

Efficacy of Physical Therapy and Intra-articular Hyaluronans on Pain and Functional Performance of Osteoarthritic Subjects

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ABSTRACT

Objective: To determine the effectiveness of physical therapy and intra-articular programs for subjects with osteoarthritis (OA) of the knee referred for physiotherapy in terms of pain and physical dysfunction. **Methods:** After a baseline assessment, one hundred twenty patients aged 60 years or older, with symptoms and radiographic evidence of unilateral or bilateral knee osteoarthritis were randomized into one of three groups. Group 1: Forty patients received weekly intra-articular hyaluronan (HA) treatment during the first 3 weeks, group 2: forty patients received physical therapy three times a week for 8 weeks, group 3: forty patients receive both physical therapy program and intra-articular injection of Hyaluronan. Outcome measures: Using a visual analogue scale (VAS), patients assessed the following clinical variables: stiffness, pain at rest, pain during weight-bearing. Objective measures of physical performance [range of motion (ROM), 6-minute walk distance, and muscle strength] were assessed at baseline, 4, 8 and 24 weeks. **Results:** All the study groups showed a significant improvement in mostly all variables measured in (e.g. pain and physical function) during the 4 week follow-up assessments. There was dramatic early improvement in mostly all variables except the muscle strength and range of the motion with hylan group after the first injection. On completion of the program group 3 demonstrated significant improvements over the other two groups. Mostly all improvements were maintained at the 6 month follow up assessments. **Conclusion:** Physical therapy, either as an individually delivered treatment or in combinations with hyaluronan, is an effective intervention for patients with knee OA. Although all patients had improvement, Physical therapy in combinations with hyaluronan was superior to hyaluronan group alone for no activity-related pain and functional performance. **Key words:** Physical therapy, Intra-articular hyaluronan treatment, Osteoarthritis, functional performance.

INTRODUCTION

Osteoarthritis is a major cause of pain and disability in the community seniors in the Western world. As prevalence increases it is expected to pose an increased burden on health care in

the future^{24,25}, and perceived as a major public health problem¹⁶, loss of articular cartilage, subchondral sclerosis, chronic synovitis, joint deterioration and osteophytes formation⁹. The pain associated with this condition is the chief complaint of most patients, prompting them to seek medical attention. Pain can originate from

the synovial membrane, joint capsule, periarticular muscles and ligaments, and periosteum and subchondral bone, among other sources^{16,22}. Treatments have generally targeted pain, assuming that disability would improve as a direct result of improvements in pain⁵.

Today, various treatment modalities are used to manage this condition. The conservative treatment focuses mainly on relieving pain, reducing inflammation, decreasing stiffness, maintaining joint mobility and preventing further deformity⁹. Individuals with knee OA may have a variety of impairments and functional limitations that prevent them from participating in regular exercise and physical activity. Physical therapists can offer a variety of supplemental treatment approaches that may help patients overcome these barriers and enhance the overall effectiveness of exercise therapy programs¹⁰.

Physical therapy agents (PTA) play an important role in the treatment of OA of the knee. Deep heat such as pulsed short waves diathermy (PSWD) and electrotherapeutic modalities such as interferential therapy are used for the treatment of acute and chronic pain which are the cardinal symptoms of OA⁵.

Current treatment of OA is limited to symptom management with analgesics, anti-inflammatory agents, and viscosupplementation devices. It has been suggested that sodium hyaluronate delays progressive joint space narrowing and improves the biomechanics of OA knee joints even in the absence of pain relief²⁹, by conveying the drug directly to the inflamed joint area, thus avoiding major systemic side effects³. At least there are four mechanisms whereby intra-articular injection of hyaluronate derivatives may provide therapeutic benefit in symptomatic osteoarthritic joints: restoration of elastic and viscous properties of the

synovial fluid; anti-inflammatory effects; anti-nociceptive effects; normalisation of hyaluronan synthesis by synoviocytes²⁹.

MATERIALS AND METHODS

Study design

A total of 120 participants recruited for the study (67 women and 53 men) with a mean age of 58.9 years suffered from OA. The participants first completed all baseline assessments and were then randomized to the three treatment groups. The patients in group 1 were given three intra-articular injections of high molecular weight hyaluronan (Orthovisc) once a week (7 days apart), by an expert orthopedic surgeon, physical therapy group (group 2), and a combination of both lines of treatment group (group 3). Patients were followed up for 21 weeks after the last injection (total study duration of 24 weeks). Informed consent was obtained from all subjects before participation in this study.

Inclusion criteria were as follows: (a) knee pain for more than 25 of the past 30 days, morning stiffness of less than 30 minutes, and crepitation in the knee or (b) osteophytes on x ray examination of the knees indicating knee OA., (In patients with bilateral disease the more painful knee was treated) and radiologically verified OA of grade I-III according to Ahlbäck (1968) (1) (grade I=loss of more than 50% of joint space, but less than 100%; grade II=complete loss of joint space; grade III=additional loss of bone substance) estimated on the basis of an anteroposterior weight-bearing radiograph with a knee flexion angle of 10–15° with no bone erosion⁸.

The exclusion criteria were: bone attrition in either knee (Ahlbäck grade IV–V); previous intra-articular fracture of the knee; rheumatoid arthritis non-compliance, or other

inflammatory joint disease as defined by American College of Rheumatology criteria; intra-articular injections of steroids or hyaluronan or other invasive procedure (e.g. arthroscopy, arthrography, surgery) less than 6 months prior to inclusion, and any quadriceps exercise program within the last 4 months. Furthermore, patients were not included if they had a known allergy to any substance related to the study, difficulty completing questionnaires, or any disabling problem of the musculoskeletal system or other organ system which could interfere with the assessment of efficacy. Patients using concomitant analgesic treatment for other reasons were excluded. Informed consent to participate in the study was obtained from all participants.

Physical therapy

Physical therapy was applied to each patient in group 2 and 3 for 3 times a week for 8 weeks. It consists of several strategies to facilitate resolution of symptoms and improve functional deficits, including ROM exercises without resistance, strengthening exercise program. A series of ice backs, interferential therapy, and pulsed short wave diathermy (PSWD) was applied for each patient in group 2 and 3.

Intervention Protocol

The intervention protocol for the group 2 or 3 consisted of 24 sessions of 20 minute induction-coil PSW diathermy therapy. The participants were positioned supine and comfortably on the treatment plinth with the affected knee extended. A towel was wrapped around the knee joint, and then the induction coil cable was applied circularly along the affected leg. All participants received treatments from the same SW diathermy machine (Enraf, Curapuls 419, the Netherlands.) The intensity of the current was

set based on each participant's sensation of warmth (a mild but pleasant sensation of heat)¹¹. 20 minute of Interferential Current (IFC) with a four electrodes around the knee joint using a standard Galva electrotherapy system (Zimmer Elektromedizin, Neu-Ulm, Germany). With IF, four permutations of frequencies can be used: the two main frequencies and their sum or their difference, with the principle of mixing a 4 kHz and a 4.001–4.005 kHz frequency to generate the single desired frequency of 1–1000 Hz. In the current study it was used on "Program 36". The patients were instructed to perform knee extensions every 5 min during the 20 min session, to prevent stiffness of the knees. For the ice backs application a towel of ice backs was wrapped around the knee joint. Strengthening exercise program for all muscle groups around the knee joint from the supine position at first in the form of straight leg raising, quadriceps drill exercises, manual resistance was applied to resist motion throughout the range of motion, exercise for each motion was applied 15 repetitions.

Intra-articular injections

A 2 ml of NaHA (Orthovisc; Biomeks) contains 15 mg sodium hyaluronate and 9 mg sodium chloride for each 1 ml. The molecular weight of NaHA is $1.55 \cdot 10^6$ D. All the intra-articular injections were given by the same physicians under aseptic procedures using a medial approach to each patient in group 1 and 3. If effusion was present, the joint was aspirated before injecting hyaluronic acid. The patients were clinically assessed before each of the first three injections (days 0, 7, 14), 7 days after the third injections (at the first month), at 8 weeks, and 24 week. No anesthetic was used either topically or intra-articularly. Only the index knee was treated.

Washout and escape medication

All analgesic and anti-inflammatory medications were discontinued prior to the start of treatment. The washout period was 2 weeks for medications with a prolonged half-life or at least five times the half-life of the drug. During the washout period, the patients were allowed to use paracetamol if necessary (up to 4 g/day).

Assessments

Baseline characteristics (weight, height, age, sex, study knee and Ahlbäck (1968)¹ radiological grade) were recorded at the first visit. The pain was assessed daily when walking on a flat surface and at rest by visual analogue scale (VAS). Mean resting pain intensity (MRPI) and Mean walking pain intensity (MWPI). Objective and functional measures of physical performance, range of motion (ROM) (measured as the degrees of passive flexion of the study knee), 6-minute walk distance (participants were instructed to cover as much distance as possible during the 6-minute time frame), and Quadriceps muscle strength (QMS). The secondary endpoint was evaluated by changes in the Western Ontario and McMaster Universities (WOMAC) score vs. baseline. The WOMAC was conceived to assess 3 domains: pain, stiffness, and physical function by 24 questions: 5 determine subject global assessment of pain, 2 assess joint stiffness, and 17 assess physical functioning¹.

Statistical Methods

SPSS for Windows software was used for data management and statistical analysis. To compare the groups concerning demographic measurements, ANOVA and chi-squared were used in group analyses. The repeated measure analysis of variance (ANOVA) was used to compare the study groups on nominal variables, and paired t test

was used to test the changes from baseline. The level of significance was set at 0.05 for all statistical tests.

RESULTS

Recruitment of participants was conducted over 6 months from referrals for assessment of osteoarthritis of the knee. A total of 120 participants completed the trial, well matched with respect to demographic data, duration of arthritis, baseline score on the visual analog scale, the concomitant use of analgesics, and radiographic stage (table 1) which summarizes their characteristics at the start of the trial. Most patients (82%) presented with unilateral knee osteoarthritis. In patients with bilateral symptoms, only the more symptomatic knee (on VAS) was used for the purposes of the study. There were no statistically significant differences in demographic and clinical data measured between the groups baseline, physical functioning, or grade of OA ($P > 0.05$). Severity of knee osteoarthritis at baseline radiograph was graded as follows: 55 grade 1, 49 grade 2, and 16 grade 3. No serious adverse events occurred during the study.

There was significant improvement in all parameters studied in group 3 at week 4 evaluation compared to baseline scores and also the two other groups (ANOVA, $P < 0.05$), the improvement continued through the study end points. Group 1 showed dramatic significant improvement in the mean resting and walking pain intensity compared to group 2 but this difference was not observed at 8 and 24 weeks assessments, while group 2 showed significant improvement in mean distance walked in 6 minutes, mean QMS and mean ROM0 in comparison with group 1 at 4 weeks assessments.

On program completion, combined treatment and physical therapy groups demonstrated significant improvements in functional performance outcomes (Mean distance walked in 6 minutes, Mean QMS and Mean ROM0) (ANOVA, $P < 0.05$) over the group 1 (Table 2). Group 2 showed a significant difference in relation to group 1, which showed return to the baseline scores of mean QMS and mean ROM0 at the 24 weeks assessment.

Although the pain at rest, mean walking pain intensity, mean distance walked in 6 minutes and mean WOMAC score were improved during the whole follow-up in all patients compared to baseline (ANOVA, $P < 0.05$), there was a statistical significant difference between the groups for these parameters which were in favor of combined treatment group (group 3) at the 4, 8 and 24 weeks ($P < 0.05$, Table 2).

Combined treatment group demonstrated more than 48.2% improvement of the resting pain, 15.4% in 6-minute walk distance, 32.2% in QMS, and 22.5% in ROM at 4 weeks. By

24 weeks, average 6-minute walk distances had improved by 17.4% over baseline values ($P < 0.05$), average QMS had improved by 37.4% over baseline values ($P < 0.05$), and average resting pain had improved by 63% over baseline values ($P < 0.05$). In the intra-articular group, 39% to 56% of patients were free or nearly free of weight-bearing pain 10 to 21 weeks after the last injection.

Improvements in the mean distance walked in 6 minutes were substantiated by significant correlated improvements in knee extensor strength and mean walking pain intensity in the physical therapy group, mean distance walked in 6 minutes, mean QMS and ROM were significantly improved (11.6%, 25.2%, and 16.6% respectively) after 4 weeks of active strengthening exercises ($P < 0.05$).

These findings suggest combination treatment may provide patients with a more physiologically dynamic viscosupplementation and hence a more responsive synovial rheology that improves pain and function in their osteoarthritic knee.

Table (1): Demographic and baseline characteristics of all participants.

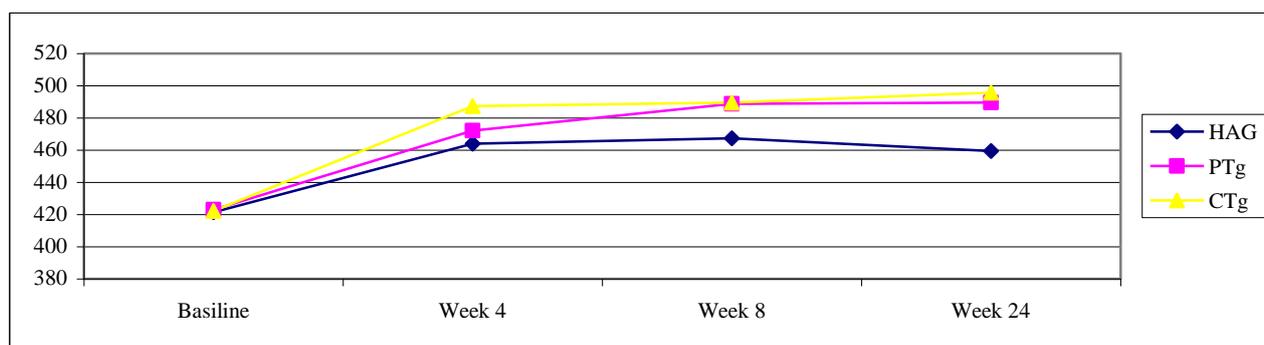
Variable	HA g, (N = 40)		PT g, N=40		CT g, (N = 40)		P* Value
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	58.3	8.1	59.2	7.2	59.4	7.9	NS
Weight (kg)	82.2	5.4	84.3	5.6	79.8	5.7	NS
Body mass index (kg.m-2)	29.7	3.9	30.6	3.2	30.2	3.5	NS
Sex M/F	18/22	-	16/24	-	19/ 21	-	NS
Mean duration of symptoms, m*	162	15.6	157	14.9	168	14.2	NS
Bilateral symptoms %	35%	-	34%	-	36%	-	NS
Medications use %	60%	-	56%	-	58%	-	NS
No (%) at each Rg stage							
Grade 1	17 (42.5)	-	20 (50.5)	-	18 (45.5)	-	NS
Grade 2	17 (42.5)	-	15 (37.5)	-	17 (42.5)	-	NS
Grade 3	6 (15.0)	-	5 (12.5)	-	5 (12.5)	-	NS

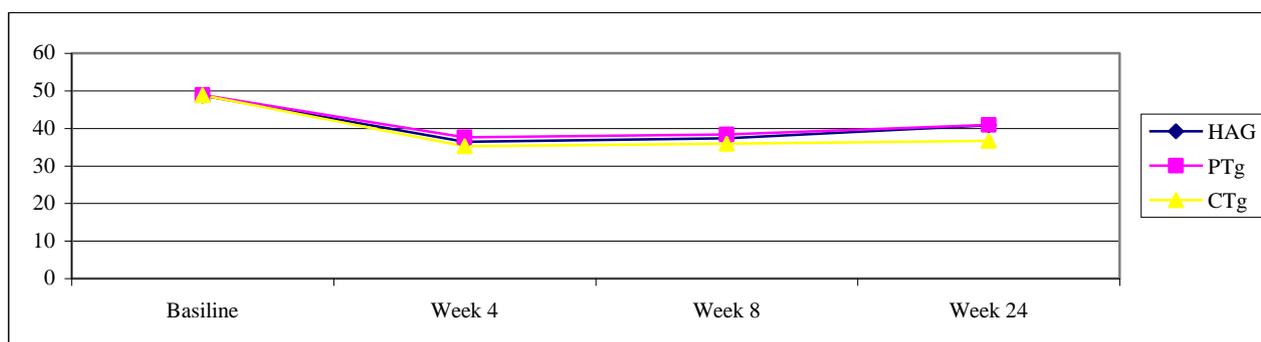
m*: month, Rg: radiographic, CT G: Combined Treatment group, HA: HA

Table (2): The treatment outcomes: changes from baseline, 4, 8 and 24 Weeks.

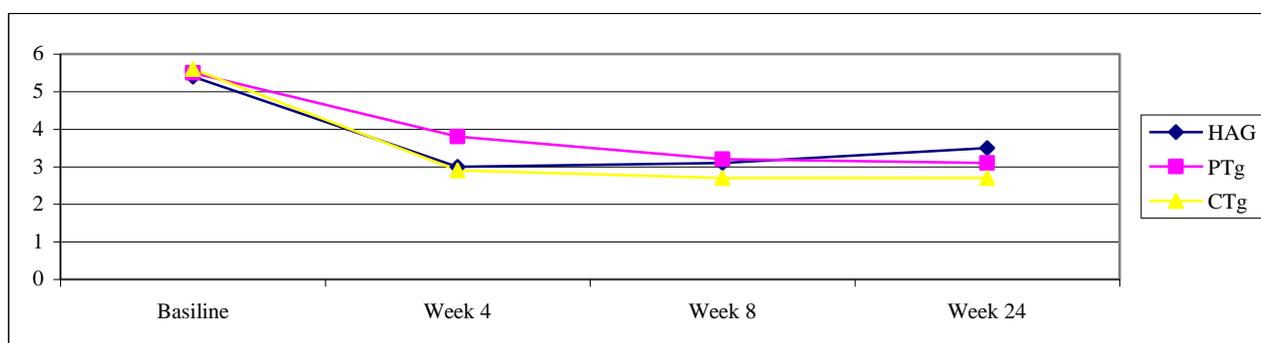
Test	Baseline	Week 4	Week 8	24 Week
WOMAC S,				
HA g	48.7 (13.3)	36.4* (10.8)	37.3* (11.8)	40.8* (13.2)
PT g	48.9 (13.6)	37.6* (12.5)	38.4* (12.6)	40.9* (15.3)
CT g	48.8 (12.9)	35.2* (11.1)	35.9* (12.8)	36.7* (12.8)
DW in 6 m, m				
HA g	421.4 (75.5)	464.0* (62.5)	467.4* (61.8)	459.4* (54.9)
PT g	422.9 (78.4)	472.1* (65.8)	488.7* (64.1)	489.6* (63.7)
CT g	422.2 (80.1)	487.3* (67.6)	489.6* (63.2)	495.6* (72.3)
RPI				
HA g	5.4 (1.8)	3.0* (1.3)	3.1* (1.5)	3.5* (1.6)
PT g	5.5 (1.7)	3.8* (1.4)	3.2* (1.5)	3.1* (1.5)
CT g	5.6 (1.6)	2.9* (1.3)	2.7* (1.4)	2.7* (1.2)
WPI				
HA g	7.4 (1.5)	4.1* (1.5)	4.4* (1.7)	4.9* (1.8)
PT g	7.4 (1.5)	4.3* (1.6)	4.2* (1.8)	4.4* (1.7)
CT g	7.3 (1.4)	3.9* (1.3)	3.8* (1.4)	4.1* (1.3)
QMS (Kgs)				
HA g	51.8 (5.6)	52.9 (7.4) (NS)	52.5 (6.8) (NS)	51.8 (5.5) (NS)
PT g	52.4 (5.9)	65.6* (5.6)	68.8* (5.9)	69.2* (6.7)
CT g	51.6 (6.2)	68.2* (7.5)	71.2* (6.6)	70.9* (6.9)
ROM 0				
HA g	1200 (12.50)	122.60 (9.7) (NS)	123.80 (11.9)(NS)	120.40 (10.5)(NS)
PT g	1180 (11.60)	130.60* (9.8)	130.90* (10.7)	132.80* (9.6)
CT g	1180 (10.30)	135.50* (9.7)	135.20* (10.8)	135.70* (8.8)

HAG: Hyaluronans group, PTG: physical therapy group, CTG: Combined Treatment group, m minutes, m^c Meter QMS: mean x- quadriceps muscle strength WOMAC S: Western Ontario and McMaster University osteoarthritis index scores, *Pain intensity was measured with a visual analog scale; a score of 0 indicated no discomfort and a score of 10 indicated severe discomfort. RPI: Mean x- resting pain intensity, WPI: Mean x- walking pain intensity, DW in 6 m: Mean x- distance walked in 6 minutes, m, ROM 0: mean x- range of motion

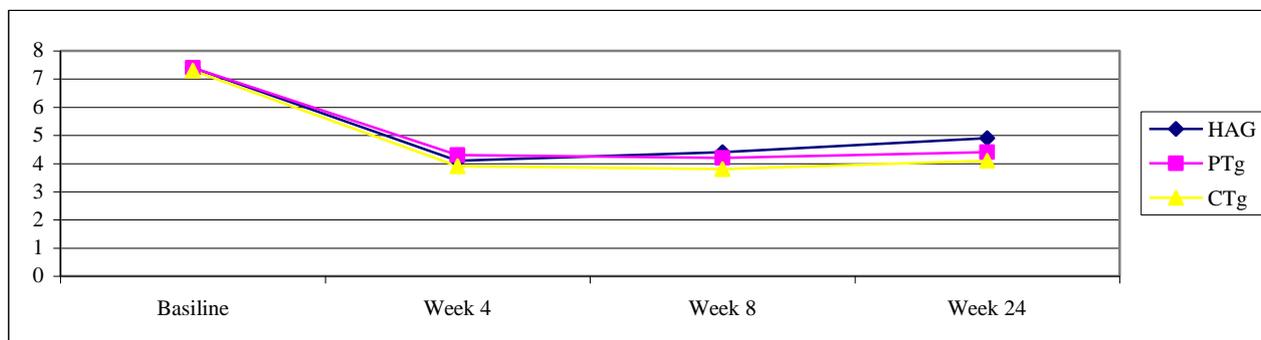
**Mean distance walked in 6 M, m**



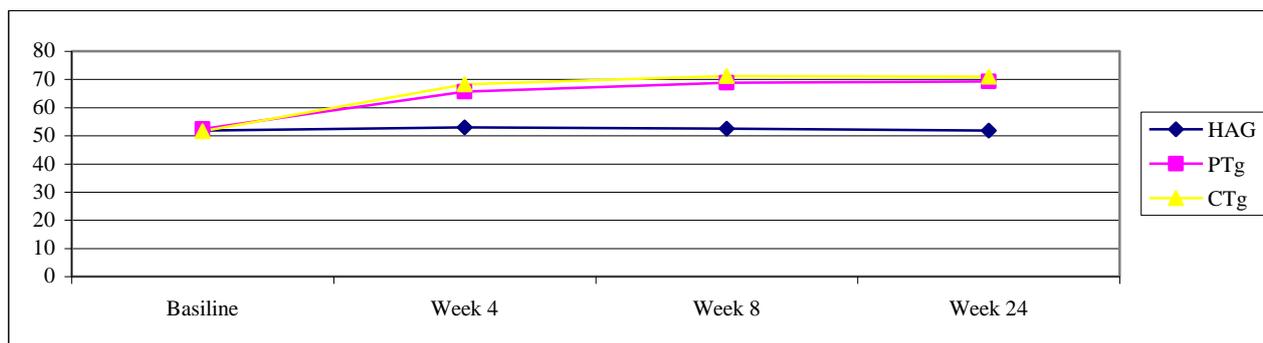
Mean WOMAC score



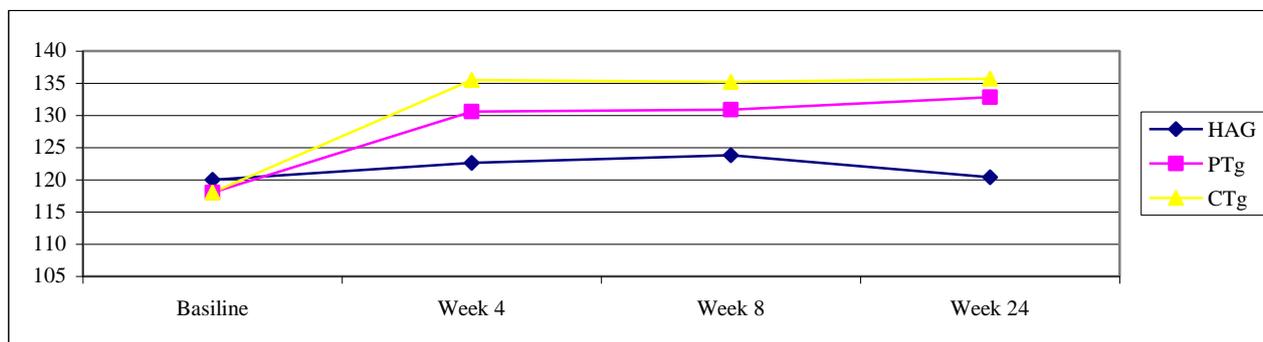
Mean resting pain intensity



Mean walking pain intensity



Mean QMS (Kgs)



Mean ROM0

DISCUSSION

Knee OA is a common but often difficult problem to manage in primary care. It is traditionally thought of as a noninflammatory type of arthritis; however, inflammatory mechanisms can be present³⁰. Despite the increasing morbidity and economic costs of osteoarthritis (OA), standard therapies have not progressed significantly over the past several years. Current therapies are directed at controlling pain and maintaining articular function rather than altering physical functioning and the disease process²⁸. Although pain relief is a chief motivator for patients with OA to seek medical attention, a secondary benefit of successful treatment is to delay the decreased quality of life associated with osteoarthritic pain²³.

Viscosupplementation is a local therapeutic approach with the objective to decrease pain and to improve joint mobility, based on the replacement of synovial fluid or exudates with an elastoviscous hyaluronan solution⁷ through increasing the viscoelasticity of the synovial fluid appears to play a role^{26,27,30}. The hyaluronic acid has become an increasingly accepted therapeutic alternative in the symptomatic management of OA. Basic science research has documented numerous potential actions of exogenous hyaluronic acid upon the diseased joint²⁶.

In our study, all the treatments programs were found effective for the management of the knee OA during the follow-up at the week 4, 8 and 24 for all parameters studied except of the mean quadriceps muscle strength (kg) and mean ROM0 for the hyaluronic acid group. These results are coincident with the results of

Mei et al. (2006)¹² who reported a significant improvement of pain in osteoarthritic patients post pulsed shortwave application. Ruth et al. (2005)²³ who reported that interferential current applied to the knee significantly reduced both chronic pain intensity and stiffness and significantly increased pain-free range of motion and pain threshold in the knee. Their results suggest that IFC is very effective in the treatment of chronic OA knee pain. They reported that the significant results of their study may in part be due to IF stimulation, as IF stimulation delivers current more deeply than conventional TENS. Pope et al. (1995)²¹ came to the conclusion that, IFC is also reported to be more comfortable to patients. Consequently, IFC offers an effective and recommended treatment for OA pain.

Also in agreement with the results of the present study Petrella et al. (2002)¹⁸ reported that aerobic and resistance exercises have been shown to help with many of the physiological and psychological factors associated with arthritis: muscle weakness; decreased flexibility; poor endurance; fatigue; depression; and low pain threshold. Certainly, in patients with osteoarthritis, regular exercise can improve pain, proprioception, strength, instability, and endurance, all of which improve functional independence. Exercise has been considered as an important non-pharmacological approach. In addition, it directly reduces disability and corrects walking. In addition to its potential impact on the disease processes themselves, exercise improves general health and well being, enhances quality of life, and preserves physical independence. No deleterious effects have been documented, despite some programs including quite vigorous activity among elderly subjects²⁰. Delitto et al. (1988)⁷ reported that by contracting and exercising the muscles that mainly control knee movement, it

can decrease knee stiffness, increase range of motion and improves the quality and viscosity of synovial fluid in the knee. Petrella and Bartha (2000)¹⁷ showed a significant effect of home based exercise therapy on both self selected speed of walking and stepping, both clinically relevant functional outcomes as recommended by OMERACT.

The results of the present study goes in accordance with that of Van Baar et al (1999)²⁸ concerned supervised individual treatment, including strengthening exercises, ROM exercises, and functional training over 12 weeks for patients with knee OA of a mean duration of >10 years find that supervised individual treatment resulted in beneficial effects and reduced disability in patients with osteoarthritis of the knee. Also the controlled, randomized, single-blinded study of Deyle et al. (2005)⁸ which demonstrated that manual therapy techniques and exercises applied by physical therapists for 8 clinical visits produced a 52% improvement in self-reports of function, stiffness, and pain as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale and a 12% improvement in 6-minute walk test scores. A placebo control group that received equal clinical attention showed no improvement in WOMAC scores or 6-minute walk test scores. Quadriceps weakness is a risk factor for incident knee osteoarthritis (OA), the rate of loss was slower with strength training (ST) than with ROM. Compared with ROM, ST decreased the mean rate of joint space narrowing (JSN) in osteoarthritic knees by 26%. The ST group retained more strength and exhibited less frequent progressive JSN over 30 months than the ROM group¹³.

Neustadt et al. (2005)¹⁵ findings came to the conclusion that viscosupplementation is an effective treatment for mild to severe OA of the knee and in those for whom other

approaches are contraindicated, or have failed. Modawal et al. (2005)¹⁴ reported that Intra-articular viscosupplementation was moderately effective in relieving knee pain in patients with osteoarthritis only 10 weeks after the last injection.

Results of the present study goes with that of Atamaz et al. (2006)³ who find that there was significant improvement in all variables measured in physical therapy agents and hylan groups during the follow-up except the WOMAC-stiffness and range of the motion. They came to the conclusion that although all patients had improvement, physical therapy was superior to hyaluronan group for no activity-related pain and functional performance. Also the results of the present study goes in parallel with that of Paker et al.,¹⁶ who find that WOMAC pain scores were statistically significant improved at the end of the first month in both the TENS and the viscosupplementation group. WOMAC stiffness scores showed a statistically significant decrease in the TENS group at the end of the first month while it did not in the second group; however, these patients exhibited improvement during the sixth month after injection. Improvement in WOMAC physical function scores was greater in the intra-articular hylan group than in the TENS group at the end of follow-up

Also the results of the present study goes with that of Modawal et al. (2005)¹⁴ reported that Intra-articular viscosupplementation was moderately effective in relieving knee pain in patients with osteoarthritis only 10 weeks after the last injection. Petrella and Bartha (2000)¹⁷ who find that Intra-articular hyaluronic acid injections were highly effective in improving resting and walking pain in patients with osteoarthritis of the knee on a first and a second treatment series.

The results of the present study are in agree with that of Petrella et al. (2005)¹⁹ who found that hyaluronate sodium group showed significantly faster self-paced walking and stepping test results at week 12 compared with baseline measures and they conclude that for pain with physical activity and functional performance, hyaluronate sodium may be superior to placebo alone or NSAIDs alone.

Kolarz et al. (2003)¹¹ reported that when intra-articular hyaluronans are used in clinical practice, one can expect between 3 months and 6 months of improvement from pain and stiffness as measured in various ways. Retreatment with a second course of intra-articular hyaluronan therapy was useful and not associated with any increase in adverse events.

Bagga et al. (2006)⁴ suggested that one possible mechanism of action of viscosupplementation is to promote endogenous hyaluronan production. They claimed the positive effect of the viscosupplementation to at least four mechanisms as intra-articular injection of hyaluronate-derivatives may provide therapeutic benefit in symptomatic osteoarthritic joints through: restoration of elastic and viscous properties of the synovial fluid, anti-inflammatory effects, anti-nociceptive effects, normalization of hyaluronan synthesis by synoviocytes.

The results show that although both physical therapy and intra-articular hialuronat injection reduce chronic pain, physical therapy is significantly more effective. This is in agreement with Ruth et al. (2005)²³ who showed that in OA pain, physical therapy, with IFC or ice cube induced significant pain relief.

Moreover, our findings showed that better results for the function and pain relief by WOMAC were obtained in combined physical therapy and hyaluronan group. Physical

therapy appears to be a promising intervention for relieving pain, decreasing knee stiffness and improving function.

The positive effect of the combined treatment in the present study is also supported by the increase of the mean maximal knee flexion angle, the decrease of the mean VAS values and the significant reduction of the mean WOMAC score.

Conclusion

Based on the aforementioned analyses, physical therapy combined with hyaluronan is an effective treatment for OA of the knee with beneficial effects: on pain, function and patient global assessment; for resting pain relief hyaluronan seems to be more effective than physical therapy. Further, for pain with physical activity and functional performance, physical therapy combined with hyaluronan is superior to intra-articular hyaluronan alone.

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الملخص العربي

دراسة كفاءة برنامج مزدوج للعلاج الطبيعي والحقن المفصلي بالهيالورونات علي الأداء الوظيفي والمخرجات العملية لمرضى خشونة المفصل

لتحديد كفاءة برنامج مزدوج من العلاج الطبيعي والحقن المفصلي للأشخاص المصابين بخشونة المفاصل والذين يعانون من الألم واختلال الوظائف البدنية . تم إختيار مائة وعشرون حالة ممن تتراوح أعمارهم بين الستون عاما أو أكثر . تم تقسيم الحالات إلي ثلاث مجموعات: المجموعة الأولى (40فرد) تلقت حقن مفصلي بالهيالورونات لمدة ثلاثة أسابيع بواقع حقنة واحدة أسبوعيا والمجموعة الثانية (40فرد) تلقت جلسات العلاج الطبيعي بواقع ثلاث جلسات أسبوعيا لمدة ثمانية أسابيع وتلقت المجموعة الثالثة (40فرد) برنامج مزدوج للنظامين السابقين . وقد تم اختيار مقياس الألم المرئي والتبيس والألم أثناء الراحة وأثناء الحركة مع تحميل وزن الجسم وكذا المدى الحركي واختبار مسافة المشى لمدة ستة دقائق وقوة العضلات . وقد أظهرت جميع المجموعات تحسنا دال احصائيا لمعظم الاختبار من خلال التقييم التبعي الذي استمر لمدة ستة أشهر . وقد أظهرت هذه الدراسة أن العلاج الطبيعي سواءا منفردا أو خلال علاج مشترك مع الحقن المفصلي بالهيالورونات لمرضى خشونة الركبة هو علاج آمن وفعال. وعلي الرغم من أن كافة المجموعات قد أظهرت تحسنا ملحوظا ودال إحصائيا إلا أن مجموعة العلاج المشترك بين العلاج الطبيعي والحقن المفصلي بالهيالورونات كانت أفضل من نتائج مجموعة الحقن المفصلي بالهيالورونات فقط من حيث إختفاء الألم المصاحب للحركة أو الأداء الوظيفي .