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Comparison of Extracorporeal Shockwave Therapy versus Intra-Articular Injections of Hyaluronic Acid for the Treatment of Knee Osteoarthritis

Muhammad Shoaib, Musab Bin Noor*, Umar Shafique, Fraz Tahir*****

Department of Rehabilitation Medicine, PAF Hospital Islamabad Pakistan, *Department of Rehabilitation Medicine, Combined Military Hospital Bahawalpur /National University of Medical Sciences (NUMS) Pakistan, **Department of Rehabilitation Medicine, Combined Military Hospital Lahore /National University of Medical Sciences (NUMS) Pakistan,***Department of Rehabilitation Medicine, Combined Military Hospital Quetta /National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To compare efficacy of extracorporeal shock wave therapy (ESWT) versus intra-articular injections of hyaluronic acid (HA) in the treatment of knee osteoarthritis.

Study Design: Quasi experimental study

Place and Duration of Study: Department of Rehabilitation Medicine, Pakistan Air Force Hospital, Islamabad Pakistan, from Jan to Jul 2022.

Methodology: The total of 100 patients meeting inclusion criteria were randomly assigned to two groups. Group A patients underwent 3 x sessions of ESWT at weekly intervals with treatment protocol of 1000 shockwave pulses at intensity of 0.25mJ/mm2. Group B, patients underwent 3 x injections of Hyaluronic Acid (32 ml/2ml) at weekly intervals. Severity of knee pain on Visual Analogue scale was calculated at baseline, four weeks and twelve weeks after the intervention.

Results: At baseline Median ESWT VAS scores were 6(3). HA group VAS score was 6(2). At 4 weeks following the intervention, VAS ratings improved in both groups, with ESWT VAS of 2(2) and HA VAS of 2(1). At 12 weeks, median (IQR) of 3(0). HA group Median VAS scores were of 2(1), a statistically significant difference between both groups. Treatment with intraarticular injections of hyaluronic acid was therefore found to be more effective than Shockwave Therapy in providing long-term pain relief in knee osteoarthritis.

Conclusion: Hyaluronic acid and ESWT are both equally effective in providing short-term pain relief in knee OA, with Hyaluronic Acid proving more effective in the long term.

Keywords: Hyaluronic Acid, Knee Osteoarthritis, SWT.

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INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease that gradually worsens over time.[1] Several factors including family history, obesity, external trauma and ageing have been associated with development of arthritis.[2] Arthritis can develop in a variety of different joint structures, ranging from cartilages to whole joints. Deterioration of the joint occurs due to pathologic processes affecting the synovium, bone, and cartilage. Hallmarks of OA include Joint cartilage breakdown, the development of osteophytes, sclerosis of the subchondral bone, meniscal breakdown, and synovial proliferation.[3] Debilitating pain, impaired mobility, and decreased quality of life are all direct results of these pathologic processes. Common OA treatment objectives are to reduce pain, increase joint mobility, treat dysfunction, and enhance quality of life.[4] The majority of treatments for osteoarthritis (OA) focus on reducing patient suffering by minimizing pain and increasing range of motion in damaged joints, treating underlying dysfunction, and boosting patients' overall quality of life.

The most commonly affected joint in osteoarthritis is the knee joint.[5] Treatments for knee OA vary from pharmacological to non-pharmacological. The best treatment combines non-pharmacological and pharmacological therapies. Exercise, muscle strengthening, and weight control are some of the non-pharmacological treatments, along with transcutaneous electrical nerve stimulation (TENS) and thermal modalities. Medications used to treat arthritis pain and inflammation include NSAIDs, acetaminophen, opioids, capsaicin, and intra-articular injections of cortisone or glucosamine and hyaluronic acid (HA). The vast majority of patients suffering from osteoarthritis of the knee are elderly individuals who also have additional medical comorbidities. Intra-

Correspondence: Dr Muhammad Shoaib, Department of Rehabilitation Medicine, PAF Hospital, Islamabad Pakistan

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articular treatments are commonly used in this setting. Knee OA patients should consider intra-articular injections of HA plus corticosteroids. In circumstances where symptomatic treatment has proven inadequate, radiofrequency ablation and surgery may be considered.[6] Although there are several options for relieving the pain of knee OA, it often persists despite treatment.[7] Therefore, it is still important to study potential novel treatments for knee OA.

The use of extracorporeal shock wave treatment (ESWT) has increased in recent years due to its effectiveness in treating musculoskeletal disorders and relieving pain. ESWT has been shown to be effective in treating a wide variety of conditions, including epicondylitis, shoulder calcific tendonitis, plantar fasciitis, patellar tendonitis, Achilles tendinopathy, delayed union and non-union of long bone fractures, and avascular necrosis (AVN) of the femoral head.[8] Some animal studies have shown that ESWT can completely reverse knee OA.[9] These studies show that when ESWT is applied to an animal's arthritic joint, the course of OA is slowed, motor dysfunction is alleviated, pain is decreased, and there is a reversal of OA and chondroprotective benefits. Recent research has shown that ESWT can help people with knee discomfort and enhance their knee's functionality. Given these findings, ESWT should be considered a viable therapy option for knee OA.

A knee OA study,[10] compared intra-articular cortisone injection to ESWT with participants who received intra-articular corticosteroids injections and ESWT experiencing significantly more pain reduction, functional improvement, and knee range of motion in comparison with control group. These effects were seen to a greater degree in the ESWT group than in the intra-articular corticosteroid injection group. When it comes to treating symptomatic cases of knee osteoarthritis in humans, however, studies directly comparing ESWT with intra-articular HA injection are quite uncommon.

Therefore, this study aimed to compare the effectiveness of ESWT with intra-articular HA injection in the treatment of knee OA.

METHODOLOGY

This Quasi experimental study was carried out among patients presenting to the Rehabilitation Medicine outpatient clinic at PAF Hospital, Islamabad Pakistan, from January 2022 to June 2022. Approval was received from the institutional ethical review committee (IH/75988/3/org dated 30 jan). The sample size was calculated using the Open Epi calculator, taking the prevalence of knee Osteoarthritis as 6.3%, a confidence interval of 95% and a 5% margin of error. A non-probability consecutive sampling method was used to recruit 100 people in the study.

Inclusion Criteria: People of both genders fulfilling the following criteria were included in the study: 1) aged 35 years or above, 2) individuals with osteoarthritis of the knee as diagnosed by the American College of Rheumatology's criteria 3) Grade II or Grade III osteoarthritis affecting at least one knee based on the Kellgren-Lawrence radiological grading system. In case of patients with bilateral knee osteoarthritis, the knee with greater symptom severity was selected for the study.

Exclusion Criteria: The following subjects were excluded from the study: 1) Patients with neurological or cognitive conditions preventing them from accurately reporting outcome measures, 2) patients with history of trauma, sepsis, intraarticular injections or surgical interventions in affected knee, 3) patients with active autoimmune or infective conditions affecting the lower limbs or knee joints.

Prior to inclusion in the study, the study objectives were explained to the subjects in detail and written informed consent was obtained. The subjects were randomly placed in two groups using lottery, with Group A (n=50) receiving Extracorporeal Shockwave therapy and Group B (n=50) receiving intraarticular Hyaluronic Acid injections. In Group A, the Extracorporeal Shockwave therapy was administered using "Modus" ESWT machine manufactured by "Inceler Medikal" in 2019. Each patient underwent 3x sessions of ESWT at weekly intervals with treatment protocol of 1000 shockwave pulses at intensity of 0.25 mJ/mm2 administered to the tender-most point of the affected knee. In Group B, patients underwent 3x injections of 2ml of Hyaluronic Acid (32ml/2ml) into affected knee at weekly intervals. The injection was performed using strict asepsis via lateral mid-patellar approach with the patients lying supine and the knee flexed at 45 degrees. Both the procedures for Group A and B were performed by trained physicians. Demographic data was collected for all subjects, including age, gender, affected side and duration of symptoms.

Severity of knee pain on Visual Analogue scale was calculated at baseline. The primary outcome measure of this study was change in pain severity on Visual Analogue Scale at four weeks after the final

intervention, while the secondary outcome measure was change in pain severity on Visual Analogue Scale at twelve weeks after the final intervention.

Data was analyzed using statistical Package for Social Science (IBM Corporation) version 25.00. Frequency and percentage were calculated for the qualitative variables, including gender, and affected side. Mean and Standard Deviation were calculated for quantitative variables including age and duration of symptoms. Median and Interquartile Range was calculated for VAS score and Mann-Whitney U test was used to analyze the hypothesis.

RESULTS

All study subjects in both interventional groups completed the study, with no subjects lost to follow-up. The mean age of the subjects was 51.86±8.90, with the mean age in group A being 50.00±9.80 and in group B being 53.72±8.30. The overall male: female ratio was 49:51, the ratio in group A was 23:27 and in group B was 24:26. The mean duration of disease was 4.06±1.53 years in group A, and 4.50±1.70 in group B (Table-I).

Table-I: Demographic Characteristic of Study Groups (n=100)

Parameters	Group A Extracorporeal Shockwave Therapy (n=50)	Group B Intraarticular Hyalgan (n=50)
Gender		
Male	23(46%)	24(48%)
Female	27(54%)	26(52%)
Mean Age (Years)	50.00+9.80	53.72+8.30
Mean Duration (Years)	4.06+1.53	4.06+1.81

At baseline, the Median VAS score was with 6(3) in the ESWT group. VAS score was 6(2) in HA group. At 4 weeks after the intervention, VAS scores improved in both groups, with VAS median of 2(2) in the ESWT group and in the HA group was 1(1). This indicated that both interventions were effective in providing pain relief in osteoarthritis, and had similar efficacy. At 12 weeks, pain scores were higher as compared to 4 weeks, but still significantly lower than baseline, with VAS median of 3(0). Vas score were 2(1) in the HA group a statistically significant difference between both groups, as Hyaluronic Acid group showed lower pain scores as compared to Shockwave Therapy group (p<0.001) shown in Table-II. Treatment with intraarticular injections of hyaluronic acid was therefore found to be more effective than Shockwave Therapy in providing long-term pain relief in knee osteoarthritis.

Table-II: Comparison of Pain Score Among Study Groups (n=100)

Parameters	Group A Extracorporeal Shockwave Therapy Median (IQR) (n=50)	Group B Intraarticular Hyalgan Median (IQR) (n=50)	p-value
Pain score at baseline	6(3)	6(2)	0.083
Pain score at 4 weeks	2(2)	2(1)	<0.001
Pain score at 12 weeks	3(0)	2(1)	<0.001

DISCUSSION

Many people with knee OA receive non-operative therapy to manage their symptoms and overcome functional restrictions. The American College of Rheumatology (ACR) 2012 recommendations suggest a treatment strategy for knee OA that combines non-pharmacological and pharmacological therapy.[11] Lateral epicondylitis, calcific tendonitis of the shoulder, and plantar fasciitis are just a few of the many musculoskeletal conditions that have benefited from ESWT.[12] It was recently suggested that it could be used as a remedy for knee osteoarthritis. Subchondral bone and articular cartilage undergo pathological alterations in OA. It is unclear how exactly ESWT helps with joint OA, but it does seem to have an impact on the underlying pathophysiology of the condition. The impact of ESWT on subchondral bone and articular cartilage has been documented in certain animal studies.[13] There have been reports of ESWT improving subchondral bone and articular cartilage in some animal trials. The benefits of ESWT for knee OA have been demonstrated through a pathohistological and immunohistochemical study by Lee *et al*.[14] They found that ESWT restored OA-induced alterations in the arthritic knees of rats and had chondroprotective effects on the damaged cartilage.[15] Applying ESWT to arthritic rabbits decreased synovial NO production and blocked chondrocyte death, as shown by Zhao *et al*.[16] By taking this course of action, the catabolic rate within the arthritic joint was reduced, which had a beneficial influence on progression of the disease.

Both ESWT and intra-articular HA injections were found to be beneficial in reducing symptoms of pain and functional impairment in the initial follow up period. However, at 12-week period ESWT's healing benefits on knee OA were in contrast to those seen in earlier research. Hyaluronic acid effect was

comparatively better in the later stages. Patients with knee OA reported less pain and better knee functions at the 12-week follow-up following ESWT compared to those who received a placebo, according to Zhao *et al*.[15] Both low-energy ESWT (0.040 mJ/mm2) and medium-energy ESWT (0.093 mJ/mm2) were successful in reducing the knee discomfort of OA patients and enhancing their physical activities, as reported by Kim *et al*.[17] When comparing the two treatment groups, however, the medium-energy ESWT group showed much more therapeutic results. ESWT was tested on people with knee OA who had suffered a persistent stroke by Cho *et al*.[18] Doppler activity was found to increase during ultrasonic wave observation, and the pain reduction and improved benefits of ESWT were confirmed.[19] There are many benefits associated with ESWT. In particular, it is less intrusive, more accessible, requires no hospitalization, and has fewer potential side effects.

Research published recently suggests that HA injections into the joint may help OA of the knee. Injecting HA directly into a joint has been shown to improve physical function and decrease discomfort, and this practice has been widely reported and documented. An updated meta-analysis study found that 3 months following therapy for knee OA, intra-articular HA injections significantly reduced pain and improved functional impairment.[20] Although specific mechanism of HA is yet to be explained, a postulated mechanism for the effectiveness of HA has been published. In particular, HA demonstrated chondroprotective properties by binding to a cluster of differentiation 44(CD44) receptors. It also reduced chondrocyte apoptosis, displayed anti-inflammatory effects by altering leukocytes and interleukins, accelerated the production of glycosaminoglycan and proteoglycan, and exhibited physical properties such as joint lubrication and shock absorption, and had a pain relieving impact.[21]

We investigated self-reported measures with objective performance testing. Metrics based on performance were found to be higher than they were at the study's outset. The HA group's increased proficiency on performance-based measures is consistent with previous research. Patients with knee osteoarthritis were given intra-articular sodium hyaluronate injections, and the researchers measured the patients' physical functions using the visual analogue scale, self-paced walking, WOMAC, and stepping tests to demonstrate the treatment's effectiveness. In their study, Sun *et al.,* found that individuals with knee OA who received intra-articular HA reported significant improvements in pain, functionality, and stability.[22] For women with knee OA, Marks found that the duration of time spent stair-walking was significantly associated with pain, more so than age, height, weight or disease severity.[23] When we take the findings of these studies into account, we can say that the reduced pain experienced by the HA group is linked to the enhancement of their performance-based functions.

LIMITATION OF STUDY

There were certain limitations on the scope of this investigation. Since there were no placebo-controlled groups, no assessment of placebo effects could be made. None of the modifiable factors associated with ESWT effects (such as treatment intervals or energy intensity) were studied. Therefore, future research must include a substantial sample size, control groups, extended follow-up periods, and evaluations of the numerous aspects that may affect the treatment's success.

CONCLUSION

Patients with knee osteoarthritis who received treatment with shock waves and hyaluronic acid in the early stages of the disease experienced a decrease in the severity of pain as well as an improvement in their capacity to engage in physically demanding activities. Therefore, hyaluronic acid and ESWT are both equally effective in providing short-term pain relief for patients with knee osteoarthritis (OA). Hyaluronic acid, on the other hand, was shown to be more effective throughout the course of time in comparison to ESWT.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MS & MBN: Data acquisition, data analysis, critical review, approval of the final version to be published.

US & FT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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