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Efficacy of Intraarticular Hyaluronic acid and Cortico-Steroid Co-Injection versus Hyaluronic acid in Knee Osteoarthritis

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ABSTRACT

Introduction: For knee osteoarthritis, intra-articular injections of Hyaluronic acid and corticosteroid have individually shown promise, nevertheless, the rate at which symptoms improve is a limiting factor for both treatments.
Aims and Objectives: To compare mean pain score in patients receiving combination of intra-articular Hyaluronic acid and corticosteroid versus Hyaluronic acid alone in osteoarthritic knee.
Place and Duration of Study: The randomized controlled trial was conducted in the Orthopedic Department of Shaikh Zayed Hospital, Lahore, from June 11, 2021, to December 11, 2021.
Materials and Methods: The study comprised a total of 64 patients fulfilling the inclusion criteria and after providing informed written consent with 32 patients each assigned to the Hyaluronic acid plus corticosteroid group (Group A) and Hyaluronic acid alone group (Group B). Lottery method was used to randomly divide patients into two groups. Pain was assessed at baseline and at 3 months via visual analog scale. All the data was recorded on preset performa and analyzed via SPSS version 20.
Results: Out of 64 patients enrolled in study, 15.6% were male and 34.4% were females in HA+CS group and 12.5% were male and 37.5% were females in HA alone group. Distribution of knee side, 9.4% patients had right while 40.6% had left side in HA + CS group and 23.4% had right while 26.6% had left side in HA alone group. Mean age of HA + CS group was 59.22±8.027 years and mean age of HA alone group was 57.34±6.378 years. Mean pain score was 01 in HA+CS group versus 4.13 in HA group ($p<0.001$).
Conclusion: In current study, we concluded that those individuals who underwent HA and CS co-treatment experienced reduction in mean pain score more as compared to those who received HA alone.

Key Words: Hyaluronic acid, Corticosteroid, Knee Osteoarthritis, Visual Analog Scale

INTRODUCTION

One of the most common chronic arthritic conditions, osteoarthritis (OA) of the knee usually affects middle-aged and older individuals. 10% of men and 13% of women over 60 have symptomatic osteoarthritis of the knee, making it a major source of disability. Women are more likely than men to develop osteoarthritis (OA) and factors such as age, weight, genetics and biomechanical characteristics all increase the risk of developing and worsening OA[1]. Over the course of a lifetime, over 14-20% of persons in the Pakistan develop symptoms of knee osteoarthritis and there is currently no pharmaceutical treatment that may stop or reverse the disease progression. Osteoarthritis in the knee significantly impacts a person's quality of life and productivity at work. A knee replacement is a complex surgical treatment that involves extensive postoperative rehabilitation and has a 30-day mortality rate of 1 in 500. Despite this, it may be a beneficial therapy for many of these patients. A great number of patients are either unsuitable candidates or do not desire knee arthroplasty. In conservative treatment of osteoarthritis (OA), non-steroidal anti-inflammatory medications (NSAIDs) and oral opioids provide short-term therapeutic relief. Many of these analgesics are not advised for individuals with gastrointestinal or cardiovascular problems. To prevent systemic complications, it might be preferable to inject therapeutic drugs directly into the arthritic joint[2–6]. The employment of non-surgical techniques is also an option for the management of knee osteoarthritis. Clinical evidence supports the efficacy of Hyaluronic acid and corticosteroid (CS) treatment in managing knee osteoarthritis symptoms[7-9]. Numerous studies have shown that HA and CS injections are secure and

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efficient therapies that help patients with knee arthritis feel less discomfort and have improved joint functionality. It has been claimed that because of its anti-inflammatory properties, CS are superior to HA in decreasing acute pain. In contrast to HA, the duration of pain alleviation in CS is shorter. When administered in tandem, HA and CS may provide long lasting analgesic effects compared to when used alone. Injections of any drug used over an extended period may lead to needless damage and possibly infection of the arthritic joint. According to reports, when corticosteroid is injected into an osteoarthritic joint, it accelerates the apoptotic process of cartilage cells. For this reason, physicians must carefully balance the dosage of corticosteroid to prevent unintended consequences[10–15]. Wang et.al conducted a study to evaluate the efficacy of combination of injection of Hyaluronic acid and corticosteroid versus Hyaluronic acid alone in knee osteoarthritis. At baseline, visual analog score was 7.13±1.00 in HA & CS group and 7.15±0.99 (p=0.927) in HA group. At 3 months it was 5.30±1.11 in HA & CS group and 6.07±1.06 in HA group (p< 0.001).[1] The main goals of OA treatment for patients are pain management and increased joint mobility. The current study aims to investigate whether a single shot combined intra-articular injection of CS and HA leads to improved functional outcomes and a longer duration of pain alleviation. Therefore, rather than utilizing either of the two medicines alone, co-injection of HA and CS could be used as a single conservative treatment approach in the future to treat osteoarthritis in the knee.

MATERIALS AND METHODS

A single-blind randomized clinical trial was conducted in the Orthopedic Department of Shaikh Zayed Hospital, Lahore, from 11-06-2021 to 11-12-2021 after approval from institutional review committee Vide No:CPSP/ REU/ 45021. The study comprised a total of 64 patients selected through non-probability consecutive sampling. Sample size was calculated with 80% of power of test, 95% confidence level and taking expected score in HA and CS group as 5.3±1.1 and HA alone group as 6.07±1.06. Written informed consent was taken from every patient. Lottery method was used to randomly divide patients into 2 groups. Group A went through combination of Hyaluronic acid and corticosteroid and group B got Hyaluronic acid alone. Inclusion criteria were to involve both male and female patients aged 30-80 years with knee osteoarthritis Kellgren and Lawrence grade 1–3 and VAS > 3. Patients with inflammatory, septic, post traumatic arthritis and undergoing physiotherapy were excluded. For intra-articular injection, anterolateral approach was used in all patients lying in supine position and knee flexed 90 degrees. After preparing the skin with chlorhexidine solution, sterile needle aims vertically midline towards intra-articular space, inserted lateral to patellar tendon around 1 cm above the surface of tibial plateu and at angle of 45 degree from anterior knee surface. Pain was assessed at baseline and at 3 months via visual analog scale. All the data was collected via a performa, entered and analyzed in SPSS version 20. Qualitative variable like gender and knee side were presented as frequency and percentage. Quantitative variables like BMI, age, VAS at baseline and at 3 months were presented as mean±S.D. Effect modifiers were controlled by stratification on the basis of age, gender, duration of symptoms and BMI. Comparison of mean pain in both group was done using t-test taking p< 0.05 as statistically significant.

RESULTS

Distribution of gender was done which showed that 15.6% (n=10) were male and 34.4% (n=22) females in HA +CS group and 12.5% (n=8) were male and 37.5% (n=24) were females in HA alone group. Distribution of knee side was done which showed that 9.4% (n=6) had right and 40.6% (n=26) left side in HA + CS group and 23.4% (n=15) right and 26.6% (n=17) have left side in HA alone group. Age distribution of the patients was done, it shows that out of 64 patients (32 in each), 7.8 %(n=5) were in age group of 30-50 years and 42.2%(n=27) were in age group of 51-80 years were in HA +CS group and 4.7 %(n=3) were in age group of 30-50 years and 45.3%(n=29) were in age group of 51-80 years were in HA alone group, mean age of HA + CS group was calculated as 59.22±8.027 years and mean age of HA alone group was 57.34±6.378 years. None of patients left study. Distribution of BMI, VAS score at baseline and VAS score at 3 months was calculated which was 27.92±7.074 in HA+CS group, 27.14±3.342 in HA alone group, 8.63±1.185 in HA+CS, 8.13±1.008 in HA alone group, 1.00±1.136 in HA+CS group and 4.13±1.755 in HA alone group respectively. The data was stratified for age, gender, duration of symptoms and BMI. Mean pain score was 1 in HA+CS group versus 4.13 in HA group (p=0.000).

Table no. 1: Distribution of BMI, VAS at baseline and VAS at 3 months N= 64

Variables	HA + CS Mean±SD	HA alone Mean±SD	p-value
BMI(kg/m2)	27.92±7.074	27.14±3.342	0.579
VAS at baseline	8.63±1.185	8.13±1.008	0.074
VAS at 3 months	1.00±1.136	4.13±1.755	0.000

Table no.2: Comparison of mean pain score in both groups using t-test N= 64

	Groups	N	Mean	S.D	p-value
Mean Pain Score	HA+CS	32	1.00	1.136	0.000
	HA alone	32	4.13	1.755	

DISCUSSON

The second most common cause of disability is knee OA, a chronic, degenerative joint disease that is heavily burdened socially and economically[16]. The current study is carried out to identify the ideal intra articular injection regimen for patients with knee OA and to establish a medical guideline, as the appropriate course of treatment for these individuals is still unclear. The current study's conclusion is that, when compared to HA alone, HA plus CS demonstrated a lower mean pain score. One molecule from the class of glycosaminoglycans is hyaluronic acid (HA). HA is a heterogeneous set of chemicals rather than a single molecule since its characteristics depend on its molecular weight and structure. The two primary functions of HA are joint lubrication and chondroprotection against mechanical damage[17]. In recent years, HA compounds have acquired higher quality. As a result, high-molecular-weight HA (HMWHA) was developed, and it was thought to affect the joint more favorably than low-molecular-weight HA (LMWHA).

The present study conducted on 64 patients revealed a significant alleviation in pain with HA+CS administration after three months of having received a single dose of both drugs versus HA alone.

In comparison a trial conducted by Wang et al. on 120 patients and assigned to the HA or HA&CS therapy groups (n=60/group) in basic variables such as, mean age, sex distribution, mean body mass index, mean VAS score, mean knee range of motion and mean Western Ontario and McMaster Universities Osteoarthritis Index did not show any significant variations between the groups. Most of the enrolled participants had clinical evaluations at the conclusion of the trial. Three patients in the HA&CS group were no longer followed up with at month six. Two patients in the HA group were not followed up with at month three, and two more patients were not followed up at sixth month. Before starting therapy, the VAS scores of the HA&CS and HA groups were not significantly different (7.45±2.05 vs. 7.30±1.96, respectively). After therapy, the HA&CS group's VAS score dropped considerably as compared to the HA group. By the sixth month, neither group's mean VAS score had changed substantially. In fact, it had grown. Following injection, patients in both groups had lower VAS scores; however, neither group's VAS score at month six differed significantly from the baseline[16]. The mean difference in pain reduction score within the first month was −4.24 (95% CI: −6.19 to −2.29, favoring IA-HA+anti-inflammatory drugs; ($P < 0.0001$), according to a study by Euppayo et al.. For the mean difference in pain reduction score from the second to the twelfth month, the ES of the random effects model was −1.39 (95% CI: −1.95 to −0.82; $P < 0.0001$). For the mean difference in pain reduction score within a year, the random effects model's ES was −1.63 (95% CI: −2.19 to −1.08, favoring IA-HA+anti inflammatory drugs; ($P < 0.0001$). For the heterogeneity test, the I 2 value was 83.48% and the P value was less than 0.0001. According to these findings, utilizing IA-HA+anti-inflammatory drugs considerably decreased pain scores in the first month following injection by 4.24 times ($P < 0.0001$) when compared to IA-HA alone. When compared to IA-HA alone, the use of anti inflammatory drugs + IA-HA reduced pain scores by 1.39 times between the second and the twelfth month ($P < 0.0001$). Using IA-HA +anti inflammatory drugs for a year significantly decreased pain scores over IA-HA alone by 1.63 times ($P < 0.0001$)[22]. The acute symptoms of OA may be significantly reduced by the anti-inflammatory properties of CS. Patients with osteoarthritis (OA) usually exhibit joint inflammation, which includes stiffness, warmth, discomfort, and joint effusions in the morning. These effusions are partially caused by thickening of the synovial membrane or synovial fluid. In the early phases of the inflammatory response, CS can

decrease leukocyte infiltration, edema, and capillary expansion due to its potent anti-inflammatory properties[18,19]. One of the patients who left the research early because of inadequate pain management eventually had total knee arthroplasty (TKA) at Southeast University's Affiliated Zhongda Hospital. Degenerative alterations to the knee joint and chronic synovial inflammation were revealed by radiographic pictures of the joint synovium and through pathological sections. An injection of HA alone usually isn't enough to reduce inflammation and ease pain in patients with OA and acute synovitis. In order to get the intended result, co-administration of a CS injection could be required[20]. Jüni et.al[21] found in a latest comprehensive review that corticosteroid injection had no effect at all after six months. The Department of Orthopaedics at The Affiliated Zhongda Hospital of Southeast University does not advise single corticosteroid injections because of cartilage loss linked to it and possible cardiovascular side effects. The current study's findings indicate that corticosteroid intra-articular injection cannot sustain pain alleviation for longer than six months, not even in conjunction with Hyaluronic acid. Therefore, for patients with knee osteoarthritis, it could be beneficial to co-inject HA and CS once every six months. When HA and CS are used in tandem, pain alleviation and improved knee function can be seen both in the short and long term. In the meantime, Hyaluronic acid may help to shield the cartilage erosion from corticosteroid, enhancing the safety of corticosteroid application. Limitation of study was to not assess and compare adverse reactions in both groups.

CONCLUSION

In the current study, we examined the mean pain score between individuals with osteoarthritis in their knee who received a combination of Hyaluronic acid and corticosteroid with those who received Hyaluronic acid alone. The results were significant (p=0.000). In comparison to patients who received HA alone, we found that patients who received co-treatment with HA and CS had a lower mean pain score.

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