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**ORIGINAL ARTICLE**

# Comparison of Disease Progression in Patients with Osteoarthritis of Knee Treated with Versus without Intraarticular Injection of Corticosteroids

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## ABSTRACT

**Objectives:** To compare the frequency of disease progression in patients with osteoarthritis of knee treated with versus without intra-articular injection of corticosteroids.

**Design:** The present study was a randomized single-blind controlled trial.

**Study Settings:** The current study was conducted at Department of Orthopedic Surgery at Sir Ganga Ram Hospital Lahore over 1 year from May 2020 to April 2021.

**Study Procedure:** The present study was conducted over 186 patients of both genders aged between 40-70 years presenting in outpatient department of orthopedic surgery with osteoarthritis of knee joint. The sampled patients were randomly allotted into two treatment arms. Patients from Group-A received intraarticular injection of steroids in addition to conservative management while those in Group-B were taken as controls and were managed conservatively without intraarticular injection of steroids. Outcome variable was frequency of disease progression over KL grading which was noted and compared between the groups. An informed on paper consent was obtained from every participant.

**Results:** The mean age of the patients was 52.5±8.7 years. There was a female predominance with a male to female ratio of 1:1.7. The mean BMI of these patients was 28.3±3.6 Kg/m$^2$ and 60 (32.3%) patients were obese. 103 (55.4%) patients had grade 2 while 83 (44.6%) patients had grade 3 osteoarthritis. Disease progression was noted in 30 (16.1%) patients after 6 months follow-up. The frequency of disease progression was significantly higher in patients receiving intra-articular injection of corticosteroids as compared to controls (26.9% vs. 5.4%; p-value<0.001). When stratified, comparable difference was observed across various subgroups of patients based on patient's age, gender, BMI and baseline Kellgren-Lawrence Grade.

**Conclusion:** In the present study intraarticular injection of steroids was found to be associated with articular cartilage damage evident from increased frequency of disease progression following intraarticular injection as compared to controls which advocates that intraarticular injection of steroids should be avoided in the management of osteoarthritis and should be reserved only for patients with advanced disease and who are already planned for joint replacement.

**Keywords:** Osteoarthritis, Intraarticular Steroids, Chondrotoxicity

## INTRODUCTION

Knee joint osteoarthritis is a fairly common presentation in orthopedic outdoors[1] affecting mainly middle aged to elder citizens.[2] Pain and limitation of movement are primary concerns of these patients.[1-3] Conservative measures like weight reduction, walking aids and avoidance of squatting position are usually advised along with calcium and vitamin D supplements and oral analgesics like paracetamol.[4,5] Patients with more advanced disease and those who fail to respond to these measures are usually advised intraarticular injections of corticosteroids[4,5] which are quite beneficial in relieving pain and stiffness with an effect size of up to 0.70 in published literature.[5]

However, there has been a growing body of evidence which suggests that these intraarticular steroids are chondrotoxic and by damaging the reminiscent articular cartilage, they may worsen the disease.[6-10] Until now, the evidence only came from laboratories where addition of steroids to sampled chondrocytes was seen to be associated with cell destruction and apoptosis[6-10], yet no clinical trial was available to challenge this clinical practice which is a routine in most of orthopedic centers worldwide.

Zeng et al.[11] (2019) conducted a first ever clinical trial in human subjects suffering osteoarthritis of knee receiving intraarticular steroids compared to a cohort of patients with similar disease severity managed without intraarticular steroids. They confirmed the previously existing laboratory evidence and reported that the frequency of disease progression was significantly higher in patients with intraarticular steroids (21.7% vs. 7.1%; p-value=0.001) as compared to controls. In the light of this evidence, the current practice of intraarticular steroids to treat osteoarthritis knee appears inappropriate as it can itself lead to progression of disease so that after an initial improvement more and more patient will develop severe disease and will end up in joint replacement. However, as mentioned before intraarticular steroids are routinely given at most of orthopedic centers worldwide.[4,5] Although the laboratory evidence has been there for almost a decade, it didn't seem to affect the practice.[6-10] This trial is first of its kind and sounds an alarm.[11] Keeping in view, the limited available evidence[11], the purpose of the current study was to repeat this trial and further confirm the results. If the results of the present study revealed disease progression with intraarticular steroids, it would add to the growing body of evidence against intraarticular steroids thus strengthening the case for a change of practice. The results of the present study would thus help in the appropriate management of patients presenting with osteoarthritis of knee in future orthopedic practice.

**Study Procedure:** The current study was a randomized single-blind controlled trial conducted at Department of Orthopedic Surgery at Sir Ganga Ram Hospital Lahore over 1 year period from May 2020 to April 2021. Sample size of 186 cases (93 cases in each group) was estimated with 80% power of test and 5% significance level while taking expected frequency of disease progression to be 21.7% with and 7.1% without intraarticular steroids in patients with knee osteoarthritis.[11] Non-probability, consecutive sampling was done and patients of 40-70 years age from both genders presenting with osteoarthritis of knee were included. Disease severity was graded using Kellgren and Lawrence Grading[12]. Patients with grades-II and III disease at presentation were included. Patients with history of previous intraarticular injection of steroids or hyaluronate, soft tissue contractures, disorders of spine, hip or ankle which hindered the rehabilitation were excluded. We also excluded diabetics, morbidly obese patients, those with deranged coagulation profile and those with active local infection. These patients were randomly divided into two treatment groups using lottery method. Patients in both the groups were evaluated for KL grading of osteoarthritis at their first visit by getting an X-ray AP standing and Lateral views. Patients in

the experimental group were injected inj. triamcinolone acetonide 80 mg intraarticular after standard aseptic measures. Patients in both the groups were given routine treatment of osteoarthritis as per department protocols. Patients were followed at 6 months after the first session and upon follow-up repeat X-rays were advised. These X-rays were assessed by KL grading and a 1 grade or more progression was considered as worsening of disease.

## RESULTS

The mean age of the patients was 52.5±8.7 years. There was female predominance (1:1.7) and 60 (32.3%) patients were obese. 103 (55.4%) patients had grade 2 while 83 (44.6%) patients had grade 3 osteoarthritis. Both the groups were comparable in terms of demographic characteristics as shown in Table 1. Disease progression was noted in 30 (16.1%) patients after 6 months follow-up. The frequency of disease progression was significantly higher in patients receiving intraarticular injection of corticosteroids as compared to patients managed without intraarticular steroids (26.9% vs. 5.4%; p-value<0.001) as shown in Table 2.

Table 1: Demographic Characteristics of Studied Groups n=186

| Characteristic | Intraarticular Steroid Injection n=93 | Conventional Management alone n=93 | P-value |
|---|---|---|---|
| Age (years) | 52.6±8.1 | 52.4±9.2 | 0.873 |
| • 40-50 years | 38 (40.9%) | 37 (39.8%) | 0.954 |
| • 50-60 years | 34 (36.6%) | 36 (38.7%) | |
| • 60-70 years | 21 (22.6%) | 20 (21.5%) | |
| Gender | | | |
| • Male | 35 (37.6%) | 34 (36.6%) | 0.879 |
| • Female | 58 (62.4%) | 59 (63.4%) | |
| BMI (Kg/m$^2$) | 28.2±3.8 | 28.4±3.5 | 0.708 |
| • 20-25 Kg/m$^2$ | 25 (26.9%) | 24 (25.8%) | 0.983 |
| • 25-30 Kg/m$^2$ | 38 (40.8%) | 39 (41.9%) | |
| • 30-35 Kg/m$^2$ | 30 (32.3%) | 30 (32.3%) | |
| Kellgren-Lawrence Grade | | | |
| • Grade-2 | 51 (54.8%) | 52 (55.9%) | 0.883 |
| • Grade-3 | 42 (45.2%) | 41 (44.1%) | |

Insignificant difference was observed on Independent sample t-test and Chi-square test

Table 2: Comparison of Disease Progression between the Study Groups n=186

| Disease Progression | Intraarticular Steroid Injection n=93 | Conventional Management n=93 | P-value |
|---|---|---|---|
| Yes | 25 (26.9%) | 5 (5.4%) | <0.001* |
| No | 68 (73.1%) | 88 (94.6%) | |
| Total | 93 (100.0%) | 93 (100.0%) | |

* Significant difference was observed on chi-square test

## DISCUSSION

Osteoarthritis is chronic, progressive, degenerative arthropathy characterized by gradual loss of articular cartilage, subchondral bone remodeling, osteophyte formation and joint inflammation.[13] Knee joint is the most commonly involved joint in osteoarthritis.[14] The most common presentation of osteoarthritis is pain in the affected joint and intraarticular steroids are routinely given in such patients for pain relief.[15] A recent study claimed that this intraarticular injection of steroids was associated with worsening of disease and advocated that it should be avoided in future practice.[11] However, the available evidence was limited and presently there was no local such published material and that is why need for the present study was felt.

The objective of this study was to compare the frequency of disease progression in patients with osteoarthritis of knee treated with versus without intraarticular injection of corticosteroids.

In the present study, the mean age of the patients presenting with osteoarthritis of knee joint was 52.5±8.7 years. Ghaznavi et al.[16] (2017) stated similar mean age of 52.2±9.3 years among patients presenting with osteoarthritis of knee at Liaquat National Hospital, Karachi. A similar mean age of 52.6±8.8 has been described by Khalid et al.[17] (2015) among such patients presenting at Bahawal Vitoria Hospital Bahawalpur while Kidwai et al.[18] (2016) observed it to be 50.7±10.2 years at an Industrial Hospital at Karachi. Moseley et al.[19] (2002) reported similar mean age of 52.0±11.1 years among American such patients. This observation is also in line with that of Tripathy et al.[20] (2020) and Sanghi et al.[21] (2013) who observed a comparable mean age of 51.0±6.7 years and 53.2±9.6 years respectively in Indian patients with OA knee. Akhter et al.[22] (2021) observed a comparable mean age of 53.5±6.9 years in Bangladeshi such patients.

In the presents study, there were 37 (37.1%) male and 63 (62.9%) female patients with a male to female ratio of 1:1.7. A similar female predominance with a male to female ratio of 1:1.6 has been reported by Ghaznavi et al.[16] (2017) among OA knee patients presenting at Liaquat National Hospital, Karachi. Khalid et al.[17] (2015) also reported similar female predominance (m:f; 1:1.5) among such patients at Bahawal Victoria Hospital, Bahawalpur while Kidwai et al.[18] (2016) observed it to be 1:1.7 in Karachi. This observation is also in line with that of Tripathy et al.[20] (2020), Rao et al.[23] (2020) and Sanghi et al.[21] (2013) who observed a comparable female predominance in Indian patients with OA knee and reported a male to female ratio of 1:1.6, 1:1.5 and 1:1.5 respectively. Akhter et al.[22] (2021) reported a comparable male to female ratio of 1:1.5 in Bangladeshi such patients.

We observed that the frequency of disease progression was significantly higher in patients receiving intraarticular injection of corticosteroids as compared to patients managed without intraarticular steroids (26.9% vs. 5.4%; p-value<0.001). Our observation is comparable to that of parent study from Zeng et al.[11] (2019) where the author reported that the frequency of disease progression was significantly higher in patients with intraarticular steroids (21.7% vs. 7.1%; p-value=0.001) as compared to controls.

The present study is first of its kind in Pakistani population and has established that intraarticular injection of steroids has detrimental effects on articular cartilage as evident from previous laboratory[6-10] and clinical[11] studies. Another indirect contributing factor to this disease progression can be the loss of pain after the injection. Pain is however a defensive mechanism and subsequent lack of caution may add to this disease progression. In the light of this evidence, we advocate that intraarticular injection of steroids should be avoided in the management of osteoarthritis and should be reserved only for patients who have advanced disease and are already planned for joint replacement.

A very strong limitation to the present study was that we only considered worsening of disease on KL grading and ignored other important aspects like risk of infection, complications during subsequent total knee replacement and final outcome of joint replacement surgery among such patients which could have further weighed the detrimental effects of intraarticular steroids. Such a study is highly recommended in future research.

## CONCLUSION

In the present study intraarticular injection of steroids was found to be associated with articular cartilage damage evident from increased frequency of disease progression following intraarticular injection as compared to controls which advocates that intraarticular injection of steroids should be avoided in the management of osteoarthritis and should be reserved only for patients with advanced disease and who are already planned for joint replacement.

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