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Efficacy of mesenchymal stem celltherapy in the management of osteoarthritis: a randomized controlled trial

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Abstract

Objective

To assess the efficacy of mesenchymal stem cell therapy in the management of osteoarthritis.

Methods

In this study, 45 participants who had obvious symptoms of osteoarthritis were randomly selected and placed in three groups such as control group, single-dose, and double-dose injection therapy groups. Each group consists of 15 participants. Two groups of participants received intra-articular mesenchymal stem cell therapy consisting of either a single or double dose of injection therapies whereas the control group has been treated through a conservative method.

Results

The results of the study revealed that the participants did not experience any severe adverse consequences. Although the participants who received mesenchymal stem cell therapy were placed in single & double dose injection therapy groups experienced significant pain but functional improvement was observed after twelve months of follow-up.

Conclusion

The study has concluded that mesenchymal stem cell therapy is one of the most effective treatments for osteoarthritis and further prevents the progression of the disease.

Keywords

Efficacy, mesenchymal stem cell therapy, osteoarthritis

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Introduction

Osteoarthritis has a considerable role in morbidity and among the aging population, due to which it is expected to continue to be a huge social and financial burden in society. The most prevalent type of joint dysfunction is osteoarthritis¹. Articular cartilage degeneration and reactive new bone growth at the articular margins are its defining characteristics, which results in discomfort and stiffness in the affected joints². All synovial joints are susceptible to osteoarthritis but specifically, hip and knee joints are where it most frequently manifests itself resulting in physical impairment. It is one of the most common degenerative illnesses that causes persistent pain and functional loss³. It is the most prevalent type of joint condition and places an enormous strain on the world's healthcare systems. Without a reliable treatment option, for osteoarthritis, it offers a singular opportunity for therapeutic innovation⁴. The intrinsic potential of mesenchymal

stem cells for tissue repair and regeneration has been suggested to develop a mesodermal lineage, such as osteoblasts and chondrocytes⁵⁻⁶. Mesenchymal stem cells have immunomodulatory and anti-inflammatory effects by suppressing inflammatory T-cell proliferation, inhibiting monocyte maturation, and expression of anti-inflammatory cytokines⁶. Stem cells have the potential to replace organs like osteoarthritic joints, which sets them apart from conventional treatments focused on medicines, proteins, or antibodies⁷. It is recognized worldwide as the fourth greatest cause of disability and a significant factor influencing disability-adjusted life years². Symptomatic arthritis affects almost 10% of men and 18% of women belonging to the age group of 45 years, with radiological prevalence reaching up to 80% of the population at the age of 65 years⁸. This prevalence rate of osteoarthritis increases with the age of an individual. Instead of changing the course of the disease, traditional conservative medical treatments for osteoarthritis include symptomatic management. These pharmaceutical treatments have sporadic and limited advantages leading to severe negative consequences in the body⁹.

The studies have revealed that approximately 20% of patients experience prolonged pain or loss of function during 12 months. Although the preferred treatment for symptomatic osteoarthritis is surgical replacement¹⁰. Traditionally, osteoarthritis is always considered an age-related and degenerative syndrome, but with time, the pathophysiology of this disorder has been understood in a better way that it is caused by an imbalance between the pathways of catabolic and anabolic¹¹. As chondrocyte cell senescence releases reactive oxygen due to mechanical or biological stressors as a result of which there is a rise in inflammatory cytokine expression¹². Data revealed from pre-clinical studies have proved that Intra-articular mesenchymal stem cell therapy has been beneficial for the relief of pain and functional improvement¹¹. The degenerative nature of osteoarthritis cannot yet be reversed by any effective therapy². The therapeutic use of stem cells, however, may be a component of one of the promising treatments. The use of Mesenchymal stem cells, with their property of multi-lineage differentiation towards cell types in the joints, has been beneficial for stem cell treatments which are readily now available. This may be effective for both cartilage regeneration and subchondral bone remodeling in the treatment of osteoarthritis injuries. In this study efficacy of mesenchymal stem cells has been evaluated along with pain and other functional changes taking place in the body.

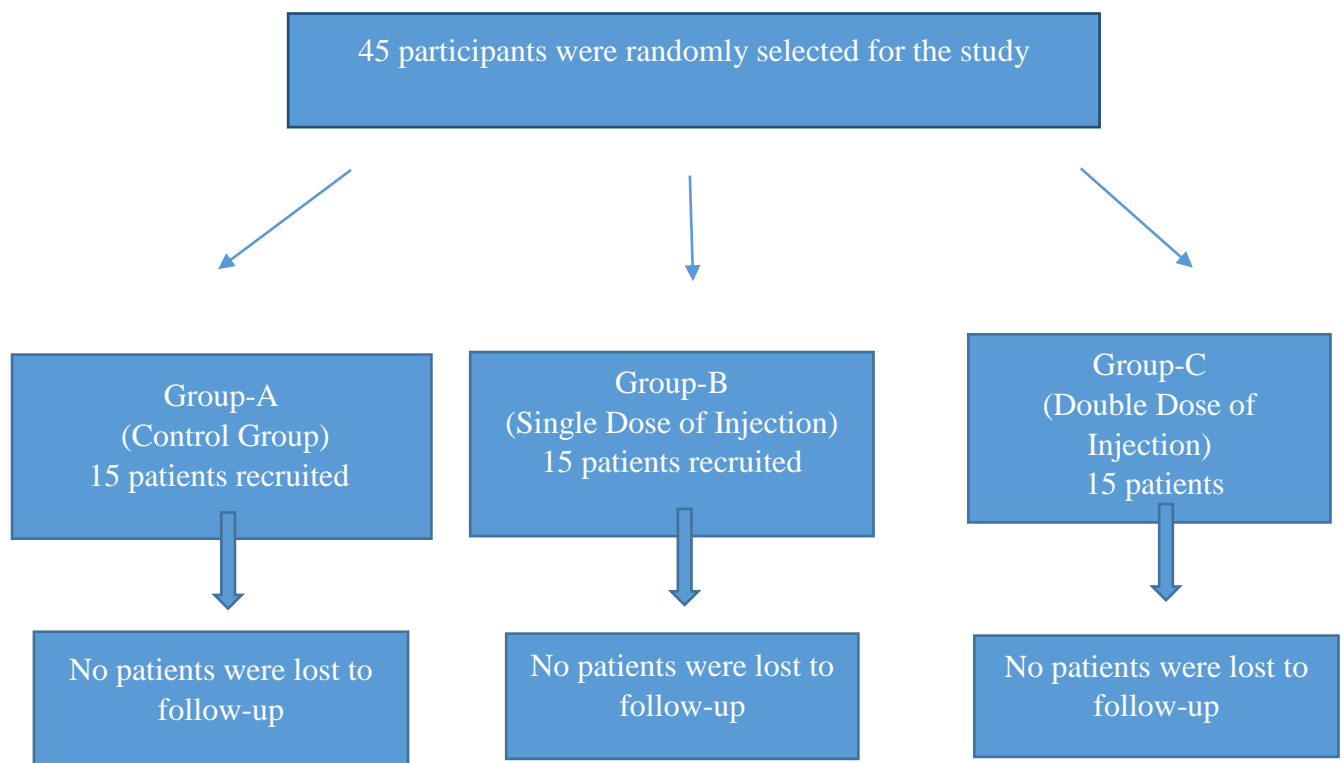
Material and methods

A randomized control trial was conducted among 45 participants recruited from the public hospital of Karachi, Pakistan. The study was approved by the ethical committee of the Hospital. Before starting the study all the participants were informed regarding the objective and aim of the study. Hence all 45 participants were equally and randomly distributed into the control and treatments group. The control group received conservative treatment only on the contrary one treatment group received a single dose of intra-articular injection whereas the other treatment group received a double dose of intra-articular injections. The inclusion criteria of the study

included 18 years and above with a moderate complaint of osteoarthritis. Although all these participants have received conservative management previously. The pain of participants was assessed by using a validated scale called Numeric Pain Rating Scale (NPRS) from 0-10¹³. For quantitative assessment of pain, a validated tool Western Ontario and McMaster Universities Arthritis Index (WOMAC Index 3.0) was used¹⁴. For the calculation of sample size, it was difficult as enough information has not been published regarding the effects of mesenchymal stem cells. The sample size has been chosen according to previously published study guidelines¹⁵.

Hence, Statistical analysis was performed by using SPSS version 21. To assess the mean differences of independent and dependent variables Two Way Repeated Measures ANOVA was used. For the analysis of data categorically Chi-square tests were used.

Figure-1 Flow chart for the selection of patients in the study



Results

In the study total, 45 participants were selected randomly. Out of which 15 patients were randomly placed in the control group, the other 15 were placed in the single dose injection group, and the remaining 15 were placed in the double dose injection group. The results of the study revealed that fifty percent were men in the control group, seventy percent were placed in the single-dose injection therapy group, and forty percent were placed in the double-dose injection therapy group as shown in Table 1. Body mass index was different among the groups. Hence the participants of the control group were normally overweight and in the treatment

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groups, the participants were obese. Validated scale NPRS was used to assess pain and functional outcomes among single and double-dose injection therapy groups. The results were statistically significant (<0.05) in both single and double injection therapy groups as compared to baseline. Hence the participants in both groups experience less pain at twelve months as compared to the control group. No significant difference was observed among both therapy groups.

The WOMAC scores throughout follow-up showed improvements in the single and double-dose of injection therapy group with baseline values of 84 (9.4) and 87.3 (8) increasing to 84 (9.4) and 87.3 (8) at 12 months, respectively. As early as one month and up until the last follow-up at 12 months, statistically significant improvement compared to baseline measurements was seen. At 12 months, there was a statistically significant improvement in both treatment groups as compared to the control group. As shown in Table-2 when pain and functional outcome measures were combined, the percentage of patients attaining a minimal clinically relevant difference was 84.2 and 86.9% in single and double-dose injection therapy groups, respectively. Further, gender and age did not affect mesenchymal stem cell therapy. The participants of single and double-dose injection therapy experienced discomfort and swellings which were later resolved with time.

Table 1- Demographic characteristics of the participants placed in the following groups

Demographic Variables	Control group	Single Dose Injection therapy	Double Dose Injection therapy	p-value
Total sample size	15	15	15	
Gender (% male)	50	70	40	
Age (years)	50.2(6.1)	53.6(6.2)	54.7(11.2)	0.57
Height (m)	1.72(0.1)	1.75(0.1)	1.6(0.2)	0.60
Weight (kg)	75(14.0)	96.8(21.0)	87.2(24.5)	0.06
BMI (kg/m ²)	24.2(3.3)	32.1(5.3)	31.2(5.7)	0.022

Table-2 Comparison of baseline data with control, single dose, and double dose injection therapy group

Outcome	Control group	Single-dose injection	Double-dose injection
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measures		therapy	therapy
NPRS	40	88.9	99
WOMAC	20	99	89
Average	24.9	84.2	86.9

Table-3 Adverse consequences of the single and double dose of injection therapy groups.

The Severity of Adverse Consequences	Single-dose injection therapy at baseline	Double-dose injection therapy at baseline	Double dose injection therapy after 6 months (%)
Nil	25%	15%	0%
Slight	55%	60%	35%
Moderate	5%	25%	55%
Severe	5%	5%	2%

Chi-square analysis shows no significant difference between the groups

Discussion

With the emerging technology the utilization of mesenchymal stem cells as a therapeutic approach is not surprising. Studies conducted earlier have shown that mesenchymal stem cells have been beneficial for the management of osteoarthritis¹⁶. This study is conducted to assess the efficacy of intra-articular mesenchymal stem cell therapy consisting of either a single or double dose of injection for the management of osteoarthritis. The results of the study revealed that mesenchymal stem cells are safe and effective for the management of osteoarthritis as it also slows the course of the disease. Hence statistically significant change was seen in both groups by utilizing the scales called NPRS and WOMAC. Various studies have shown that mesenchymal stem cell therapy is not associated with age but is directly linked to decreased function¹⁷. The results of the study revealed that intra-articular mesenchymal stem cell therapy slows down the spread of disease which is similar to several previous clinical studies conducted globally. A study conducted by Vega A et al, revealed that mesenchymal stem cell therapy is beneficial in stabilizing osteoarthritis and improving the quality of cartilage¹⁸. The results of the study revealed that the double dose of injection therapy led to a trend of better disease stabilization as compared to a single dose of injection therapy. Several trials have failed to provide evidence that mesenchymal stem cells are significantly incorporated into regenerating cartilage tissue¹⁹. Further, the results of the study revealed that most of the participants in both therapy groups showed considerable relief in pain although previous research has revealed that synovitis is highly associated with pain among the patients of osteoarthritis²⁰. This result was similar to a study conducted earlier by Teichtahl AJ et al²¹. On the contrary, there was an RCT conducted earlier

which showed that bisphosphonate medication did not improve the pain in knees²². The results of the study revealed that no serious adverse effects were observed in mesenchymal stem cell therapy during the management of osteoarthritis. Although two participants experienced significant pain and edema, eventually pain was resolved by using oral analgesics/anti-inflammatories. The main limitation of this study is the small sample size. Hence more research should be done in this area by using more techniques.

Conclusion

In this randomized control study, mesenchymal stem cells have been linked successfully for the modification of disease. Mesenchymal stem cells have been effectively utilized for the management of osteoarthritis without any adverse consequences and showed a dynamic achievement as compared to conventional methods. The results provide a significant improvement in the pain and function of an individual. According to the comparison of treatment plans double intra-articular injection therapy of the mesenchymal stem resulted in more consistent stabilization of osteoarthritis as compared to a single injection regime.

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