



Kinetics features changes before and after intra-articular hyaluronic acid injections in patients with knee osteoarthritis

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KEYWORDS

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ABSTRACT

Objectives: To examine the kinetic features in patients with knee osteoarthritis (OA) after intra-articular hyaluronic acid (IAHA) injections in different time periods.

Design: A single group repeated measures study.

Setting: Gait laboratory in a tertiary hospital.

Participants: Twenty-five subjects with bilateral symptomatic knee OA and 15 healthy control subjects.
Intervention: Gait analyses were performed in both control and OA groups before (baseline), and after the completion of IAHA injections (1 week, 3 months, and 6 months).

Main Outcome Measures: Knee pain and functional indices were assessed using a visual analogue scale (VAS) and the Lequesne function Index (LI). Joint kinetic changes were analyzed in the frontal and sagittal planes with 6-camera motion analysis system and two AMTI force plates.

Results: VAS and LI scores were both improved in OA group after IAHA injections ($p < 0.001$). In the frontal plane, increased knee adduction moment ($p < 0.001$) after IAHA treatment was observed and would last up to a period of 6 months. In the sagittal plane, lower knee extension moments at early stance, and larger knee flexion moments at terminal stance were demonstrated after the completion of IAHA injections ($p < 0.05$).

Conclusions: This study revealed that IAHA injections can provide significant pain relief and improvement in activity of daily living function for patients with knee OA. However, the reduction in pain and the increase in knee adduction moment may last up to 6 months. This may cause excessive loading on the knee joints, which may further accelerate the rate of knee degeneration. As a result, longer study time is needed to determine whether the observed kinetic findings in this study are associated with detrimental outcomes on the knee joints.

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1. Introduction

Osteoarthritis (OA) is a very common progressive degenerative disease of the knee. Complications of knee OA include pain and muscle weakness of the knee, proprioceptive deficits, altered gait mechanics, deterioration in lower limbs activities of daily living and decreased quality of life. During ambulation, up to 70% of knee joint load passes through the medial compartment due to the effect of ground reaction force passing medially [1]. As a result, changes in knee OA occur most predominantly in the medial compartment of knee joint [2].

In gait studies, the knee adduction moment assessed during walking plays an important role in patients with medial compartment knee OA. It has been shown that increased adduction moment is the major cause of high joint loading at

the knees in patients with OA [3,4]. Other gait changes at the knee joint associate with knee OA include decrease in walking speed, cadence, and lower knee flexion moment during the stance phase [1,4]. These changes could alter knee joint loading and should be analyzed as part of outcome measurements in patients with knee OA [5].

Hyaluronic acid (HA), also known as hyaluronan, is a major component of synovial fluid (SF). It plays an important role in regulating the biochemical balance and matrix structure of the intra-articular (IA) environment [6]. The US Food and Drug Administration (FDA) approved its use in 1997, and a series of three to five injections are delivered once per week [7]. Both high and lower molecular weight (MW) hyaluronic acid are efficacious in treating patients with knee OA [8]. The intra-articular hyaluronic acid (IAHA) treatment of knee OA has been investigated in randomized controlled clinical trials [9,10]. Several studies have compared the efficacy of HA to that of cortisone IA injections [11], non-steroid anti-inflammatory drugs [12], and placebo injections (saline injections or arthrocentesis) [13,14]. Results from these studies have indicated that IAHA

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injections may provide patients with longer beneficial effects as compared with these treatment options.

In previous studies, primary outcome measures demonstrating the efficacy of IAHA injections are typically average self-reported scores of knee symptoms and functions [11–15]. The long-term effect of IAHA injection on kinetic variables on the knee joints of the lower extremity is seldom thoroughly examined [1,16,17]. As a result, the purpose of this study was to investigate the long-term effects of IAHA treatment by evaluating the frontal and sagittal plane joint kinetics during walking in patients with medial knee OA. We hypothesize that the joint kinetics in both the frontal and sagittal planes are significantly changed after IAHA injections in knee OA patients, and the effect would last up to six months.

2. Methods

2.1. Subjects

Subjects were divided into 2 groups: the control group, and patients with knee OA. The OA group consisted of 25 patients with bilateral medial knee OA (9 male and 16 female subjects, mean age: 65.0±8.3 years; height: 156.5±7.3 cm; weight: 62.6±10.4 kg), with grade I or II based on Kellgren-Lawrence (K/L) grading system [18]. Fifteen age-, height-, and weight-matched healthy subjects were recruited as the control group (5 male and 10 female patients, mean age: 64.7±7.3 years; height: 158.3±7.1 cm; weight: 61.5±6.9 kg).

The inclusion criteria for the group with knee OA included bilateral knee pain for at least 6 months and showing no improvements after conservative non-steroid anti-inflammatory agents and physiotherapy treatments. Subjects with histories of other arthritis (non osteoarthritis), injuries to the lower limb joints, musculoskeletal diseases or a history of prolonged knee pain were excluded. Subjects in the control group had no history of lower limb arthritis, no knee pain for at least one year, and no neurological or vascular diseases involving the lower extremities. This study was approved by the Medical Ethics and the Human Clinical Trial Committee of the Institute. Informed consents were obtained from all participants.

2.2. Procedure

In the knee OA group, IAHA injections were performed to bilateral knee joints. An amount of 2.5 mL of hyaluronate (Artz, 1% HA solution; molecular-weight (MW) of 860 kilodaltons (kd); Seikagaku Corporation, Tokyo, Japan) was injected into each knee joint once a week, for a total of five consecutive weeks without the application of local anesthetics. The injection technique followed the standard lateral approach with the knee extended and patient in the supine position. Sterilized procedures were strictly followed to prevent any septic infection.

2.3. Clinical assessment

Clinical assessment was made by an investigator for each patient before IAHA injections (as baseline), and 1 week, 3 months and 6 months after the completion of the fifth injection. The level of knee pain on walking was evaluated by the use of a 100 mm visual analog scale (VAS). Functional impairments in patients with knee OA was assessed by Lequesne's function index (LI) [19]. The LI questionnaire included knee discomfort, endurance of ambulation, and difficulties in daily life. A maximum score of 26 indicated the greatest degree of dysfunction. The degree of disability was graded by the scoring as follows: >14 points = extremely severe; 11–13 points = very severe; 8–10 points = severe; 4–7 points = moderate; 1–3 points = mild.

2.4. Gait analysis

For the analysis of spatiotemporal gait parameters, a 6-camera motion analysis system (Vicon 370, Oxford Metrics, Oxford, UK) and two AMTI force plates (Advanced Mechanical Technology, Watertown, MA, USA) were synchronized to collect the three-dimensional (3D) marker trajectories at a sampling rate of 120 Hz and ground reaction force (GRF) at a frequency of 960 Hz. The reflective markers were placed on anatomic landmarks including bilateral anterior superior iliac spines, lateral thighs, medial/lateral epicondyles of femur, lateral shanks, medial/lateral malleoli, calcaneus, base of second metatarsal bones, and sacrum. Three successful gait cycles for each limb were recorded for each subject. Each subject was asked to walk at a self-selected, comfortable pace on a 10-m walkway in the gait laboratory.

Gait analyses were performed before the IAHA injections as baseline, and 1 week, 3 months, and 6 months after the completion of IAHA injections for the knee OA group. During the entire six-month post-IAHA period, patients in the knee OA group did not receive any additional nutritional supplements (e.g. glucosamine), non-steroidal anti-inflammatory agents or physiotherapy treatments.

Three-dimensional joint moments were calculated via the inverse dynamics approach. The detailed procedures were described previously [20]. All joint moments in the frontal and sagittal planes were normalized according to the participant's body mass (Nm/kg). Gait velocity and step length were normalized according to the body height (%BH/sec and %BH).

2.5. Statistical analysis

The SPSS version 12 software was used for the statistical analysis. Group differences in age, body height, body mass, joint moments, walking speed, and step length were compared using an independent t-test. Gender differences between groups were determined using a Chi-square test. The non-parametric Wilcoxon signed-rank test was used for the comparison of VAS and LI scores before and after IAHA injections. The gait variables were compared using repeated measures analysis of variance (ANOVA) to determine significant differences among baseline, 1 week, 3 months, and 6 months after injections. *Post hoc* Bonferroni tests were used to evaluate the significance of pairwise comparisons. Pearson correlation coefficients were used to find associations between VAS pain scores and kinetic variables. The level of significance was set at $p < 0.05$.

3. Results

The average scores of VAS and LI were significant improved after IAHA injections ($p < 0.001$) in patients with knee OA (Table 1). VAS score was reduced from 54.6±12.4 at baseline to 38.5±11.2 at 1 week and 42.4±10.0 at 6 months after IAHA injections. As indicated by LI, pain, maximum distance walked, and difficulties in daily life scores were all significantly improved after IAHA injections from 1 week to 6 months ($p < 0.001$) when compared with the baseline. Total scores of LI was significant improved from 14.8±3.6 at baseline, to 7.4±3.0 at 1 week and 8.7±3.0 at 6 months after IAHA injections. The OA knee group showed significantly slower walking speed (49.4%±11.7 %BH/s) ($p < 0.001$) and shorter step length (30.8±5.2 %BH) ($p = 0.01$) at baseline. These parameters significantly increased after the completion of IAHA injections (Figure 1).

Comparisons of the knee joint angles in the frontal plane between baseline, after IAHA injections in the knee OA and the control groups are shown in Figure 2. At 1 week and 3 months after IAHA injections, the knee adduction angles increased (more

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