Original Article

Comparison of Intraarticular Injection of Hyaluronic Acid and Steroids in Reducing Pain of Initial Stages of Knee Osteoarthritis

Muhammad Aamir[1], Kashif Saddiq[1]. Sajjad Ahmad[1], Irfan Ali Shujah[1], Muhammad Khizer Hayat Makki[1] and Adnan Nazir[2]

ABSTRACT

Objective: To compare the mean change in VAS score after intra-articular injection of Hyaluronic acid and Steroids in patients with initial stages of knee osteoarthritis.
Study Design: Randomized controlled trail study.
Place and Duration of Study: This study was conducted at the department of Orthopedics, BVH Bahawalpur from September 2017 to February 2018.
Materials and Methods: To compare the mean change in VAS score after intra-articular injection of Hyaluronic acid and Steroids in patients with initial stages of knee osteoarthritis
Results: The mean age in group A was 59.55 ± 7.60 years and group B 59.37 ± 8.26 years. Out of these 80 patients, 52 (65.0%) were females and 28 (35.0%) males with 1.85:1 female-male ratio. Mean pre-treatment VAS score in group A was 6.30 ± 1.38 while in group B was 5.95 ± 1.50. Mean post-treatment VAS score in group A was 4.48 ± 1.26 while in group B was 1.60 ± 0.93. Mean reduction in VAS score in group A was 1.82 ± 0.12 while in group B was 4.35 ± 0.57.
Conclusion: We recommend hyaluronic acid in patients with initial stages of knee OA because significant reduction in mean VAS score (at 6 months) observed with intra-articular hyaluronic acid as compared to corticosteroid use.
Key Words: Knee osteoarthritis, hyaluronic acid, corticosteroid, intra-articular injection

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INTRODUCTION

Knee Osteoarthritis is a degenerative joint disease with gradually advancing softening and wearing of knee joint cartilage. It is characterized by following changes in subchondral bone like sclerosis, osteophytes and cyst formation along with synovitis and fibrosis of joint capsule[1]. Pain, tenderness, stiffness and joint swelling are common symptoms in early stages, while deformity and loss of function occur in late stages. Although osteoarthritis (OA) can affect any synovial joint but osteoarthritis of knee is most cumbersome in terms of prevalence and disability[2,3]. It is an age related disease[4]. It is most common cause of disability around the world and widespread musculoskeletal problem[5].

Department of Orthopedics, Civil Hospital, Bahawalpur.

Correspondence: Dr. Muhammad Aamir, Senior Registrar of Orthopedic Surgery, Civil Hospital Bahawalpur.
Contact No:0345 8709062
Email: drmaamir586@gmail.com

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The estimated prevalence of symptomatic osteoarthritis of knee in the USA has been 12%. Sever pain results in functional impairment with limitation of daily life activities and poor quality of life of patients[6].
It is divided into primary when no etiology found and secondary when there is definite etiology leading to disease. Risk factors are joint dysplasia, trauma, obesity, occupation and family history. On radiographic basis it can be divided into five stages, 0 to 4, with normal joint space to complete loss of joint space. Treatment options are, non-pharmacologic, pharmacologic and surgical. Non-pharmacologic are weight reduction, low impact exercise and physical therapy. Pharmacologic options are NSAIDs, intra-articular (IA) steroids and Hyaluronic acid (HA). Surgical options are joint debridement, realignment osteotomy, joint replacement and arthrodesis.
In one study conducted by Seth S. Leopold[7] "Intra-articular injection of Steroids is compared with HA for initial stages of knee OA. Another study conducted by Adrian C. Jones[8] also compared steroids with HA for initial stages of knee OA. As few studies have been done in Pakistan to compare the intraarticular injection of Steroids with Hyaluronic acids, so I have decided to carry-out study. If results of my study shows which recommended for use in Pakistan..

MATERIALS AND METHODS

This RCT conducted at department of Orthopedics BVH Bahawalpur from September 2017 to February 2018. Using non-probability consecutive sampling, 80 patients were enrolled with their consent including male and female, aged 40-70 years & Knee OA stage 1, 2 and 3 according to Kellgren and Lawrence classification. Patients with stage 4 Knee osteoarthritis, insufficiency of collateral ligaments, insufficiency of anterior and posterior cruciate ligaments, intraarticular injection within 3 months of registering into study, thrombocytopenia with platelet count less than $100x10^9$/liter, radiographic findings of chondro-calcinosis, any systemic disease, cardiovascular, hematologic, tumor or anesthesia.immunosuppression were excluded from the study.

Two groups made as A and B, each containing 40 patients. Group A patients were injected depomedrol 80 mg intra-articularly using 22-G needle after local anesth Patient may ask for another injection of steroid at any time during study period. Group B patients treated by Hyaluronic acid; three injections given at weekly interval.Year three Post graduate trainees performed the procedures. Following the injection patients were asked to take rest for 15 minutes before leaving and instructed to limit exercise for 24 hours and use only acetaminophen to relieve pain. Assessment of group A & B by VAS score was performed at 3 months and final outcome at 6 months. SPSS 21 used to analyze the data. Mean deviation and SD was calculated for age and mean reduction in pain score. Student 't' test used to evaluate the mean reduction in pain score in both groups and p-value ≤0.05 was regarded significant. For both groups stratification was performed regarding age, gender and stage of knee osteoarthritis to minimize the confounding effects.

RESULTS

Table No.I: Age distribution for both groups (n=80).

Age (years)	A (n=40)		B (n=40)		Total (n=80)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
40-50	09	22.50	12	30.0	23	28.75
51-60	12	30.0	10	25.0	23	28.75
61-70	19	47.50	18	45.0	34	42.50
Mean ± SD	59.55 ± 7.60		59.37 ± 8.26		59.46 ± 7.89	

Table No. 2: Mean pre & post therapy VAS score

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.30	1.38	5.95	1.50
Post-treatment (at 6 months)	4.48	1.26	1.60	0.93
Reduction in pain score	1.82	0.12	4.35	0.57

P-value <0.0001 which is statistically significant.

Table No. 3: Comparison of Mean reduction in VAS score in both groups for age 40-50 years.

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.40	1.42	5.83	1.53
Post-treatment (at 6 months)	4.80	1.03	1.75	0.87
Reduction in pain score	1.60	0.39	4.08	0.66

P-value <0.0001 which is statistically significant.

Table No. 4: Comparison of Mean reduction in VAS score in both groups for age 51-60 years.

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.28	1.32	6.40	1.43
Post-treatment (at 6 months)	4.43	1.34	1.40	0.97
Reduction in pain score	1.85	0.02	5.00	0.46

P-value <0.0001 which is statistically significant.

Table No. 5: Comparison of Mean reduction in VAS score in both groups for age 61-70 years.

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.25	1.48	5.78	1.56
Post-treatment (at 6 months)	4.31	1.35	1.61	0.98
Reduction in pain score	1.94	0.13	4.17	0.58

Table No. 6: Comparison of Mean reduction in VAS score in both groups for Male gender.

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.19	1.36	5.92	1.53
Post-treatment (at 6 months)	4.41	1.12	1.60	0.96
Reduction in pain score	1.78	0.24	4.32	0.57

P-value <0.0001 which is statistically significant.

Table No. 7: Comparison of Mean reduction in VAS score in both groups for Female gender.

VAS Score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.54	1.45	6.0	1.51
Post-treatment (at 6 months)	4.62	1.56	1.60	0.91
Reduction in pain score	1.92	0.11	4.40	0.60

P-value <0.0001 which is statistically significant.

Table No. 8: Comparison of Mean reduction in VAS score in both groups for Stage 1.

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.53	1.50	5.94	1.39
Post-treatment (at 6 months)	4.59	1.37	1.63	1.02
Reduction in pain score	1.94	0.13	4.31	0.37

P-value <0.0001 which is statistically significant.

Table No. 9: Comparison of Mean reduction in VAS score in both groups for Stage 2.

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.21	1.31	5.78	1.63
Post-treatment (at 6 months)	4.57	1.22	1.50	0.94
Reduction in pain score	1.64	0.09	4.28	0.69

Table No. 10: Comparison of Mean reduction in VAS score in both groups for Stage 3.

VAS score	A (n=40)		B (n=40)	
	Mean	Standard Deviation	Mean	Standard Deviation
Pre-treatment (baseline)	6.00	1.32	6.20	1.62
Post-treatment (at 6 months)	4.11	1.17	1.70	0.82
Reduction in pain score	1.89	0.15	4.50	0.80

P-value <0.0001 which is statistically significant.

DISCUSSION

Osteoarthritis (OA) is, no doubt, one of the most common types of chronic arthritis, with radiographic evidence of medial compartment and patellofemoral part of knee joint involved in greater than 50% of population over 65 years of age.[9] Around, 18% women and 10% males have symptomatic Osteoarthritis. It is a degenerative joint disease with gradually advancing softening and wearing of knee joint cartilage characterized by mobility impairment and joint pain. Currently there is no definitive cure and treatment goals are symptomatic relief, improvement in function and joint mobility thus optimizing quality of patient,s life.[10]Non-pharmacological as well as pharmacological methods are used to manage OA of the hip and/ or knee (and other sites). Patients having advanced osteoarthritis and unresponsive to medicines are offered joint replacement surgery.[9,10]

Analgesics, NSAIDs, IA steroids injection and IA hyaluronan injections are main drugs to control pain of knee osteoarthritis. Recently disease modifying drugs have been introduced to slow up degenerative process in the cartilage along with pain relief for examples chondroitin sulfate, glucosamine sulfate and hyaluronan.[11] IA injections of HA have been found beneficial in the management through improving synovial fluid viscosity, lubrication of joint, inhibiting proteoglycan degradation, optimizing hyaluronan production, and expressing anti-inflammatory and analgesic effects.[12,13] IA corticosteroid injections inhibit inflammatory cytokines and appeared relatively safe for treatment of OA in the past decad.[14] However, symptom free interval is considerably low than the suggested interval between the doses of IA corticosteroids.[15]The effects of Corticosteroids and placebos, Hyaluronan and other placebos have been studied in various systematic reviews but CS and HA effects comparing studies are very few. So, this randomized controlled study has compared mean change in VAS score after intra-articular Steroids and Hyaluronic acid injection to treat initial stages of osteoarthritis knee.

Primary osteoarthritis is often asymptomatic and commonly affects the elderly group with radiographic evidence in approximately 80-90% of individuals older than 65 years.[16] Symptoms Typically after the age of 50 years early symptoms appear. The prevalence rises dramatically after 50 years because joint cartilage tensile strength decreases with age associated changes in proteoglycans & collagen and reduced supply of nutrients to cartilage.[16] The age ranged 30-70 years in our study while mean was 59.46 ± 7.89 years. The mean age in group A was 59.55 ± 7.60 years and in group B was 59.37 ± 8.26 years. 34 (42.50%) patients constituting main bulk were found between 61-70 years.

The predominance ratio of female gender to male (1.85:1) in our study coincides with results of many previous studies.[17,18,19,20] Similarly erosive osteoarthritis more common in females with a ratio 12:1 (female-to-male).[16]

In a meta-analysis done by Wang F et al[21], high quality trials with 583 participants reflected equal effectiveness for CS and HA following one month. VAS mean difference was 1.66 (95% CI; -0.90, 4.23). However, 03 months later, the mean difference was -12.58 (95% CI; -17.76, -7.40), while 06 months later, the difference was -9.01 (95% CI; -12.62, -5.40), preferring HA. Hence in comparison with CS, HA possessed greater relative effect. In our study, mean pre-treatment VAS score in group A was 6.30 ± 1.38 while in group B was 5.95 ± 1.50. Mean post-treatment VAS score was 4.48 ± 1.26 in group A while in group B was 1.60 ± 0.93. Mean reduction in VAS score was 1.82 ± 0.12 in group A while in group B was 4.35 ± 0.57. So statistically significant difference exist between the two groups (p<0.0001). Jones AC et al[20] in his study has shown the mean VAS at the start and end of study in Hyaluronic acid and steroids groups respectively as 53.2 ± 5.6 and

55.3 ± 5.3, 28.2 ± 7.2 and 48.6 ± 9.6 with the mean reduction of 6.7 ± 4.3 and 2.5 ± 1.6 respectively.

Other studies[22-23], consisting 116 CS treated and 129 patients with HA (n=245),expressed reduce VAS score (mean 1.66 mm) with CS in comparison with the HA group following one month but statistically the difference was not significant (P=0.20; I2=48%; 95% CI, −0.90, 4.23). Three studies[24,25,26], involving 165 HA treated and 155 patients treated with CS (n=320), favoring efficacy of HA with significant reduction in VAS score(mean of 12.58 mm, range 7.40 - 17.76) following 03 months when compared with steroid group (95% CI; P<0.00001; I2=42%). A conclusion of five studies[20,22-25] after six months of treatment with 217 HA and 194 patients of CS injection (n=411) showed results favoring HA intraarticular knee injection therapy with significant reduction in VAS score (mean 9.01 mm, range 5.40 to 12.62), in comparison with CS group (P<0.00001; I2=47%, 95% CI).

Narayanan SS et al[27] in his study concluded that a regime of three intraarticular injection of hyaluronic acid administered in three consecutive weeks has a significant effect on functional outcome and reduction of osteoarthritic knee pain for at least six months. Gydek A et al[28] has shown VAS pain score at rest and during walking before treatment with hyaluronic acid as 3.4 ± 2.2 and 5.0 ± 2.1 respectively. After treatment the VAS pain score at rest and during walking decreased to 1.5 ± 1.5 and to 2.2 ± 1.7 respectively.

Results of many studies are expressing short term functional improvement and symptomatic relief with intraarticular corticosteroids in osteoarthritis of Hip and Knee. Ravaud et al[29] RCT study of 6 months concluded that corticosteroids injection into joint improved symptomatic outcome for initial four weeks and gradually effect decreased over 12 weeks. A quality review consisting of 1973 patients (knee osteoarthritis) in 28 RCTs expressed improvement in pain for 1–34 weeks without improvement in function with intraarticular steroids. Nine trials assessed HA and hylan derivatives vs IA steroids. HA products showed similar outcome along with more durable benefit over 5–13 weeks after injection.[30]

Stretching over 6.7 years, Petrella et al[31] recent study with 537 patients having osteoarthritis of knee given weekly three hyaluronic acid (500-730 kD) injections intraarticularly. The same cycle repeated if patient desired so. There was 27±7 weeks interval between the two courses. The outcome assessed at 6 months follow up. Some long term benefit of hyaluronic acid also noted. Overall this study concluded reduction in mean VAS score with IA hyaluronic acid vs IA steroid in Knee osteoarthritis patients.

CONCLUSION

This study concluded that there is significant reduction in mean VAS score (at 6 months) with hyaluronic acid compared to IA injection of corticosteroid in patients with initial stages of knee OA. So, we recommend that intra-articular hyaluronic acid injection should be used routinely in the management of knee OA for reducing pain as well as morbidity of these particular patients..

Author's Contribution:

Concept & Design of Study:	Muhammad Aamir
Drafting:	Kashif Saddiq, Sajjad Ahmad,
Data Analysis:	Irfan Ali Shujah, Muhammad Khizer Hayat Makki and Adnan Nazir
Revisiting Critically:	Muhammad Amir Kashif Saddiq
Final Approval of version:	Muhammad Aamir

Conflict of Interest: The study has no conflict of interest to declare by any author.

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