Viscosupplementation Effect on Proprioception in the Osteoarthritic Knee

Michael W. Payne, MSc, Robert J. Petrella, MD, PhD

ABSTRACT. Payne MW, Petrella RJ. Viscosupplementation effect on proprioception in the osteoarthritic knee. Arch Phys Med Rehabil 2000;81:598-603.

Objective: To test the hypothesis that treatment of the osteoarthritic knee with intraarticular hyaluronan may improve proprioception.

Methods: Forty-six patients with unilateral osteoarthritis of the knee were recruited for this study from primary care clinics in the Department of Family Medicine at the University of Western Ontario. Inclusion required (1) the presence of pain with activities of daily function and (2) radiographic confirmation of medial compartment osteoarthritis. Proprioception was measured with an electrogoniometer attached to the study knee. Subjects performed an angle reproduction test in the closed kinetic position. The difference between the target test angle and the reproduced angle was labeled the absolute angular error (AAE). Eleven angles were tested in random order before beginning therapy, after 3 weeks, and after 12 weeks.

Results: Twenty-one men and 19 women completed the study (22 subjects received hyaluronan injections and 18 subjects received a placebo injection). No significant differences existed between the study groups in age, the timing of injections, or proprioceptive testing. A 2×3 repeated measures analysis of variance (ANOVA) comparing injection groups at all times revealed no significant differences in AAE. The AAE proprioception data was examined for differences due to fatigue caused by the number of test angles ($p < .001$) and differences explained by angulations in various divisions of the normal range of motion ($p < .001$). After accounting for these potential confounds, a two-way ANOVA still did not detect any significant differences in AAE between hyaluronan and placebo groups.

Conclusion: Other studies have found that proprioception may be impaired in osteoarthritic knees and that viscosupplementation therapy with hyaluronan may decrease pain and increase function in these knee joints. The results of the present study suggest that this therapy does not adversely affect proprioception and that a longer, longitudinal study is required to determine if viscosupplementation treatments could attentuate proprioceptive decline.

Key Words: Knee proprioception; Viscosupplementation; Hyaluronan; Osteoarthritis; Rehabilitation.

From the Faculties of Medicine and Health Sciences, and Centre for Activity and Ageing, University of Western Ontario, London, Ontario, Canada.

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Reprint requests to Dr. Robert J. Petrella, Heart Health and Exercise Laboratory, Centre for Activity and Ageing, 1490 Richmond Street North, London, Ontario N6G 2M3.

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OSTEOARTHRITIS (OA) is a degenerative condition associated with a decrease in the hyaluronan concentration of the synovial fluid in the joint and a decrease in the molecular weight of the hyaluronan molecules.[1] Hyaluronan is a major component of both synovial fluid and articular cartilage, and is responsible for the elastoviscosity of synovial fluid.[2] Molecular catabolism of hyaluronan by oxygen derived free radicals[1] reduces the molecular weight of the molecule. Consequently, both the elasticity and viscosity of synovial fluid are reduced, resulting in poor shock absorption and poor lubrication within the joint[3] and leading to pain or loss of joint function. In cases where the elastoviscosity is reduced, hyaluronan can be infused into the articular space in an attempt to reestablish the preexisting environment of fluid and tissue around the joint.[3] Viscosupplementation, the intraarticular infusion of hyaluronan, may restore the normal rheological state and reduce symptoms of the arthritic joint.[3]

A correlation has been described between a worsening of OA and impaired proprioception,[4-7] although a causal relationship between OA and proprioception has yet to be fully developed. The loss in proprioception in elderly people with knee OA increases their susceptibility to falls.[8] Viscosupplementation with hyaluronan may improve function and decrease pain in the knee[3,9-11]; however, it is unknown if these benefits correlate with a change in proprioception. In the present study, we tested the hypothesis that by improving symptoms of OA including joint function, we may also improve proprioception. Accepting the alternate hypothesis could prove important in reducing the risk of OA-related falls. Conversely, if hyaluronan injections did not change or in fact worsened proprioception (null hypothesis), this treatment may be useful only in limited situations involving restricted movement, since the treatment may put patients at risk of falling. However, if hyaluronan injections improve proprioception, or attenuate the decline in proprioception associated with OA, this treatment may offer an advantage to patients at risk of falling.[12] We have previously shown[13] that regular physical activity in older patients can improve proprioception and range of motion, while others[14] have shown that treatment with intraarticular steroids and exercise therapy[15] improve osteoarthritic symptoms including joint function. Proprioception was not measured in these studies. One might anticipate that intraarticular hyaluronan therapy may also improve joint function including proprioception.

The purpose of the present study was to investigate the effect of intraarticular hyaluronan injections on proprioception in osteoarthritic knee joints in patients with mild to moderate knee OA. The null hypothesis that a course of hyaluronan injections will not improve proprioception using active, closed-kinetic angle reproduction tests when compared with placebo injections was tested using a randomized, double-blind, placebo controlled design.

METHODS

Subjects and Setting

Forty-six subjects (23 men, 23 women; age, 67 ± 8.2yrs, range 57 to 76yrs) from the community volunteered to participate in this study of proprioceptive function. Subjects were eligible for inclusion if they had pain or a decrease in usual activity because of knee OA, and mild to moderate (Grades I to III) knee OA confirmed clinically and radiographically.[16] Subjects were excluded if they had non-OA arthritides; were cognitively impaired, pregnant, or were surgical candidates; had known avian allergies; or had current or previous (<6 months) intraarticular therapy. All subjects were asked to refrain from starting any other forms of treatment for OA for the duration of the study. All testing was conducted in the Heart and Health Exercise Laboratory at the Centre for Activity and Ageing, London, Ontario. The study protocol was approved by the university's Review Board for Health Sciences Research Involving Human Subjects.

Instrumentation

Proprioception is commonly measured in a clinical setting by evaluating a subject's ability to reproduce static joint angles using a clinical electrogoniometer. We used an electrogoniometer[a] designed for the "measurement of angular movement" in a clinical or laboratory setting[17]; this device consisted of a fixed endblock and a telescopic endblock connected by a series of strain gauges in a composite wire enclosed by a flexible, protective spring. The electrogoniometer was taped directly to the skin across the joint of interest, and joint angles were determined from the change in strain along the length of the wire.

Study Protocol

Study participants were randomly assigned to one of two treatment groups by means of a random number table; the first group received three weekly 2-mL injections of 2% hyaluronan in the form of 730kD hyalgan (Suplasyn[b]) and the second received three weekly 2-mL injections of saline as a placebo injection. Both groups were given a program of stretching and flexibility exercises and could use acetaminophen as needed for pain. The number of exercises/repetitions and number of acetaminophen tablets were recorded. Injections were administered on the medial side with the knee in full extension to 5°[18] by the same physician, who was blinded to the group assignment. Subjects received injections in only one knee during the treatment schedule.

Proprioception measurements were taken before the subject's first injection, after 3 weeks of treatment, and after 3 months. The same investigator performed all proprioception measurements.

Proprioception Measurement

Measurement of proprioception was done with subjects in the standing (closed kinetic chain) position to more accurately mimic true functional movement of the lower extremity. The feet were placed "comfortably" apart (ie, 10 to 12 inches, or shoulder width apart, with a slight external rotation). The subject stood on both legs for the duration of the test, with the electrogoniometer attached to the test knee. Since fatigue impairs proprioception,[18,19] all subjects were instructed to refrain from heavy activity during the day of testing. Subjects were instructed to wear shorts, loose pants, skirts, or gowns; no tight or restrictive clothing was permitted below the mid to upper thigh.[4,20]

Test angles at the knee included 5° increments from 10° to 60° of knee flexion. All 11 test angles were attempted at each of the three testing sessions. The order in which the angles were tested was randomly assigned by a computer program for each test session.

The electrogoniometer was attached to the lateral side of the leg across the study knee using adhesive tape placed so that the endblocks of the goniometer corresponded with the axis of the leg when viewed in the sagittal plane. The subject was first asked to stand in a neutral position (knees fully extended). The electrogoniometer was zeroed in this position.

The subject was then asked to flex both knees (as if performing a deep knee bend) until the predetermined test angle was reached, as indicated by the output display unit of the electrogoniometer. When the test angle was reached, the subjects were instructed to remain at this angle for 2 to 3 seconds. The subjects were then instructed to return to the neutral standing position and remain there for 2 to 3 seconds. After returning to the neutral position, the subjects were given five seconds to reproduce the test angle and acknowledge verbally when they believed they had reproduced it. The primary outcome variable was the absolute angular error (AAE), which was the absolute difference between the true and perceived test angle (AAE = test angle perceived minus test angle true).

To minimize muscular fatigue during the test, subjects were encouraged to return to the neutral standing position immediately after verbally indicating their perception of the desired test angle in order to reduce the amount of time spent in active weight-bearing flexion at the knees. The subjects were instructed to keep their eyes closed during testing to eliminate visual cues, and were not verbally encouraged during test angle reproduction. A 5-second rest was given between each test sequence. Testing of each subject was done at the same time of day and under similar laboratory conditions.

Statistical Analysis

AAE values for each subject at each session were averaged. The mean AAE values for each treatment group at each session were compared using a 2 × 3 repeated-measures analysis of variance (ANOVA) to determine any statistically significant differences between the groups at any time. The .05 level was adopted as the maximum probability value denoting a statistically significant difference.

Lattanzio and colleagues[18] and Marks and Quinney[19] indicated that an increase in mean AAE of 1° was a clinically detectable proprioceptive deficit. Using 1° as clinically detectable significance, .05 as the alpha error, 0.8 as the statistical power, and the mean and standard deviation from Lattanzio,[18] who measured knee proprioception by the angular reproduction test in the standing position using the same electrogoniometer as the present study, we calculated the sample size for the present study to be 20 people (10 per group).

RESULTS

Of the 46 people meeting the inclusion criteria, six dropped out before initiating the injection therapy for reasons unrelated to the study protocol. Twenty-one men (64.7 ± 7.2yrs) and 19 women (67.5 ± 9.5yrs) received the complete injection series. Twenty-two subjects were randomized into the hyaluronan group (15 men, age 67.8 ± 6.4yrs), leaving 18 subjects (12 women, age 63.9 ± 10.0yrs) to receive placebo injections. Although the hyaluronan injection group was older than the placebo group, this difference was not significant as determined by a *t* test for independent samples.

Injection series. Proprioception was measured at three times during the study for 38 subjects; two participants were lost before their final follow-up visit. No significant differences were found for chronology of proprioception measurements between groups at any level of time.

ANOVA. A 2 × 3 repeated-measures ANOVA on the dependent variable (AAE) with injection group and time as factors found no significant interactions or main effects (fig 1). Thus, proprioception was not affected by the hyaluronan injections when compared with the placebo group.

Angle limitations. Some subjects had difficulty performing some of the angles, and others were unable to bend to the larger angles. This difficulty may have either increased the AAE values or, at greater angles, decreased the AAE results because of a "ceiling effect." This limitation could have prevented subjects from achieving the same range of variability surrounding a certain angle (ie, a subject with a maximum angulation of 52° may not overshoot 50° by more than 2°, whereas a subject with a greater maximum angulation might introduce more variability into their AAE results). A one-way ANOVA on AAE as a function of the test angle found significant differences in AAE with different degrees of bending ($F(10, 1165) = 6.93$, $p < .001$). Linear regression showed a steady decrease in AAE as the test angle increased, potentially indicating a ceiling effect of reduced variability toward higher angles ($R = .384$, $F(1, 121\ 1) = 209.89$, $p < .001$) (fig 2). Using a 2 × 3 repeated-measures ANOVA with AAE data from only 25° to 60°, we found no significant differences within the main effects of time or treatment group. Similar null responses were accepted for identical analyses with AAE data from 35° to 60°, and 10° to 20°. Since many subjects expressed a feeling that they were approaching their maximum angulation in the closed-kinetic position for angles greater than 50°, we further reduced the data sample by removing AAE values from 55° to 60° in an attempt to determine significant proprioceptive differences with a narrower range of angles. A 2 × 3 repeated-measures ANOVA on AAE data from 35° to 50° (ie, with 55° and 60° findings removed from the previous data set) found no significant differences within main effects of time and injection group.

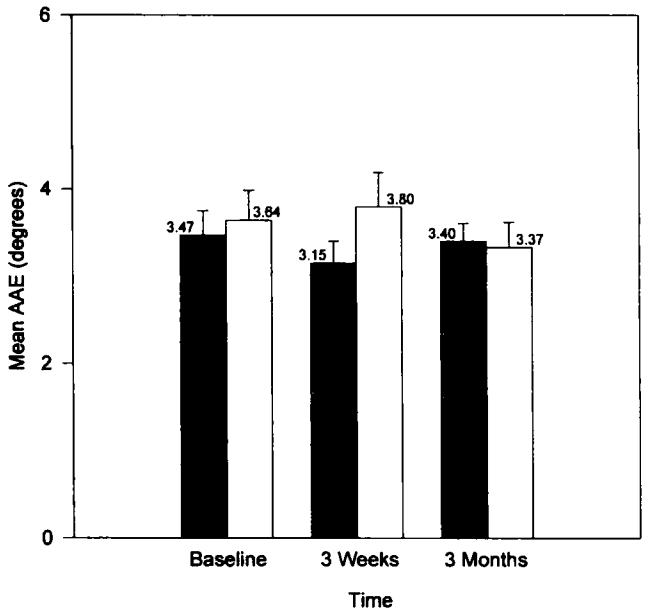

Fig 1. Mean absolute angular error (AAE) proprioception measurements at each time in the placebo group (■) and the hyaluronan group (□). Values are mean ± SEM. There were no significant differences between treatment groups at any time during the study.

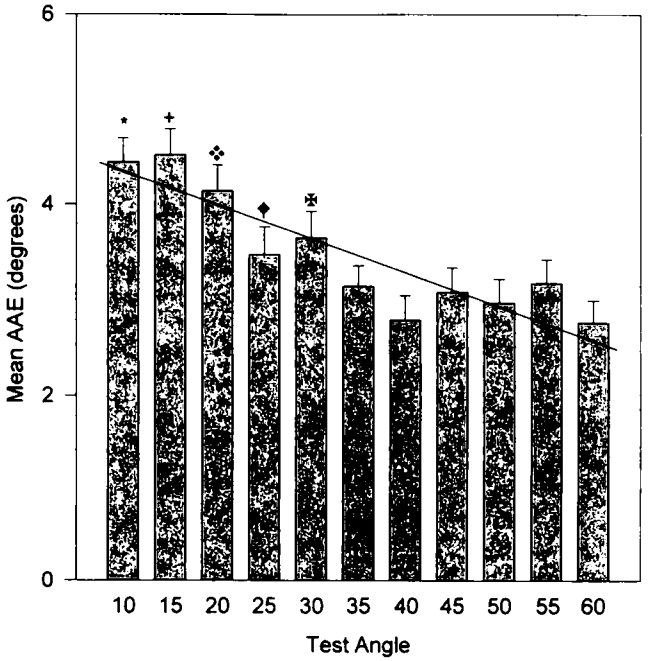

Fig 2. Limitations in absolute angular error (AAE) measurements due to test angle. Values are mean ± SEM. Regression line equation: 5.517 − (.102 · test angle). *Significantly different from test angles 35, 40, 45, 50, 55, 60 ($p < .05$); +significantly different from test angles 25, 35, 40, 45, 50, 55, 60 ($p < .05$); ❖ significantly different from test angles 35, 40, 45, 50, 55, 60 ($p < .05$); ♦ significantly different from test angles 40, 50, 60 ($p < .05$); *significantly different from test angles 40, 45, 50, 60 ($p < .05$).

Knee proprioception and fatigue. The effects of fatigue due to the number of repetitions during testing may inflate the AAE results in a population unaccustomed to performing this type of activity. To eliminate fatigue as a potential confound from the main analysis, a one-way ANOVA was performed on the AAE of the combined sample using the number of repetitions as the independent factor. AAE values were significantly greater in the latter angles compared with angles performed earlier in that testing period ($F(10, 1\ 165) = 1.89$, $p = .042$), although fatigue may only account for 1.4% of the variability in AAE ($\eta^2 = .01407$). This trend for poorer matching performance in later repetitions was confirmed by linear regression ($R = .124$, $F(1, 121\ 1) = 18.80$, $p < .001$) (fig 3). Tukey's HSD post hoc analysis revealed significant differences in the amount of AAE between the second angle reproduction and angles numbered 4, 6, 7, 9, 10, and 11, and also between angle number 5 and number 11.

The 2 × 3 repeated-measures ANOVA was reanalyzed eliminating AAE values calculated from angles performed either 10th or 11th. The 11th angle was removed because it differed significantly from two other repetitions; however, in subjects unable to perform all angle repetitions, this angle (numbered 11) may not actually have been the 11th angle performed during that testing period. Thus, the 10th angle was also eliminated. The reduced data set did not show any significant differences in proprioception between active treatment and placebo groups at any time. Since the second angle had a significantly lower AAE than six other reproduction attempts, this trial was examined alone for proprioceptive differences between treatment groups. A 2 × 3 repeated-

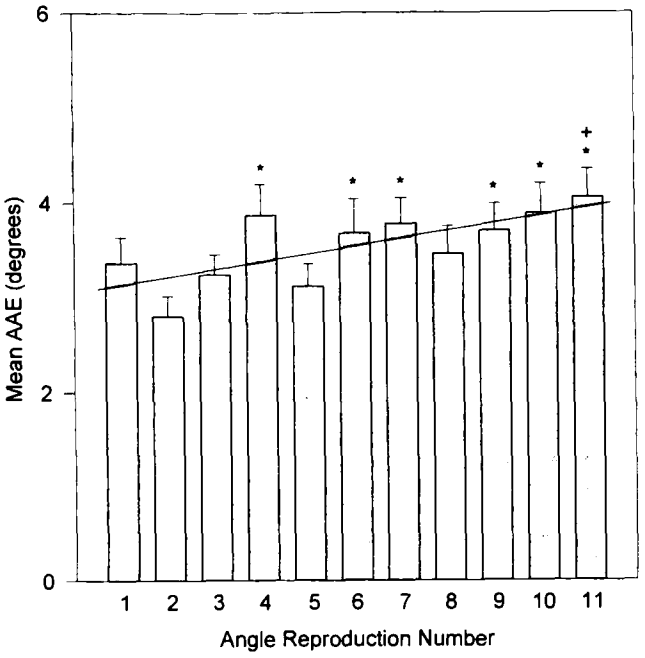

Fig 3. Mean absolute angular error (AAE) proprioception measurements at each repetition. Values are mean ± SEM. Regression line equation: 1.099 + (.161 · order number). *Significantly different from second angle reproduction ($p < .05$); +significantly different from fifth angle reproduction ($p < .05$).

measures ANOVA found no significant differences at any time during the study.

DISCUSSION

This study examined the effect of viscosupplementation therapy on knee joint proprioception in patients with mild to moderate OA of the knee. Subjects were given either a series of three hyaluronan injections or three placebo injections; proprioception was measured at three times during the study period. Since a 2 × 3 repeated-measures ANOVA revealed no effect of hyaluronan viscosupplementation on clinical measures of proprioception compared with placebo injections at any time, the null hypothesis was not rejected. These results may be attributed to failure of hyaluronan injections to restore the joint's rheological state; hyaluronan being inefficacious in reparation of damaged proprioceptors of ligaments, menisci, cartilage, or synovium; an insignificant contribution of articular proprioceptors to proprioception irrespective of hyaluronan effects; or a lack of sensitivity in the clinical, closed-kinetic, angle reproduction test for measuring unilateral knee proprioception, thus introducing a type II error into the analysis.

Treatment/Protocol Determinants of Function

Viscosupplementation studies report effects of hyaluronan injections on pain and function lasting up to 6 months or 1 year.[3,11] The present study's 3-week measurement may be too short to show changes in proprioception if the process is slow; further measurements after 6 months would not be expected to find any proprioceptive changes in the hyaluronan subjects because the injected hyaluronan molecules would have been catabolized back to their preexisting osteoarthritic state.[1] It may therefore be reasonable to expect any changes in proprioception to be detectable after 3 months into the treatment, approximately in the middle of the treatment schedule. Thus, the timing of measurements in this study (pretherapy, at 3 weeks, and at 3 months) ensures that no acute changes in proprioception occur from one treatment series. The present study's total time frame may have been too short to accurately show proprioceptive benefits of hyaluronan in knee OA. A longer study using the same measurement protocol on subjects receiving multiple series of injections may confirm the hypothesis that, although hyaluronan has no acute effect on proprioception, repeated treatments of it may attenuate osteoarthritic decline. A long-term treatment plan using hyaluronan to maintain the knee's rheological state may also maintain proprioception.

Viscosupplementation was developed to treat patients with symptoms of OA; no direct effect on proprioception is necessarily expected. Attenuated proprioceptive decline in patients treated with viscosupplementation, while a placebo group's proprioception declines normally, would indicate that OA may have a greater effect on impairing proprioception than poor proprioception has on advancing OA. Conversely, if a viscosupplementation group's osteoarthritic symptoms, such as pain, improved while their proprioceptive ability steadily declined, that finding would help to eliminate the bottom pathway in the causative factors from OA to proprioception. If OA has no influence on proprioception, proprioceptive decline would be due only to aging effects, and persons with accelerated proprioceptive impairment would be more likely to develop OA in one knee or the other.

Results from a longer term study (determining if viscosupplementation does or does not have an effect on proprioception) would contribute to previous work examining the causal relationship between OA and proprioception. In an earlier study, proprioception was worse in both knees in patients who had unilateral knee OA, leading to the conclusion that impaired proprioception was not a result of localized OA.[6] It follows that impaired proprioception may cause OA. If this is the case, viscosupplementation should not have an acute effect on proprioception, as supported by this study, but may aid in the longer term by reducing the effect of osteoarthritically induced pathology to proprioceptors in the knee. Since hyaluronan in the knee joint space is unlikely to directly affect muscle spindle receptors (because of no contact and no potential mechanism), any changes to proprioception would occur because of changes to articular receptors.

Other Determinants of Treatment Effect

Because viscosupplementation therapy fails to improve proprioception, physical therapy remains the most effective method to restore or maintain proprioception in a population with OA of the knee. Traditional exercise programs have included range-of-motion isometric quadriceps exercise ("quad-setting") and, occasionally, aerobic workouts.[15,21,22] Although aerobic programs have no effect on reducing joint pain or increasing strength, flexibility, or function, they affect aerobic power, walking time, depression, anxiety, and exercise time.[22] Quad-setting and range-of-motion exercises can be performed in the home, and they increase function, decrease pain, and improve proprioception while incurring OA-related symptoms in only a few cases.[23] In the present study, the exercises were not designed to improve proprioception but merely to aid perception of joint position through home-based stretching and flexibility maneuvers.

The largest separation in AAE between the two groups occurred after 3 weeks, although this increased difference in AAE did not reach statistical significance. The increased reproduction error in the hyaluronan group after 3 weeks may be attributable to mechanical effects of increased fluid in the joint, since a 3-week period would be too short to restore degenerated proprioceptors. However, it was unlikely that

injected hyaluronan was still be resident in the joint.[1] Little evidence exists to either expect or refute that the mechanical influence of increased fluid volume in the joint space would have any effect on proprioception. In the present study it appeared that neither the amount of fluid injected (2mL per injection) nor the amount of swelling associated with OA had any effect on proprioception.

Protocol Limitations

We saw four limitations to the present study: the selection of sample size, subjects' fatigue, closed versus open kinetic testing, and the angle reproduction test versus a threshold detection test. We used the convention of Marks and Quinney[19] that a minumum clinically detectable AAE was 1°. Whether this 1° of AAE is clinically important is beyond the scope or intention of the present study. Indeed, if differences in AAE were observed between treatments, it would be important to investigate whether this is related to some other clinical determinant of fall risk, pain, or function. Therapy aimed at producing "favorable" changes in AAE could then be studied in the context of improved proprioception measures in patients with OA.

Fatigue increased AAE in knee reproduction tests.[18,22] Some effects due to fatigue were shown in the present study, but even when data from fatigued conditions (ie, later joint angulations) were removed from the analysis, we found no differences in proprioception between hyaluronan and placebo injection groups at any time point. Consideration was also given to potential difficulties associated with certain angles being more difficult to reproduce (especially those at extremes of range of motion). Permutations of groups of angles with similar errors throughout the articular range of motion (10° to 20°, 25° to 60°, 35° to 60°, 35° to 50°) also failed to introduce any information regarding differences in proprioception between groups at any time. By removing confounds due to fatigue and amount of knee bend, it can safely be concluded that viscosupplementation had no effect on our closed-kinetic clinical measure of proprioception.

We chose the closed-kinetic chain position to reproduce normal, active, weight-bearing movements of the lower extremity encountered in daily activities, whereas numerous other studies have utilized open-kinetic positions to isolate one specific knee.[4,7,20,23] The closed-kinetic chain protocol is sensitive to change,[18] but the open-kinetic positioning may be more sensitive to variations in proprioception. A study similar to the present one using open-kinetic proprioception measurements may detect more subtle changes in proprioception.

Of the two most common clinical proprioception measurement techniques currently used, the angle reproduction test and the threshold to detection test, we determined subjects' proprioception exclusively by means of the angle reproduction test. Although thought to measure the same phenomenon, these two tests may either involve different neural mechanisms or may measure different aspects of proprioception.[7] Thus, it may be erroneous to report that viscosupplementation has no effect on proprioception before all aspects of proprioception potentially affected by this therapy have been investigated.

CONCLUSIONS

The present study determined that viscosupplementation therapy in mild to moderate OA of the knee using three weekly injections of hyaluronan (2mL of 2% hyalgan) had no effect on clinical measures of knee proprioception compared with placebo. Further studies involving the angle reproduction test in the open-kinetic position or threshold to detection of motion testing following hyaluronan therapy may more sensitively address the effects of viscosupplementation on proprioception. Longitudinal study of repeated hyaluronan injection series coupled with age-matched normal controls could determine if multiple viscosupplementation treatments would attenuate proprioceptive decline over time and may provide insight into the causal relations between OA and proprioception.

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References

1. Aviad AD, Houpt JB. The molecular weight of therapeutic hyaluronan (sodium hyaluronate): how significant is it? J Rheumatol 1994;21:297-301.
2. Weiss C, Band P. Musculoskeletal applications of hyaluronan and hylan. Potential uses in the foot and ankle. Implantable Biomaterials 1995;12:497-517.
3. Peyron JG. Intraarticular hyaluronan injections in the treatment of osteoarthritis: state-of-the-art review. J Rheumatol 1993;20:10-5.
4. Barrett DS, Cobb AG, Bentley G. Joint proprioception in normal, osteoarthritic and replaced knees. J Bone Joint Surg Br 1991;73: 53-6.
5. Pai YC, Rymer WZ, Chang RW, Sharma L. Effect of age and osteoarthritis on knee proprioception. Arthritis Rheum 1997;40: 2260-5.
6. Sharma L, Pai YC, Holtkamp K, Rymer WZ. Is knee joint proprioception worse in the arthritic knee versus the unaffected knee in unilateral knee osteoarthritis? Arthritis Rheum 1997;40: 1518-25.
7. Skinner HB, Barrack RL. Joint position sense in the normal and pathologic knee joint. J Electromyogr Kinesiol 1991;1:180-90.
8. Lord SR, Clark RD, Webster IW. Physiological factors associated with falls in an elderly population. J Am Geriatr Soc 1991;39:1194-200.
9. Lussier A, Cividino AA, McFarlane CA, Olszynski WP, Potashner WJ, De Medicis R. Viscosupplementation with hylan for the treatment of osteoarthritis: findings from clinical practice in Canada. J Rheumatol 1996;23:1579-85.
10. Towheed TE, Hochberg MC. A systematic review of randomized controlled trials of pharmacological therapy in osteoarthritis of the knee, with an emphasis on trial methodology. Semin Arthritis Rheum 1997;26:755-70.
11. Maheu E. Hyaluronan in knee osteoarthritis: a review of the clinical trials with hyalgan. Eur J Rheumatol Inflamm 1995;15: 17-24.
12. Kaplan FS, Nixon JE, Reitz M, Rindfleish L, Tucker J. Age-related changes in proprioception and sensation of joint position. Acta Orthop Scand 1985;56:72-4.
13. Petrella RJ, Lattanzio PJ, Nelson MG. The effect of age and activity on knee-joint proprioception. Am J Phys Med Rehabil 1997;76:235-41.
14. Srinivasan A, Amos M, Webley M. The effects of joint washout and steroid injection compared with either joint washout or steroid injection alone in rheumatoid knee effusion. Br J Rheumatol 1995;34:771-3.
15. Ettinger WH Jr, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis: the Fitness Arthritis and Seniors Trial (FAST). JAMA 1997;277:25-31.
16. Altman R, Fries JF, Block DA, Carstens J, Cooke TD, Genant H, et al. Radiographic assessment of progression in osteoarthritis. Arthritis Rheum 1987;30:1214-25.
17. Penny and Giles Biometrics Limited. Goniometer and torsiometer operating manual. Blackwood, Gwent, UK: Penny and Giles Biometrics Limited; 1993.
18. Lattanzio PJ, Petrella RJ, Sproule JR, Fowler PJ. Effects of fatigue on knee proprioception. Clin J Sport Med 1997;7:22-7.
19. Marks R, Quinney HA. Effect of fatiguing maximal isokinetic quadriceps contractions on ability to estimate knee-position. Percept Mot Skills 1993;77:1195-202.

20. Perlau R, Frank C, Fick G. The effect of elastic bandages on human knee proprioception in the uninjured population. Am J Sports Med 1995;23:251-5.
21. Balazs EA, Denlinger JL. Viscosupplementation: a new concept in the treatment of osteoarthritis. J Rheumatol 1993;20:3-9.
22. Fisher NM, Pendergast DR, Gresham GE, Calkins E. Muscle rehabilitation: its effect on muscular and functional performance of patients with knee osteoarthritis. Arch Phys Med Rehabil 1991;72: 367-74.
23. Horch KW, Clark FJ, Burgess PR. Awareness of knee joint angle under static conditions. J Neurophysiol 1975;38:1436-47.

Suppliers

a. Penny & Giles Biometrics Ltd., 36 Nine Mile Point Industrial Estate, Cwmfelinfach, Gwent, NP1 7HZ, United Kingdom.
b. Bioniche Inc., Canada, 383 Sovereign Road, London, Ontario, Canada N6M 1A3.