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Is Intraarticular Enjections Effective on Pain Management in Patients with Late Stage Primer Gonarthrosis During COVID-19 Pandemic? A Single Centre Experience

COVID-19 Pandemisi Sırasında Geç Evre Primer Gonartrozu Olan Hastalarda Eklem İçi Enjeksiyonlar Ağrı Yönetiminde Etkili Midir? Tek Merkez Deneyimi

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Abstract

Background: Primary gonarthrosis is a progressive disease that increases with age and leads to limitations in activities of daily living. Until surgery is performed, nonsteroidal anti-inflammatory drugs, intraarticular injections, and physical therapy methods are used.

Purpose: This study aims to compare the clinical effects of intra-articular corticosteroid (CCS) and hyaluronic acid (HA) injections for pain relief in primary gonarthrosis during the COVID-19 pandemic.

Material and Method: In this retrospective cohort study., 88 patients who underwent intra-articular CCS and HA injection between August 2020 and March 2021 due to Kellgren-Lawrence stage 2 and higher gonarthrosis were investigated. Patients were divided into two groups. Group I contains the patients who received HA injections, and group II contains the patients who received CCS injection. Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Knee Society Score (KSS) scores were used for the preoperative and postoperative functional evaluations of the patients. Grading of the severity of gonarthrosis was based on the Kellgren-Lawrence classification.

Results: Group I included 40 patients and group II included 48 patients. The mean age was 59.4±7.3 years, and the average follow-up period was 12±2,6 months. The pre-intervention WOMAC scores were 13,5 in Group I and 13.6 in Group II, KSS scores were 26,5 in Group I and 25,2 in Group II. While there was a significant change in the control at month 1 in both groups, no difference was found between the groups. At the 6th month control, the improvement in group 1 continued at a significant level compared to the pre-injection period, while group 2 returned to the pre-injection level. ($p<0,01$). After the injection, three patients in group 1 were hospitalized for one day because of sudden onset of pain and then discharged. Apart from this situation, no patient had septic arthritis or hemarthrosis.

Conclusion: Our study shows that both injections have a similar effect in the first month, but the palliative effect of intra-articular HA may be beneficial for a longer period of time.

Keyword: Corticosteroid injection, COVID-19 pandemic, hyaluronic acid, gonarthrosis, pain relief

Öz

Giriş: Primer gonartroz, yaşla birlikte artan ve günlük yaşam aktivitelerinde kısıtlamalara yol açan ilerleyici bir hastalıktır. Ameliyat yapılana kadar nonsteroid antienflamatuar ilaçlar, eklem içi enjeksiyonlar ve fizik tedavi yöntemleri kullanılır.

Amaç: Bu çalışma, COVID-19 pandemi döneminde primer gonartrozda ağrının giderilmesi için eklem içi kortikosteroid (CCS) ve hyalüronik asit (HA) enjeksiyonlarının klinik etkilerini karşılaştırmayı amaçlamaktadır.

Gereç ve Yöntem: Bu retrospektif kohort çalışma Kellgren-Lawrence sınıflamasına göre evre 2 ve üzeri gonartrozu olan ve Ağustos 2020 ile Mart 2021 tarihleri arasında eklem içi CCS ve HA enjeksiyonu yapılan 88 hasta incelendi. Hastalar iki gruba ayrıldı. Grup I, HA enjeksiyonu yapılan hastaları, grup II ise CCS enjeksiyonu yapılan hastaları içermektedir. Hastaların ameliyat öncesi ve ameliyat sonrası fonksiyonel değerlendirmelerinde Western Ontario ve McMaster Universities Arthritis Index (WOMAC) ve Knee Society Score (KSS) skorları kullanıldı.

Bulgular: Grup I'de 40 hasta ve grup II'de 48 hasta yer aldı. Ortalama yaş 59.4±7.3 yıl, ortalama takip süresi 12±2,6 ay idi. Enjeksiyon öncesi WOMAC skorları Grup I'de 13,5 ve Grup II'de 13.6, KSS skorları Grup I'de 26,5 ve Grup II'de 25,2 idi. Her iki grupta 1. ayda kontrolde anlamlı bir değişiklik varken, gruplar arasında fark bulunmadı. 6. ay kontrolünde, grup 1'deki iyileşme enjeksiyon öncesi döneme göre anlamlı düzeyde devam ederken, grup 2 enjeksiyon öncesi seviyeye döndü. ($p<0,01$). Enjeksiyondan sonra grup 1'deki üç hasta ani başlayan ağrı nedeniyle bir gün hastanede yatırılarak taburcu edildi.

Sonuç: Çalışmamız, her iki enjeksiyonun ilk ay içerisinde benzer etkisinin olduğunu ancak intraartikuler HA'nın palyatif etkisinin daha uzun süre faydalı olabileceğini göstermektedir

Anahtar Kelimeler: Kortikosteroid enjeksiyonu, COVID-19 pandemisi, hyaluronik asit, gonartroz, ağrı kesici

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INTRODUCTION

Primary gonarthrosis is one of the most common and progressive diseases of the musculoskeletal system.[1,2] Gonarthrosis is a leading cause of restrictive joint disease in elderly patients and will be the fourth leading cause of disability by 2020 due to increased life expectancy.[3] The incidence of gonarthrosis increases from the age of 55 and occurs in 10% of men and 18% of women over 60.[4,5] Gonarthrosis impairs quality of life through limited mobility and decreased independence.[5,6] Age, concomitant diseases, and duration of symptoms should be considered when deciding on treatment for patients with gonarthrosis. While conservative treatment consists of exercise, physical therapy applications, and drug treatments, surgical treatment is the current method of treatment for patients who do not respond to these methods.

Conservative treatments include patient education, daily living adjustments, braces, analgesic and anti-inflammatory treatments, and intra-articular corticosteroid (CCS) and hyaluronic acid injections (HA). Long-term use of nonsteroidal anti-inflammatory drugs is not recommended because of their limited ability to pass through the joint capsule and the high risk of side effects associated with chronic use.[5] There are publications in the literature reporting successful results of intra-articular CCS and HA injections.[1,7] Therefore, intra-articular injections are used as a palliative option in patients who do not accept surgery.

During these efforts to delay the spread of the disease and protect patients and staff after the World Health Organization declared the COVID-19 pandemic, hospitals were forced to halt most non-COVID-19 pandemic related activities and postpone most elective surgeries, including knee arthroplasties, with hospital stays exceeding 23 hours.[8-10] The inability to perform elective total knee arthroplasty in patients with severe gonarthrosis has resulted in increased joint pain, decreased functional capacity, and increased use of analgesics and opioids.[8] After the first case was reported in our country on March 11, 2020, elective surgeries were restricted in many hospitals in line with the recommendations of the COVID-19 scientific committee of the Ministry of Health. During this period, intra-articular injections have become more important to relieve patients' pain, maintain their functional capacity, and minimize the side effects that may occur when taking multiple medications.[11]

The aim of our study is to evaluate the effects of two different intra-articular injection treatments on pain relief and function in patients with symptomatic primary gonarthrosis and to compare the efficacy of nonemergency surgery during the COVID-19 pandemic period when nonemergency surgery cannot be performed because of perioperative risks and hospital density.

MATERIAL AND METHOD

Institutional review board approval (22-KAEK-21) was obtained from the clinical research ethics committee before starting the study. This retrospective study evaluated presented with knee pain and received intra-articular injections between August 2020 and March 2021. Patients older than 45 years with stage 2 or more severe osteoarthritis on direct radiography according to the Kellgren-Lawrence criteria were included in the study. Patients with a previous intra-articular fracture, neuromuscular disease, acute lumbar disc disease, flexion contracture greater than 10 degrees, varus-valgus alignment greater than 7 degrees, and follow-up of less than six months were excluded from the study. Patients were randomized by days of admission. Those who underwent HA were placed in Group I, and those who underwent CCS were placed in Group II. A prestudy power analysis based on previous data determined a sample size 66 patients to reach the desired power of >0.8.

All procedures were performed in an outpatient clinic. Injections were performed by the orthopedic surgeon. Before the injection, while the patients were seated on a stretcher and their knees were flexed 90 degrees, after sterile staining and draping, the anterolateral arthroscopy portal was found and marked. All injection were made with 21 G x 16mm needle. (Beybi Medical, İstanbul, Turkey). After entering this point with an empty syringe and confirming that it was in the joint, Hyaluronic acid 36 mg/2 ml (Diart, Adamfarma Ankara, Turkey) was injected into the patients in Group 1, and a combination of 1 mL 40mg methylprednisolone acetate (Depo-Medrol 40 mg/mL flakon, Pfizer Drugs Ltd.Şti. İstanbul, Turkey) 4 mL %0,5 bupivacaine hydrochloride (Buvicaine, Polifarma Drugs, Tekirdağ, Turkey) was injected into the patients in Group 2 (**Figure 1**). Injections were performed by a single surgeon using a standardized method, whereas follow-up was performed by a blinded observer.

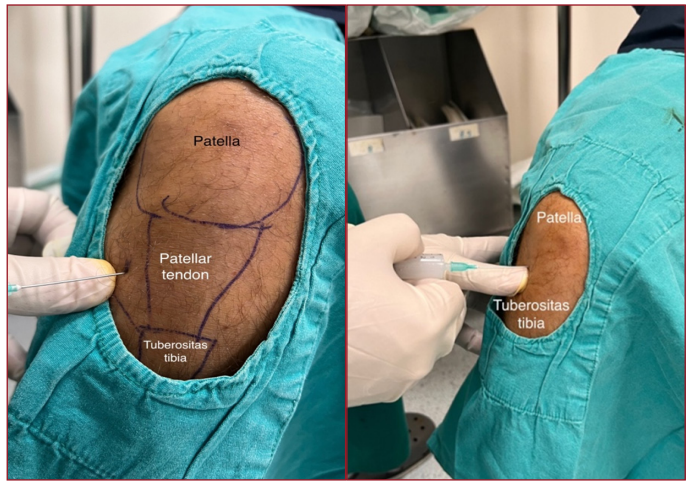

Figure 1. injection technique. In all our patients, an injection was made through the anterolateral portal while the knee was at 90 degrees of flexion.

Qualitative variables of patients (injected knees, age, sex), degrees of osteoarthritis according to Kellgren-Lawrence classification, literature including WOMAC and KSS knee function scores were reviewed and recorded on a form we prepared. The data were analyzed using SPSS Statistics Software (version 23.0, IBM Corp.). The distribution of the data was evaluated with the Kolmogorov-Smirnov test. The categorical data were assessed with the Pearson Chi-square, Fisher exact, and Fisher-Freeman-Halton tests. The parametric and non-parametric data were evaluated with the Student t-test and Mann-Whitney U test, respectively. The dependent groups (for non-normally distributed data) were evaluated with the Wilcoxon test. A p-value of <0.05 was considered significant in all the tests.

RESULTS

Between August 2020 and March 2021, 115 patients received intra-articular injections. Among these patients, 88 patients who met the inclusion and exclusion criteria and came to the last examination were included in our study. Fifteen of our 27 patients who did not participate in the study could not come because they were out of town. We could not reach 12 of our patients from the contact number they gave at the beginning of the study. Fifty-eight of our patients were female and 30 were male. Group I consisted of 40 (23 F/17 M) patients and Group II consisted of 48 (35 F/13 M) patients. The mean age of our patients was 59.4±7.3 years. The mean follow-up time was 12±2.6 months. Bilateral injection was performed in 24 patients enrolled in the study. 64 patients had a single knee injection. Injections were made to the left knee of 34 patients and to the right knee of 30 patients. It was found that 26 of 88 patients had Kellgren-Lawrence stage 2, 29 had stage 3, and 33 had stage 4 osteoarthritis. No significant difference was found in demographic data between the groups (**Table 1**).

Table 1: Demographic data and features of patients

	Group I	Group II	p
Age	59.4±8.6	59.5±6.2	0.965
Gender (Female/Male)	23/17	35/13	0.129
Follow-up period (Months)	12.42	11.66	0.146
Side Right	18	12	
Left	16	18	0.036
Bilateral	6	18	
Kellgren-Lawrence Classification;			
Type II	11	15	
Type III	14	15	0.906
Type IV	15	18	

Data presented as Mean±SD. Ki kare test was used. (p<0.05 was considered significant.)

It was found that WOMAC and KSS scores for knee function before and after injection had significantly improved in both groups at first month control. There was no difference in score improvement between groups, while scores in group 1 improved significantly in controls after month 3 and month 6 (**Table 2**).

Table 2: Difference into groups WOMAC and KSS scores

	WOMAC		p	KSS		p
	Group I	Group II		Group I	Group II	
Pre-intervention	13.5	13.6	0.774	26.5	25.2	0.361
1st Month	7.9	7.6	0.575	69.7	69.5	0.510
3rd Month	8.8	10.1	0.021	61.6	53.3	<0.001
6th Month	10.7	12.2	0.009	53.5	38.6	<0.001
Last Control	13.1	13.4	0.660	33.5	31.9	0.074

(WOMAC: Western Ontario and McMaster Universities Arthritis Index, KSS: Knee Society Score). (p<0.05 was considered significant.)

At long-term follow-up of patients after the procedure, 3 patients in group 1 experienced sudden onset of pain after the injection, which was followed up with 1-day hospitalization for pain management, and their pain resolved with medical treatment. Septic arthritis and hemarthrosis were not observed during the follow-up period.

DISCUSSION

In patients with gonarthrosis, HA and CCS injections are a widely used treatment method between analgesic therapy and joint replacement. Our study showed that both of injection techniques had successful results. In the controls performed at the third month, significant improvement in WOMAC (p=0,021) and KSS (p<0,001) scores was observed in both groups. It was observed that the improvement in functions in patients receiving HA injection continued at the sixth month follow-up (p<0,001).

Intra-articular CCS injection is another widely used treatment method. It is known that its effect starts faster and ends sooner, and if repeated frequently, it has more side effects.[12] Our study showed similar results in the treatment of gonarthrosis with both drug injections in terms of reduction of pain and restoration of functions in the initial phase. However, when comparing the groups, it was found that the effect of CCS injection wore off earlier.

Looking at the literature, we find that there are many publications on the results of intra-articular injections, especially to increase the incidence of gonarthrosis and maintain the quality of life. In a meta-analysis of 1767 patients evaluating intra-articular CCS injection by Jueni et al, they reported that efficacy began within 1 week and lasted approximately 6 weeks.[13] Similarly, a study by Godwin et al. reported that the effect began in the first week after CCS injection and ended toward the end of the fourth week.[14] Other studies of intra-articular CCS injection have shown significant improvement in pain, joint stiffness, and range of motion.[14-16] The guideline published by the American Academy of Orthopedic Surgeons in 2008 recommends its use in the short-term pain management of patients who have gonarthrosis.[16] It is found that WOMAC pain scores of our patients who received CCS injection improved significantly in the first month, but the efficacy decreased in the long term.

Table 3: Summary of publications in the literature

	Annaniemi et al. (2019)	Tammachote et al. (2016)	Leighton et al. (2014)	Bostan et al. (2010)	Matzkin et al. (2017)	Caborn et al. (2004)	Present study
Age (year)	65.7±9.2	62	61.6	53±9	61.2±8.5	63.1	59.4±7.3
Number of patients	86	89	433	11 (22 knees)	96	226	88
Gender (F/M)	50/36	79/20	213/220	9/2	-	123/93	58/30
Average follow-up (months)	17.1±7.3	6	12	5.8±0.8	6	7	12
Injection agent (HA/CCS)	HA	HA + CCS	HA + CCS	HA	CCS	HA+CCS	HA + CCS
Kellgren-Lawrance Classification	Grade 1=4 Grade 2=46 Grade 3=36	Grade 1=22 Grade 2=22 Grade 3=41 Grade 4=14	Grade 2=156 Grade 3=277	Grade 2=10 Grade 3=12	Grade 1=28 Grade 2=28 Grade 3=29 Grade 4=11	Grade 2=26 Grade 3=128 Grade 4=60	Grade 2=26 Grade 3=29 Grade 4=33
Score	VAS=69.3 WOMAC=36.7±14.6	VAS 53→24 WOMAC=43→21	WOMAC pain score=10→6	HSS=75→83 KFS=64→73 KSS=74→88 WOMAC pain score=11.9→6.5	WOMAC pain=8.2→4.4 SF-36=50→62 VAS=5.5→4.6	WOMAC (HA)=54→18 WOMAC (CCS)=53→7.5	WOMAC pain score (HA)=13.5→10.7 WOMAC pain score (CCS)=13.6→12.2 KSS (HA)=26.5→53.5 KSS (CCS)=25.5→38.6

HA:Hyaluronic acid, CCS:Corticosteroid, WOMAC: Western Ontario and McMaster Universities Arthritis Index, KSS: Knee Society Score, KFS: Knee Functional Score

Hyaluronic acid, an important viscoelastic glycosaminoglycan that occurs naturally in healthy synovial fluid, is a relatively new agent that is currently in common use.[17] It imparts a number of protective properties to synovial fluid, including shock absorption, dissipation of traumatic energy, protective coating of the articular cartilage surface, and lubricity.[18] Synthetic HA is used to increase the viscosity of synovial fluid.[19] In a study by Bostan et al, 22 patients were injected intra-articularly with HA and it was observed that the patients showed significant improvement in pain and functional scores.[1] A study by Annaniemi et al. compared the efficacy of PRP and HA and found that total knee replacement (TKP) surgery could be delayed.[20] In another study by Conrozier et al, pain was reported to be reduced for up to 26 weeks and functional recovery was maintained when intra-articular HA application was repeated three times at one-week intervals.[21] It can be observed that the improvement in WOMAC pain scores and CSS function scores of our patients who received HA injection persisted until the sixth month control.

In a study conducted by Caborn et al. comparing intra-articular CCS and HA injections, it was found that pain reduction was better in the first two weeks in patients receiving CS injection, whereas patients receiving HA improved in controls at week 12 and week 26.[22] In meta-analyses comparing the efficacy of the two agents, it has been shown that the onset of action is later and lasts longer in patients who have undergone HA.[17,23] In their study, Tammachote et al. reported that at the end of the first week, a similar level of effect was achieved between the two groups and that patients given HA benefited from pain and functionality for a longer period of time.[19] When examining the results of our patients, it was found that scores improved and pain decreased in both groups in the first month of control, while in accordance with the literature, it was found that patients who received HA injection in the third month, in the sixth month, and at the last control examination benefited longer from the injection

Our study is not without limitations. Limitations of our study are that body mass index, activity level, smoking, and chronic drug use of patients were not evaluated because of the retrospective design. The strengths of our study are that patients were randomized before injection, procedures were performed by a single surgeon, and assessments during follow-up were performed by an independent observer.

CONCLUSION

This experience, gained in the COVID-19 pandemic, has led us to believe that intra-articular injection of HA and CCS can provide temporary pain relief and short-term functional enhancement in primary gonarthroses for which surgical treatment is indicated. When both injections, which have similar effects, are administered simultaneously, the palliative effect of intra-articular HA injection may be beneficial over a longer period of time.

In symptomatic primary gonarthrosis, in times of crisis when the health care system is intensified, and in patients who have refused surgical treatment, temporary pain relief and functional recovery can be achieved with intraarticular CCS and HA injections.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Gaziosmanpasa University Ethics Committee (Decision No:22-KAEK-21).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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