF FINDINGS:

One systematic review¹ and three RCTs^{7,8,10} assessed the clinical effectiveness of VS with hyaluronic acid (HA) in patients with ankle OA. The systematic review¹ concluded that there was evidence for pain reduction with HA treatment, but that there was a lack of evidence for functional improvement. The three RCTs^{7,8,10} concluded that treatment of ankle OA with HA was safe, and improved pain relief and function, but all stated that larger studies were needed to confirm results.

Two systematic reviews^{2,3} and four RCTs^{4,5,9,11} assessed the clinical effectiveness of VS in patients with hip OA. The two systematic reviews^{2,3} concluded that HA seemed to be effective and safe for patients with hip OA, but cited methodological limitations of the included literature. Two RCTs^{4,11} concluded that HA treatment for patients with hip OA was clinically effective and safe. Two larger RCTs^{5,9} indicated that treatment with HA resulted in a small, but not significant, clinical improvement for patients with hip OA.

One RCT⁶ addressed VS in patients with persistent shoulder pain; patients with shoulder OA were included, but the number of OA patients was not specified. The study concluded that HA was clinically effective and well-tolerated for patients with shoulder OA that was refractory to conventional therapy.

Details of the included studies are provided in Table 1.

Table 1: Summary of included studies				
Author; year	Study type; no. of studies or patients	Study arms	Results	Study Conclusions
Ankle osteoarthritis				
Martin and WorkSafe BC ¹ 2009	Systematic review; 8 studies (4 RCTs and 4 case series)	Included studies evaluating Hylan G-F 20, Hyalgan, and studies not specifying type of HA	4 RCTs lacked enough evidence of pain reduction with hyaluronic acid (HA) and did not provide evidence on functional improvement in patients with ankle OA; 4 case series provided evidence of pain reduction, but did not specify if the pain reduction was clinically significant	Lack of evidence for functional improvement with HA treatment in patients with ankle OA; Evidence for pain reduction with HA treatment, but clinical significance not indicated
Cohen et al. ⁷ 2008	RCT; 30 patients	HA (Hyalgan) versus phosphate-buffered saline; 5 weekly intra-articular injections of 2 mL	At 3 months, HA group showed significant improvement in movement and weightbearing compared with the control group; Few AEs	Suggests HA may be safe and effective for patients with ankle OA, but larger studies are needed
Karatosun	RCT; 30	HA versus	At 12 months, both	HA injections and

Table 1: Summary of included studies

Author; year	Study type; no. of studies or patients	Study arms	Results	Study Conclusions
et al. ⁸ 2008	patients	exercise therapy; 3 weekly intra-articular injections of HA or 6 weeks of exercise therapy	groups improved in pain, function, and alignment scores, with no statistically significant differences between groups	exercise therapy both provide functional improvement in patients with ankle OA; larger, longer trials needed for more definite conclusions
Salk et al. ¹⁰ 2006	RCT; 20 patients	HA (Hyalgan) versus saline; 5 weekly intra-articular injections (1 mL of HA 10 mg/mL or 1 mL saline solution)	Significant improvement in pain and function in both groups from 1 to 6 months; Greater percentage of patients in HA group (5/9) showed >30 mm improvement in the ankle arthritis score compared with control group (1/8); No severe AEs	Suggests HA can provide sustained pain relief, improve function, and is well-tolerated in patients with ankle OA; Confirmation in a large RCT required
Hip osteoarthritis				
van den Bekerom et al. ² 2008	Systematic review; 16 studies; 509 patients	Included studies evaluating Hylan G-F 20, Hyalgan, Ostrnil, Durolane, Fermatron, and Orthovisc	Level of evidence fairly low; VS with HA is safe and well-tolerated, and seems to be effective for treatment of hip OA	Intra-articular HA guided by fluoroscopy or ultrasound seems effective for patients with hip OA, but cannot be recommended as standard therapy for wider populations
Fernandez Lopez and Ruano-Ravina; ³ 2006	Systematic review; 8 studies (2 RCTs, 5 other clinical trials, 1 review)	Type of HA not specified in abstract	Included literature had methodological limitations; Pain relief with HA in most studies was estimated to be 40% to 50%, but duration of effect was not specified	HA treatment should be used with caution in patients with hip OA, only when other treatments have failed
Migliore et al. ⁴ 2009	RCT; 42 patients	HA (Hyalubrix) versus local analgesia (mepivacaine); 2 (once a month) intra-articular injections guided	HA group experienced significantly reduced functional impairment and pain compared with local analgesia group at 3 and 6 months; Minimal AEs	Suggests HA is clinically effective and safe for management of patients with hip OA

Table 1: Summary of included studies

Author; year	Study type; no. of studies or patients	Study arms	Results	Study Conclusions
		by ultrasound		
Richette et al. ⁵ 2009	RCT; 85 patients	HA versus placebo; single intra-articular injection (2.5 mL) guided by fluoroscopy	At 3 months, no difference in decrease in pain score, secondary end points, or AEs between the 2 groups	Indicates that a single injection of HA is not more effective than placebo for patients with hip OA
Qvistgaard et al. ⁹ 2006	RCT; 101 patients	HA versus corticosteroid versus saline; 3 intra-articular injections given at 14-day intervals	No significant difference for HA versus saline in 'pain on walking' at 2 weeks; No significant difference for any treatment group at 3 months; No significant AEs	Treatment outcomes with HA in patients with hip OA were not significant, but there was a small clinical improvement
Tikiz et al. ¹¹ 2005	RCT; 43 patients (56 hips)	Low molecular weight HA (Ostenil) versus high molecular weight HA (Hylan G-F 20, Synvisc); 3 weekly injections guided by fluoroscopy	Significant improvement in functioning and pain in both groups through 6 months follow-up; No significant difference between the 2 groups; No systemic AEs	Both types of HA showed significant clinical improvement in patients with hip OA, with no significant differences in outcomes between the 2 types of HA
Shoulder osteoarthritis				
Blaine et al. ⁶ 2008	RCT; 660 patients with persistent shoulder pain (no. of shoulder OA patients not specified)	HA (Hyalgan) versus phosphate-buffered saline solution; 5 weekly injections of HA, or 3 weekly injections of HA followed by 2 weekly injections of saline solution, or 5 weekly injections of saline solution (all intra-articular)	In patients with shoulder OA, HA groups had significantly greater pain relief than the controls, through 26 weeks; No serious AEs	Overall findings indicate that HA is clinically effective and well-tolerated in patients with shoulder OA that is refractory to conventional therapy

AEs=adverse events; HA=hyaluronic acid; no=number; OA=osteoarthritis; RCT=randomized controlled trial

REFERENCES SUMMARIZED:

Health technology assessments

No literature identified

Systematic reviews and meta-analyses

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See: Summary, p.6
2. Van den Bekerom MP, Lamme B, Sermon A, Mulier M. What is the evidence for viscosupplementation in the treatment of patients with hip osteoarthritis? Systematic review of the literature. *Arch Orthop Trauma Surg.* 2008 Aug;128(8):815-23. [PubMed: PM17874246](#)
3. Fernandez Lopez JC, Ruano-Ravina A. Efficacy and safety of intraarticular hyaluronic acid in the treatment of hip osteoarthritis: a systematic review. *Osteoarthritis Cartilage.* 2006 Dec;14(12):1306-11. [PubMed: PM16979914](#)

Randomized controlled trials

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5. Richette P, Ravaud P, Conrozier T, Euller-Ziegler L, Mazieres B, Maugars Y, et al. Effect of hyaluronic acid in symptomatic hip osteoarthritis: a multicenter, randomized, placebo-controlled trial. *Arthritis Rheum.* 2009 Mar;60(3):824-30. [PubMed: PM19248105](#)
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11. Tikiz C, Unlu Z, Sener A, Efe M, Tuzun C. Comparison of the efficacy of lower and higher molecular weight viscosupplementation in the treatment of hip osteoarthritis. *Clin Rheumatol*. 2005 Jun;24(3):244-50. [PubMed: PM15647968](#)

Controlled clinical trials

No literature identified

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APPENDIX – FURTHER INFORMATION:

Guidelines and recommendations

12. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage*. 2010 Apr;18(4):476-99. [PubMed: PM20170770](#)
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See: *Recommendation 30, p.43*
14. *Osteoarthritis: the care and management of osteoarthritis in adults* [Internet]. London: National Institute for Health and Clinical Excellence; 2008 [cited 2010 May 3]. (NICE clinical guideline 59). Available from: <http://www.nice.org.uk/nicemedia/pdf/CG59NICEguideline.pdf>
See: *Intra-articular injections, p.14*

Review articles

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