STEM CELLS: HYPE OR HOPE?

REGENERATIVE MEDICINE FOR YOUR PATIENT

Saunora Prom, DO, CAQSM
WHO AM I?

- Philadelphia College of Osteopathic Medicine
- Riverside Family Medicine Residency
- Osteopathic Manipulation Fellowship
- Sports Medicine Fellowship
- TPMG
OBJECTIVES

• Overview regenerative medicine
• Overview of regenerative procedures
• Overview of stem cells types
• Research review
• Dangers/Side effects
• Case presentations
• Future research
Regenerative medicine: "process of replacing, engineering or regenerating human cells, tissues or organs to restore or establish normal function". This field holds the promise of engineering damaged tissues and organs by stimulating the body's own repair mechanisms to functionally heal previously irreparable tissues or organs.

The regeneration or replacement of cells, tissues or organs to restore or establish normal function.”
The concept of creating irritation or injury to stimulate healing has been recorded as early as Roman times where hot needles were poked into the shoulders of injured gladiators.

_Gua sha_ (Chinese: 刮痧; pinyin: guā shā), meaning "scraping sha-bruises", is a traditional Chinese medical treatment in which the skin is scraped to produce light bruising. Practitioners believe _gua sha_ releases unhealthy elements from injured areas and stimulates blood flow and healing.
There are 3 Different Types of Regenerative Medicine Procedures

- Prolotherapy - 1930
- Stem Cell: Embryonic - 1981
  Bone Marrow - 1990’s
  Adipose - 2000’s
  Amniotic - 2000’s
PROLOTHERAPY

- Injection using irritant solution, typically dextrose.
- Chronic musculoskeletal injuries
- Multiple small injections
- Has been used for 75 years
- Few high quality studies
  "Dextrose Prolotherapy for Knee OA"
Dextrose Prolotherapy for Knee Osteoarthritis: A Randomized Controlled Trial

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ABSTRACT

PURPOSE Knee osteoarthritis is a common, debilitating chronic disease. Prolotherapy is an injection therapy for chronic musculoskeletal pain. We conducted a 3-arm, blinded (injector, assessor, injection group participants), randomized controlled trial to assess the efficacy of prolotherapy for knee osteoarthritis.

METHODS Ninety adults with at least 3 months of painful knee osteoarthritis were randomized to blinded injection (dextrose prolotherapy or saline) or at-home exercise. Extra- and intra-articular injections were done at 1, 5, and 9 weeks with as-needed additional treatments at weeks 13 and 17. Exercise participants received an exercise manual and in-person instruction. Outcome measures included a composite score on the Western Ontario McMaster University Osteoarthritis Index (WOMAC; 100 points); knee pain scale (KPS; individual knee), post-procedure opioid medication use, and participant satisfaction. Intention-to-treat analysis using analysis of variance was used.

RESULTS No baseline differences existed between groups. All groups reported improved composite WOMAC scores compared with baseline status (P < .01) at 52 weeks. Adjusted for sex, age, and body mass index, WOMAC scores for patients receiving dextrose prolotherapy improved more (P < .05) at 52 weeks than did scores for patients receiving saline and exercise (score change: 15.3 ± 3.5 vs 7.6 ± 3.4, and 8.2 ± 3.3 points, respectively) and exceeded the WOMAC-based minimal clinically important difference. Individual knee pain scores also improved more in the prolotherapy group (P = .05). Use of prescribed postprocedure opioid medication resulted in rapid diminution of injection-related pain. Satisfaction with prolotherapy was high. There were no adverse events.

CONCLUSIONS Prolotherapy resulted in clinically meaningful sustained improvement of pain, function, and stiffness scores for knee osteoarthritis compared with blinded saline injections and at-home exercises.

PRP (PLATELET RICH PLASMA)

Consists of drawing blood from a patient and then spinning it down to concentrate platelets and growth factors.

- Plasma makes up the liquid part of human blood, and it contains red cells, white cells, and platelets.
- Play a significant role in blood clotting during an injury and with injury repair.
- Once activated, they start releasing proteins responsible for healing, called Growth Factors.
PRP re-formulated per Indication

- **PRP**
  - Platelets
  - Growth factors
  - WBCs
  - RBCs

- **Uses:**
  - Tendinopathy
  - Ligament and Tendon healing
  - OA
Evidence for use of PRP

- Lateral Epicondylitis: Yes
- RTC Repair: No
- Patellar Tendinopathy: Yes
- Achilles Tendinopathy: No
- Acute Injury: No
- Intra-operatively: No
- Chondral Defects: No
- OA symptoms: Yes
- Muscle regeneration: ?

Level I Evidence
Lateral Epicondylitis

- 3 Largest RCTs showing efficacy greater than corticosteroid and Dry needling
- Not much difference between PRP and autologous blood
- Evidence: LR-PRP
STEM CELLS
MESENCHYMAL STEM CELLS & DIFFERENTIATION

MSC's start from an undifferentiated state and convert into a number of necessary cell types depending on the environment they are placed in.
BONE MARROW DERIVED STEM CELLS

Bone marrow contains a significant amount of the biologic materials necessary for regeneration
• Comes from the patient’s own body
• Bone marrow produces cells that are vital to existence including platelets, white blood cells and red blood cells.
• Three types of adult stem cells in the human body: Blood Components, Lining of the endometrium, and **Mesenchymal Stem Cells**
Get back to doing the things you love, faster & without surgery.

Receive a Regenexx® Patient Info Packet by Email

Your Email

Call 888-525-3005  Are You a Candidate?

Join Us for a Regenexx Webinar!
ADIPOSE ?
AMNIOTIC DERIVED FLUID

- Immunologically Privileged - do not create a rejection reaction

**High Concentration of Stem Cells**
- Full Complement of Growth Factors
- Other biological components include Hyaluronic Acid (joint lubrication) Fibrin & Collagen (scaffold for cellular attachment).
- Anti-inflammatory and Anti-Adhesion Qualities
- Anti-Microbial - minimal infection risk
- No Ethical Concerns - no fetal tissue
- Show benefits for an immense number of medical conditions.
<table>
<thead>
<tr>
<th></th>
<th>Cryopreserved (ReNu)</th>
<th>Dehydrated Suspension Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Morselized cryopreserved amnion and amniotic fluid from the same donor</td>
<td>Morselized sterilized amnion/chorion in saline</td>
</tr>
<tr>
<td>Viable Cells</td>
<td>Yes -MSCs</td>
<td>No live cells</td>
</tr>
<tr>
<td>Growth Factors</td>
<td>Yes</td>
<td>Yes-However some of the growth factors do not survive the drying process</td>
</tr>
<tr>
<td>Storage</td>
<td>Freezer</td>
<td>Shelf Storage</td>
</tr>
<tr>
<td>Processing</td>
<td>GMP Pharmaceutical Grade Manufacturing</td>
<td>GTP Manufacturing</td>
</tr>
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Biologic Treatment is Interactive

KEY ELEMENTS ALL REQUIRED:

- Growth factors, cells, scaffold
- Mechanically favorable environment

A “Nutrient Rich Soup” includes-

- Cells (RBC, white cells, MSC)
- Growth factors (from platelets or plasma)
- Scaffolds

Potential sources of this “Soup”:

- Bone Marrow Aspirate, Amniotic Fluid
Contents in Each Therapy

**PRP (Platelet Rich Plasma)**
- Growth Factors

**BMA (Bone Marrow Aspirate)**
- Growth Factors
- Multipotent Cells

**Amniotic Tissue Graft**
- Growth Factors
- Multipotent Cells
- Scaffold

All three elements are believed to be essential for tissue healing.

**PRP**
1 Element

**BMA**
2 Elements

**Amniotic**
All Elements
Amniotic Derived Stem Cells

- Derived from amniotic fluid obtained during scheduled c-sections from consenting donors
- Amniotic fluid surrounds fetus during pregnancy, feeding it.
- Normally, this fluid is simply discarded
- Researchers have discovered that amniotic fluid has an extremely high concentration of stem cells.
- Higher volume than bone marrow in adults
- Amniotic stem cells are actually immunopriviliged, so they do not create a rejection reaction when injected into a patient.
MESENCHYMAL STEM CELLS IN PARTIAL MENISECTOMY

Adult Human Mesenchymal Stem Cells Delivered via Intra-Articular Injection to the Knee Following Partial Medial Meniscectomy; Vangsness et al

- This was the first randomized, doubleblind, controlled study to evaluate the safety, regenerative effects, and clinical outcomes of human mesenchymal stem cells delivered by intra-articular injection into the human knee. The results demonstrated that high doses of allogeneic mesenchymal stem cells can be safely delivered in a concentrated manner to an enclosed space (knee-joint capsule) without abnormal tissue formation.
- Overall, the study injections were well tolerated. There were no adverse events that led to treatment discontinuation or study termination.
- The results of this study suggest that mesenchymal stem cells have the potential to improve the overall condition of the knee joint.
- Here, controlled data in an exploratory study showed that some patients had an increase in meniscal volume, particularly at one year, indicating de novo tissue regeneration. Preclinical studies have suggested that mesenchymal stem cells may promote tissue regeneration through mesenchymal stem cell adherence, production of trophic factors, extracellular matrix deposition, and differentiation into meniscal cells, all of which may contribute to tissue regeneration. A higher proportion of those with osteoarthritic changes experienced a reduction in pain following the treatment with mesenchymal stem cells.

Increased meniscal volume in post-meniscectomy patients who received adult MSC injections into the knee.
Adult human mesenchymal stem cells delivered via intra-articular injection to the knee following partial medial meniscectomy: a randomized, double-blind, controlled study.

Vangness CT Jr, Farr J, Boyd J, Dellaero DT, Mills CR, LeRoux-Williams M.

Abstract

BACKGROUND: There are limited treatment options for tissue restoration and the prevention of degenerative changes in the knee. Stem cells have been a focus of intense preclinical research into tissue regeneration but limited clinical investigation. In a randomized, double-blind, controlled study, the safety of the intra-articular injection of human mesenchymal stem cells into the knee, the ability of mesenchymal stem cells to promote meniscus regeneration following partial meniscectomy, and the effects of mesenchymal stem cells on osteoarthritic changes in the knee were investigated.

METHODS: A total of fifty-five patients at seven institutions underwent a partial medial meniscectomy. A single superolateral knee injection was given within seven to ten days after the meniscectomy. Patients were randomized to one of three treatment groups: Group A, in which patients received an injection of $50 \times 10^6$ allogeneic mesenchymal stem cells; Group B, $150 \times 10^6$ allogeneic mesenchymal stem cells; and the control group, a sodium hyaluronate (hyaluronic acid/hyaluronan) vehicle control. Patients were followed to evaluate safety, meniscus regeneration, the overall condition of the knee joint, and clinical outcomes at intervals through two years. Evaluations included sequential magnetic resonance imaging (MRI).

RESULTS: No ectopic tissue formation or clinically important safety issues were identified. There was significantly increased meniscal volume (defined a priori as a 15% threshold) determined by quantitative MRI in 24% of patients in Group A and 6% in Group B at twelve months post meniscectomy ($p = 0.022$). No patients in the control group met the 15% threshold for increased meniscal volume. Patients with osteoarthritic changes who received mesenchymal stem cells experienced a significant reduction in pain compared with those who received the control, on the basis of visual analog scale assessments.

CONCLUSIONS: There was evidence of meniscus regeneration and improvement in knee pain following treatment with allogeneic human mesenchymal stem cells. These results support the study of human mesenchymal stem cells for the apparent knee-tissue regeneration and protective effects.

TRIAL REGISTRATION: ClinicalTrials.gov NCT00225095.
INTRA-ARTICULAR MSC INJECTION FOR KNEE OA

- Journal Transplantation, April 2015
- Prospective Randomized Trial for Knee OA
- Allograft MSC vs Hyaluronic Acid injected in knee
- One year follow up
- MSC patients improved clinical outcomes, including pain vs. HA
- MSC patients showed actual IMPROVEMENT in cartilage quality and quantity on MRI vs. HA
Treatment of Knee Osteoarthritis With Allogeneic Bone Marrow Mesenchymal Stem Cells: A Randomized Controlled Trial.


Author information

Abstract

BACKGROUND: Osteoarthritis is the most prevalent joint disease and a common cause of joint pain, functional loss, and disability. Conventional treatments demonstrate only modest clinical benefits without lesion reversal. Autologous mesenchymal stromal cell (MSC) treatments have shown feasibility, safety, and strong indications for clinical efficacy. We performed a randomized, active control trial to assess the feasibility and safety of treating osteoarthritis with allogeneic MSCs, and we obtain information regarding the efficacy of this treatment.

METHODS: We randomized 30 patients with chronic knee pain unresponsive to conservative treatments and showing radiological evidence of osteoarthritis into 2 groups of 15 patients. The test group was treated with allogeneic bone marrow MSCs by intra-articular injection of 40 × 10(6) cells. The control group received intra-articular hyaluronic acid (60 mg, single dose). Clinical outcomes were followed for 1 year and included evaluations of pain, disability, and quality of life. Articular cartilage quality was assessed by quantitative magnetic resonance imaging T2 mapping.

RESULTS: Feasibility and safety were confirmed and indications of clinical efficacy were identified. The MSC-treated patients displayed significant improvement in algofunctional indices versus the active controls treated with hyaluronic acid. Quantification of cartilage quality by T2 relaxation measurements showed a significant decrease in poor cartilage areas, with cartilage quality improvements in MSC-treated patients.

CONCLUSIONS: Allogeneic MSC therapy may be a valid alternative for the treatment of chronic knee osteoarthritis that is more logistically convenient than autologous MSC treatment. The intervention is simple, does not require surgery, provides pain relief, and significantly improves cartilage quality.
A Novel Biological Approach to Treat Chondromalacia Patellae

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1 Stems Medical Clinic, Seoul, Republic of Korea, 2 National Leading Research Laboratory, Department of Biological Sciences, Myongji University, Yongin, Gyeonggido, Republic of Korea

Abstract

Mesenchymal stem cells from several sources (bone marrow, synovial tissue, cord blood, and adipose tissue) can differentiate into variable parts (bones, cartilage, muscle, and adipose tissue), representing a promising new therapy in regenerative medicine. In animal models, mesenchymal stem cells have been used successfully to regenerate cartilage and bones. However, there have been no follow-up studies on humans treated with adipose-tissue-derived stem cells (ADSCs) for the chondromalacia patellae. To obtain ADSCs, lipoaspirates were obtained from lower abdominal subcutaneous adipose tissue. The stromal vascular fraction was separated from the lipoaspirates by centrifugation after treatment with collagenase. The stem-cell-containing stromal vascular fraction was mixed with calcium chloride-activated platelet rich plasma and hyaluronic acid, and this ADSCs mixture was then injected under ultrasonic guidance into the retro-patellar joints of all three patients. Patients were subjected to pre- and post-treatment magnetic resonance imaging (MRI) scans. Pre- and post-treatment subjective pain scores and physical therapy assessments measured clinical changes. One month after the injection of autologous ADSCs, each patient’s pain improved 50–70%. Three months after the treatment, the patients’ pain improved 80–90%. The pain improvement persisted over 1 year, confirmed by telephone follow ups. Also, all three patients did not report any serious side effects. The repeated magnetic resonance imaging scans at three months showed improvement of the damaged tissues (softened cartilages) on the patellae-femoral joints. In patients with chondromalacia patellae who have continuous anterior knee pain, percutaneous injection of autologous ADSCs may play an important role in the restoration of the damaged tissues (softened cartilages). Thus, ADSCs treatment presents a glimpse of a new promising, effective, safe, and non-surgical method of treatment for chondromalacia patellae.
Amniotic MSC = Bone Marrow MSC?
Amnio vs BMA: MSC Volume Comparison

Amniotic
440,000 MSC’s/1ml

Bone Marrow Aspirate
1,600 MSC’s/1ml

Umbilical Cord Tissue Offers the Greatest Number of Harvestable Mesenchymal Stem Cells for Research and Clinical Application: A Literature Review of Different Harvest Sites.

Vangsness CT Jr¹, Stemberg H², Harris L³.

Abstract

PURPOSE: Recent years have seen dramatic increases in the techniques used to harvest and isolate human mesenchymal stem cells. As the potential therapeutic aspects of these cells further develop, informative data on the differences in yields between tissue harvest sites and methods will become increasingly valuable. We collected and compared data on cell yields from multiple tissue harvest sites to provide insight into the varying levels of mesenchymal stem cells by tissue and offer primary and alternative tissue types for harvest and clinical application.

METHODS: The PubMed and Medline databases were searched for articles relating to the harvest, isolation, and quantification of human mesenchymal stem cells. Selected articles were analyzed for relevant data, which were categorized according to tissue site and, if possible, standardized to facilitate comparison between sites.

RESULTS: Human mesenchymal stem cell levels in tissue varied widely according to tissue site and harvest method. Yields for adipose tissue ranged from 4,737 cells/mL of tissue to 1,550,000 cells/mL of tissue. Yields for bone marrow ranged from 1 to 30 cells/mL to 317,400 cells/mL. Yields for umbilical cord tissue ranged from 10,000 cells/mL to 4,700,000 cells/cm of umbilical cord. Secondary tissue harvest sites such as placental tissue and synovium yielded results ranging from 1,000 cells/mL to 30,000 cells/mL.

CONCLUSIONS: Variations in allogeneic mesenchymal stem cell harvest levels from human tissues reflect the evolving nature of the field, patient demographic characteristics, and differences in harvest and isolation techniques. At present, Wharton’s jelly tissue yields the highest concentration of allogeneic mesenchymal stem cells whereas adipose tissue yields the highest levels of autologous mesenchymal stem cells per milliliter of tissue.

CLINICAL RELEVANCE: This comparison of stem cell levels from the literature offers a primer and guide for harvesting mesenchymal stem cells. Larger mesenchymal stem cell yields are more desirable for research and clinical application.

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Bone marrow-derived mesenchymal stromal cells differ in their attachment to fibronectin-derived peptides from term placenta-derived mesenchymal stromal cells

Jan K. Maerz¹, Lorenzo P. Roncoroni¹, David Goldeck², Tanja Abruzzese¹, Hubert Kalbacher³, Bernd Rolauffs⁴, Peter DeZwart⁴, Kay Nieselt⁵, Melanie L. Hart¹, Gerd Klein⁷ and Wilhelm K. Aicher¹*

Abstract

Introduction: Human mesenchymal stromal cells (MSCs) can be isolated from different sources including bone marrow and term placenta. These two populations display distinct patterns of proliferation and differentiation in vitro. Since proliferation and differentiation of cells are modulated by cell–matrix interactions, we investigated the attachment of MSCs to a set of peptide-coated surfaces and explored their interactions with peptides in suspension.

Methods: Human MSCs were isolated from bone marrow and term placenta and expanded. Binding of MSCs to peptides was investigated by a cell-attachment spot assay, by blocking experiments and flow cytometry. The integrin expression pattern was explored by a transcript array and corroborated by quantitative reverse transcription polymerase chain reaction and flow cytometry.

Results: Expanded placenta-derived MSCs (pMSCs) attached well to surfaces coated with fibronectin-derived peptides P7, P15, and P17, whereas bone marrow-derived MSCs (bmMSCs) attached to P7, but barely to P15 and P17. The binding of bmMSCs and pMSCs to the peptides was mediated by β1 integrins. In suspension, expanded bmMSCs barely bind to P7, P13, P15, and less to P14 and P17. Ex vivo, bmMSCs failed to bind P7, but displayed a weak interaction with P13, P14, and P15. In suspension, expanded pMSCs displayed binding to many peptides, including P4, P7, P13, P14, P15, and P17. The differences observed in binding of bmMSCs and pMSCs to the peptides were associated with significant differences in expression of integrin α2-, α4-, and α6-chains.

Conclusions: Human bmMSCs and pMSCs show distinct patterns of attachment to defined peptides and maintain differences in expression of integrins in vitro. Interactions of ex vivo bmMSCs with a given peptide yield different staining patterns compared to expanded bmMSCs in suspension. Attachment of expanded MSCs to peptides on surfaces is different from interactions of expanded MSCs with peptides in suspension. Studies designed to investigate the interactions of human MSCs with peptide-augmented scaffolds or peptides in suspension must...
Changes in Chondrogenic Progenitor Populations Associated with Aging and Osteoarthritis.

Brady K1, Dickinson SC1, Hollander AP1.

Abstract
Chondrogenic progenitor populations, including mesenchymal stem cells, represent promising cell-based transplantation or tissue engineering therapies for the regeneration of damaged cartilage. Osteoarthritis (OA) predominantly affects the elderly and is a leading cause of disability worldwide. Advancing age is a prominent risk factor that is closely associated with the onset and progression of the disease. Understanding the influence that aging and OA have on chondrogenic progenitor cells is important to determine how these processes affect the cellular mechanisms of the cells and their capacity to differentiate into functional chondrocytes for use in therapeutic applications. Here, we review the effect of age- and OA-related changes on the growth kinetics and differentiation potential of chondrogenic progenitor cell populations. Aging differentially influences the proliferative potential of progenitor cells showing reduced growth rates with increased senescence and apoptotic activity over time, while chondrogenesis appears to be independent of donor age. Cartilage tissue affected by OA shows evidence of progenitor populations with some potential for repair, however reports on the proliferative propensity of mesenchymal stem cells and their chondrogenic potential are contradictory. This is likely attributed to the narrow age ranges of samples assessed and deficits in definitively identifying donors with OA versus healthy patients across a wide scope of advancing ages. Further studies that investigate the mechanistic effects of chondrogenic progenitor populations associated with aging and the progression of OA using clearly defined criteria and age-matched control subject groups are crucial to our understanding of the clinical relevance of these cells for use in cartilage repair therapies.
Human Amniotic Membrane-Derived Products in Sports Medicine: Basic Science, Early Results, and Potential Clinical Applications.

Riboh JC\textsuperscript{1}, Saltzman BM\textsuperscript{2}, Yanke AB\textsuperscript{2}, Cole BJ\textsuperscript{2}.

\textbf{Author information}

\textbf{Abstract}

\textbf{BACKGROUND:} Amniotic membrane (AM)-derived products have been successfully used in ophthalmology, plastic surgery, and wound care, but little is known about their potential applications in orthopaedic sports medicine.

\textbf{PURPOSE:} To provide an updated review of the basic science and preclinical and clinical data supporting the use of AM-derived products and to review their current applications in sports medicine.

\textbf{STUDY DESIGN:} Systematic review.

\textbf{METHODS:} A systematic search of the literature was conducted using the Medline, EMBASE, and Cochrane databases. The search term amniotic membrane was used alone and in conjunction with stem cell, orthopaedic, tissue engineering, scaffold, and sports medicine.

\textbf{RESULTS:} The search identified 6870 articles, 80 of which, after screening of the titles and abstracts, were considered relevant to this study. Fifty-five articles described the anatomy, basic science, and nonorthopaedic applications of AM-derived products. Twenty-five articles described preclinical and clinical trials of AM-derived products for orthopaedic sports medicine. Because the level of evidence obtained from this search was not adequate for systematic review or meta-analysis, a current concepts review on the anatomy, physiology, and clinical uses of AM-derived products is presented.

\textbf{CONCLUSION:} Amniotic membranes have many promising applications in sports medicine. They are a source of pluripotent cells, highly organized collagen, antifibrotic and anti-inflammatory cytokines, immunomodulators, and matrix proteins. These properties may make it beneficial when applied as tissue engineering scaffolds, improving tissue organization in healing, and treatment of the arthritic joint. The current body of evidence in sports medicine is heavily biased toward in vitro and animal studies, with little to no human clinical data. Nonetheless, 14 companies or distributors offer commercial AM products. The preparation and formulation of these products alter their biological and mechanical properties, and a thorough understanding of these differences will help guide the use of AM-derived products in sports medicine research.
Response to ReNu™ ... A Trend Toward Long-lasting Improvement

In a small pilot study, ReNu™ was evaluated in patients with documented Kellgren-Lawrence Grade 3 and 4 OA of the knee, which represents a moderately severe to severe stage.

Early improvement with lasting results, evaluated through one year.

Patient-reported improvements in daily function maintained for up to one year.

SANE (Single Assessment Numerical Evaluation) is a patient-reported outcome measurement used to assess patients' opinions regarding their current level of function.

KOOS ADL (Knee Injury Osteoarthritis Outcome Score Activities of Daily Living) is a patient-reported outcome measurement used to assess the patient's opinion about knee-associated problems and changes induced from treatment.
An Investigation of ReNu™ Knee Injection: Monitoring the Response of Knee Function and Pain in Patients with Osteoarthritis

IRB Number: 2016-274

Institutional Review Board, Hospital for Special Surgery
WHO’S A CANDIDATE?

- Any one who does not want surgery or does not qualify for surgery
- Any one who would like to have potential for regrowth
- Cartilage patients
- Young patients
- OA prevention
PROCEDURE

- Discuss pros and cons
- Stop NSAID’s for 2 weeks prior and 3 months post
- Thaw frozen product and combine with saline.
- Ultrasound guided injection/s +/- HA
- Physical therapy Knee rehab:
  - Toe touch weight bearing 2 wks
  - Initiate strengthening week 3
  - Return to sport specific activities
    - Swimming- 3 wks
    - Cycling- 3 wks
    - Running 4-6wks
    - Cutting 6-8wks

- Office f/u in 4 weeks
- Continued increasing activity and supplements
Clinical utility of ultrasound guidance for intra-articular knee injections: a review.

Berkoff DJ, Miller LE, Block JE.

Abstract
Intra-articular corticosteroid and hyaluronic acid injections provide short-term symptom amelioration for arthritic conditions involving structural damage or degenerative changes in the knee. Conventional palpation-guided anatomical injections frequently result in inaccurate needle placement into extra-articular tissue and adjacent structures. The purpose of this review was to determine the effect of ultrasound guidance on the accuracy of needle placement, clinical outcomes, and cost-effectiveness in comparison with anatomical landmark-guided intra-articular large joint injections, with particular emphasis on the knee. A total of 13 relevant studies were identified; five studied the knee, seven studied the shoulder, one used both the knee and shoulder, and none studied the hip. Ultrasound was used in seven studies; the remaining studies utilized air arthrography, fluoroscopy, magnetic resonance arthrography, or magnetic resonance imaging. Across all studies (using all imaging modalities and all joints), needle placement accuracy ranged from 63% to 100% with ultrasound and from 39% to 100% with conventional anatomical guidance. Imaging guidance improved the accuracy of intra-articular injections of the knee (96.7% versus 81.0%, P < 0.001) and shoulder (97.3% versus 65.4%, P < 0.001). In particular, ultrasound guidance of knee injections resulted in better accuracy than anatomical guidance (95.8% versus 77.8%, P < 0.001), yielding an odds ratio of 6.4 (95% confidence interval 2.9-14). Ultrasound guidance notably improves injection accuracy in the target intra-articular joint space of large joints including the knee. The enhanced injection accuracy achieved with ultrasound needle guidance directly improves patient-reported clinical outcomes and cost-effectiveness.
To the Editor:

Commercial stem-cell clinics have been highly publicized in the lay press and operate worldwide with limited or no regulation.\(^1\) We report the case of a 66-year-old man who underwent intrathecal infusions for the treatment of residual deficits from an ischemic stroke at commercial stem-cell clinics in China, Argentina, and Mexico. He was not taking any immunosuppressive medications. In reports provided to him by the clinics, the infusions were described as consisting of mesenchymal, embryonic, and fetal neural stem cells. Progressive lower back pain, paraplegia, and urinary incontinence subsequently developed. Magnetic resonance imaging (MRI) revealed a lesion of the thoracic spinal cord and thecal sac; a biopsy specimen was obtained (Figure 1).
There are now more than 500 stem cell clinics in the United States. Many charge $5,000 to $20,000 for injections of “stem cell” solutions that may not contain the same kind of stem cells used in controlled experiments — and indeed may not contain stem cells at all.
Stem Cell Treatment: Out from the Shadows, Onto the Cutting Edge

The Jets’ Chris Johnson is one of hundreds of NFL players who’ve turned to stem cells to aid in recovery from injury. It may be the next big breakthrough in the treatment of sports ailments, but for now the use of such therapy is strictly limited in the U.S.—and questions about effectiveness outweigh the answers.
42 YO WITH RTC TEAR
51 YO KNEE OA
LONG TERM GOALS

Evaluate and treat things that can contribute to long term improvement:

- Obesity
- Bio mechanical issues (scapular dyskinesis, quad weakness, poor balance)
- Inflammatory processes- gout, RA, smoking
- Activity modification
- Supplements
VITAMINS & NUTRITIONAL SUPPLEMENTS

Glucosamine / Chondroitin Sulfate
Some positive results for moderate to advance arthritis
American Academy of Orthopedic Surgeons recommended against its use for patients with osteoarthritis of the knee (Dec, 2008)

Fish Oil (Omega-3 Fatty Acids)
Diet rich in Fruits and Vegetables
CONCLUSION

• Amniotic stem cells have great potential
  • Good pre-clinical and clinical evidence
    • Effectiveness and safety

• Promising clinical trials
  • Cartilage restoration
  • Meniscus healing

• More clinical evidence needed
  • Optimal concentrations, frequency, other areas
  • Adjuvant therapies

• Complications
  • Minimal to none
Questions????