Intra-articular Fat Derived Stem Cell Injections Effect On Pain, Stiffness, And Function In Osteoarthritis

AnMed Health Family Medicine Residency Program

William Gasque, MD; Christopher Clemow, MD; Joel E. Williams, MPH, PhD; Mark Cromer, BS

PRISMA HEALTH SM

Introduction

Osteoarthritis (OA) is one of the most common chronic diseases and a major cause of disability, with an estimated knee OA prevalence between 12-35%. Pharmacologic therapies used for OA include analgesics, NSAIDs, steroid injections, Platelet Rich Plasma (PRP), viscosupplementation, and surgery/joint replacement. Unfortunately, current treatments are limited by: addiction, temporary relief, potential adverse effects, and limited research on efficacy. Additionally, standard treatments target symptom management rather than the underlying pathophysiology of OA. Mesenchymal stem cells (MSCs) have known potential for developing osteogenic and chondrogenic cell lines. Adipose-derived stem cells (ASCs) are considered the MSC source of choice based on practicality, easy access, and simple harvesting procedure. Adipose tissue samples contain 100-fold more MSCs (ASCs) than identical bone marrow samples. Highly beneficial characteristics of MSCs are their non-immunogenic profile and immunomodulatory properties. MSCs also release bioactive substances and stimulate growth factor production which provide a rich environment to support and sustain local tissue regeneration. Clinical studies have indicated that MSCs are capable of stimulating chondrocyte proliferation and extracellular matrix (ECM) synthesis. Other studies evaluated the use of concomitant PRP intra-articular injection with MSCs in knee OA which showed promising functional and radiographic improvements. The current research is still relatively new with many of the studies being rated as low quality or having small sample sizes. More studies and data are needed to clarify the efficacy of adipose derived MSC injections regarding improvement in pain, function, and stiffness.

Purpose

1. To analyze the impact of fat derived MSC injections (SCI) using a Lipogems technique on pain, stiffness, and function associated with OA.
2. To evaluate trends in pain medication usage, Kellgren-Lawrence (KL) scales, and correlation with leukocyte-poor PRP (lp-PRP) injections.

Method

A prospective observational study using questionnaires and WOMAC Scores at 1 month before SCI, 1 month after SCI, and in the recent month. 52 patients were treated with fat derived SCI, with/without a 1-2 week post lp-PRP injection. We used a Within-Subject Repeated Analysis of Variance (ANOVA) where time (**Pre-SCI**, **Post-SCI**, **Recent**) was the within-subject factor and WOMAC scores for Pain, Stiffness and Function were the outcomes of interest. Alpha was set at (.05). A Greenhouse-Geisser and Bonferroni correction was applied to protect the family wise error rate for multiple comparisons.

Patient Population:		
Patient Population:	62	
Number of Responses:	52	
Average Age (years):	69.97	Min: 43, Max: 85
Number of Injections:	86	Location: 79 knees, 4 shoulders, 1 hip, 2 ankles Indication: 80 for OA, 2 for OA and Torn Meniscus, 2 for post traumatic arthritis, 2 for psoriatic arthritis
Average KL Score:	2.9	
Patients with Post lp-PRP injections	26	Injections: 44
Average Months on Recent Survey:	9.07	Min: 3, Max: 23

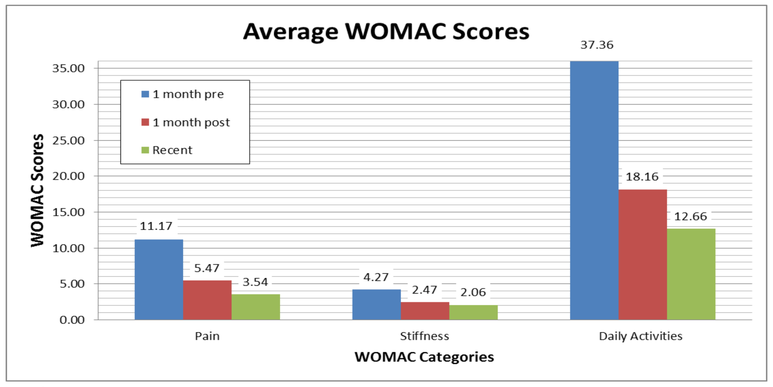
Results

WOMAC Score Summary			
	Pain	Stiffness	Activities
# of Categories	5	2	17
Maximum Scores	20	8	68

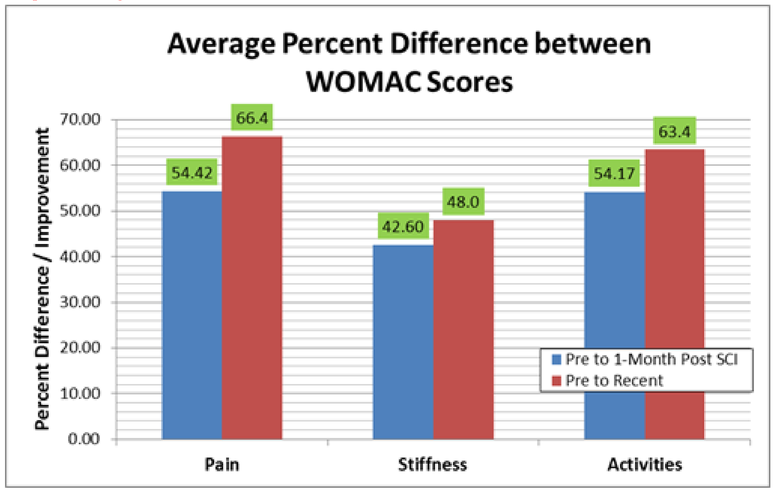
Table 1: WOMAC Scoring Guide

Post Hoc Tests Using Bonferroni Correction			
SCI Comparison	Pain	Stiffness	Activities
Pre vs Post	11.18 ± 4.54 vs 5.30 ± 4.44 p = 0.000	4.28 ± 2.02 vs 2.38 ± 2.03 p = 0.000	37.32 ± 16.31 vs 17.63 ± 14.44 p = 0.000
Post vs Recent	5.30 ± 4.44 vs. 3.55 ± 3.38 p = 0.002	***2.38 ± 2.03 vs. 2.06 ± 1.90*** ***p = 0.250***	17.63 ± 14.44 vs. 12.70 ± 11.65 p = 0.003
Pre vs Recent	11.18 ± 4.54 vs 3.55 ± 3.38 p = 0.000	4.28 ± 2.02 vs 2.06 ± 1.90 p = 0.000	37.32 ± 16.31 vs 12.70 ± 11.65 p = 0.000

Table 2: Post Hoc Testing Using Bonferroni Correction comparing Pain, Stiffness, and Activities



Graph 1: Average WOMAC Scores



Graph 2: Average Percent Difference between WOMAC Scores

Comparing Womac Scores between Pre-Injection and Recent	Number of Injections	% of injections
Pain scores that worsened	2	2.33%
Pain scores that did not change	4	4.65%
Pain scores that improved	80	93.02%
Stiff scores that worsened	6	6.98%
Stiff scores that did not change	13	15.12%
Stiff scores that improved	67	77.91%
Activity scores that worsened	3	3.49%
Activity scores that did not change	2	2.33%
Activity scores that improved	81	94.19%

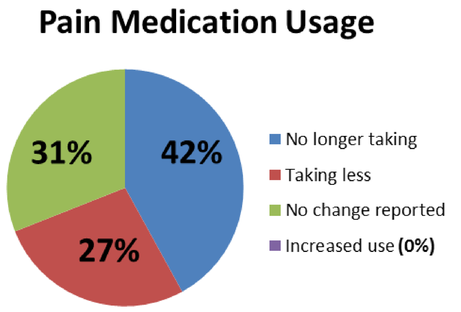
Table 3: Overall Change in Pain, Stiffness, and Function between Pre SCI and Recent Scores

Recent WOMAC Scores								
Months since SCI	Number of Injections		Average Percent Difference (%) between Pre and Recent					
			Pain	Stiff	Activities			
3	2							
4	15	27	64.5	52.5	60.3			
5	10							
6	7							
7	3							
8	5	32	64.8	39.2	58.7			
9	8							
10	9					Average % excluding 2 outliers at 22 and 23 months		
						Pain	Stiff	Activities
11	5							
12	1							
13	10							
14	2							
15	2	27 (25)	61.2	42.4	60.6	72.5	49.5	74.8
17	1							
18	1							
20	2							
22	1							
23	2							

Table 4: Average Percent Difference between Pre SCI and Recent Scores divided into time line since the SCI

Kellgren-Lawrence Score	# of Knee Injections	Average Pre-SCI Score			Average % Difference b/w prior & recent		
		Pain	Stiffness	Activities	Pain	Stiffness	Activities
1	2	11	4	45	72.7	50.0	73.3
2	18	10.3	3.7	34.6	78.3	55.4	75.8
3	39	11.2	4.0	38.2	64.9	40.8	64.2
4	18	11.5	5.1	36.3	54.6	49.4	49.7

Table 5: Average Percent Difference between Pre SCI and Recent Scores divided into the severity of the OA based on Kellgren-Lawrence Scores



Graph 3: Pain Medication use between Pre SCI and Recent Scores

Injections that were NOT for Knee OA only	Months since SCI and Recent Womac Scores	Percent Difference b/w prior and recent		
		Pain	Stiff	Activities
Knee with psoriatic arthritis	7	100.00	100.00	100.00
Knee with psoriatic arthritis	7	100.00	100.00	100.00
Knee with OA and torn meniscus	5	92.31	62.50	96.30
Knee with OA and torn meniscus	9	92.86	66.67	86.54
Shoulder with OA	8	100.00	100.00	100.00
Shoulder with OA	4	76.00	50.00	73.49
Shoulder with OA	9	100.00	100.00	100.00
Shoulder with post traumatic arthritis	8	75.00	83.33	84.44
Ankle with post traumatic arthritis	13	75.00	12.50	50.00
Ankle with post traumatic arthritis	4	100.00	100.00	100.00
Hip with OA	4	83.33	100.00	80.23
Average	7.09	90.41	79.55	88.27

Table 6: Average Percent Difference between Pre SCI and Recent Scores among injections that were not for Knee OA only

Discussion

Results showed statistically significant reduction in scores for **Pain**, **Stiffness**, and physical **Function** between **Pre-SCI** and **Post-SCI**. Score reductions continued from **Post-SCI** to the **Recent** survey but were significant in **Pain** and **Function**. These reductions occurred while patients also reported decreased pain medication usage. The percent change remained consistent from 3 months to 2 years. Benefits appeared to extend to various msk conditions although more data is needed for these groups. Less severe OA (< 4 KL) appeared to have greater improvement in **Pain** and **Function**. No significant difference was found in those receiving lp-PRP after SCI. The primary areas of potential bias/confounders include historical recall which is more prone to ascertainment, a varied timeline, and varied pain medication usage. Areas of improvement include a larger patient population, a control/comparison group, a longer timeline, and post SCI radiographic comparison.

Conclusion / Significance

The vast majority of patients reported overall improvement in pain, stiffness, and function after receiving SCIs while at the same time reporting decreased pain medication usage. Fat derived SCI appears to be a promising treatment for musculoskeletal pathologies, particularly knee OA. Patients that are without relief from standard therapy, poor candidates for surgery, or requiring frequent pain medication could benefit significantly. With these promising results, additional research is certainly warranted to add to the current data, compare to alternative therapies, and increase the timeline measured.