[Review]

Viscosupplementation for the treatment of osteoarthritis of the knee

N Bellamy, J Campbell, V Robinson, T Gee, R Bourne, G Wells

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Abstract

Background
Osteoarthritis (OA) is the most prevalent chronic joint disorder worldwide and is associated with significant pain and disability.

Objectives
To assess the effects of viscosupplementation in the treatment of OA of the knee. The products were hyaluronan and hylan derivatives (Adant, Arthrum H, Artz (Artzal, Supartz), BioHy (Arthrease, Euflexxa, Nuflexxa), Durolane, Fermathron, Go-On, Hyalgan, Hylan G-F 20 (Synvisc Hylan G-F 20), Hyruan, NRD-101 (Suvenyl), Orthovisc, Ostenil, Replasyn, SLM-10, Suplasyn, Synject and Zeel compositum).

Search strategy
MEDLINE (up to January (week 1) 2006 for update), EMBASE, PREMEDLINE, Current Contents up to July 2003, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched. Specialised journals and reference lists of identified randomised controlled trials (RCTs) and pertinent review articles up to December 2005 were handsearched.

Selection criteria
RCTs of viscosupplementation for the treatment of people with a diagnosis of OA of the knee were eligible. Single and double-blinded studies, placebo-based and comparative studies were eligible. At least one of the four OMERACT III core set outcome measures had to be reported (Bellamy 1997).

Data collection and analysis
Each trial was assessed independently by two reviewers for its methodological quality using a validated tool. All data were extracted by one reviewer and verified by a second reviewer . Continuous outcome measures were analysed as weighted mean differences

(WMD) with 95% confidence intervals (CI). However, where different scales were used to measure the same outcome, standardized mean differences (SMD) were used. Dichotomous outcomes were analyzed by relative risk (RR).

Main results

Seventy-six trials with a median quality score of 3 (range 1 to 5) were identified. Follow-up periods varied between day of last injection and eighteen months. Forty trials included comparisons of hyaluronan/hylan and placebo (saline or arthrocentesis), ten trials included comparisons of intra-articular (IA) corticosteroids, six trials included comparisons of nonsteroidal anti-inflammatory drugs (NSAIDs), three trials included comparisons of physical therapy, two trials included comparisons of exercise, two trials included comparisons of arthroscopy, two trials included comparisons of conventional treatment, and fifteen trials included comparisons of other hyaluronans/hylan. The pooled analyses of the effects of viscosupplements against 'placebo' controls generally supported the efficacy of this class of intervention. In these same analyses, differential efficacy effects were observed for different products on different variables and at different timepoints. Of note is the 5 to 13 week post injection period which showed a percent improvement from baseline of 28 to 54% for pain and 9 to 32% for function. In general, comparable efficacy was noted against NSAIDs and longer-term benefits were noted in comparisons against IA corticosteroids. In general, few adverse events were reported in the hyaluronan/hylan trials included in these analyses.

Authors' conclusions

Based on the aforementioned analyses, viscosupplementation is an effective treatment for OA of the knee with beneficial effects: on pain, function and patient global assessment; and at different post injection periods but especially at the 5 to 13 week post injection period. It is of note that the magnitude of the clinical effect, as expressed by the WMD and standardised mean difference (SMD) from the RevMan 4.2 output, is different for different products, comparisons, timepoints, variables and trial designs. However, there are few randomised head-to-head comparisons of different viscosupplements and readers should be cautious, therefore, in drawing conclusions regarding the relative value of different products. The clinical effect for some products, against placebo, on some variables at some timepoints is in the moderate to large effect-size range. Readers should refer to relevant tables to review specific detail given the heterogeneity in effects across the product class and some discrepancies observed between the RevMan 4.2 analyses and the original publications. Overall, the analyses performed are positive for the HA class and particularly positive for some products with respect to certain variables and timepoints, such as pain on weight bearing at 5 to 13 weeks postinjection.

In general, sample-size restrictions preclude any definitive comment on the safety of the HA class of products; however, within the constraints of the trial designs employed no major safety issues were detected. In some analyses viscosupplements were comparable in efficacy to systemic forms of active intervention, with more local reactions but fewer systemic adverse events.

In other analyses HA products had more prolonged effects than IA corticosteroids.

Overall, the aforementioned analyses support the use of the HA class of products in the treatment of knee OA.

Plain language summary

Osteoarthritis (OA) is the most common form of chronic arthritis worldwide. Hyaluronan and hylan (HA) products provide opportunity to treat OA in individual knee joints. To evaluate the efficacy, effectiveness and safety of HA products, in knee OA, we have conducted a systematic review using Cochrane methodology. The analyses support the contention that the HA class of products is superior to placebo. There is considerable between-product, between-variable and time-dependent variability in the clinical response. The clinical effect for some products against placebo on some variables at some time points is in the moderate to large effect size range. In general, sample size restrictions preclude any definitive comment on the safety of the HA class of products, however, within the constraints of the trial designs employed, no major safety issues were detected. The analyses suggest that viscosupplements are comparable in efficacy to systemic forms of active intervention, with more local reactions but fewer systemic adverse events, and that HA products have more prolonged effects than IA corticosteroids. Overall, the aforementioned analyses support the use of the HA class of products in the treatment of knee OA.