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VISCOSUPPLEMENTATION VERSUS PHYSIOTHERAPY IN KNEE OSTEOARTHRITIS: Short-term effects on biomechanical parameters of gait

DİZ OSTEOARTRİTİNDE VİSKOSUPLEMENTASYON FİZYOTERAPİYE KARŞI: Kısa dönemde yürüyüşün biyomekanik özelikleri üzerine etkileri

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ABSTRACT

Aim: This aim of this prospective, controlled, single-blind study was to compare the efficacy and side effects of intraarticular Hyaluronan or Hylan G-F 20 injections and a three weeks of physiotherapy (PT) program in treatment of knee osteoarthritis (OA).
Methods: Thirty patients with knee OA were assigned into one of the three groups. Groups received intraarticular injections of Hyaluronan or Hylan G-F 20, or physiotherapy program, respectively. The outcome parameters measured before and one week after 3 weeks' intervention were Western Ontario McMaster Universities Osteoarthritis Index (WOMAC), and kinematic and kinetic gait characteristics.
Results: Pain subscore and total score of WOMAC, sagittal plane excursions of the knee, extensor and adductor moments and scaled vertical forces improved in all of the groups. However, the statistically significant difference was observed in only subjective clinical assessments (pain subscore and total score of WOMAC) of PT group.
Conclusion: Intra-articular viscosupplements are found to be effective and safe not only in relieving pain but in altering the natural history of the knee OA, by decreasing joint loading, as well.

Key words: Osteoarthritis, hyaluronan, hyalan, physiotherapy

ÖZET

Amaç: Bu prospektif, kontrollü, tek-kör çalışmanın amacı diz osteoartritinin (OA) tedavisinde diz içi Hyaluronan veya Hylan G-F 20 enjeksiyonları ile 3 haftalık fizyoterapi (FT) programının etkinliği ve yan etkilerinin karşılaştırılmasıdır.
Metod: Diz OA'sı olan 30 hasta üç gruptan birisine dahil edildi. Gruplara diz içi Hyaluronan veya Hylan G-F 20 enjeksiyonları veya 3 haftalık fizyoterapi (FT) programı verildi. Sonuç değerlendirme ölçekleri
Western Ontario McMaster Universities Osteoarthritis Index (WOMAC), ve yürüyüşün kinematik ve kinetik özellikleri 3 haftalık tedaviden önce ve sonra uygulandı.
Bulgular: WOMAC ağrı alt skoru ve toplam skoru, diz sagital plan toplam hareket açısı, ekstansor ve adduktor momentler ve vertical yer reaksiyon kuvvetleri her üç grupta da düzeldi. Ancak subjektif klinik değerlendirmelerdeki (WOMAC ağrı ve toplam skoru) değişim sadece FT grubunda anlamlıydı.
Sonuç: Eklem içi viskosuplementler diz OA'da ağrının azaltılmasında ve eklem yüklenmesini azaltarak hastalık seyrinin düzeltilmesinde etkin ve güvenli bulundu.

Anahtar kelimeler: Osteoartrit, hyaluronan, hyalan, fizyoterapi

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INTRODUCTION

Osteoarthritis is the most prevalent and costly joint disease in older adults. According to the American College of Rheumatology (ACR) Guidelines for the Medical Management of Osteoarthritis (OA), the goals of management for patients with OA of the knee are to control pain and other symptoms, maintain/improve joint mobility, minimize disability, and educate patients and their families about the disease and its therapy [1]. Guidelines specify two major treatment modalities: non-pharmacological therapy (patient education, physiotherapy, weight loss, ambulatory assisstive devices and orthotics) and pharmacological therapy (simple, topical or opioid analgesics, non-steroidal anti-inflammatory drugs (NSAID), muscle relaxants, antidepressants, intra-articular steroids and hyaluronic acid (HA) injections) [2]. At present, pharmacologic therapy for OA is only palliative and is based on the use of analgesic or anti-inflammatory agents, which are singly or in combination. Also, therapies devised to alter the course of the disease are few (such as weight loss and exercise) and may depend on the underlying etiopathogenetic processess. Therefore, therapies that will be analgesic, anti-inflammatory and ideally, that may alter the natural history of the disease are needed [3].

Intraarticular viscosupplementations have been proposed as effective and safe alternatives for the management of knee OA [4-10]. Hyaluronan (Orthovisc®) and hylan G-F 20 (Synvisc®) are the viscosupplements administered intra-articularly, as a course of three injections, to supplement and restore the shock absorbing, protecting, and lubricating properties of the synovial fluid. They may also decrease production of prostoglandins and cytokiness [4]. The net result is a knee joint that has reduced pain and improved mobility. They requires 3-8 weeks to have its maximum effect. Different studies confirm that HA therapy relieves pain, reduces consumption of non-steroidal anti-inflammatory drugs (NSAIDs) and delays surgery [6]. However, the outcome parameters used in most of those clinical trials are relatively subjective, self administered questionnaires such as visual analogue scales, Lequesne Index, Lysholm scale, SF-36, Western Ontario McMaster Universities Osteoarthritis Index (WOMAC), physician and patient global assessments [6,9,11]. Being a developing country in financial crisis, before prescribing expensive viscosupplementations in the routine of our outpatient clinic, we would like to investigate the objective efficacy of intra-articular hyaluronic acid injections.

The effectiveness, safety and low economical burden of physiotherapy (PT) for OA of the knees are well known in most of the European countries. Relieving pain and muscle spasms, and strengthening quadriceps and hamstring muscles, PT programs increase mobility and decrease disability in patients with knee OA. A comprehensive graded exercise program with isotonic resistive exercises for OA of the knee has been shown to result in increased quadriceps and hamstring strength and increased ability to perform chair rises, walking, and climbing [12].

The purpose of that prospective, single-blind, controlled study was to compare the efficacy and side effects of intraarticular Hyaluronan or Hylan G-F 20 injections and a three weeks of PT program in treatment of knee OA, in terms of pain and stiffness severity, physical functioning and biomechanical parameters of gait.

METHODS

Subjects

Thirty patients, (4 men, 26 women) from an outpatient clinic of Physical Medicine and Rehabilitation, with OA of the knees according to ACR [11] were assigned into one of the three groups, according to their chart numbers. Entry criteria consisted of, willingness to participate in the study, older than 40 years of age, radiographic evidence of Kellgren and Lawrence grade I-III OA of the knee, symptomatic disease for more than 1 year, no intra-articular hyaluronic acid injection for 1 year, no intra-articular corticosteroid injection within 3 months. None of the patients were on oral glucosamine or chondroitin supplements. Adjuvant medication with paracetamol was allowed during the study if necessary. Informed consent was obtained from all of the patients.

Interventions

First and second groups received a single course of three 2ml bilateral intraarticular injections of Hyaluronan or Hylan G-F 20, respectively. Third group was delivered a physiotherapy program, applied by physiotherapists at our outpatient clinic, five days a week for 3 weeks. After superficial heat application with hot packs to relieve pain and muscle spasms, patients received isotonic quadriceps and hamstring strengthening exercises. All patients started the program performing 20 repetitions with no resistance (isotonic) throughout the full existing range of motion. If no pain was performed resistance was added, it began at 0.5kg and progressed by 0.5kg increments. The physical therapist determined the rate of progression based on the patients' tolerance.

Outcome parameters

The outcome parameters, measured by two blinded evaluators, before and one week after the three weeks' intervention were 1) Pain, stiffness and physical functioning subscores of WOMAC [13]. 2) Time-distance, kinematic and kinetic characteristics of gait using a three-dimensional computerized gait analysis system.

Western Ontario McMaster Universities Osteoarthritis Index is a tri-dimensional, disease-specific, self-administered, health status measure. It probes clinically important, patient-relevant symptoms in the areas of pain, stiffness and physical function in patients with the hip and/or knee. The index consists of 24 questions (5 pain, 2 stiffness, 17 physical function) and can be completed in less than 5 minutes. WOMAC is valid, reliable, and sufficiently sensitive to detect clinically-important changes in health status following a variety of interventions [14].

Computerized gait analysis has been used to quantify objectively the changes on biomechanics of walking for patients with knee OA [15-20]. Sagittal plane knee joint rotation angles, peak extensor and adduction moments and peak scaled vertical forces are the most recommended variables for the outcome studies of knee OA [16-18,20]. Fifteen passively reflective markers were placed on standard and specific anatomical landmarks: sacrum, bilateral anterior superior iliac spine, middle thigh, lateral knee (directly lateral to axis of rotation), middle shank (the middle point between the knee marker and the lateral malleolous), lateral malleolous, heel and forefoot between the second and third metatarsal head (21). After the subjects had been instrumented with retro-reflective markers, they were instructed to walk at a self-selected speed over a 10-meter walkway during which data capture was completed. Best data of three trials used in analysis. The trial, in which all the markers were clearly and automatically identified by the system, was determined as best data. Three dimensional gait data were collected with the Vicon 370 systema and two Bertec forceplates. Concomitant vidotape recordings of the subjects' gait were also performed. Five cameras recorded (at 60Hz) the three-dimensional spatial location of each marker as the subject walks. Time-distance (cadence, walking velocity, stride time, stride length), kinematic (joint rotation angle of knee in sagittal plane) and kinetic (scaled vertical forces, extensor and adductor moments of knee) variables were processed using Vicon Clinical Manager software. Calibration of the motion analysis system was performed daily. Anthropometric data including height, weight, leg length and joint width of the knee and ankle were collected.

DATA ANALYSIS

Data analysis was done using SPSS for Windows version 9.0b. Baseline characteristics of the groups were compared using Kruskal-Wallis H test and chi-square. WOMAC subscores (pain, stiffness and physical functioning), time-distance parameters, kinematic and kinetic variables of each group before and after treatment were compared using Wilcoxon's matched pairs signed-rank test.

RESULTS

Demographic data and disease characteristics were presented in Table 1. No statistically significant difference was detected between baseline age, gender, disease duration, radiographic grade, and pain, stiffness, and physical functioning WOMAC subscores of the

Tablo-I

Demographic data and disease characteristics of the patients

		Hyaluronan	Hyalan G-F 20	Physiotherapy	P value
Age (years)		62.4 ± 10.5	63.2 ± 4.4	57.4 ± 10.0	0.393*
Gender Male/Female		1/9	2/8	1/9	0.749**
Disease duration (years)		7.6 ± 7.4	12.0 ± 6.2	9.0 ± 7.4	0.234*
Radiographic grade	I	4	6	-	
	II	5	2	7	0.054**
	III	1	2	3	
Pain		12.1 ± 4.2	9.2 ± 2.7	9.7 ± 2.3	0.118*
Stiffness		4.4 ± 2.4	3.2 ± 1.6	4.4 ± 1.6	0.187*
Physical functioning		41.0 ± 9.4	29.7 ± 13.8	36.1 ± 7.6	0.154*
WOMAC total score		57.5 ± 14.6	42.1 ± 15.2	50.2 ± 10.5	0.112*

* Kruskal-Wallis Test
** Chi-square

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Comparison of average scores of clinical parameters before and after treatment

Agent/variable	Before treatment	After treatment	Z value	P value
Hyaluronan (n=10)				
Pain	12.1 ± 4.2	9.8 ± 4.5	-1.4	0.171
Stiffness	4.4 ± 2.4	4.5 ± 2.4	.00	1.000
Physical functioning	41.0 ± 9.4	42.6 ± 7.7	-1.0	0.322
WOMAC total	57.5 ± 14.6	56.1 ± 11.0	-1.4	0.173
Hylan G-F 20 (n=10)				
Pain	9.2 ± 2.7	7.8 ± 3.1	-0.77	0.441
Stiffness	3.2 ± 1.6	3.4 ± 1.3	-1.0	0.323
Physical functioning	29.7 ± 13.8	30.7 ± 12.4	-1.0	0.325
WOMAC total	42.1 ± 15.2	41.9 ± 13.5	-0.12	0.910
Physiotherapy (n=10)				
Pain	9.7 ± 2.3	4.1 ± 2.0	-2.8	0.005
Stiffness	4.4 ± 1.6	4.4 ± 1.5	.00	1.000
Physical functioning	36.1 ± 7.6	36.1 ± 7.5	.00	1.000
WOMAC total	50.2 ± 10.5	44.6 ± 9.5	-2.8	0.005

Likert scale for pain, stiffness and physical functioning: 1=none and 5=worst possible

groups. Comparison of average scores of clinical and biomechanical gait parameters, before and after treatment, was shown in Table 2 and 3. Pain subscore and total score of WOMAC, sagittal plane excursions of the knee, extensor and adductor moments and scaled vertical forces improved in all of the groups. However, the statistically significant difference was observed in only subjective clinical assessments (pain subscore and total score of WOMAC) of PT group. There were no withdrawals for adverse effects for three of the groups.

DISCUSSION

This study revealed the beneficial impact of viscosupplementations on the gait patterns of patients with knee OA. The gait in knee OA is characterized by slow speed, limited peak knee flexion and extension degrees, decreased weight bearing and increased adductor and extensor moments at the knee [15,17,22]. In order to document the effectiveness of different interventions on knee joint loading and gait deviations because of knee pain and stiffness, we used knee excursion in sagittal plane, extensor and adductor moments of the knee and scaled vertical forces. Carlson et al suggested to use the total excursion (peak flexion - peak extension joint rotation angles in degrees) of pelvis, hip, knee and ankle in the data analysis rather than actual maximum and minimum values to minimize errors inherent in minor changes in marker placement between sessions [23]. Although the difference was not statistically significant, an increase in knee excursions and scaled vertical forces was observed after treatment for three of the groups, which show decreased pain and stiffness, and increased

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Comparison of average scores of biomechanical gait parameters before and after treatment

Agent/variable	Before treatment	After treatment	Z value	P value
Hyaluronan (n=10)				
Knee excursion (degrees)	40.6 ± 6.5	47.0 ± 8.1	-1.15	0.251
Knee extensor moment (Nw/kg)	0.38 ± 0.15	0.22 ± 0.04	-1.5	0.144
Knee adductor moment (Nw/kg)	0.44 ± 0.16	0.43 ± 0.12	-0.22	0.789
Scaled vertical force Peak 1	87.7 ± 4.1	90.7 ± 2.3	-1.8	0.071
Hylan G-F 20 (n=10)				
Knee excursion (degrees)	41.2 ± 8.1	43.3 ± 8.5	-.21	0.833
Knee extensor moment (Nw/kg)	0.26 ± 0.20	0.14 ± 0.07	-1.8	0.066
Knee adductor moment (Nw/kg)	0.45 ± 0.11	0.44 ± 0.12	-0.23	0.689
Scaled vertical force Peak 1	85.8 ± 4.5	88.4 ± 5.4	-0.2	0.027
Physiotherapy (n=10)				
Knee excursion (degrees)	40.8 ± 7.1	41.8 ± 5.6	-0.24	0.812
Knee extensor moment (Nw/kg)	0.18 ± 0.16	0.20 ± 0.11	-0.28	0.783
Knee adductor moment (Nw/kg)	0.44 ± 0.12	0.43 ± 0.12	-0.25	0.785
Scaled vertical force Peak 1	89.0 ± 4.7	89.5 ± 4.6	0.00	1.000

weight bearing, respectively. Higher adductor and extensor moments are the major determinants of the higher loading at the knees with OA [18-19]. The patients with knee OA try to reduce internal knee extensor moments to reduce the knee joint loading. In this study, we observed that intra-articular Hyaluronan and Hyalan G-F 20 injections decreased the adductor and extensor moments of knee.

Physiotherapy was selected as a control intervention instead of placebo because, 1) it is the most prescribed intervention in physical medicine and rehabilitation departments in Europe, 2) ethically better than placebo. In terms of subjective clinical parameters such as pain severity, PT was better than viscosupplementations. Clinically but not statistically significant improvements were found in stiffness and physical functioning for the viscosupplementation groups. PT did not affect the severity of stiffness and physical functioning or gait parameters. The use of superficial heat for pain relief in patients with arthritis is well known. Application of both superficial and deep heat produce sedation and analgesia by acting on free nerve endings of both peripheral nerves and gamma fibres of muscle spindles [24]. This may explain the decrease in pain severity for PT group. The benefits of PT on knee OA (for at least 6 weeks) has been shown in previous studies [12,25-28]. This study shows that 3 weeks time duration is not enough to examine objective strengthening of the quadriceps and hamstring muscles, which are mainly responsible for the biomechanical characteristics of the OA gait.

Viscosupplementation is a process whereby exogeneous hyaluronic acid provides a replacement for the lubrication that has been lost because of the disease. It has also been shown that intra-articular hyaluronic acid stimulate the synovial cells to synthesize endogeneous hyaluronic acid; decrease the entry of polymorphonuclear cells into the synovial fluid, reflecting a decrease in the severity of inflammation; and intercalate itself into the folds of the soft tissues within the joint, insulating pain fibers in the synovium and thereby decreasing nociceptive activity; play role in the aggregation of cartilage proteoglycans and increase proteoglycan synthesis [3]. It has been suggested that patients with knee OA who have failed conventional therapy, including an education program aimed at decreasing potential exacerbating factors (such as obesity); physical therapy; and analgesics, with or without NSAIDs, might be candidates for intra-articular hyaluronic acid therapy [3]. Because the treatment is expensive the use of this modality must be carefully considered.

Hyaluronan (hyaluronic acid, HA or hyaluronate) is a glycosaminoglycan with a repeating disaccharide unit of N-acetylglucosamine and glucuronic acid. Hylan is the generic name for crosslinked hyaluronan chains when the crosslink does not affect the two specific groups of the molecule, namely the carboxylic and N-acetyl groups. Superiority of high molecular weight sodium hyaluronate (HA) and lower molecular weight HA preparations to each other in the treatment of joint disease has been discussed by various authors [5,29]. High molecular-weight products theoretically are superior to lower molecular-weight products, in part because of their greater elastic and viscous properties [8,29]. Wobig et al supported this theory with their clinical comparative study using a 3-injection regimen [7]. In this study we could not demonstrate any significant difference between Hyaluronan and Hylan G-F 20 in terms of clinical or biomechenical parameters.

There were no withdrawals for adverse effects for three of the groups. Intraarticular hyalan was associated with significant local inflammatory reactions of which mechanism and long term sequelae is unclear [30]. However, we did not observe such a side effect.

The low statistical power of clinical improvements in this study can be explained by the low number of patients in the groups. Because of financial limitations the number of the patients could not have been increased. Moreover, viscosupplementations require 3-8 weeks to have its maximum effect. If we had made the second gait analysis in 8 weeks, instead of 4 weeks time after the first injection, we might have found more significant improvement in biomechanical gait characteristics. Schnitzer et al, investigated the effects of piroxicam on gait characteristics of patients with OA and suggested the agents capable of relieving pain while reducing loads at the knee would be desirable [15]. In this study, intra-articular viscosupplements are found to be effective and safe not only in relieving pain but in altering the natural history of the knee OA, by decreasing joint loading, as well.

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SUPPLIERS

a VICON, Oxford Metrics Limited, 14 Minns Estate, West Way, Oxford, OX2 OJB

b Statistical Package for the Social Sciences (SPSS) for Windows, Version 9.0; SPSS Inc., 444 N. Michigan Avenue, Chicago, IL.