

Efficacy of intraarticular hyaluronic acid injection through a lateral approach under fluoroscopic control for advanced hip osteoarthritis

Floroskopik lateral yaklaşımla intraartiküler hyaluronik asit enjeksiyonunun ileri evre kalça osteoartritinde etkinliği

Can EYİĞÖR,¹ Alihan PİRİM,¹ Sibel EYİĞÖR,² Meltem UYAR¹



Summary

Objectives: Hyaluronic acid (HA) is used for intraarticular treatment of hip osteoarthritis (OA). The objective of this study was to determine the efficacy of intraarticular injection of HA through a lateral approach under fluoroscopic control for advanced hip OA.

Methods: The study included 21 patients with advanced hip OA. All patients received 2.5 ml HA injection once a week for 3 weeks by lateral approach under fluoroscopic control. Disability (Lequesne index), pain scores (visual analog scale-VAS) and analgesic use of patients were assessed before treatment and 1, 3 and 6 months after the treatment.

Results: Lequesne index and VAS pain scores measured 1, 3 and 6 months after treatment were significantly lower compared to baseline scores ($p < 0.001$). Although analgesic use was significantly reduced 1 and 3 months after treatment compared to baseline ($p < 0.05$), no difference was determined in analgesic use at the 6th month ($p > 0.05$). No side effect was observed.

Conclusion: In conclusion, intraarticular HA injection through a lateral approach under fluoroscopic control was shown to be a safe and effective method for patients with advanced hip OA.

Key words: Fluoroscopic lateral approach; hyaluronic acid; advanced hip osteoarthritis.

Özet

Amaç: Hyaluronik asit (HA) kalça osteoartriti (OA) tedavisinde intraartiküler olarak kullanılmaktadır. Bu çalışmanın amacı, floroskopik lateral yaklaşımla intraartiküler HA enjeksiyonunun, ileri evre kalça OA'lı hastalarda etkinliğini saptamaktır.

Gereç ve Yöntem: İleri evre kalça OA'lı 21 hasta çalışmaya alındı. Tüm hastalara lateral yaklaşımla floroskopi kılavuzluğunda birer hafta ara ile 3 kez 2.5 ml HA enjeksiyonu yapıldı. Hastaların tedavi öncesi ve son enjeksiyondan sonra 1., 3. ve 6. aylarda özür-lülük (Lequesne indeksi), ağrı (Vizuel analog scale-VAS) skorları ve analjezik tüketimleri değerlendirildi.

Bulgular: Lequesne indeksi ve VAS ağrı skorları 1., 3., ve 6. aylarda başlangıç değerlerine göre istatistiksel olarak anlamlı azaldı ($p < 0.001$). Analjezik tüketimi 1. ve 3. aylarda başlangıç değerine göre istatistiksel olarak azalırken ($p < 0.05$), 6. ayda analjezik tüketiminde fark saptanmadı ($p > 0.05$). Herhangi bir yan etki gözlenmedi.

Sonuç: Sonuç olarak, floroskopi eşliğinde, şiddetli kalça OA'sında lateral yaklaşımla HA enjeksiyonu etkili ve emniyetli bir uygulamadır.

Anahtar sözcükler: Floroskopik lateral yaklaşım; hyaluronik asit; ileri evre kalça osteoartriti.

Departments of ¹Anesthesiology and Reanimation, ²Physical Therapy and Rehabilitation, Ege University Faculty of Medicine, Izmir, Turkey
Ege Üniversitesi Tıp Fakültesi, ¹Anesteziyoloji ve Reanimasyon Anabilim Dalı, Algoloji Bilim Dalı, ²Fizik Tedavi ve Rehabilitasyon Anabilim Dalı, İzmir
Submitted - January 2, 2010 (Başvuru tarihi - 2 Ocak 2010) Accepted after revision - March 15, 2010 (Düzeltilme sonrası kabul tarihi - 15 Mart 2010)

Correspondence (İletişim): Can Eyigör, M.D. Ege Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Algoloji Bilim Dalı, Bornova 35100 İzmir, Turkey.
Tel: +90 - 232 - 390 21 55 **e-mail (e-posta):** can.eyigor@yahoo.com.tr

Introduction

Osteoarthritis (OA) is a degenerative joint disease characterized by cartilage erosion, changes in subchondral bone, osteophyte formation and synovial inflammation. It is a common cause of chronic pain, particularly in the elderly. Although there is no treatment that has been proved to prevent or reverse the structural changes that occur in OA, a proper treatment that alleviates symptoms may improve the patient's quality of life.^[1] Simple analgesics, non-steroid anti-inflammatory drugs (NSAID), tramadol, physical therapy agents, intraarticular injections (hyaluronic acid, steroid etc.) and surgical methods are used in the treatment of OA.^[2,3] But there is no consensus about the effects of each treatment on cartilage and synovial tissue.

Hyaluronic acid (HA) used intraarticularly in the treatment of OA is a major constituent of the synovial fluid and cartilage. HA is known to increase viscosity of the synovial fluid; facilitate gliding via layer formation on the cartilage and protect soft tissue from trauma by acting as a shock absorbant; also soothes the pain and exerts an immunomodulatory effect on inflammatory cells.^[4] Although commonly used in clinical practice, there are no strict rules concerning the injection technique, age, radiographic staging of osteoarthritis, severity of symptoms, physical activity level, previous trauma or deformity; therefore patient selection has not been clearly delineated.^[5]

Although numerous studies on knee OA has been published in the recent years, there are limited studies on hip OA in the literature.^[6-8] Possible reasons for this include difficulty of administration, deep localization of the hip joint, indistinct descriptions for the injection site, close proximity to the neurovascular structures and fear and inexperience of the doctors about this technique.^[4,9] Today, intraarticular injections of hip are performed under image control because of safety and efficacy reasons. Fluoroscopy and ultrasound are commonly used imaging techniques; computed tomography is also employed. Anterolateral approach is more frequently preferred for injections to hip joint to treat hip OA, few studies have used lateral approach in the literature.^[8,10] However, there are studies that suggest intraartic-

ular injection to hip by lateral approach might be safer and more effective.^[9,11]

Therefore, purpose of our study was to determine the efficacy and safety of intraarticular HA injection through lateral approach under fluoroscopic control for patients with advanced hip OA.

Materials and Methods

Patients presented to outpatient clinic of Algology Department of School of Medicine of Ege University for hip pain were reviewed retrospectively and 21 of these patients that were diagnosed as primary hip OA by physical, laboratory and radiologic examinations according to American College of Rheumatology (ACR) criteria;^[12] rated as grade 3 or 4 according to Kellgren-Lawrence criteria;^[13] and had symptoms for 2 years or more, with no intraarticular injection within the last 6 months, and suffered from severe pain despite WHO second line medical treatment were enrolled into the study. Patients that had inflammatory joint disease (rheumatoid arthritis, ankylosing spondylitis etc), active synovitis of the joint, a history of hip surgery or replacement, intraarticular injection within the last 6 months, a history of trauma within the last 6 months or use of an oral or muscular steroid, or had any disease that precludes exercising or that caused loss of muscle power, advanced cardiovascular disease, pregnancy, malignancy, bleeding diathesis, mental disease were excluded from the study.

Demographic and clinical characteristics of the patients (age, gender, length, weight, duration of the symptoms) were recorded. All patients were assessed by the following scales before the injections and 1, 3 and 6 months after the injections:

- * Visual analog scale (VAS) 100 mm (scale 0 = no pain, 100 = worst pain possible) was used.
- * Severity of pain, walking capacity and disability in daily activities were assessed by Lequesne index^[14]
- * Analgesic use was determined according to WHO analgesic ladder^[15] (1st step paracetamol ≤ 2 g/day, if this did not provide

Table 1. Demographic characteristics of the patients

| | |
|------------------------------------|-----------|
| Patients (n) | |
| Men | 5 |
| Women | 16 |
| Age in years (mean±SD) | 61.3±12.3 |
| Symptom duration (years) (mean±SD) | 6.9±3.0 |
| BMI (kg/m ²) | 25.7±4.8 |
| Radiological grade (n) | |
| III | 14 |
| IV | 7 |
| Analgesic usage (n) | |
| No | 0 |
| 1st step | 5 |
| 2nd step | 16 |

sufficient analgesia, tramadol PO ≤200 mg/day was used as 2nd step medicine).

Each patient enrolled for the study was informed comprehensively about the study and their consents were obtained. All patients received three injections of 2.5 ml HA (Adant®) once a week. Patients were laid supine on the application table. C-arm fluoroscopy was set in the anterolateral position to view the hip joint. Intersection of the imaginary line at the level of trochanter major on lateral of femur with the line corresponding to the superior of the hip joint in the anterolateral view was determined as the



Fig. 1. Fluoroscopic image of the hip joint after injection of the radiopaque dye.

injection point and local anesthesia was achieved by %2 prilocaine. Injection was performed by 15 cm long 22 G needle. Access to hip joint was confirmed by 0.5 ml of contrast material (Fig. 1). Patients were monitored for side effects throughout the study.

Statistical Analysis

All analyses were performed by SPSS version 15.0 software package. Changes in VAS pain scores and Lequesne scores were assessed by general linear model, repeated measurement were assessed by ANOVA, paired comparisons were assessed by Bonferroni test, and changes in analgesic use were assessed by McNemar test. A value of $p < 0.05$ was considered as significant.

Results

Study included 21 patients. Clinical and demographical characteristics of the patients are presented in Table 1.

VAS pain scores

VAS pain scores of the patients 1, 3 and 6 months after treatment showed statistically significant reduction compared to that of before treatment ($p < 0.001$). Reductions in the pain scores 1, 3 and 6 months after treatment were 62.6%, 61.3% and 39.9% respectively (Fig. 2).

Lequesne index

Lequesne indexes of the patients 1, 3 and 6 months after treatment showed statistically significant reduction compared to that of before treatment ($p < 0.001$). Reductions in the Lequesne indexes 1, 3 and 6 months after treatment were 25.6%, 22.8% and 17.4% respectively (Fig. 3).

Analgesic use

Analgesic use of the patients before treatment is presented in Table 1. One month after the treatment 6 patients (28.6%) need no analgesics. Twelve patients (57.1%) used 1st step analgesics, whereas 3 patients (14.3%) required 2nd step analgesics. Three months after the treatment 4 patients (19%) required no analgesic. Twelve patients (57.1%) used 1st step analgesics, whereas 5 patients (23.8%) used 2nd step analgesics. Reduction in analgesic use 1 and 3 months after treatment were statistically sig-

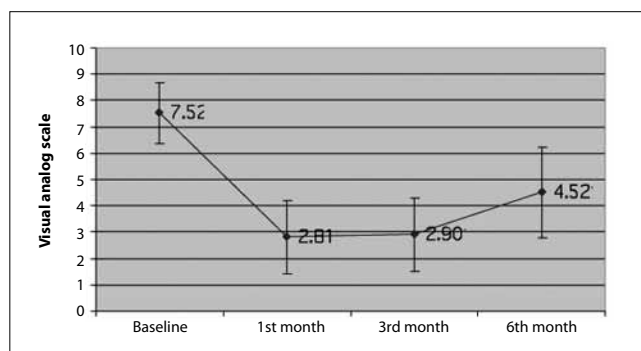


Fig. 2. Pain (VAS) changes in 1st, 3rd and 6th months. * $p < 0.001$

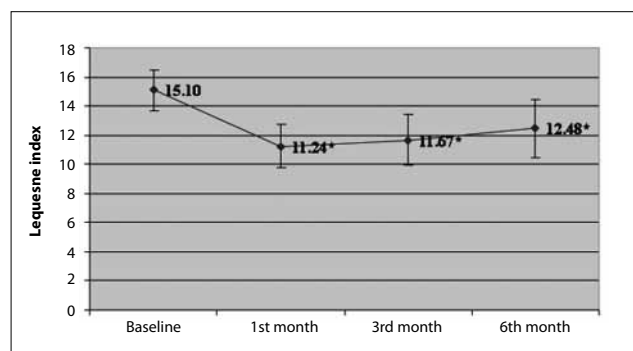


Fig. 3. The Lequesne index changes in over time. * $p < 0.001$

nificant ($p < 0.05$). Six months after the treatment, 3 patients (14.3%) need no analgesics. Seven patients (33.3%) used 1st step analgesics, whereas 11 patients (52.4%) used 2nd step analgesics. Analgesic use 6 months after the treatment did not show significant difference compared to baseline ($p > 0.05$) (Table 2).

Safety

None of the patients developed a systemic side effect during the study period. Three of the 21 patients (14.29%) reported a moderate pain around the needle insertion site on the lateral side of the hip that lasted 3-5 days. No complication was observed in other patients during injection and within the follow-up period.

Discussion

Our study showed that intraarticular HA injection through lateral approach under fluoroscopic control provided significant reduction in pain scores, disability scores and analgesic use in advanced hip OA. In our study, VAS pain scores showed significant reduction consistent with the studies in the literature. [7,8] VAS pain scores at the 6th month were higher compared to 1st and 3rd months, yet still lower than the baseline VAS scores. Migliore et al. [6] has

also reported higher VAS scores at 6th month compared to 2nd month, but still significantly lower than the baseline.

Lequesne index scores were also reduced significantly similar to the VAS pain scores during and at the end of the treatment period. However percent reduction of the Lequesne index scores were considerably lower compared to reduction in VAS pain scores. In contrast with the results reported by several studies in the literature, reduction of the Lequesne index scores at the 1st, 3rd and 6th months compared to baseline were 25.6%, 22.8% and 17.4% respectively. [6-8] At the 6th month, Tıkız et al. [7] reported 50% and Migliore et al. [6] reported 47% decrease in these scores compared to baseline. Lack of corresponding improvement in disability scores despite a significant decrease in the pain scores was attributed to selection of patients with advanced OA for the study. It should also be remembered that pain is only a symptom, whereas improvement of disability depends on several factors.

Tramadol is a weak opioid in the second step of analgesic ladder of WHO which is used in patients that paracetamol and NSAIDs are not able to alleviate the pain. [15] Due to risks posed by long-term use

Table 2. Analgesic consumption of the patients

| Analgesic usage (n) | 1st month* | 3rd month* | 6th month |
|---------------------|------------|------------|-----------|
| No | 6 | 4 | 3 |
| 1st step | 12 | 12 | 7 |
| 2nd step | 3 | 5 | 11 |

* $p < 0.05$

of NSAID analgesics,^[16,17] tramadol is being increasingly prescribed particularly for geriatric patients in the recent years.^[18,19] Analgesic use was not restricted as the study included patients with advanced stage of hip OA. Analgesic use was significantly reduced in the follow-up examinations at the 1st and 3rd months, which was consistent with the literature.^[6,7,20] However, this tendency of reduction in analgesic use did not persist until the 6th month. Our results at the 6th month suggest that the effect of intraarticular HA in advanced OA is diminished 6 months after injection and the injection may be repeated if required. Studies in the literature that have a follow-up period of 6 months or longer showed that reduction in analgesic use compared to baseline may persist for up to 12 months.^[6,7,20] The cause of discrepancy between our study and the literature may be explained by enrollment of advanced stage hip OA patients into our study.

Ultrasound is frequently used for intraarticular injections to hip joint and usually anterior approach is preferred.^[6,8,21] However there is no widely accepted consensus on imaging method and the approach used (anterior-posterior or lateral). In their cadaveric study, Leopold et al.^[9] have demonstrated that lateral approach was safer for injections to hip joint and provided higher rates of access into the joint. Our study is the first study to perform intraarticular HA injections through lateral approach under fluoroscopic control for patients with advanced OA. Similar to the literature, no significant side effect was observed in our patients.^[6-8] It is not possible to conclude only by this study that lateral approach is superior to other approaches in terms of easy access to hip joint. Thus further studies are required to compare these two approaches in terms of efficacy, patient satisfaction and complications.

Our study has several limitations. We have not considered forming a placebo group as patients enrolled for the study had advanced stage OA with higher pain and disability scores. Additionally, lack of assessment of quality of life and the psychological status of the patients and relatively insufficient follow-up period may be considered as other limitations of our study.

In conclusion, intraarticular HA injection through

lateral approach under fluoroscopic control has proved to be a safe and effective method for patients with advanced hip OA. Results of our study obtained by 6 months of follow-up are encouraging. But our results have to be supported by studies that have higher number of patients with control group and a long-term follow-up.

References

1. Thomas E, Wilkie R, Peat G, Hill S, Dziedzic K, Croft P. The North Staffordshire Osteoarthritis Project--NorStOP: prospective, 3-year study of the epidemiology and management of clinical osteoarthritis in a general population of older adults. *BMC Musculoskelet Disord* 2004;5:2.
2. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheum* 2000;43(9):1905-15.
3. Ling SM, Bathon JM. Osteoarthritis in older adults. *J Am Geriatr Soc* 1998;46(2):216-25.
4. Pelletier JP, Martel-Pelletier J. The pathophysiology of osteoarthritis and the implication of the use of hyaluronan and hylan as therapeutic agents in viscosupplementation. *J Rheumatol Suppl* 1993;39:19-24.
5. Brockmeier SF, Shaffer BS. Viscosupplementation therapy for osteoarthritis. *Sports Med Arthrosc* 2006;14(3):155-62.
6. Migliore A, Tormenta S, Martin Martin LS, Iannessi F, Mas-safra U, Carloni E, et al. The symptomatic effects of intra-articular administration of hylan G-F 20 on osteoarthritis of the hip: clinical data of 6 months follow-up. *Clin Rheumatol* 2006;25(3):389-93.
7. Tikiz C, Unlü Z, Sener A, Efe M, Tüzün C. Comparison of the efficacy of lower and higher molecular weight viscosupplementation in the treatment of hip osteoarthritis. *Clin Rheumatol* 2005;24(3):244-50.
8. Caglar-Yagci H, Unsal S, Yagci I, Dulgeroglu D, Ozel S. Safety and efficacy of ultrasound-guided intra-articular hylan G-F 20 injection in osteoarthritis of the hip: a pilot study. *Rheumatol Int* 2005;25(5):341-4.
9. Leopold SS, Battista V, Oliverio JA. Safety and efficacy of intraarticular hip injection using anatomic landmarks. *Clin Orthop Relat Res* 2001;(391):192-7.
10. Gaston MS, Tiemessen CH, Philips JE. Intra-articular hip viscosupplementation with synthetic hyaluronic acid for osteoarthritis: efficacy, safety and relation to pre-injection radiographs. *Arch Orthop Trauma Surg* 2007;127(10):899-903.
11. Conrozier T, Bertin P, Mathieu P, Charlot J, Bailleul F, Treves R, et al. Intra-articular injections of hylan G-F 20 in patients with symptomatic hip osteoarthritis: an open-label, multicentre, pilot study. *Clin Exp Rheumatol* 2003;21(5):605-10.
12. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis Rheum* 1991;34(5):505-14.
13. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis* 1957;16(4):494-502.
14. Lequesne MG. The algofunctional indices for hip and knee osteoarthritis. *J Rheumatol* 1997;24(4):779-81.
15. Cancer Pain Relief. Geneva: World Health Organization; 1984.

16. Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ES-CISIT). *Ann Rheum Dis* 2003;62(12):1145-55.
17. Page J, Henry D. Consumption of NSAIDs and the development of congestive heart failure in elderly patients: an underrecognized public health problem. *Arch Intern Med* 2000;160(6):777-84.
18. Malonne H, Coffiner M, Sonet B, Sereno A, Vanderbist F. Efficacy and tolerability of sustained-release tramadol in the treatment of symptomatic osteoarthritis of the hip or knee: a multicenter, randomized, double-blind, placebo-controlled study. *Clin Ther* 2004;26(11):1774-82.
19. Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:16-20.
20. Migliore A, Tormenta S, Massafra U, Carloni E, Padalino C, Iannessi F, et al. Repeated ultrasound-guided intra-articular injections of 40 mg of Hyalgan may be useful in symptomatic relief of hip osteoarthritis. *Osteoarthritis Cartilage* 2005;13(12):1126-7.
21. Sofka CM, Saboeiro G, Adler RS. Ultrasound-guided adult hip injections. *J Vasc Interv Radiol* 2005;16(8):1121-3.