Diz Osteoartritli Hastalarda Eklem İçi Viskosuplement Enjeksiyonunun İzokinetik Kas Gücü Üzerine Etkileri

Effects of Intra-Articular Viscosuplement Injection on The Isokinetic Muscle Test Values of Patients with Knee Osteoarthritis

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ÖZ

GİRİŞ ve AMAÇ: *Diz osteoartriti hayat kalitesini önemli derecede etkileyen yaygın bir hastalıktır. Rehabilitasyon protokolleri diz eklemi üzerindeki yükü azaltmak amacıyla kas güçlendirme egzersizleri içermelidir. bu çalışmada intraartiküler olarak uygulanan hyaluronik asit, kondroitin sülfat ve glukozamin içeren viskosuplementasyon enjeksiyonlarının diz kaslarının izokinetik kuvvetleri üzerindeki etkilerini araştırdık.*

YÖNTEM ve GEREÇLER: *Çift-kör ve randomize yapılan bu çalışmada demografik veriler ve izokinetik kas gücü ölçümü Biodex (System 3) ile yapıldı. Enjeksiyondan önce ve 3 ay sonra kuadriseps kasının 60°/sn ve 240°/sn açısal hızlarında izokinetik kas gücü testi uygulandı. SPSS for Windows programı ile istatistiksel analizler yapıldı.*

BULGULAR: *60°/sn ve 240°/sn açısal hızlarında yapılan izokinetik testlerde istatistiksel olarak anlamlı fark bulundu. Diz osteoartriti tedavisinde hyaluronik asit, kondroitin sülfat ve glukozamin içeren viskosuplementasyon enjeksiyonlarının kuadriseps ve hamstring kaslarında total ve fonksiyonel izokinetik kas gücünü arttırdığı saptandı.*

TARTIŞMA ve SONUÇ: *Hyaluronik asit, kondroitin sülfat ve glukozamin içeren viskosuplementasyon enjeksiyonları kuadriseps ve hamstring kaslarında 60°/sn ve 240°/sn açısal hızlarında izokinetik kas gücünün artmasını sağlamaktadır. Tedavi protokollerinde daha fazla yer alabileceği düşünülebilir.*

Anahtar Kelimeler: *izokinetik kuvvet, kas gücü, gonartroz, viskosuplementasyon, hyaluronik asit, gukozamin*

ABSTRACT

INTRODUCTION: *Knee osteoarthritis is a common disease that seriously decrease the quality of life. Rehabilitation protocols include muscle strenthening exercises to decrease loading of the knee joint. We aimed to identify and analyse the outcome of the isokinetic muscle test of the knee joint after injection of intra-articular viscosupplement containing hyaluronic acid, chondroitin sulphate and glucosamine.*

METHODS: *This study is designed as a prospective and double-blind study. Demographic data was recorded, and the isokinetic test was measured with Biodex (System 3) for the measurement of quadriceps muscle strength before and 3 months after the injection. The device is set to measure at angular velocities of 60°/s and 240°/s. SPSS for Windows was used for statistical analyses.*

RESULTS: *There were statistically significant results with isokinetic measurements were evaluated at angular velocities of 60°/s and 240°/s. In the treatment of knee osteoarthritis, the hyaluronic acid, chondroitin sulphate and glucosamine injection were found to increase total and functional strength in isokinetic quadriceps and hamstring muscle strength.*

DISCUSSION AND CONCLUSION: *Hyaluronic acid, chondroitin sulphate and glucosamine injection were found to increase total and functional strength at angular velocities of 60°/s and 240°/s in isokinetic quadriceps and hamstring muscle strength.*

Keywords: *isokinetic strength, muscle strength, gonarthrosis, viscosupplementation, hyaluronic acid, glucosamine*

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INTRODUCTION

Knee osteoarthritis (OA) is a common disease which causes pain and disability with increasing age (1, 2). In developed countries, it is considered to be one of the ten diseases which most decreases functionality (3). With a prevalence between 22% - 39% in the general population, 7% of which are patients who are over 65 years old. The examination of worldwide statistics show that knee OA is present in 18% of women and 9.6% of men. Knee OA is characterized by pain, functional loss and progressive immobility where motions are require physical activity of the lower extremity. The disease causes 80% of restriction on motion and 25% of restrictions on the activities of daily life. Additionally, along with the loss of proprioception, it can result in defects of static and dynamic postural stability and the loss of balance (4,5). The disease causes reduced muscle strength, defects in muscle functionality and reduced workout capacity. According to the radiographic classification of Kellgren and Lawrence, quadriceps muscle weakness is frequently seen without atrophy and pain in early phases of knee OA of which degree is 0 or 1. If the symptoms are accompanied by knee pain, there will be an increase in the muscle weakness and cause dysfunction and progression of disease. An increase of strength in the muscles of quadriceps and hamstrings play a positive role for stability and mobility of joints and pain tolerance (3,6).

In the advanced phases of the disease, along with the pain, a decrease of, particularly, extensor dynamic muscle strength is observed (7). Isokinetic tests are the most objective measurement tools for evaluating the dynamic muscle strength. With isokinetic tests, isometric, eccentric and angular velocity of contractions of concentric type with the velocities of 60°/s, 90°/s and 120°/s are evaluated. Reduced angular velocity means that mechanical overload is much greater (8). In isokinetic tests, concentrically evaluated muscle strength gives more meaningful results in terms of the patients' performances. Making the concentric contraction tests slower is in an important factor for indicating the performance of muscle and the pain more accurately. In the isokinetic tests which are made more quickly, angular torque is specified accurately (7).

Among the current treatments of knee OA are the use of analgesic and non-steroidal anti-inflammatory medicines, surgical interventions (arthroscopy, total knee replacement), intra-articular injections, physiotherapy, weight control, exercise, the use of orthotic support and the training of the patient. Intra-articular injection is one of the effective non-operative treatments for reducing pain and increasing functionality (9). Among the most reliable substances for intra-articular injections are hyaluronic acid, chondroitin sulphate and glucosamine. Hyaluronic acid (HA) is an important component of synovial fluid and articular cartilage and is responsible for elastoviscocity of synovial fluid which allows the effective movement of knee joints. The amount of HA in synovial fluid (concentration and molecular weight) decreases in the osteoarthritic knee which causes a restriction of normal joint biomechanics and potential physical damage in the knee. The injections of HA replace the HA lost and stimulate the production of endogenic HA in the osteoarthritic joint. Chondroitin sulphate (CS) is tied to high molecular weight monomers in the articular system. Proteoglycane aggregate shows viscoelastic and hydration features and the ability to interact with the electric charges of surrounding tissues, and it provides a protection of cartilaginous tissue. In addition, chondroitin sulphate is the inhibitor of extracellular protease which plays role in metabolism of connective tissues and as in vitro, it stimulates the production of chondrocyte and proteoglycane; additionally, it inhibits the production of cartilage cytokine and induces the apoptosis of joint chondrocyte (5). Glucosamine (GA), provides chondroprotective, analgesic and shock absorbent effects oncartilage and synovium of the joint. Altogether; HA, chondroitin sulphate and glucosamine are cartilaginous matrix initiators containing cytokine modulators. These molecules are thought to be effective on the structural impairment of the joint by limiting the progression of pathological changes in osteoarthritis and are classified as modifying agents. The use of viscosupplementation (HA, CS and GA) in the treatment of OA is preferred because of the positive effects of pain relief and functional improvement of the joint. In addition to HA with potentially chondroprotective effects in the joint, CS and GA

play an important role in maintaining joint homeostasis (10,11).

In the literature, studies with intra-articular HA injection in the treatment of knee OA are frequently seen, but the number of studies about the co-injection of HA, CS and GA are scarce. In addition, proprioception increases that is related with the decreasing of the pain as a result of viscosuplement injection. By this way the neuromuscular control increases. This mechanism probably results increasingin isokinetic muscle strength. Therefore, we aimed to investigate the effects of HA, CS and GA injection on isokinetic quadriceps and hamstring muscle strengths in our study.

MATERIAL AND METHODS

This study is a prospective and double-blind study performed in Private Ortospor Polyclinic, Istanbul Yeni Yuzyil University Faculty of Health Sciences, Physiotherapy and Rehabilitation Department and Bahçeşehir University Medical Park Fatih Hospital. Before the study commenced, approval was obtained from the Istanbul Yeni Yüzyıl University Clinical Research Ethics Committee in 12.05.2017 and with approval number 028, including the required verbal and written consent of patients. Thirteen patients with stage 3 and stage 4 knee OA, according to Kellgren-Lawrence classification, were included in the study. All patients who participated in the study were female.

Participants

The inclusion criteria for the study are being over 40 years of age, being diagnosed with Stage 3 and 4 knee OA, according to the Kellgren-Lawrence classification. The number of participants was identified by power analyses. Exclusion criteria include any lower extremity deformity (knee flexion contracture, knee hyperextension, varus and valgus deformities), septic arthritis, rheumatoid arthritis, major dysplasia, congenital anomalies, acromegaly, primary osteochondromatosis, Ehler-Danlos syndrome, neuropathic arthropathy, hyperparathyroidism, hypothyroidism, diabetes mellitus, active synovitis, severe knee traumas, previous surgery and in the last year; knee arthroscopy, injections and fracture history and pregnancy.

Intervention

An injection, containing hyaluronic acid, chondroitin sulphate and glucosamine, was applied on one occasion and took place with the knee joint in the supine position and the knee in extension. The injection materail was commercial kit (Genvisc Plus) which is menufactured by Phibio GmbH Ltd. Com. and the cost of the kit was paid by researchers.

Assessment

Age, height, weight, body mass index, body fat mass, body water percentage, metabolic age, basal metabolism were recorded and isokinetic test was measured with Biodex (System 3) for the measurement of quadriceps muscle strength before the injection and then 3 months later. Measurements were performed at angular velocities of 60°/s and 240°/s. Biodex (System 3) and isokinetic systems were used to evaluate knee flexion angles and the muscle strengths applied at these angular velocities. The patients were asked to wear casual clothes for the test. The testing environment is maintained as a quiet environment, in normal daylight, with below 50% humidity and at an appropriate temperature (25°C). Before the test, patients undertook warm up exercises for 50 minutes at 50 RPM on an exercise bike, followed by a short stretching program undertaken immediately after the warm up. The assesment process commences with the patient being placed in an upright position with the knee stabilized in 90° flexion. The patient was asked to perform full knee flexion extensions passively. The device is set to measure at angular velocities of 60°/s and 240°/s. After a full explanation about the test, the patient had 2 trial attempts, then made 4 repetitions at 60°/s, 240°/s angular velocities 20 times the extension and flexion, and peak torque, peak torque /body weight and total work parameters in isokinetic measurements were evaluated before and after the injection that contains the velocity of the device, torque body weight, total work (J), acceleration time (ms), deceleration time (ms). Knee extension and flexion were recorded and the best measurement was made.

Statistical Analysis

Kolmogorow Smirnov tests were performed to determine the suitability of the data for normal distribution.

Wilcoxon test was used to compare measurement parameters before and after treatment. P value < 0.05 was accepted as meaningful for all statistical levels.

RESULTS

13 female patients with knee OA aged between 42-63 years participated in the study.

Variables	Mean ± SD (min-max)
Age (years)	53.61 ± 5.47 (42-63)
BMI	34.35 ± 5.22 (26.20 -43.30)
Body fat mass (kg)	36.85 ± 10.82 (21.50-54.70)
Body water%	41.30 ± 3.17 (36.80-45.70)
Age of	60.31 ± 9.47 (40.80-73)
Metabolism	
Basal metabolism	1523.83 ± 158.08 (1242-1764)

Demographic characteristics of patients are shown in Table 1.

Table 1. Demographic characteristics of patients
BMI: Body mass index

When the isokinetic measurements of the patients were evaluated before and after the injection, we found a statistically significant improvement in left knee peak torque and peak torque / body weight at 60°/s angular velocity (p = 0.023, 0.007) (Table 2).

Table 2. Comparison of isokinetic measurements at 60°/s angular velocity during knee flexion before and after injection

	60°/s	60°/s	60°/s	60°/s
Action	**Preinjection**	**Postinjection**	**Difference**	**p**
PT-R (Nm)	27.10±13.41	28.65±10.14	1.54±4.99	0.221
PT-L (Nm)	23.46±10.85	28.62±9.02	5.16±6.89	0.023*
PTQ/BW-R (Nm)	30.14±14.87	32.57±11.19	2.43±6.52	0.235
PTQ/BW-L (Nm)	26.93±13.36	45.30±41.09	18.36±42.43	0.007*
TW-R (J)	107.59±77.59	120.93±64.10	13.34±49.20	0.345
TW-L (J)	100.10±69.70	123.60±58.17	23.49±42.29	0.086
ACT-R (msn)	106.15±30.14	101.53±18.18	-4.61±29.04	0.429
ACT-L (msn)	102.30±38.76	127.69±72.24	25.38±73.21	0.244
DCT-R (msn)	130.76±42.90	139.23±40.30	8.46±54.90	0.582
DCT-L (msn)	124.61±15.06	156.92±70.28	32.30±70.61	0.098

p<0.05, Wilcoxon Test. PT:Peak tork, BW: Body weight, TW:Total work, ACT:Acceleration time, DCT: Deceleration time, R:Right, L:Left.

In the pre-treatment and post-treatment comparisons, it was found that there was a statistically significant improvement in the total labor force values in the right knee with peak torque, peak torque / body weight and total workforce at 240°/h angular velocity (p = 0.013, 0.013, 0.046, 0.003) (Table 3).

Table 3. Comparison of isokinetic measurements at 240°/s angular velocity during knee flexion before and after injection

	240°/s	240°/s	240°/s	240°/s
Action	**Preinjection**	**Postinjection**	**Difference**	**p**
PT-R (Nm)	14.03±9.56	16.79±10.04	2.75±6.54	0.173
PT-L (Nm)	10.60±7.96	19.30±10.00	8.70±9.26	0.013*
PTQ/BW-R (Nm)	15.13±9.43	18.20±10.39	3.06±7.94	0.221
PTQ/BW-L (Nm)	11.81±8.60	21.77±11.25	9.96±10.20	0.013*
TW-R (J)	142.50±166.68	246.51±177.57	104.01±143.08	0.046*
TW-L (J)	97.87±148.54	245.06±169.21	147.19±142.08	0.003*
ACT-R (msn)	163.84±39.90	145.38±49.26	-18.46±48.10	0.097
ACT-L (msn)	160.00±37.85	149.23±29.28	-10.76±21.77	0.079
DCT-R (msn)	133.07±23.93	123.84±18.50	-9.23±24.98	0.187
DCT-L (msn)	130.00±23.80	148.46±62.82	18.46±45.24	0.103

p<0.05, Wilcoxon Test. PT:Peak tork, BW: Body weight, TW:Total work, ACT:Acceleration time, DCT: Deceleration time, R:Right, L:Left.

	60°/s			
Action	**Preinjection**	**Postinjection**	**Difference**	
PT-R (Nm)	68.40±31.21	71.28±21.95	2.87±18.95	0.600
PT-L (Nm)	56.28±14.01	59.73±19.86	3.45±16.09	0.463
PTQ/BW-R (Nm)	75.31±30.00	80.99±23.06	5.67±18.96	0.311
PTQ/BW-L (Nm)	65.48±20.94	69.79±24.98	4.30±15.75	0.382
TW-R (J)	316.24±149.99	352.62±113.06	36.37±87.72	0.133
TW-L (J)	265.60±86.23	290.40±104.92	24.79±81.08	0.345
ACT-R (msn)	114.61±39.71	103.84±34.77	-10.76±47.16	0.502
ACT-L (msn)	129.23±26.62	130.76±18.00	1.53±31.05	0.472
DCT-R (msn)	139.23±28.12	151.53±77.11	12.30±85.55	0.370
DCT-L (msn)	103.07±33.01	98.46±29.67	-4.61±34.30	0.531

p<0.05, Wilcoxon Test. PT:Peak tork, BW: Body weight, TW:Total work, ACT:Acceleration time, DCT: Deceleration time, R:Right, L:Left.

Table 4. Comparison of isokinetic measurements at 60°/s angular velocity during knee extension before and after injection

When the isokinetic measurements during knee extension were examined, there was no significant difference in the angular velocity between 60°/s before and after the injection (p> 0.05) (Table 4).

When the isokinetic measurements at knee extension at 240°/s angular velocity before and after injection were compared, it was found that there was a statistically significant increase in right knee total workforce (p = 0.028) (Table 5).

	240°/s	240°/s	240°/s	240°/s
Action	**Preinjection**	**Postinjection**	**Difference**	
PT-R (Nm)	42.94±12.01	43.75±12.13	0.80±6.03	0.814
PT-L (Nm)	36.10±6.56	38.53±6.82	2.43±7.22	0.196
PTQ/BW-R (Nm)	48.86±12.48	49.76±12.48	0.90±6.50	0.807
PTQ/BW-L (Nm)	41.59±8.13	44.74±9.94	3.15±7.90	0.152
TW-R (J)	920.80±299.72	1061.77±321.21	140.97±177.35	0.028*
TW-L (J)	817.28±232.55	913.61±162.07	96.33±213.82	0.152
ACT-R (msn)	117.69±36.77	114.61±51.73	-3.07±50.39	0.474
ACT-L (msn)	122.30±33.70	115.38±33.06	-6.92±30.38	0.331
DCT-R (msn)	126.15±40.52	130.00±12.90	3.84±35.48	1.000
DCT-L (msn)	135.38±23.66	126.92±16.01	-8.46±28.23	0.310

***p<0.05, Wilcoxon Test. PT:Peak tork, BW: Body weight, TW:Total work, ACT:Acceleration time, DCT: Deceleration time, R:Right, L:Left.**

Table 5. Comparison of isokinetic measurements at 240°/s angular velocity during knee extension before and after injection (Page 5)

DISCUSSION

Knee OA is a serious disease which is common and causes muscle weakness and loss of functionality over time (12, 13). In most of the studies towards its remedy, the effect of intraarticular HA injection on pain levels in patients with knee osteoarthritis was investigated, however, in our study, the effect of HA, CS and GA injection on concentric muscle strength was investigated. In previous studies investigations into the effect of injection on muscle strength, HA has often been used alone, so an equivalent or similar study to our study has not been located in our literature searching. As a result of our study, it was determined that the knee flexion and extension strength increase in the isokinetic muscle strength measurement of patients with knee OA injected by HA, CS and GA.

The knee joint contains 3 different structural and functional afferent fibers. These fibers receive signals from 4 different receptors in the surrounding tissues (Pacinian, Ruffini's and Golgi-Mazzoni corpuscles; muscle spindles). In degenerative changes in the joint, the release of various mediators results in secondary stimulation of the nociceptors. Interaction between mechanoreceptors and these nociceptors can lead to changes in the coordination and muscle functions of the affected limb.

Injection of intra-articular viscosuplementation can lead to an increase in total work and peak torque secondary to the improvement of neuromuscular function in knees (14). Muscle strength in the knee OA may be decreased due to secondary muscle atrophy as a result of arthrogenic inhibition, joint pain and swelling. With a decrease in pain and inflammation, muscle strength can be increased (15). In our study, we determined that concentric muscle strength could be increased by the effects of a viscosupplementation injection.

With isokinetic evaluation, the clinician is able to observe muscle performance in a safe and objective manner. Evaluation of the muscle performance is undertaken by performing tests at different velocities and recording and monitoring performance with various objective data. The balance between muscle groups in the tested area can be evaluated (16). Isokinetic tests are usually the preferred methods to determine muscle strength, loss of balance between muscles and effectiveness of treatment. In isokinetic evaluation, total work (J) and peak torque (Nm) are reliable parameters for evaluation of joint and muscle function (17). Therefore, in our study, we evaluated peak torque, peak torque / body weight and total work parameters in isokinetic measurements before and after the injection.

The viscoelastic properties of the degenerative joint are greatly reduced compared to normal conditions. In an in vitro study, Rainer reported an 8-10-fold increase in pathological joint fluid viscosity following high-molecular HA administration, suggesting an improved elasticity of the synovial fluid and joint biomechanics (18, 19). Brandt et al. found a significant correlation between total work and muscle torque increase in muscles and radiographic changes in patients with osteoarthritis (20). In the study by Schneider et al.,

it was determined that isokinetic evaluations of 18 knee OA patients after the injection of HA improved total labor force during both flexion and extension, particularly in knee extension (15).

According to the studies, when HA is injected 3 times intra-articularly, maximal isokinetic muscle strength increases in the short term (14, 18). It is believed that this effect, caused by the injection, affects the muscle performance and decreases the friction with increased viscosity. According to a study, this force increase was seen only at 60 and 240°/s angular velocities and at the right lower extremity. It was thought that the greater increase in the muscle strength of the right extremity is often the dominant side and more sensitive to the treatment applied (22). In our study, no significant difference was found between right and left lower extremity measurements. In order to obtain more meaningful results, isokinetic measurements were evaluated at angular velocities of 60 and 240°/s. At the same time, it is observed that the injection does not change the agonist / antagonist muscle strength ratio but this result does not have any negative effect on flexor-extensor muscle balance.

When we review the literature, injection and increased muscle strength correlations were show similar results to our study. Tang et al. showed that muscle strength increases upto 6 months after an HA injection in patients with knee OA (15), and another study of the same study group reported that concurrent muscle power and eccentric muscle strength increased by 27.7%, a 5 times increase after the injection of HA (13). In a study by Miltner et al., they applied a total of 5 HA injections to 43 knee OA patients once a week, and stated that while an HA injection resulted in a total increase in total work and peak torque during flexion and extension compared to the control group, but an increase to the maximum peak torque at, low angular velocities(60°/s) and the maximum peak torque at high angular velocities (180°/s) during flexion and extension after injection (23) was also found. Demirhan et al., performed HA injections on 63 patients with bilateral grade 2 and 3 knees OA, compared the results of isokinetic test results with 3 HA injections with the control group. The result was a significant improvement in the peak torque at 60°/s angular velocity, while, at 180°/s and 240°/s. They did not determine any significant difference in angular peak torque (22). In our study, it was found that increase a 22% in peak torque of the left lower limb in the flexion direction at 60°/s angular velocity and a 68% in peak torque / body weight ratio ; also, increase a 82% in peak flexion direction in peak torque of the left lower limb in peak flexion direction at 240°/s angular velocity, and a 84% in peak torque / body weight ratio after injection. Besides, it was shown that increase a 250% in total workface of every 2 lower limbs flexion at 240°/s angular velocity, in extension there is only 16% increase in the total work force in the flexion direction.

There are some limitations of our study. The first of these limitations is the lack of long-term follow-up on how long the muscle strength increase continues, the second is not being able to make a comparison with a control group, and finally the study had a small sample size.

In conclusion, as well as confirming that the injection of intra-articular viscosupplementation is a safe and effective treatment in patients with knee OA; when treating knee OA, an HA, CS and GA injection was found to increase total and functional strength at angular velocities of 60°/h and 240°/h in isokinetic quadriceps and hamstring muscle strengths.

Authors' contributions: The design of the study was conceived by IHU, MTH, TD and MU. Data collection, management and analysis were performed by IHU, MTH, TD and MU. All authors participated in the interpretation of the results and manuscript writing. All have read and approved the final version of the manuscript for publication.

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