ORIGINAL ARTICLE

THE EFFECTIVENESS OF INTRA-ARTICULAR INJECTIONS HYALURONIC ACID AND CORTICOSTEROIDS IN THE TREATMENT OF PATIENTS WITH KNEE OSTEOARTHRITIS SYMPTOMS

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ABSTRACT

Introduction: Knee osteoarthritis (OA) is a degenerative condition that is caused by the gradual wear and tear of the cartilage that cushions the bones of the knee. This study will find out the effectiveness of intra-articular hyaluronic acid (IAHA) and intra-articular corticosteroids (IACS) in the management of knee OA.

Material & Methods: A randomized control trial was conducted in Hayatabad Medical Complex Peshawar and Pak Military Hospital Rawalpindi from March 2019 to June 2021. Total one eighty-two patients were randomly assessed in the study. Treatment group A received intra-articular hyaluronic acid (IAHA), while treatment group B received intra-articular corticosteroids for three months. This study has used Western Ontario and McMaster Universities Arthritis Index (WOMAC) to evaluate the effectiveness of treatment in both groups of knee OA.

Results: The study participants mean age was 56.344 ± 7.25. Out of 182 patients, 2 of the patients reported as "loss to follow up" from IACS Tx group b. Treatment groups include 95 (52.7%) female patient while 85 (47.22%) were male patients. 96 (53.33%) received intra-articular hyaluronic acid (IAHA), while 84 (46.66%) received intra-articular steroids (IACS). The pre- and post-treatment mean difference in WOMAC scores in the hyaluronic acid group was 5.52 ± 4.756, while that in the corticosteroid group was 9.495 ± 1.24 (p value < 0.01).

Conclusion: Intra-articular steroids (IACS) and hyaluronic acid (IAHA) alone reduces OA symptoms and pain significantly. Yet intra-articular steroids are more effective than intra-articular hyaluronic acid in reducing symptoms of OA at knee.

Key Words: knees; osteoarthritis; corticosteroids**;** hyaluronic acid; effectiveness.

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INTRODUCTION

Knee osteoarthritis (OA) is a degenerative condition that is caused by the gradual wear and tear of the cartilage that cushions the bones of the knee.[1-2] According to the National Health

and Nutrition Examination Survey (NHANES), about half of patients diagnosed with knee OA complained of knee pain.[3] There is a profound effect on the knee with the demographic risk factors of age, sex, and body mass index (BMI).[4, 5] Knee osteoarthritis is a typical condition that is present globally due to an increase in metabolic disorders and obesity. [5]

Knee OA affects over 9% of the world's population. The prevalence of OA increases with age, with older adults being at the highest risk.[4,5] Additionally, OA is more common in women than men. In the US, it is estimated that more than 30 million adults have OA. Patients who come to the hospital are usually more anxious to relieve their pain (5). By the time people enter a tertiary hospital setting, enough time has passed, so the assumptions are high for tertiary care physicians to accurately treat their worsening symptoms.[6] OA is the leading cause of knee sign and symptoms worldwide. Many interventions have been used to reduce side effects. NSAIDs, steroids, and hyaluronic acid are often used by rheumatologists until the patient receives a total knee replacement. [7]

In recent years, several trials and surveys have been published to determine the effective response of treatment to support patients with knee OA, which plays a vital role in weight bearing of the body. Alireza Askari et al in 2016 led a RCT to evaluate the efficacy of steroids and hyaluronic acid (HA). According to the findings of this study, hyaluronic acid provides long-term pain relief, whereas IACS have a short-term effect that is inserted at regular intervals, making HA intervention a better option. [8] Another randomized controlled trial in 2016 compared intra-articular infusion of Hylan G-F 20 Hyaluronic acid (IAHA) with injection of intra-articular corticosteroids (IACS) and concluded that the two drugs had similar efficacy.[9] Christopher Smith et al published a systematic review in 2019 that concluded that combination of IAHA and IACS resulted in pain reduction at 2–4, 24–26 and 52 weeks compared to HA injection alone.[10]

Total knee replacement (TKR) is a treatment option for patients with knee OA, but it is not feasible for all patients. In this particular situation, as far as practicality and cost-effectiveness are concerned, the recommended interventions of IAHA and IACS are appropriate and should be used routinely.[11] This study fills a gap in the nearby population literature by looking at the feasibility of intra-articular infusion of IAHA and IACS for the management of patients with knee OA in the rheumatology departments of Hayatabad Medical Complex, Peshawar and Pak Military Medical Hospital, Rawalpindi.

MATERIAL AND METHODS

Prior to starting the study, permission was obtained from the institution's ethics committee vide NCS/DPT/1274/19. The study participants were patients diagnosed with knee OA who presented to the rheumatology department of Hayatabad Medical Complex Peshawar and Pak Military Medical Hospital Rawalpindi between March 2019 and June 2021. The ages of these persons were between 18 and 60 years old and patients who fulfills the criteria of American College of Rheumatology classification criteria 1997. [12]

WHO sample size calculator was used to calculate the sample size using the population ratio of 14.6%. A convenient sampling method of non-probability sampling technique was used to collect the sample size required for this study. [13] Randomization was done using free accessible website (http://www.randomization.com) which were used to randomly assign patients to two treatment groups (A and B). [8]

Patients having conditions other than OA were excluded. Patients having history of bone fracture and surgery, multivitamins deficiency or other metabolic disorder etc. leading to bone pain, were excluded from the study. Patients who used alternative therapies and having history at which IACS and IAHA causes adverse effects were also excluded from the trial. Patients who can't follow up for three months were also excluded from the trial.

Patients signed an informed consent form before enrolling, that included a detailed description of the study as well as the risks of drugs and intraarticular (IA) procedures. Total one eighty patients were randomly assessed in the study using online accessible randomization website. Treatment group A received intra-articular hyaluronic acid (0.6-6 mg), while treatment group B received intra-articular corticosteroids (methylprednisolone 80 mg) for three months. WOMAC questionnaire was used at baseline and after three months of

management to evaluate the effectiveness of treatment in both treatment group A and B. [14,15] The patients' responses were evaluated using the WOMAC. It covers all the major characteristics of osteoarthritis in three domains: stiffness, physical functioning and pain. In patients suffering from osteoarthritis, twenty-four elements span all three areas. A score might range from 0 to 100 based on the sum of all the patients' responses. [16] Patients in both groups were evaluated using WOMAC before beginning medication and again three months later. Differences in WOMAC scores pre and post treatment were compared between the two groups. SPSS 23.0 was used for statistical analysis. Means and standard deviations were calculated for patients' ages, WOMAC scores difference pre and post management and length of illness. A student's t-test, with a p-value less than or equal to 0.05 was used to assess WOMAC scores pre and post management of knee OA. [15,16]

RESULTS

Many OA patients were omitted from the study due to strict inclusive and exclusive criteria. Of 192 patients contacted 182 (94.79%) individuals with knee OA were included in the study. Of them 12 (6.25%) refused to volunteer, the final stood at 182 (94.79%). Out of 182, 2 of the participants were reported as "loss to follow up" from treatment group B (IACS) as shown in figure 1.

Table I shows the mean age of study participants in groups A and B was 56 and 56.878 respectively, resulting in a mean age of research participants of 56.439 ±7.35. out of 180 participants, 95 (52.7%) female patients were included, while 85 (47.22%) participants were men. The average duration of symptoms prior to management was 14.12 ± 3.455 months. Out of 182 patients who were randomly randomized to one of two treatments. 96 (53.33%) received IAHA and 84 (46.66%) received IACS. As shown in Table II that the mean difference in WOMAC score pre and post management of IACS was 9.495±1.24, whereas in the IAHA group was 5.52 ± 4.756(p-value <0.01).

DISCUSSION

Developed countries and developing countries have a long waiting list for TKR. Few patients with knee OA undergo standard treatment of TKR because of the many complications. Consequently, this study was designed to evaluate the effectiveness of IAHA and IACS in the management of knee OA.

Wei-Wei He et al. published a systematic review and meta-analysis that concluded that IACS treatment options were more effective in managing pain in the short term, while IAHA was effective in the long term. Both were effective treatments, but the IAHA treatment caused more adverse outcomes than IACS.[17] Egemen Ayhan et al. (2014) published literature on IACS and IAHA for the treatment of knee OA. This study concluded that intra-articular injections are safe and have good outcomes. However, the study was not sure about the disease-modifying effect and the placebo effect of these drugs. The choice of CS is reasonable for severe and persistent synovitis in patients who cannot undergo surgery. CS has good efficacy in the short term. In this study, patients who were unwilling to undergo surgery preferred long-term IAHA intervention. [18]

Vito Pavone et al. in 2021 concluded a systematic review which aims to point out the effectiveness of intra-articular injections of the main drugs. Caution should be done using CS with repetitive use due to potential harm as CS reduce pain intensity. HA has shown good outcomes in terms of functional improvement and pain reduction. In conclusion, the authors confirm that IA steroids are effective, but their efficacy may be short-lived (<4 weeks). [19] One study has concluded that a combination of IACS and IAHA resulted in pain reduction at 2-4, 24-26 and 52 weeks compared to HA injection alone. [20]

The current study provides significant evidence regarding the use of IACS in the management of knee OA. In our study patient feedback was only collected after three months of treatment. There are some limitations in the current study. First, follow-up in case of chronic knee pain could have generated good results, due to which long-term effects of treatment of IAHA and IACS are still questionable and are not reported. Future studies with better design preferably systematic review should be carried out for reviewing the evidence present and the generalizability of results.

CONCLUSION

IACS and IAHA reduces knee OA symptoms and pain significantly. Yet intra-articular steroids were more effective than intra-articular

hyaluronic acid in reducing knee osteoarthritis symptoms.

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Table 1: Characteristics of the individuals with osteoarthritis knee

Table 1 shows the characteristics of the individuals with osteoarthritis knee who participated in the study	
Total patients included in study(n)	N=182
Gender	
Male	85 (47.22%)
Female	95 (52.7%)
Age (years)	18 years-60 years
Mean age of Group A	56
Mean age of Group B	56.978
Mean + SD	56.439±7.35
Range (min-max)	57 year - 18 years = 39 years
Mean duration of Symptoms (months)	14.1 ± 3.455 months

Table 1. Difference in WOMAC Score Pre and Post Treatment of Knee Osteoarthritis

Table II: Difference in WOMAC score in both the groups before and after the treatment	
Groups	N
Corticosteroid	96(53.33%)
Hyaluronic Acid	84(46.66%)
Difference in WOMAC score	
Corticosteroid	9.495±1.24
Hyaluronic Acid	5.52±4.756
p-Value	<0.001

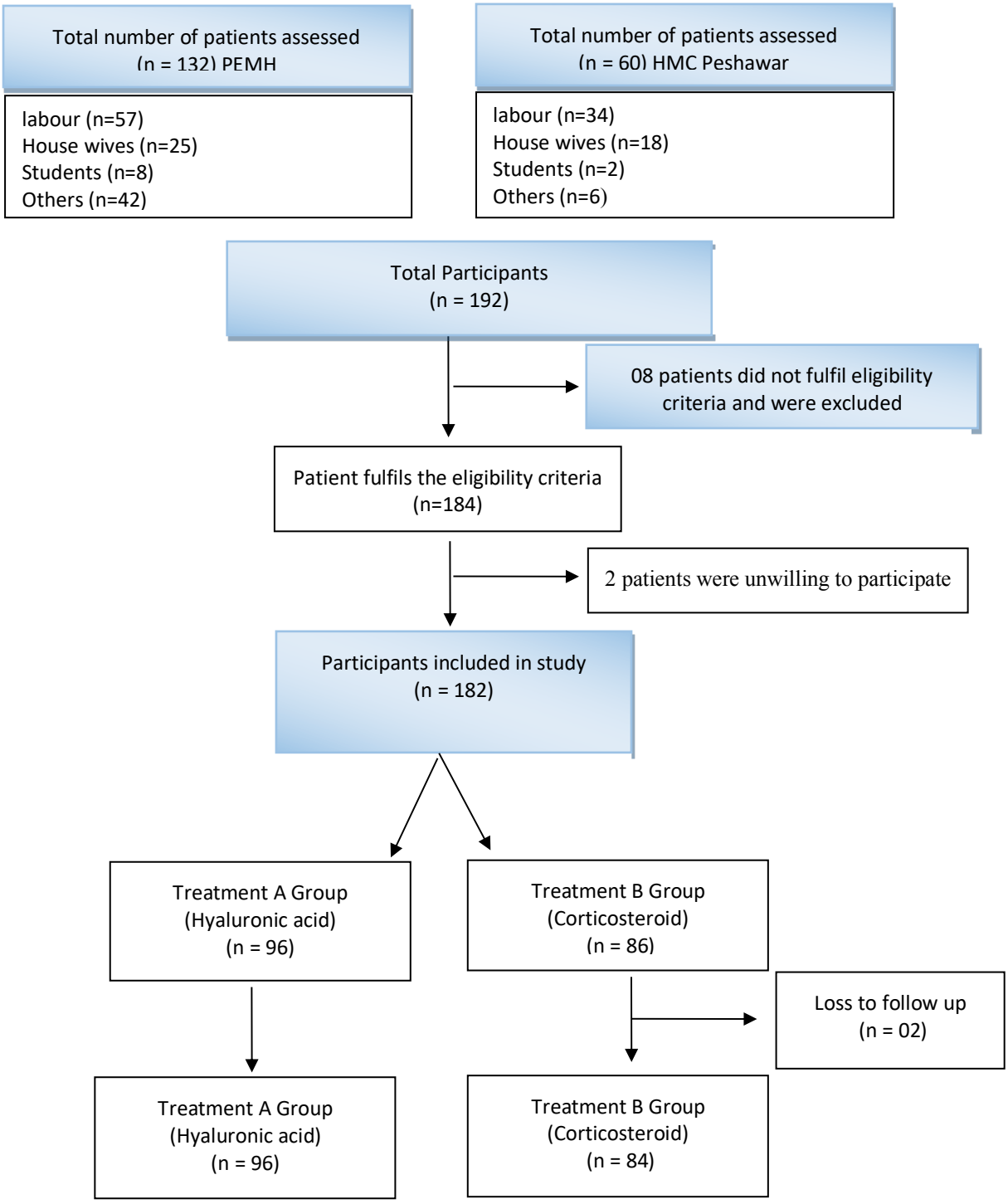

Figure 1: Flowchart of participants in the study