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Case Report
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Adipose Tissue Injections for Severe Hip Osteoarthritis: A Case Series

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Abstract

Objectives: Adipose tissue is a source of Mesenchymal Stem Cells (MSCs), which have primarily been evaluated for treatment of knee Osteoarthritis (OA). The purpose of this study was to evaluate the effect of adipose tissue hip injections at reducing pain and improving function in severe hip OA, and to assess for adverse effects.

Case Report: Five patients (5 male, mean age 59.9 ± 5.9 years) with hip pain attributed to severe OA, and who had failed conservative management, underwent adipose cell harvesting followed by an ultrasound-guided adipose tissue injection into the affected hip joint. Pain and quality of life were assessed at baseline, and at 1-, 3-, 6-, 12-, and 24-months post-injection, using a Visual Analog Scale (VAS) and the International Hip Outcome Tool-12 (iHOT-12). VAS scores improved at all follow-up visits, with the greatest improvement noted at 3 months post-injection. iHOT-12 scores progressively increased throughout follow-up, corresponding to a poorer quality of life. Two participants had consultations with an orthopedic surgeon during follow-up, and one underwent a Total Hip Arthroplasty (THA). There were no significant adverse effects noted as a result of the injection.

Discussion: Hip injections with adipose tissue appear to be safe and to improve pain in severe hip OA, with maximum improvement noted at 3 months post-injection. However, quality of life scores progressively worsened post-injection and one participant ultimately underwent a THA. Future studies comparing intraarticular hip injections of adipose tissue to other substances will help further elucidate their long-term efficacy at treating symptoms associated with hip OA.

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Introduction

Hip Osteoarthritis (OA) is a condition resulting from intraarticular cartilage loss and affects approximately 1 in 4 individuals throughout their lifetime [1-4]. Hip OA is typically characterized by pain localized to the hip or groin, and can be severely debilitating [2]. The condition is often classified using the Kellgren and Lawrence (K&L) grading system, which assigns a score of 0-4 based on the amount of cartilage loss seen on X-ray [5]. Management typically starts with non-operative measures consisting of activity modification, oral pain medications and physical therapy [3,4]. However, significant proportions of individuals are refractory to these treatments and necessitate more invasive interventions, which typically begin with a Corticosteroid Injection (CSI). CSIs have been found to reduce pain due to hip OA for up to 3 months [3,4]; however, they are associated with adverse effects, including elevations in blood sugar, and worsening of arthritis [4,6-8]. Furthermore, CSIs do not treat the underlying cause of hip OA, and research has found that approximately 1 in 10 individuals will ultimately undergo a Total Hip Arthroplasty (THA) [1,2]. Given the drawbacks of CSIs and the high risk of requiring an operative intervention for end-stage OA, intraarticular injections of substances other than corticosteroid have been evaluated as a potential alternative non-operative means of managing hip OA, though they have not shown significant success. Viscosupplementation of the hip joint with Hyaluronic Acid (HA) has not been found to be more successful at relieving pain compared to intraarticular saline [9,10]. Intraarticular hip injections of Platelet-Rich-Plasma (PRP) have not been found to be more effective than HA [4,11-13]. Lastly, injections of NSAIDs directly to the hip joint have not been found to be more successful than injections of corticosteroids [8]. A substance that has not been extensively studied for injection into the hip joint is adipose tissue. Adipose tissue is often harvested from the abdomen and contains Mesenchymal Stem Cells (MSCs), which have been shown *in vitro* to have the ability to mature into

different types of cells based on the stimuli to which they are exposed [4]. As such, unlike other substances used for intraarticular injections, adipose tissue has the theoretical potential to slow the progression of OA instead of solely treating pain. Furthermore, injections of bone marrow concentrate, which contains MSCs, into the knee joint have shown promise at treating pain associated with knee OA [14], and have not been associated with any significant adverse effects [15]. When evaluating the use MSCs for the hip, research performed in dogs has shown that intraarticular injections of adipose-derived MSCs improved quality of life at 6 months post-injection and were not associated with any adverse effects [16]. Limited research in humans with mild-moderate OA found that adipose-derived MSC injections into the hip were associated with improvement in pain and function at the 6-month mark with no adverse effects [3]. However, this data is based on a small study population (n=6) with only mild-moderate OA, and there is a lack of data regarding outcomes beyond 6 months post-injection. The purpose of this case series was to evaluate the effects of intra-articular hip injections with adipose tissue in reducing pain and improving function in patients with severe hip OA at various intervals up to 2 years post-injection, as well as to evaluate for adverse effects.

Case Presentation

Patient's ≥ 18 years of age who presented to our outpatient sports medicine clinic with hip pain secondary to severe OA were considered for inclusion into the study. Patients had to have completed a minimum of 6 weeks of conservative management, including physical therapy, weight loss, activity modification, or oral anti-inflammatory medication. Furthermore, patients were required to have had at least one intraarticular hip injection of corticosteroid with little to no sustained effect. Exclusion criteria included having taken an anti-inflammatory medication within 14 days of study entry, having taken an anti-rheumatic disease medication within 3 months of study entry, or having received an injection of any substance to the treated hip within 2 months of study entry. Patients were not considered for inclusion into the study if they were pregnant, breast-feeding, or carried any of the following diagnoses: A systemic rheumatic or inflammatory disease of the joint, an ongoing infectious disease, diabetes mellitus, cancer, or a clinically significant cardiovascular, renal, hepatic, or endocrine disease. Lastly, participants were required to have not participated in a study of an experimental drug or medical device within 30 days of study entry. Consent and IRB approval were obtained through Stanford University. Patients who enrolled in the study completed the following baseline assessments: (1) a visual Analog Scale (VAS) measuring average pain and peak pain during the past week on a scale from 0 to 10 (with higher scores correlating with increased pain levels), and (2) International Hip Outcome Tool-12 (iHOT-12) questionnaire designed to measure health-related quality of life, consisting of 12 questions scored from 0 to 10 (with higher scores correlating with poorer health-related quality of life) with the final score calculated as the sum of each question [17]. Patients then underwent autologous adipose cell harvesting from the abdomen at our outpatient clinic. A qualitative analysis of the adipose cells was performed before undergoing MSC isolation using a centrifugation system. A qualitative analysis of the MSC isolate was then performed. The patient then received an injection of the adipose-derived MSC isolate into the affected hip joint, along with 5 mL of 1% lidocaine, 40 mL of 0.9% sterile saline, 0.4 mL of 4.2% bicarbonate, and 1:100,000 epinephrine, using a standardized ultrasound-guided technique by the same physician. Following the injection, the patients were instructed to undergo a period of relative rest for 1 week in conjunction with range of motion exercises, followed by a gradual increase in activity level that progressed to normal daily activity at week 3. Patients were then followed up at 1-, 3-, 6-, 12-, and 24 months post-injection, at which time they repeated the VAS and iHOT-12. Patients were advised that they could drop out of the study at any point, including if they did not receive optimal pain relief and wanted to seek other treatments. A total of 5 participants met inclusion criteria for the study and agreed to participate. All participants were male, mean age was 59.9 years (range 52-67), and all participants had grade 4 OA (K&L classification) at the time of their injection, indicative of severe OA (Table 1). All participants completed baseline assessments. One participant was lost to follow-up at 1 month, one participant was lost to follow-up at 6 months, and one participant was lost to follow-up at 12 months. Two participants completed the full 24 months of follow-up. When evaluating baseline VAS pain assessments, mean VAS scores were 6.0 (average pain) and 7.0 (peak pain) (Table 2). These values improved at all follow up visits, with the most significant improvement noted at 3 months post-injection (mean average pain of 2.5, peak pain of 3.5). Similarly, participants noted the greatest percentage improvement in their pain at 3 months post-injection (mean of 61.25% improvement). When evaluating iHOT-12 assessments, the baseline mean score was 37.6. Scores at follow up were higher at all visits, with the highest mean iHOT-12 score being 85.9 at 24-months post-injection (Table 3). One participant underwent a THA during the follow up period, which was performed at 19 months post-injection. Of the remaining four participants, one had a consultation with an orthopedic surgeon due to ongoing pain from hip OA, but ultimately did not undergo a surgical intervention. One participant reported an adverse reaction post-injection, as he endorsed severe pain radiating from his affected hip to his anterior thigh several hours after returning home from his injection. However, the symptoms resolved with over-the-counter analgesics. Otherwise, no adverse events were reported by any patient during the 2-year follow up period.

Table 1: Demographics.

Participant	Age	Gender	K&L grade
1	58.2	M	4
2	67.3	M	4
3	62.2	M	4
4	54.3	M	4
5	52.6	M	4
Mean	**58.9**		

Abbreviation: K&L: Kellgren and Lawrence

Discussion

We found that intra-articular hip injections with adipose tissue for severe hip OA improved pain up to 2 years post-injection, with the greatest improvement noted at 3 months post-injection. The participants who completed the full 2 years of follow-up noted approximately 50% improvement of their pain at 12- and 24-months post-injection. These findings are notable given that all individuals had severe hip OA at the time of their injection and had previously failed conservative management, including a CSI. However, we noted the opposite trend with the iHOT-12 questionnaire as patients noted the best health-related quality of life at baseline, with a general trend of worsening quality of life as time elapsed. Ultimately, one participant underwent a THA, which occurred 19 months post-

Table 2: VAS pain data.

Participant	Baseline		1MO			3MO			6MO			12MO			24MO		
	Avg Pain	Peak Pain	Avg Pain	Peak Pain	% Imp	Avg Pain	Peak Pain	% Imp	Avg Pain	Peak Pain	% Imp	Avg Pain	Peak Pain	% Imp	Avg Pain	Peak Pain	% Imp
1	10	10	6	8	20	3	3	60	3	4	75	3	4	50	5	5	40
2	4	6	4	4	70	2	4	75									
3	4	5	2	7	10	2	4	50	5	5	0						
4	7	7	3	4	50	3	3	60	3	3	60	3	3	60	4	3	50
5	5	7															
Mean	**6**	**7**	**3.75**	**5.75**	**37.5**	**2.5**	**3.5**	**61.25**	**3.67**	**4**	**45**	**3**	**3.5**	**55**	**4.5**	**4**	**45**

Abbreviations: VAS: Visual Analogue Scale; MO: Month; % Imp: Percent Improvement

Table 3: iHOT-12 data.

Participant	Baseline	1MO	3MO	6MO	12MO	24MO
1	23.4	50.8	85.3	69	80.7	69.7
2	48.3	77.9	89.4			
3	46.1	43.5	38	43.9		
4	35.1	92.1	95	92.1	90.9	102.1
5	35.1					
Mean	**37.6**	**66.1**	**76.9**	**68.3**	**85.8**	**85.9**

Abbreviations: iHOT-12: International Hip Outcome Tool-12; MO: Month

injection. Notably, we saw no significant adverse events associated with adipose tissue injections into the hip, in conjunction with prior research [3,15]. Limitations of this study include the small sample size, the limited percentage of participants who completed the full 24 months of follow up, and the lack of a control group. Future prospective studies comparing intraarticular hip injections of adipose tissue to other substances will help further elucidate the long-term effects of adipose tissue injections at reducing pain and improving function in individuals with severe hip OA.

Conclusion

Based on results from a small cohort, intraarticular hip adipose tissue injections may improve pain in patients with severe osteoarthritis up to two years post-injection. These injections do not appear to be associated with any significant adverse effects.

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