



2017

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Recommended Citation

Stewart, Dennis W., "Use of Mesenchymal Stem Cells for the Treatment of Osteoarthritis" (2017).
Physician Assistant Scholarly Project Posters. 56.
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Use of Mesenchymal Stem Cells for the Treatment of Osteoarthritis

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Abstract

- Healthy articular cartilage protects and provides smooth functioning of the joint. The deterioration of the articular cartilage leads to the crippling disease known as osteoarthritis (OA).
- OA is a leading cause of disability in the United States. Although some of the current treatment modalities, along with pharmacological treatment, may offer short term improvement with pain and function, they do not offer long term relief, and are ineffective in preventing the progression of OA.
- In advanced stages, surgery in the form of total knee arthroplasty (TKA), is sometimes needed. This is an invasive procedure and typically requires hospitalization.
- Now, there is a safe and effective modality on the horizon. This minimally invasive treatment is the injection of mesenchymal stem cells (MSCs) directly into the affected joint.
- These are multipotent progenitor cells that offer immunosuppressive and anti-inflammatory action, have the capacity of self-renewal, and have high plasticity. MSCs can be harvested from the patient themselves, autologous, or can be from a donor, allogeneic.
- A review of the literature suggests treatment of moderate to severe OA of the knee with MSC injections are a viable treatment option when compared to other treatments that include a total knee replacement. MSCs are the only treatment option that have evidence of cartilage regeneration in addition to improvement of functional mobility, pain relief, and overall improvement in quality of life.

Introduction

- Osteoarthritis (OA) is a leading cause of joint disease characterized by the degeneration of articular cartilage. OA leads to pain, stiffness, swelling, tenderness, and loss of mobility and flexibility in the affected joint. These symptoms lead to reduced activity, which leads to weight gain, which worsens OA. (Burke, et al. 2016). There is no cure for this disease.
- Most treatments are short lived, and only offer little relief. For severe OA, surgical treatment, such as total knee arthroplasty (TKA), may offer longer relief, however, this procedure is invasive, requires hospitalization, causes moderate to severe pain, and has risks for infection and failure.
- According to new research, a promising treatment could be on the horizon.
- The newest treatment that is being researched for the treatment of moderate to severe OA is mesenchymal stem cell injections. When compared to TKA surgery, this treatment is much less invasive, has a much quicker recovery time, less chance for adverse events, and is much less expensive



Statement of the Problem

- Current treatments for OA such as weight loss, physical therapy, and pharmaceuticals help lessen the pain and increase mobility in cases of mild to moderate OA. In severe cases, the standard of care in the U.S. is TKA. Although effective in most cases, the procedure itself is invasive, has the potential for failure and infection, is costly, and still takes several weeks for rehabilitation.

Research Question

- In patients with moderate to severe osteoarthritis, could mesenchymal stem cell injections, compared to current treatments, offer longer pain relief and improved function?
- In patients with severe osteoarthritis, is treatment with mesenchymal stem cells, compared to total knee arthroplasty, less expensive?

Literature Review

Pathophysiology of osteoarthritis:

- Proper, non-painful joint function in the human body is dependent upon the wellness of the articular cartilage that covers the opposing articulating bones. Deterioration of the articular cartilage leads to the crippling disease known as OA (Correa and Lietman, in press).
- Patients with OA experience loss of flexibility, stiffness, swelling and pain, leading to loss of mobility which leads to weight gain, which is worse on OA affected joints (Burke et al. 2016).
- OA also involves structures such as subchondrial bone, synovial fluid, and the synovial membrane, causes hypertrophic bone changes with osteophyte formation and subchondrial bone remodeling (Pearle et al. 2005).

Current treatments for osteoarthritis:

- Aquatic exercises improved pain symptoms, but only for a short term following conclusion of treatment (Bartels et al. 2016).
- Land based physical therapy results in pain reduction and improved function and quality of life for up to 6 months following the completion of the program (Fransen et al. 2015).
- Intra-articular corticosteroid injections showed improvement with function for up to 6 weeks and pain relief for up to 13 weeks post injection (Jüni et al. 2015).
- Viscosupplementation injection in the knee with hyaluronan showed significant improvement with pain and function up to 13 weeks post injection (Bellamy et al. 2005).
- Total knee arthroplasty (TKA) leads to reduction in pain, improvement of function, and better quality of life for treatment of severe OA (Singh et al. 2013).

Mesenchymal stem cells for treatment of osteoarthritis:

- Recent evidence suggests that MSC injection can boost repair and limit further destruction of joint (Diekman and Guilak, 2013).
- MSC injection significantly improves cartilage quality resulting in pain relief and improved quality of life (Mehrabani et al. 2016).
- MSC sheet implantation show greater efficacy over MSC injections in promoting meniscus regeneration while inhibiting progression of OA (Qi et al. 2016).

Cont. Literature Review

Cost comparison of treatments used for osteoarthritis:

- The average cost of TKA is \$49,500 for uninsured patients (Greengard 2015).
- MSC injections for OA is currently under research and is not covered by insurance. It is estimated at \$3,000-\$3,500 to inject one joint and \$4,000-\$5,000 for two joints (Dr. Robert J. Daley, n.d.).

Discussion

Function and mobility improvement by treatment.

Treatment	sample size	improvement ≥ 8 weeks	improvement ≥ 12 weeks	improvement ≥ 6 months	improvement ≥ 12 months
hyaluronan or hyal derivatives (HA)	76 trials	yes	yes	no	no
TKA (total knee arthroplasty)	122 patients	yes	yes	yes	yes
electromagnetic field treatment	636 patients	no	no	no	no
therapeutic ultrasound	341 patients	yes	no	no	no
corticosteroid injection	1767 patients	no	no	no	no
land based exercise	3913 patients	yes	yes	yes	no
Mesenchymal Stem Cell (MSC) injection low dose	30 patients	yes	yes	yes	no
Mesenchymal Stem Cell (MSC) injection high dose	30 patients	yes	yes	yes	yes

Improvement in pain by treatment.

Treatment	sample size	improvement ≥ 8 weeks	improvement ≥ 12 weeks	improvement ≥ 6 months	improvement ≥ 12 months
hyaluronan or hyal derivatives (HA)	76 trials	yes	yes	no	no
TKA (total knee arthroplasty)	122 patients	yes	yes	yes	yes
electromagnetic field treatment	636 patients	yes	yes	no	no
therapeutic ultrasound	341 patients	yes	no	no	no
corticosteroid injection	1767 patients	yes	yes	no	no
land based exercise	3913 patients	yes	yes	yes	no
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Applicability to Clinical Practice

- Clinicians are taught to always have their patients best interest in mind. For treatment of OA, there are many different conservative choices such as land and water exercise therapy, electromagnetic therapy, oral pain medications, and injectable steroids to name a few, that are non-invasive and inexpensive, however, they each have a varying degree of success with pain control, functional improvement, and improvement in quality of life, but none show regenerative properties for the cartilage that is damaged.
- Based on moderate quality of evidence, treatment of OA, mostly in the knee, with mesenchymal stem cell injections, are the only option that show regeneration of cartilage. This leads to improvement of functional mobility, pain relief, and overall improvement in quality of life.
- When compared to a TKA, which is the current standard of care for severe OA, it is minimally invasive, less painful, has minimal associated risks, requires less rehabilitation time, and causes a lower burden of cost on the health care system.

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Thanks...

- To my family for their understanding and commitment for these demanding past two years.
- Dr. Hovey for volunteering to be my primary preceptor and for suggesting this topic for my research.
- Jay Metzger for his direction and help as my program advisor.
- Professor Klug for offering her statistical expertise for this project.
- To all other faculty of the Physician Assistant Program for their guidance, instruction, and dedication to their students.