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Stem Cell Intraarticular Protocol for Knee Injection (SCIPKI)

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Abstract

Osteoarthritis (OA) is a chronic degenerative joint disease that begins in early-to-mid life and progresses with age. Because the baby boomer generation is in their 60s and 70s, the financial burden to provide symptomatic treatment for OA will continue to impose an increasing burden on society unless disease-modifying therapies are developed. Mesenchymal stem cells implantations (MSCs) offer a potential regenerative solution given their ability to differentiate to all tissues within a joint and modulate the local inflammatory response, which support the theoretical premise that MSCs can deter degenerative joint disease.

Purpose: To follow patients who have received MSCs via intervals of 3-month, 6-month, 9-month, and one year after stem cell injection(s).

Objectives: Report pain levels of patients who underwent mesenchymal stem cell (MSC) injections in knees; summarize patients' perceptions of pain prior to and after IA injection, and report patients' deviations from post-procedure instructions.

Sample: One hundred five 105 patients in this clinic receiving (MSC) Intraarticular (IA) joint injections in one or both knees over the period of one year from August 1,2017 to July 30, 2018.

Methods: Data was collected via a retrospective chart review and an electronic survey every 3 months for one year post procedure.

Findings: In this study, there was a significant difference of right knee pain severity between BMI Category 30+ and BMI Category 18.5-24.9.

Keywords: Osteoarthritis, Mesenchymal, Stem cells, Degenerative joint disease, Protocol

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Osteoarthritis (OA) is a chronic degenerative joint disease that begins in early-to-mid life and progresses as we age. Because the baby boomer generation is in their 60s and 70s, the financial burden to provide symptomatic treatment for OA will continue to impose an increasing burden on society unless disease-modifying therapies are developed. The current standard of care includes risk factor identification and modification, pain management therapies, and joint replacement. However, with this population living longer and wishing to live stronger and have an improved quality of life, these modalities will not meet the needs of this population or of society now or in the future (Sierra, Wyles, Houdek, & Behfar, 2015).

Mesenchymal stem cells (MSCs) are used as an optimal regenerative cellular therapeutic for degenerative musculoskeletal conditions like OA (Sampson, Bemden, & Aufiero, 2015; Kim & Koh, 2016). MSCs are found in a variety of tissues and have the ability to rapidly proliferate and differentiate to musculoskeletal lineages including bone and cartilage (Atkinson, 2016). A significant body of research has also demonstrated that these cells orchestrate important immunologic functions through modulation of the local inflammatory response (Glenn & Whartenby, 2014). MSCs Mesenchymal stem cells implantations offer a potential regenerative solution given their ability to differentiate to all tissues within a joint and modulate the local inflammatory response, which support the theoretical premise that MSCs can deter degenerative joint disease (Marędziak, Marycz, Tomaszewski, Kornicka, & Henry, 2016; Rodriguez-Fontan et al., 2017). More recently, Wang et al. (2017, 08) found exosomes from embryonic mesenchymal stem cells are beneficial in the treatment of OA because they balance synthesis and degradation of chondrocyte extracellular matrix. Because MSCs can specialize to all tissues within the joint, this theoretically would enable them to repair lesions (Wang et al., 2017,08).

Treating patients with OA presents a significant challenge for providers because no therapies have demonstrated efficacy in curing or halting OA progression. So a provider toolbox starts with pain management and recommending altered activities that relieves joint stress. This involves weight loss, modifying painful activities, initiating a program of low-impact exercise and stretching, the use of braces or gait aids, and over the counter analgesic medications and creams (Hockberg et al., 2012). When the conservative approach fails, patients may pursue alternative and complementary medicine or they may return to their provider for the second level of care in which a trial of corticosteroid

injections may be pursued. Corticosteroids suppress inflammation and decrease tenderness of the joint by alterations in neutrophil function, stabilization of cellular lysosomal membranes, and alterations in synovial fluid (Bert & Glasser, 2002). Steroid injections are not without drawbacks. They are known to be toxic to chondrocytes and MSCs, thus potentiating OA progression in exchange for temporary pain relief (Wyles et al., 2015). If corticosteroid injections fail to provide relief, then injectable hyaluronic acid preparations may be pursued, although there is no conclusive evidence supporting pain relief or improved function (Rutjes et al., 2012).

The final tool in providers' tool box is a referral to Orthopedic Surgery for an evaluation for total joint replacement. Total joint replacement complications are relatively rare but still exist, prosthetic joints cannot match the functionality of a native joint and falls short of demand (Lozito, Kolf &Tuan, 2009; Goldenberg, Mello, & Asensi, 2017). Clearly, there is a substantial unmet need for this chronic disease that would benefit greatly from disease-modifying therapy (Sierra, Wyles, Houdek, & Behfar, 2015, 08).

This is an opportunity for an alternate treatment, which is mesenchymal stem cells introduced via intra-articular injections (Jo et al., 2014; Jo et al., 2017, 07). Because of their proliferation, differentiation, and immunomodulatory capacity, MSCs are a potential therapeutic tool for treating osteoarthritis, as well as other chronic orthopedic diseases (Bauge & Boumediene, 2015; Marędziak et al., 2016).

Purpose

The purpose of this study was to follow patients via electronic survey who received MSCs via intervals of 3-month, 6-month, 9-month, and one year after stem cell injection(s). Because this is a relatively new and untested treated, it was important to ascertain the effectiveness and duration of this new treatment. More important, because standards have not yet been developed, it was important to determine if hypothesized post-procedure instructions were indicated and helpful. It was further determined that the ability of patients to understand and follow these instructions were extremely important. During the clinic visit, patients were recruited for the survey and given standard post-procedure instructions. Those instructions were developed as a result of phone interactions with clinic managers locally and nationally. After University Institutional Review Board (IRB) review and clinic consent by owners, this was approved as an expedited study.

Objectives

In order to develop an initial MSC IA (knee) protocol, it was important to obtain baseline pain scores on first clinic visit, and to electronically collect data at regular intervals for the first year after MSC injections in one or both knees. Demographic data included age; gender; BMI; initial pain score; OA location, OA grade for each knee injected. OA was graded by physical examination and radiographic interpretation determined by the APRN training in orthopedics. Validity of OA grade was established with two physicians who independently graded OA via weight bearing knee radiographs (xrays) using anterior/posterior and lateral technique. Results were compared to the APRN results. There was an overall agreement of 92%, which this inter-rater reliability was deemed acceptable for this study, and the APRN was deemed qualified to grade OA.

The objectives of this study were three-fold as follows:

1) report initial pain levels of patients who underwent MSC injections in one or both knees

2) summarize patients' perceptions of pain prior to and after IA injection

3) report patients' deviation(s) from post-procedure instructions.

Sample

Total patients seen in this clinic during this time period for joint injections were 198 individual patients. Of those 198, 93 patients excluded from the study. Of those 93 patients, 67 received similar injections in other major joints; another 26 participants who received knee injections lacked a personal email address or reported they were unable to maneuver online surveys. The sample size consisted of 105 patients receiving MSC- IA injections in one or both knees over the period of one year from August 1 to July 30, 2018. They each listed a valid email, and volunteered to participate in the survey.

Methods

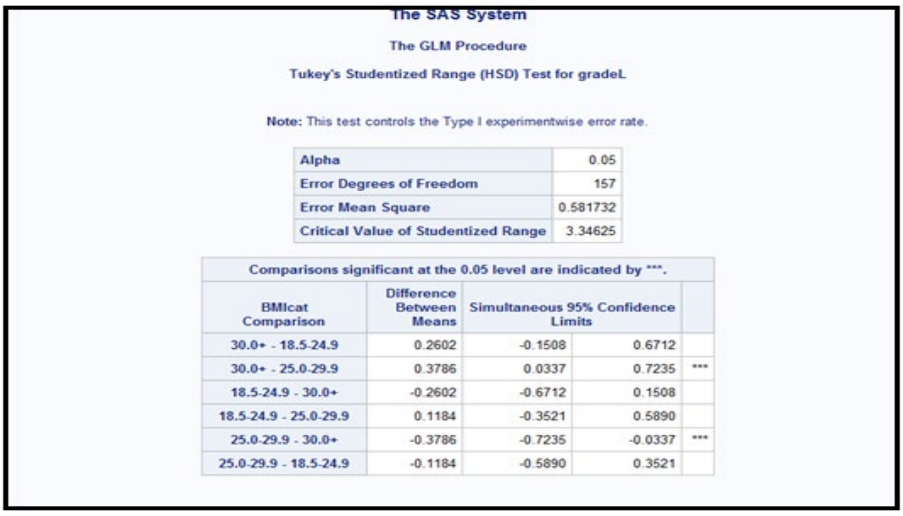
A retrospective chart review to collect demographic data was completed from February – August 2018 monthly after patients were seen in clinic to determine pain levels before and after injection at 3-month intervals for up to one year; patients' perceptions of pain secondary to IA injection, and their perceived deviations from post-procedure instructions and underlying rationale for why they deviated from plan. Because the clinic was newly established, patient volume was slow during the first three months, which resulted in fewer nine months and one year follow-up electronic surveys. The electronic survey was distributed anonymously. The electronic survey method was selected due to patient convenience and the ability to de-identify patients.

Demographic Data on Pain Levels

Of all clinic patients, 35 patients presented with complaint of right knee pain on a scale of 0 being no pain, and 10 being the worst pain imaginable, the right knee mean pain score 7.60; 30 patients presented with complaint of left knee pain with a mean pain score 7.61, and 40 patients presented with complaints of bilateral knee pain with a mean pain score of 7.71. Median age for this sample was 66.7 years, mean weight was 208. 9 pounds, and Body Mass Index (BMI) was 33.6.

Mean pain scores on a scale of 0 being no pain, and 10 being the worst pain imaginable was 7.6. Of the 105 patients, 87 patients presented with bilateral knee pain. Of those 87 patients, BMI category 18.5 – 24.9 yielded 9 patients; 25.0 – 29.9 had 27 patients, with 51 patients falling into the 30.0+ BMI category. Those 87 patients were included in both left and right knee pain scores. This profile matched most patients seen in this clinic presenting with complaints of knee pain.

Multivariate statistics were calculated using SAS® with General Linear Modeling (GLM) procedure using Tukey's Studentized Range (HSD) Test. Results indicate there a significant difference of right knee pain severity between BMI Category 30+ and BMI Category 18.5-24.9. There is also a statistically significant difference of left knee pain severity between BMI Category 30+ and BMI Category 25.0-29.9. See Tables 1 and 2.



The SAS System

The GLM Procedure

Tukey's Studentized Range (HSD) Test for gradeL

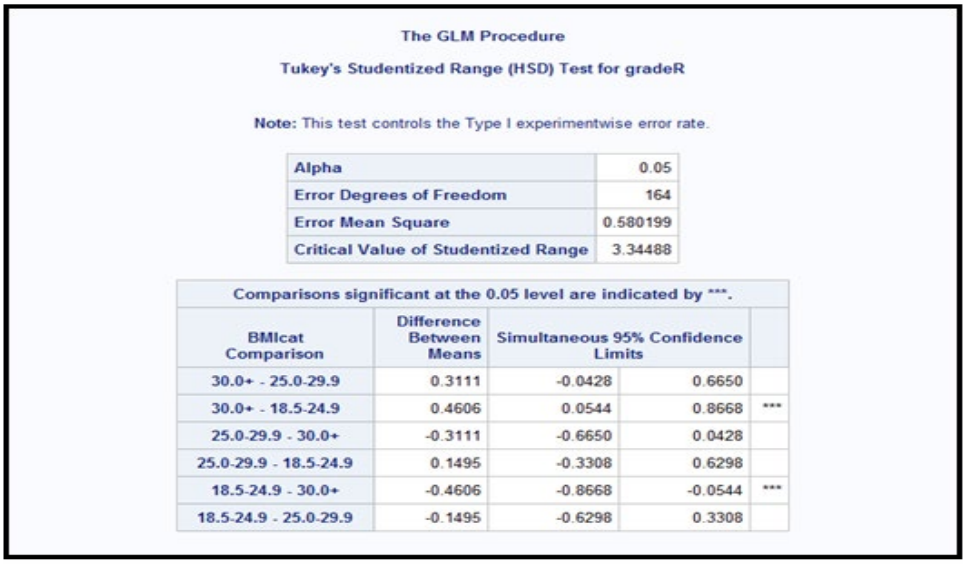
Note: This test controls the Type I experimentwise error rate.

Alpha	0.05
Error Degrees of Freedom	157
Error Mean Square	0.581732
Critical Value of Studentized Range	3.34625

Comparisons significant at the 0.05 level are indicated by ***.

BMIcat Comparison	Difference Between Means	Simultaneous 95% Confidence Limits		
30.0+ - 18.5-24.9	0.2602	-0.1508	0.6712	
30.0+ - 25.0-29.9	0.3786	0.0337	0.7235	***
18.5-24.9 - 30.0+	-0.2602	-0.6712	0.1508	
18.5-24.9 - 25.0-29.9	0.1184	-0.3521	0.5890	
25.0-29.9 - 30.0+	-0.3786	-0.7235	-0.0337	***
25.0-29.9 - 18.5-24.9	-0.1184	-0.5890	0.3521	

Table 1 : BMI and Severity of Pain - Left Knee



The GLM Procedure

Tukey's Studentized Range (HSD) Test for gradeR

Note: This test controls the Type I experimentwise error rate.

Alpha	0.05
Error Degrees of Freedom	164
Error Mean Square	0.580199
Critical Value of Studentized Range	3.34488

Comparisons significant at the 0.05 level are indicated by ***.

BMIcat Comparison	Difference Between Means	Simultaneous 95% Confidence Limits		
30.0+ - 25.0-29.9	0.3111	-0.0428	0.6650	
30.0+ - 18.5-24.9	0.4606	0.0544	0.8668	***
25.0-29.9 - 30.0+	-0.3111	-0.6650	0.0428	
25.0-29.9 - 18.5-24.9	0.1495	-0.3308	0.6298	
18.5-24.9 - 30.0+	-0.4606	-0.8668	-0.0544	***
18.5-24.9 - 25.0-29.9	-0.1495	-0.6298	0.3308	

Table 2 : BMI and Severity of Pain – Right Knee

Caution should be used when interpreting small data sets, but from this demographic data, it appears that weight categories of overweight and obese both indicate an increase in patients' reported pain levels prior to injection.

Online Survey Results

Demographic data was analyzed for the participants of the survey. Because it was anonymous, it was not possible to denote patients' time period since injection. Therefore, it was examined collectively. Fifty-seven patients responded to part or all survey questions. Of the 57 respondents, 42.9% (24) were male, and 57.1% (32) were female. Seven respondents had their left knee injected, 11 had their right knee injected, but the majority (67.9%) 38 patients had both knees injected. Respondent age ranges are seen in Table 3.

Range	Percent	Number
21-29	1.8%	1
30-39	0.0%	0
40-49	1.8%	1
50-59	14.0%	8
60-69	49.0%	28
70-79	28.1%	16
80-89	3.5%	2
90-99	0.0%	0
90-99	1.8%	1
TOTAL	100%	57

Table 3: Survey Respondents' Ages by Range

Patients' Perceptions of Pain

It was not possible to correlate prior to and after injection pain levels by patient due to confidentiality and anonymity of the survey. However, a review of the retrospective data yielded a mean pain level of 7.6/10 for all 105 patients seen prior to or at the time of injection. The range of pain levels reported for the 57 respondents prior to having the injection was 0-10; a median score of 5.0/10, and a mean pain level score 5.89/10, both statistically significant P<.001 . Using the universal pain scale for adults, pain scores as self-reported at a level of 7.6 would indicate severe to very severe pain and a definite need for pain management. A mean pain medication. See figure 1 to illustrate correlation of pain level to severity of pain (McCaffery and Beebe, 1989).

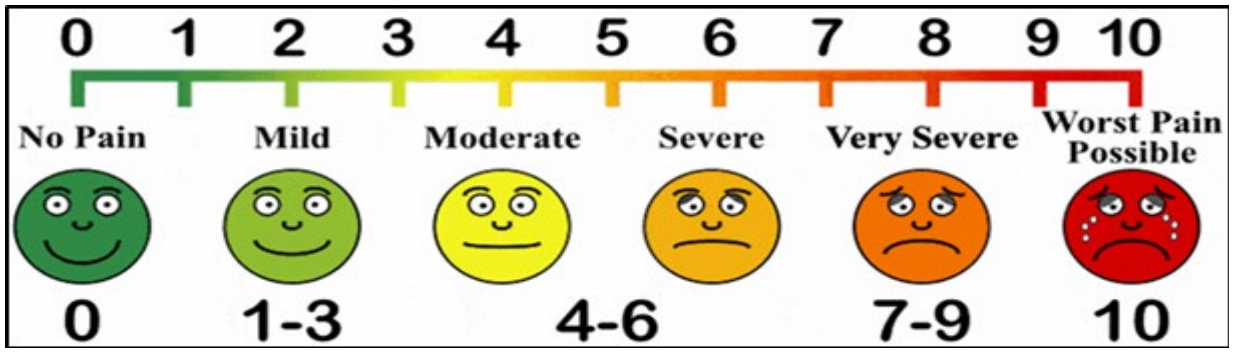


Figure 1: Universal Pain Scale and Scores

Self-reported pain levels after the injection(s) via survey results indicated a range of 1-9 for the 57 respondents, a median pain score 3.0 and an overall mean score 3.63. By self report, the pain score levels decreased from 5.89 to 3.63, which with note to the small sample size, p<0.001.

Deviations from Instructions

Forty-five percent of patients reported they deviated from the post-procedure instructions. The most common deviation selected was taking NSAIDS within 8 weeks after procedure. Follow-up phone interviews revealed they felt they had waited long enough after four weeks. With further conversation, the patients reported they relied on NSAIDS – and felt that because many surgery post-operative restrictions lasted for six weeks, they felt 4-6 weeks was adequate. However, six patients reported they had reduced the amount and frequency of NSAIDS. They attributed this to the previous clinic visit where they received education about medications commonly used to treat OA.

Limitations

The limitation most noticed in this study was the inability to survey patients without anonymity. Second, the sample size was adequate for the number of survey questions, but the return rate was 54% which was marginal at best. Third, 'pain score severity recall' accuracy is most valid within 24 hours of pain onset, and has been established in the literature for decades (McCaffery & Beebe, 1989). However,

retrospective self-reports of pain are not as reliable, so patients may have under-reported or over-reported their pain levels at the initial clinic visit or online at 3, 6, 9, or 12 months post-procedure. Four, pain is subjective and therefore it is not possible to 'measure' each person's pain comparatively. Fifth, it may have been better to track 15 patients over the year, and conduct phone interviews instead of online methods, because it was noted that the more elderly patients were more likely not to have a personal email, use email, or be computer literate. Last, the purpose of this study was to use actual patients' information to create an IA Knee MSC Protocol.

Development of IA Knee MSC Protocol

From the experience of patient interaction before, during, and the MSC IA injection procedures, an exhaustive literature search and multiple phone calls to similar clinics, an initial data collection assessment tool was developed to guide practice to establish a standard method of patient interview and examinations. See figure 2.

PATIENT NAME:	DOB: AGE:	
CHIEF COMPLAINT:		
HISTORY OF PRESENT ILLNESS:		
PAST MEDICAL HISTORY: PAST SURGICAL HISTORY:		DRUG ALLERGIES
FAMILY HISTORY:	SOCIAL HISTORY:	

REVIEW OF SYSTEMS		
SYSTEM	PATIENT DENIES: □	PATIENT REPORTS: □
Constitutional □	Recent illness, fever; NSAIDS, aspirin, warfarin, fish oil use ~ 24 hours	
HEENT	Altered taste, smell, vision; sore throat, gingivitis, or nosebleeds	
Respiratory □	Respiratory infections, asthma, chest congestion, wheezing, cough, frequent sneezing	
CV	Chest pain, palpitations, tachycardia, edema in extremities, anemia	
GI	Stomach pain, cramps, constipation, GERD, gas, bloating, N/V	
GU	Cancer, prostate problems, hematuria, pyuria	
Hematology/Lymph	Lymphadenopathy, excessive bruising, fatigue, anorexia	
Skin	Scrapes, wounds, lesions or injuries, hair loss, numbness/tingling	
Neuro	Migraines, headaches, tinnitus, slurred speech	
Psychiatric	Depressed mood, anxiety, mood swings, irritability, memory loss, confusion	
Musculoskeletal	Joint pain, muscle pain, chronic pain, muscle aches, arthritis	Joint pain: _____

□ HOME MEDICATIONS REVIEWED WITH PATIENT

MEDICATION INSTRUCTIONS: Continue all home medications / Do not take NSAIDS for 8 weeks / Consult your PCP before stopping medication

PHYSICAL EXAMINATION

Vital Signs: T ____ (° F) **BP**____ / ____ **HR** ____ **RR** ____ **Ht.** _____ **Wt.** _____ **Current Pain Level** ___/10

EXAM	NORMAL □	ABNORMAL □
Constitutional	Well nourished, in no acute distress	
HEENT/Lymph	PERRLA, conjunctiva clear. Pharynx pink. Uvula midline. Neck non-tender to palpation; thyroid non-palpable. Neck supple.	□Lymphadenopathy; □ ear, □ eye, □ nasal drainage; □ sinus tenderness, □ lid ptosis
Respiratory	Eupneic, lungs clear to auscultation, bilaterally, posteriorly	
CV	Heart tones S1S2; regular rate, rhythm; peripheral pulses present /4.	□Rub □murmur o □extra systole □ carotid bruits present
GI	Abdomen soft, non-tender to light palpation, bowel sounds present	
Skin	Intact; injection site soft, clean with minimal hair. Injection site with skin intact	□wound □scrape □rash □bite □lesion □cellulitis □ecchymosis at site
Neuro	PERRLA, smile symmetric, CN grossly intact. Oriented time, place, and person. Grips equal, strong.	
Psychiatric	Bright affect, conversational, memory intact, has insight	
Musculoskeletal	Shoulders symmetric, full ROM Knees symmetric, full ROM Hips laterally symmetric, full ROM Ankles symmetric, full ROM Gait normal, toes forward	**Knee** □ **Left** □ limited ROM < 80° flexion < 180 °extension □ effusion □ crepitus □ click □ **Right** □ limited ROM < 80° flexion < 180 °extension □ effusion □ crepitus □ click **Hip** □ **Left** □ limited ROM <30° adduction <45 ° abduction □ click □ **Right** □ limited ROM <30° adduction <45 ° abduction □ click□ **Gait** □ antalgic □ ataxic □ steppage □ Valgus □ Varus □N/A, immobile □ wheelchair
DTRs upper DTRs lower Muscles	Grade □ 3/4 □ 4/4 Grade □ 3/4 □ 4/4 Grade □ 4/5 □ 5/5	ABSENT Grade □1/4 □2/4 ABSENT Grade □1/4 □2/4 Grade □ 0 □1/5 □2/5 □3/5

X-ray: A/P bilateral knees weight bearing taken on ____/ ____/ _____ reviewed.
IMP: □ Osteoarthritis Right knee: Grade 1 / 2 / 3 / 4 Osteophytes □ Yes □ No □ Osteoarthritis Left knee: Grade 1 / 2 / 3 / 4 Osteophytes □ Yes □

Figure 2: Data Collection Initial Visit

Figure 2 Data Collection Initial Visit

The post-procedure instructions were developed first. They were reviewed with patients at the initial visit, before the procedure, and after the procedure. Family members were typically present during the post-procedure instructions. After reviewing the literature, collecting data over one year, and analyzing results of this small study, the following post-procedure protocol was introduced and was called the Stem Cell Intraarticular Protocol for Knee Injection (SCIPKI). See Table 4.

Before Procedure (at time of initial interview):

1. If you are taking blood thinners, consult with the ordering physician prior to scheduling procedure. Do **NOT** discontinue any blood thinner without consent of ordering physician.

2. Wear loose fitting clothing so the joint/site is easily accessible.

3. Do NOT take non-steroidal anti-inflammatory drugs **(NSAIDS)** for at least **3 days** prior to procedure and for **8 weeks** after your procedure. This includes over-the-counter and/or prescription drugs:

Aspirin Aleve Advil Celecoxib (Celebrex) Ibuprofen, Tab-Profen, Vicoprofen (Motrin), Meloxicam (Mobic) Naproxen (Anaprox, Naprelan, Naprapac) Ketorolac (Toradol) Diclofenac (Cataflam, Voltaren, Arthrotec Difunisal Dolobid) Indomethacin (Indocin, Indo-Lemmon, Etodolac (Lodine) Fenoprofen (Nalfon)	Flurbirofen (Ansaid) Ketroprofen (Orovail) Mefenamic Acid (Ponstel) Nabumetone (Relafen) Oxaprozin (Daypro) Piroxicam (Feldene) Sulindac (Clinoril) Indomethagan) Tolmetin (Tolectin)

4. Do **NOT** take these natural remedies for at least **3 days** prior to and for **8 weeks** after the procedure:

Aloe Curcumin Turmeric Fish Oil Green tea Ginger Noni Flax Oil Cod Liver Oil	Alpha-Lipoic Acid Astaxanthin Spirulina Resveratrol Walnut Oil Goji Berries Omega-3 supplements

Day of Procedure:

1. You may be sore today; this is normal.
2. The numbing agent will wear off in 1-2 hours.
3. DO NOT APPLY **ICE** TO injection site.

At Home Instructions:

1. You may use Tylenol for pain relief. Do not exceed 3,000 mg in any 24 hour period.
2. Do not use NSAIDs for **8 weeks** after the procedure. See list above.
3. DO NOT apply ice to injection site(s) for **8 weeks**.
4. Refrain from high impact activities for **2 weeks.** (EX: Jumping, jumping jacks, squat jumps, ANY jumps).
5. You may continue all other activities and may be weight bearing in supportive shoe gear.

CALL THE OFFICE IF YOU EXPERIENCE excessive pain, redness, swelling in the area of the procedure.

Table 4: Pre and Post-procedure Instructions

The combination of a thorough history and physical examination of patients prior to determining if they are suitable candidates for this procedure is essential, and thorough post-procedure instructions are essential for continued success with MSC IA injections in knees. In addition, a quick protocol is necessary to determine if patients are good candidates for this procedure. See table 5 for an example of initial questions.

Stem Cell Intraarticular Protocol for Knee Injection (SCIPKI)			Points	SCORE	Notes
1. Have you been evaluated and participated in physical therapy?	Yes		3	3	
	No	Go to No. 2	0		
Was it helpful?	Yes		3	3	
	No		1		
2. Have you used opioids for OA pain?	Yes		3		
	No		1	1	
3. Do you currently take opioids?	No	Go to No.4	1	1	
	Yes		3		
Are you under a pain contract?	Yes		3		Request a copy of pain contract
	No		1	1	
Do you see a pain specialist?	Yes		3		Notify pain specialist prior to procedure
	No		1	1	
4. Have you seen an orthopedic surgeon?	Yes		3		Note othopedic surgeon's name, clinic address
	No	Go to No. 6	1	1	If grade 3- 4, recommend an orthopedic consult prior to MSCs
5. If so, what was the recommendation?	Knee surgery	STOP	0		Refer to orthopedic surgeon for surgery
	Diabetes Mellitus Type II		-2		Careful history of HgA1Cs; continue medications day of surgery
	Weight loss		-1		>30 BMI, weight management prior to injection; >25 <30 continue
	Increase exercise		-1		Reinforce this; continue if no other STOPS
	Stop smoking		-1		Evaluate smoking history, educate, offer smoking cessation program
	Palliative treatment		2		If so, continue if no STOPS no matter score
6. Have you had an injection of steroids in the past 3 months?	Yes	STOP	0		Establish return visit 3 months' after steroid
	No		2	2	
7. Do you take any form of anticoagulant to protect you from heart attack?	Yes	STOP	0		Refer to Primary Care Provider for clearance to stop anticoagulant for 3 days prior to procedure
	No		2	2	
8. Do you have an artificial heart valve requiring anticoagulants?	Yes	STOP	0		Refer to cardiology for clearance to stop anticoagulant for 3 days prior to procedure
	No		2	2	
9. Have you had a pulmonary embolus requiring anticoagulation?	YES	STOP	0		Refer to pulmonology for clearance to stop anticoagulant for 3 days prior to procedure
	No		2	2	
10. Are you allergic to lidocaine, novacaine, or any other medication.	Yes		2		Careful patient history; note on record to avoid.
	No		1	1	Note on record
			TOTAL POINTS	20	≥20: Proceed if no STOPS
			15- 19: Proceed with education/evaluation of patient if no STOPS		
			< 15: Review notes, history, physical exam, xrays, determine plan		
			STOPS = Do not schedule; refer and reschedule when consult complete		

Table 5: Stem Cell Intraarticular Protocol for Knee Injection (SCIPKI)

Conclusion

It is not unexpected that patients who have BMIs calculated as 'obese' experience faster joint deterioration secondary to the increase work placed on the joints to sustain mobility. However, baseline data collected on 105 patients indicated statistically significant relationships between BMI and grade of OA in overweight and obese patients, which was unexpected. From this information, it may be most important to stress weight management along with activity to patients who are 'just a few pounds' overweight. Another take recommendation is to stress the importance of BMI calculations at every clinic visit. Tell the patient what it is. In the day of Internet accessibility, BMI may make more impact on them than their weight in pounds.

Survey results indicate patients' satisfaction with results at 3-month, 6-month, and 12-month follow-up survey responses with 78% of all patients reporting overall satisfaction with less knee pain after the injections. Patients' perception of pain after IA injection(s) was significant P<.001 in this sample .

MSCs are effective for one year post-IA injection, and most patients are satisfied with the results. More rigorous and cautionary patient education regarding the effect of NSAIDS on MSCs is needed prior to, immediately after, and weekly to minimize the effects on MSCs on the clinical outcomes is needed. This study will build on current knowledge to determine long term effects pain after MSC injections in patients with osteoarthritis of the knee.

This study was concluded after the first year because of the enormity of data collected, time spent in such activities, and participation waned during the last month of survey distributions. According to patients' feedback that they felt one follow-up survey was adequate.

References

1. Atkinson, K. (2016, 11). The mesenchymal stem cell, the mesenchymal stromal cell, and the mesenchymal stromal cell exosome. The Biology and Therapeutic Application of Mesenchymal Cells, 1-7. doi:10.1002/9781118907474.ch1

2. Baugé, C., & Boumédiene, K. (2015). Use of Adult Stem Cells for Cartilage Tissue Engineering: Current Status and Future Developments. Stem Cells International, 2015, 1-14. doi:10.1155/2015/438026

3. Bert, J. M., & Gasser, S. I. (2002, 11). Approach to the osteoarthritic knee in the aging athlete: Debridement to osteotomy. Arthroscopy: The Journal of Arthroscopic & Related Surgery, 18(9), 107-110. doi:10.1053/jars.2002.36513

4. Glenn, J. D. (2014). Mesenchymal stem cells: Emerging mechanisms of immunomodulation and therapy. World Journal of Stem Cells, 6(5), 526. doi:10.4252/wjsc.v6.i5.526

5. Goldenberg, R., Mello, D., & Asensi, K. (2017). Mesenchymal Stem/Stromal Cells from Adult Tissues. Mesenchymal Stromal Cells as Tumor Stromal Modulators, 39-63. doi:10.1016/b978-0-12-803102-5.00002-1

6. Hochberg, M. C., Altman, R. D., April, K. T., Benkhalti, M., Guyatt, G., Tugwell, P. (2012, 03). American College of Rheumatology 2012 recommendations for the use of nonpharmacologicaland pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care & Research, 64(4), 465-474. doi:10.1002/acr.21596

7. Jo, C. H., Lee, Y. G., Shin, W. H., Kim, H., Chai, J. W., Jeong, E. C., . . . Yoon, K. S. (2014, 04). Intra-Articular Injection of Mesenchymal Stem Cells for the Treatment of Osteoarthritis of the Knee: A Proof-of-Concept Clinical Trial. Stem Cells, 32(5), 1254-1266. doi:10.1002/stem.1634

8. Jo, C. H., Chai, J. W., Jeong, E. C., Oh, S., Shin, J. S., Shim, H., & Yoon, K. S. (2017, 07). Intra- articular Injection of Mesenchymal Stem Cells for the Treatment of Osteoarthritis of the Knee: A 2-Year Follow-up Study. The American Journal of Sports Medicine, 45(12), 2774-2783. doi:10.1177/0363546517716641

9. Khorraminejad-Shirazi, M., Farahmandnia, A., & Monabati, A. (2017, 10). Aging and stem cell therapy: AMPK as an applicable pharmacological target for rejuvenation of aged stem cells and achieving higher efficacy in stem cell therapy. Hematology/Oncology and Stem Cell Therapy. doi:10.1016/j.hemonc.2017.08.001

10. Kim, Y. S., & Koh, Y. G. (2016, 05). Injection of Mesenchymal Stem Cells as a Supplementary Strategy of Marrow Stimulation Improves Cartilage Regeneration After Lateral Sliding Calcaneal Osteotomy for Varus Ankle Osteoarthritis: Clinical and Second-Look Arthroscopic Results. Arthroscopy: The Journal of Arthroscopic & Related Surgery, 32(5), 878-889. doi:10.1016/j.arthro.2016.01.020

11. Lozito, T. P., Kolf, C. M., & Tuan, R. S. (2009). Micro environmental Regulation of Adult Mesenchymal Stem Cells. Regulatory Networks in Stem Cells, 185-210. doi:10.1007/978-1-60327-227-8_17

12. Marędziak, M., Marycz, K., Tomaszewski, K. A., Kornicka, K., & Henry, B. M. (2016). The Influence of Aging on the Regenerative Potential of Human Adipose Derived Mesenchymal Stem Cells. Stem Cells International,1-15. doi:10.1155/2016/2152435

13. McCaffery, M., Beebe, A . (1989). Pain: Clinical manual for nursing practice. Mosby St. Louis, MO.

14. Rodriguez-Fontan, F., Piuzzi, et al. (2017, 03). Stem and Progenitor Cells for Cartilage Repair: Source, Safety, Evidence, and Efficacy. Operative Techniques in Sports Medicine, 25(1), 25-33. doi:10.1053/j.otsm.2016.12.005

15. Rutjes, A. W., Jüni, P., Costa, B. R., Trelle, S., Nüesch, E., & Reichenbach, S. (2012, 08). Viscosupplementation for Osteoarthritis of the Knee. Annals of Internal Medicine, 157(3), 180. doi:10.7326/0003-4819-157-3-201208070-00473

16. Sampson, S., Bemden, A. B., & Aufiero, D. (2015, 04). Stem Cell Therapies for Treatment of Cartilage and Bone Disorders: Osteoarthritis, Avascular Necrosis, and Non-union Fractures. PM&R, 7(4). doi:10.1016/j.pmrj.2015.01.023

17. Sierra, R., Wyles, C., Houdek, M., & Behfar, A. (2015, 08). Mesenchymal stem cell therapy for osteoarthritis: Current perspectives. Stem Cells and Cloning: Advances and Applications, 117. doi:10.2147/sccaa.s68073

18. Wang, Y., Yu, D., Liu, Z., Zhou, F., Dai, J., Wu, B., . . . Liu, H. (2017, 08). Exosomes from embryonic mesenchymal stem cells alleviate osteoarthritis through balancing synthesis and degradation of cartilage extracellular matrix. Stem Cell Research & Therapy, 8(1). doi:10.1186/s13287-017-0632-0

19. Wyles, C. C., Houdek, M. T., Wyles, S. P., Wagner, E. R., Behfar, A., & Sierra, R. J. (2014, 09). Differential Cytotoxicity of Corticosteroids on Human Mesenchymal Stem Cells. Clinical Orthopaedics and Related Research®, 473(3), 1155-1164. doi:10.1007/s11999-014-925-y