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ORIGINAL ARTICLE

Intra-articular injection of autologous fat tissue in the treatment of patients with chronic knee pain due to osteoarthritis

Osteoartrite bağlı kronik diz ağrısı mevcut hastaların tedavisinde otolog yağ dokunun eklem içi enjeksiyonu

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Summary

Objectives: The purpose of this study was to evaluate the safety and efficacy of autologous fat tissue injection into the knee joint for the treatment of osteoarthritis.

Methods: We reviewed 165 patients who received an intra-articular injection of autologous fat tissue for knee osteoarthritis. The efficacy of the treatment was evaluated at 1, 3, 6, and 12 months follow-up using the Visual Analogue Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Oxford Knee Score (OKS). Patients with knee arthritis were classified as grades I-IV according to the Kellgren-Lawrence scale (K-L). The clinical and demographic information of the patients, NSAIDs or opioid use, and the side effects related to the procedure were recorded.

Results: There were 62 male and 103 female patients. The mean age was 61.28±11.4 years, and the mean BMI was 26.23±4.49. A significant improvement ($p<0.001$) was observed in VAS, WOMAC, and OKS values of patients with K-L grade I-III osteoarthritis. Patients with K-L grade IV osteoarthritis showed no statistically significant improvement. No serious complications were observed in the patients. In addition, a statistically significant decrease was found in the daily doses of paracetamol/tramadol and in the number of patients who continued to use NSAIDs after 12 months of follow-up.

Conclusion: The results of the study suggest that minimally manipulated autologous fat tissue injections are effective and safe treatment methods for patients with grade I-III knee osteoarthritis. The results may not be satisfactory in severe osteoarthritis due to the limited capabilities.

Keywords: Injections; intra-articular; knee; osteoarthritis; subcutaneous fat.

Özet

Amaç: Bu çalışmanın amacı, osteoartrit tedavisinde diz eklemine enjekte edilen otolog yağ dokusunun güvenilirliğini ve etkinliğini değerlendirmektir.

Gereç ve Yöntem: Diz osteoartriti için intraartiküler otolog yağ dokusu enjeksiyonu yapılan 165 hastayı inceledik. Tedavinin etkinliği 1, 3, 6 ve 12 aylık takiplerde Vizüel Analog Skala (VAS), Western Ontario ve McMaster Üniversiteleri Osteoartrit İndeksi (WOMAC) ve Oxford Diz Skoru (OKS) kullanılarak değerlendirildi. Diz artritli hastalar Kellgren-Lawrence (K-L) skalasına göre evre I-IV olarak sınıflandırıldı. Hastaların klinik ve demografik bilgileri, NSAİİ veya opioid kullanımı ve işleme ilişkin yan etkiler kaydedildi.

Bulgular: 62 erkek ve 103 kadın hasta mevcuttu. Ortalama yaş 61,28±11,4 yıl ve ortalama VKİ 26,23±4,49 idi. K-L evre I-III osteoartriti olan hastaların VAS, WOMAC ve OKS değerlerinde anlamlı bir iyileşme ($p<0.001$) gözlendi. K-L evre IV osteoartriti olan hastalar istatistiksel olarak anlamlı bir iyileşme göstermedi. Hastalarda ciddi bir komplikasyon gözlenmedi. Ayrıca, günlük parasetamol/tramadol dozlarında ve 12 aylık izlemde NSAİİ kullanmaya devam eden hasta sayısında istatistiksel olarak anlamlı azalma saptandı.

Sonuç: Çalışmanın sonuçları, minimal manipüle edilmiş otolog yağ dokusu enjeksiyonunun evre I-III diz osteoartriti mevcut hastalarda etkili ve güvenli bir tedavi yöntemi olduğunu düşündürmektedir. Şiddetli osteoartritte sınırlı iyileştirme yeteneği nedeniyle sonuçlar tatmin edici olmayabilir.

Anahtar sözcükler: Cilt altı yağ; diz; eklem içi; enjeksiyon; osteoartrit.

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Introduction

Osteoarthritis is an important cause of chronic knee pain due to degenerative changes of the joint space, especially in the elderly. Narrowing of the joint space, subchondral sclerosis, synovitis, and osteophytes are the most common radiological changes in patients.[1] The pain, which increases with activities such as walking, going uphill, and climbing stairs, usually starts insidiously and impairs quality of life. The primary goal of treatment is to reduce pain and maintain functionality. Diverse pharmacological treatments are available for knee osteoarthritis pain, including paracetamol, oral/topical NSAIDs, and tramadol. Conservative treatments (weight loss, physical therapy), minimally invasive methods (intra-articular injections, radiofrequency ablation, etc.), and surgical arthroplasty could be alternative treatments for these patients. Injections of hyaluronic acid, PRP (Plasma Rich Platelet), corticosteroids, and local anesthetics offer additional but imprecise options for joint degeneration.[2]

Intra-articular injection of minimally manipulated adipose tissue in clinical practice has started to be a novel approach in regenerative medicine after adipose tissue is easily obtained.[3] Adipose tissue-derived mesenchymal stem cells have features such as self-renewal, differentiation, and immunomodulatory capacity that activate the microenvironment by secreting different growth factors and cytokines.[4] Standardization has not yet been achieved in clinical use due to the body area where the adipose tissue would be taken, the technique to be applied, and the type of stem cell materials to be used. Previous studies reported different results for both pain relief and functionality after intra-articular injection of the adipose tissue-derived mesenchymal cells, which require isolation and processing techniques.[5,6] On the other hand, fat micrograft can be used by injecting directly into the knee joint without any processing technique or manipulation of lipoaspirate.[7] Information on this subject is still being researched. The novelty of this approach is the use of tissue instead of cells and avoiding processing and manipulation of the adipose tissue.

In this study, the purpose is to evaluate the short- and long-term effectiveness of autologous fat tissue injection, and the improvement in functionality and pain in patients with chronic knee pain due to osteoarthritis.

Material and Methods

We retrospectively reviewed 165 patients of both genders with grade I-IV osteoarthritis according to the Kellgren-Lawrence (K-L) classification and the American College of Rheumatology criteria [8,9] from June 2018 to December 2021 at Ankara University Faculty of Medicine, Department of Pain Medicine. Patients aged 40–80 years with body mass index (BMI) >20 kg/m^2 who underwent intra-articular injection of autologous fat tissue were included in the study. Patients with missing information in follow-up records were excluded. Being younger than the age of 40, acute knee pain, severe neurological and psychiatric disorders, other tissue diseases affecting the knee, anticoagulant therapy, malignant disease, corticosteroid therapy, and previous knee surgeries were also exclusion criteria. Patients were suffering from mild to severe knee osteoarthritis. The lipoaspiration procedure was performed with a blunt cannula (with a 1 mm tip attached to a 60 ml Luer-Lock syringe) inserted through a skin incision to harvest adipose tissue from the abdomen, according to the Coleman technique under local anesthesia and intravenous sedation with 0.01 mg/kg midazolam.[10] Preoperative antibiotic prophylaxis was performed with 1 g cefazolin. The patient was monitored for vital signs. The surgical site was injected with a solution including lidocaine hydrochloride and epinephrine. The lipoaspirate (a mean volume of 35–40 ml) was centrifuged at 3000 rpm for four minutes to collect the fat phase. Throughout the procedure, adipose tissue was subjected to only slight mechanical forces, with no detrimental effects. After decantation and separation of the liquid component, the middle-fat layer was retained for intra-articular injection, and the hematologic phases were discarded. The procedure was completed with an intra-articular injection of fat tissue. With the lateral approach, the osteoarthritic knee joint was injected with 7 to 10 ml autologous fat tissue volume, which did not produce high pressure inside the joint and pain due to the tension of the joint capsule.

The procedure was fast, safe, and did not require stem cell expansion or manipulation. After the procedure, patients were prescribed oral antibiotics and local cold application was recommended for pain.

Table 1. Demographic and clinical characteristics of patients

Parameters	Data (n)	Minimum–Maximum
Total number of patients		
Gender	165	
Female	103 (62.4%)	
Male	62 (37.6%)	
Age (year)	61.28±11.4	(40–80)
Weight (kg)	75.05±11.3	(50–115)
Height (meter)	169.19±9.3	(150–189)
Body mass index (kg/m^2)	26.23±4.49	(23.01–43.70)
Smoking		
Yes	81 (49.1%)	
No	84 (50. 9%)	
Knee osteoarthritis stage (Kellgren–Lawrence)		
I	17 (10.30%)	
II	58 (35.15%)	
III	64 (38.78%)	
IV	26 (15.75%)	
Disease duration (year)	7.86 ± 4.83	(1–20)
Side of the affected knee		
Right knee	27 (16.4%)	
Left knee	10 (6.06%)	
Bilateral knees	128 (77.6%)	
Medication		
Paracetamol (number of patients/mg)	101/913.03±663.5	
Tramadol (number of patients/mg)	130/50.60±128.67	
Other NSAIDs (number of patients)	86	

NSAIDs: Nonsteroid antiinflammatuar drugs. The data represent the mean value±the standard deviation.

Demographic data and the clinical characteristics of the patients, procedure-related adverse events and complications (such as bleeding and infection), pain evaluation, stiffness and knee functions, pre-procedure and post-procedure analgesic use were recorded. Patients' functionality and pain were evaluated at baseline and 1, 3, 6, and 12 months after the intervention. The radiological classification was made according to the K-L scales. The intensity of pain was measured with the Visual Analog Scale (VAS) score (from 0=no pain to 10=worst pain).[11] The functional capacity of patients was assessed with WOMAC and OKS scores.[12,13] WOMAC is a 24-item questionnaire and consists of 3 subscales: pain, joint stiffness, and functional status (pain 0–20, stiffness 0–8, physical function 0–68). All questions are graded on a Likert scale between 0–4. Higher scores on the WOMAC indicate worse pain, stiffness, and functional limitations. OKS is a 12-item questionnaire. Each question has 5 categories of answers corresponding to a score of 0 to 4. The overall score ranges from 0 (worst) to 48 (best).

The retrospective analysis of the patient data was approved by the Ethics Committee of Ankara University Faculty of Medicine (protocol number: I10-652-21, December 2, 2021) and the study was in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

IBM SPSS Statistics for macOS, Version 28.0.1.0 was used for data analysis. Data were presented as mean±SD and minimum–maximum or number and percentage (n, %) as appropriate. Wilcoxon test for non-parametric variables was used to compare pre-injection to post-injection values. The correlation was checked with a Spearman rank-order correlation.

Table 2. K-L stages and mean OKS values at 12 months follow-up

K-L stage (n)	Baseline	M1	M3	M6	M12	p
I (17)	39.70±3.15	46.17±2.27	46.35±1.83	47.05±1.88	43.70±1.68	<0.001
II (58)	32.10±5.64	41.05±5.01	42.25±4.19	41.17±4.05	37.67±4.02	<0.001
III (64)	20.85±5.00	30.46±5.19	32.54±4.76	30.79±4.78	26.87±4.64	<0.001
IV (26)	9.76±1.79	16.38±1.57	15.07±1.62	13.46±1.33	10.11±1.27	0.112
Total (165)	25.00±10.29	33.79±10.60	34.83±10.86	33.9±11.02	29.76±11.0	<0.001

OKS: Oxford Knee Score. Analysis conducted with the Wilcoxon test and Friedman Test.

Table 3. K-L stages and WOMAC total scores at 12 months follow-up

K-L stage	Baseline WOMAC	M1	M3	M6	M12	p 0–1M.	p 0–3 M.	p 0–6 M.	p 0–12 M.
I	31.56±3.71	21.1±2.99	16.08±3.99	18.78±4.71	20.12±4.22	<0.001	<0.001	0.028	<0.001
II	52.10±8.37	37.7±8.77	32.36±8.06	38.44±8.47	41.04±9.23	<0.001	<0.001	<0.001	<0.001
III	65.87±11.5	48.96±11.03	43.33±10.9	50.24±11.65	54.61±13	<0.001	<0.001	<0.001	<0.001
IV	86.76±7.29	79.07±9.62	72.36±10.4	77.76±9.66	79.48±9.7	0.131	0.258	0.237	0.349
Total	60.79±17.8	45.3±16.26	39.6±15.8	45.61±16.5	49.57±18.5	<0.001	<0.001	<0.001	<0.001

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. The data represent the mean value [standard deviation]. Analysis conducted with Wilcoxon test and T- test.

Table 4. K-L stages and VAS scores at 12 months follow-up

K-L stage	Baseline	M1	M3	M6	M12	p
I (17)	6.47±1.12	4.88±0.99	3.11±0.85	3.52±0.87	3.41±0.9	<0.001
II (58)	7.51±1.12	5.34±1.16	3.68±1.06	3.98±0.82	4.06±0.81	<0.001
III (64)	7.73±1.22	5.23±0.97	4.06±0.90	4.57±0.98	5.17±1.04	<0.001
IV (26)	8.69±0.92	7.69±1.12	7.03±1.03	7.80±1.16	7.76±0.99	0.078
Total (165)	7.67±1.26	5.30±1.07	3.98±1.10	4.45±1.16	4.85±1.39	<0.001

VAS: Visual Analog Scale. The data represent the mean value (standard deviation). Analysis conducted with Wilcoxon and Friedman test.

T-test was used to analyze the changes in the time for the paired data. We used the Friedman test to compare the severity changes in time. A probability of $p<0.05$ was considered statistically significant.

Results

The mean age of 165 participants (62 males and 103 females) included in the study analysis was 61.28±11.4 years. The mean BMI was 26.23±4.49. Sixty-nine patients had normal weight (BMI 20–24.9), 76 patients had overweight (BMI≥25), and 20 patients were obese (BMI>30). The period of osteoarthritis disease ranged between 1 and 20 years. Demographic data and clinical characteristics of the patients are shown in Table 1.

The affected knees were mostly bilateral, 128 (77.6%), then the right knee, 27 (16.4%), and the left knee, 10 (6.06%). Only one knee was followed up as an index knee. The medications used were tramadol (n=130), paracetamol (n=101), and other NSAIDs (n=86). Eighty-one patients were using the combination of tramadol and paracetamol.

A significant improvement ($p<0.001$) was observed in the mean VAS, WOMAC, and OKS index of patients with K-L grade I-III osteoarthritis during 12 months follow-up, as shown in Tables 2, 3, and 4.

The total WOMAC score and pain, function, and stiffness subscores were statistically significantly different from baseline at any follow-up period for patients

Table 5. Comparison of VAS, WOMAC, OKS related variables between baseline and 12-months follow-up

Clinical score	Baseline	M1	M3	M6	M12	p
VAS						
Female (103)	7.66±1.25	5.18±1.03	3.96±1.11	4.49±1.12	4.87±1.37	<0.001
Male (62)	7.69±1.28	5.51±1.12	4.03±1.11	4.38±1.23	4.82±1.43	<0.001
Total (165)	7.67±1.26	5.30±1.07	3.98±1.10	4.45±1.16	4.85±1.39	<0.001
WOMAC pain						
Female (103)	13±3.02	10.37±2.31	8.11±2.94	10.23±3.03	10.91±3.1	<0.001
Male (62)	13.46±2.91	11.12±2.27	8.87±2.45	11.01±2.30	11.6±2.50	<0.001
Total (165)	3.18±2.98	10.6±2.32	8.40±2.78	10.52±2.80	11.19±2.9	<0.001
WOMAC stiffness						
Female (103)	4.85±1.82	2.82±1.65	1.36±1.48	1.83±1.79	2.58±2.20	<0.001
Male (62)	4.56±1.70	2.80±1.46	1.14±1.10	1.54±1.36	2.17±1.84	<0.001
Total (165)	4.74±1.78	2.81±1.58	1.28±1.36	1.72±1.65	2.43±2.08	<0.001
WOMAC function						
Female (103)	40.18±14.14	30.46±13.28	27.91±12.65	31.16±13.5	31.7±13.4	<0.001
Male (62)	41.09±13.03	31.75±13.05	29.37±12.62	32.33±12.5	33.2±12.9	<0.001
Total (165)	40.52±13.70	30.95±13.17	28.46±12.62	31.60±13.1	32.2±13.2	<0.001
WOMAC total score						
Female (103)	60.37±18.53	44.60±16.68	38.89±16.09	44.96±17.3	49.1±19.1	<0.001
Male (62)	61.49±16.6	46.46±15.60	40.96±15.34	46.69±15.1	50.5±17.4	<0.001
Total (165)	60.79±17.81	5.30±16.26	39.67±15.80	45.61±16.5	49.6±18.5	<0.001
OKS						
Female (103)	26.58±10.34	35.16±10.58	36.02±10.79	34.54±11.0	30.9±11.1	<0.001
Male (62)	22.38±9.71	31.51±10.31	32.85±10.75	31.46±10.83	27.8±10.7	<0.001
Total (165)	25.0±10.29	33.79±10.60	34.83±10.86	33.38±11.2	29.7±11.0	<0.001

VAS: Visual Analog Scale.; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; OKS: Oxford Knee Score. The data represent the mean value (standard deviation). Analysis conducted with the Friedman test.

with K-L grade I-III osteoarthritis (p<0.001). Table 5 presented the female and male patients' mean VAS, WOMAC, and OKS values before and after intra-articular autologous fat injection, separately. Gender and smoking did not affect the results (p>0.05).

Knee swelling was seen in 19 patients one week after injection and 3 patients reported the feeling of being unable to move their knee freely, but this symptom waned one month after the intervention.The total WOMAC score and OKS values showed a statistically significant negative correlation at all follow-up periods, as shown in Table 6.

While a statistically significant positive correlation was found between BMI and total WOMAC scores (p<0.001), there was a negative correlation between BMI and OKS index (p<0.001). There was a statistically significant decrease in the paracetamol and tramadol doses at the end of 12 months. Doses of paracetamol were 913.03±663.5 mg/day - 747.87±603.7 mg/day (p<0.001) before and after the intervention, doses of tramadol were 150.60±128.67 mg/day - 119.09±116.43 mg/day before and after the intervention (p<0.001). The number of patients who continued to use NSAIDs after the intervention was 55 (p<0.001).

Discussion

The present retrospective study concluded that patients with K-L grade I-III osteoarthritis treated with intra-articular injection of autologous fat tissue showed significant improvement in mean VAS, WOMAC, and OKS values at 1st, 3rd, 6th, and 12th months compared to baseline. The efficacy of the procedure was limited in severe disease, and there

Table 6. Correlation of total WOMAC and OKS score

Months	WOMAC total	OKS	Correlation coefficient	p
Baseline	60.79±17.8	25.0±10.3	-0.705	<0.001
1.	45.30±16.3	33.79±10.6	-0.693	<0.001
3.	39.67±15.8	34.83±10.9	-0.688	<0.001
6.	45.61±16.5	33.38±11.2	-0.688	<0.001
12.	49.6±18.5	29.7±11.0	-0.714	<0.001

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; OKS: Oxford Knee Score. Spearman's correlation.

was no statistically significant improvement in VAS, WOMAC, and OKS values of patients with K-L grade IV osteoarthritis. Male and female gender did not affect the results. There was a positive correlation between increased disability and BMI. In this study, adipose tissue was not processed to separate mesenchymal stem cells during the intervention. The adipose tissue was separated from the hematological phase in an easy, accessible, single step by centrifugation in a closed system. After 12 months follow-up, there was a statistically significant decrease in the drug consumption of the patients. The results of the current study suggested that autologous fat tissue injections were effective and safe treatment methods in patients with grade I-III knee osteoarthritis for the long- and short-term.

With aging, the ability of chondrocytes to regenerate decreases, and progressive cartilage loss develops on the joint surface over time with the reduction of the extracellular matrix.[14] Spontaneous healing of cartilage damage is difficult because the vascularization of the cartilage tissue is weak and bone marrow progenitor cells do not have direct access to the cartilage damage. In addition, knee joint cartilage is exposed to catabolic reactions and inflammatory processes due to various cytokines released from synovium or chondrocytes.[15] Treatments such as hyaluronic acid or PRP (Platelet-Rich Plasma) injections reduce symptoms but cannot prevent the cartilage degeneration process. Mesenchymal stem cells (MSCs) capable of secreting trophic factors for differentiation and regeneration into cartilage are required for cartilage repair and can be isolated from adipose tissue.[16] It's thought that injection of intra-articular fat tissue managed the structural and biochemical changes in the cartilage with trophic and immunomodulatory mechanisms.[17]

The repair mechanism was not entirely clear. The study of Moshref et al. [18] with 80 patients reported that patients treated with an injection of nonprocessed autologous adipose tissue showed a lubricating and healing effect on the osteoarthritic joints, and patients showed significant improvement in VAS and WOMAC scores at 3, 6, and 12 months with significant pain reduction and increased mobility. In various studies, especially with MSCs, the long- and short-term efficacy and safety of intra-articular adipose tissue injection have been reported.[4] Russo et al.[19] evaluated the 1-year safety and outcome of a single intra-articular injection of autologous and micro-fragmented adipose tissue in 30 patients. They found no major complications, and the majority of the patients significantly improved in clinical condition compared to baseline. On the other hand, Panchal et al.[20] conducted a study with patients with K-L grade 3 and 4 osteoarthritis (in the late stage), and 17 patients showed significant improvements in pain and functional outcome measures at 12 months compared to baseline with no serious adverse effects. Instead, Bakowski et al.[5] concluded in their study with 37 patients that patients with knee osteoarthritis stage II benefited more from autologous intra-articular adipose tissue injection than patients with stage IV. Interestingly, they also stated that although the results reached the level of statistical significance, no clinically significant improvement was observed in the follow-up without categorizing them according to the stage of progression of osteoarthritis. Results of another microfragmented adipose tissue series (n=110 knees) showed the patients' VAS, OKS, and EQ-5D scores all improved to a statistically significant degree at 12 months follow-up.[21] In Hudetz and Boric's study, which differed from previous studies with a long clinical follow-up of up to 24 months, it was reported that VAS scores were significantly reduced at 12 and 24 months in 32 knees after intra-articular

injection of microfragmented adipose tissue. They also found an increased level of cartilage glycosaminoglycan (GAG) content on MRI.[22] Catteneo et al.[23] retrospectively analyzed the safety and efficacy of autologous adipose tissue injection as an adjuvant in the arthroscopic treatment of degenerative knee chondropathy and concluded a significant improvement in all clinical scores at 1, 3, 6, and 12 months. Adriani et al.[24] suggested that intraoperative use of autologous and nonmanipulated fat could provide a potential regenerative and biomechanical benefit in the treatment of knee osteoarthritis and showed a decrease in patients' VAS and WOMAC scores (including subscores of pain, joint stiffness, and function) after 12 months of follow-up compared to baseline. Similar to our studies, in contrast to prior adipose-derived stem cell therapies, adipose tissue was not processed to separate mesenchymal stem cells, and therefore potentially supportive biomechanical functions of the fat tissue were retained in addition to ASCs.[24] In all previous studies, the short-term and long-term treatment results of adipose tissue injections (with or without manipulation or processing methods), whether applied as adjuvant or primary treatment, have been positive. Adipose tissue is an important source of mesenchymal stem cells. In accordance with the literature, our study also showed that patients with K-L grade I-III osteoarthritis treated with intra-articular injection of autologous fat tissue (nonprocessed/manipulated) showed significant improvement in mean VAS, WOMAC, and OKS scores at 1st, 3rd, 6th, and 12th months. The use of autologous and nonmanipulated fat offered a simple, rapid, inexpensive option with low morbidity for use in outpatient settings. No significant improvement was observed in the VAS, WOMAC, and OKS values of patients with K-L grade IV osteoarthritis during the follow-up period.

Sometimes, young people may develop knee osteoarthritis earlier than usual because of trauma or increased load on the joints due to obesity or high BMI.[5] While 47% of the patients were over 65 years of age, 46.06% were overweight and 12% were obese in our study. There was a positive correlation between disability and increased BMI. Four patients had a degenerative process that developed after trauma. In addition, there was no significant effect of gender and smoking on the results. Our results also showed a statistically significant decrease in the patients' daily doses of paracetamol and tramadol after 12 months follow-up, and there was a statistically significant reduction in the number of patients who continued to use NSAIDs after the intervention.

The first-choice diagnostic method for knee osteoarthritis is direct radiography, which may be insufficient in some cases; therefore, magnetic resonance imaging (MRI) is preferred in patients with instability of the knee that indicates meniscal or ligament damage. However, there is no general agreement on when the regenerative chondral response becomes morphologically noticeable on MRI evaluation. Lee et al.[25] could not find significant cartilage regeneration in MRI at 6 months after the intra-articular injection of autologous adipose tissue-derived MSCs for the treatment of knee osteoarthritis. Unfortunately, we could not follow the patients' response to treatment with knee MRI evaluation. Some authors stated that it would be appreciable at least 24 months after the treatment unless studied by miniaturized MRI equipment.[26,27]

The proliferation and differentiation abilities of MSCs in adipose tissue may be limited and result in insufficient healing in advanced osteoarthritis cases. In our study, there was a statistically significant improvement in pain and disability scores in patients with K-L stage III osteoarthritis, but this improvement did not occur in patients with K-L stage IV. In contrast, Hudetz reported improvement in pain and clinical symptoms after intra-articular fat tissue injection in 85% of patients with stage III and IV knee osteoarthritis who were candidates for total knee replacement surgery.[28] Although studies report a successful outcome of mesenchymal stem cell treatment in late-stage knee osteoarthritis, before the intervention, patients should be informed about the adverse events and the limited capabilities of intra-articular fat tissue injection to avoid dissatisfaction. It should be known that total knee arthroplasty treatment might not be prevented in a knee with severe arthritis.[23]

The most common complications after the intra-articular injection are pain and swelling of the treated knee, but this improves after cold compression and paracetamol. In addition, abdominal discomfort due to lipoaspiration and knee pain or stiffness related

to injection may occur during the first 2–4 weeks. Increased arthralgia after the procedure could be attributed to the inflammatory response and the volume effect of injectate.[29] Bistolfi et al.[3] also have shown that intra-articular autologous and micro-fragmented adipose tissue injection in patients with knee osteoarthritis was not associated with any adverse events, including chondrotoxicity. No cases of cancer developing after adipose tissue intra-articular injection have been reported.[30] In our study, 3 patients had temporary knee stiffness, and knee swelling was observed in 19 patients after injection. In accordance with the literature, no long-term major complications (hematoma, infection) were observed in the patients.

Limitations

The retrospective nature and absence of a control group were the limitations of the present study. The VAS, WOMAC, and OKS values of the patients were compared before and after the procedure; therefore, the control group was not needed. Since the lack of information in patient records would increase over time, the follow-up period could not be extended to 24 months and was limited to one year. In addition, as in previous studies, we could not follow the participants with control knee MRI evaluation. Another limiting factor is the small sample size. Studies with larger sample sizes are needed to reach more reliable conclusions and make recommendations.

Conclusion

In conclusion, intra-articular fat tissue injection offers a new, one-step, easily accessible, non-surgical treatment of degenerative knee osteoarthritis. It has been proven safe and potentially effective. The main finding of this study was that a single intra-articular injection of nonmanipulated autologous fat tissue in patients with knee K-L grades I-III osteoarthritis reduced knee pain and stiffness, and improved function. The degeneration ability of this procedure was limited in severe diseases. The first goal of knee osteoarthritis treatment was to reduce the patient's pain and maintain functionality. In addition, no serious side effects were observed in our patients. Although further studies would be needed on this subject, we thought that intra-articular adipose tissue injection therapy could improve the quality of life in suitable patients.

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