ORIGINAL ARTICLE

A Comparative Study on Effectiveness of Intraarticular Injection of Steroid and Steroid Plus High Molecular Weight Hyaluronate in Primary Osteoarthritis Knee

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Abstract

Background: Primary osteoarthritis knee is a degenerative joint disease which is becoming a burden on the society as the aging population is increasing day by day due to increased healthcare facilities. Often, patients need nonsteroidal antiinflammatory drugs (NSAIDs) for pain reduction along with disease-modifying osteoarthritic drugs, and NSAID use in aged population is itself a risk factor for developing gastrointestinal, renal, and cardiovascular side effects. Many patients need intraarticular injection of steroid or high molecular weight (HMW) hyaluronate to reduce pain specially in those who do not respond to NSAID and are in high-risk group for developing side effects of NSAIDs. This study is an attempt to compare the effectiveness of intraarticular injection of steroid (i.e., depot-methylprednisolone) and steroid plus HMW hyaluronate in primary osteoarthritis knee, as literature survey revealed that there is a scarcity of study which compared the effectiveness of intraarticular injection of steroid and steroid plus HMW hyaluronate in primary osteoarthritis knee.

Materials and methods: This is a single-blind randomized parallel group study conducted in the Department of Physical Medicine and Rehabilitation, Institute of Post-Graduate Medical Education and Research and Seth Sukhlal Karnani Memorial Hospital, Kolkata, for a period of 18 months taking 30 subjects in each group. Patients with Kellgren–Lawrence radiological grading II and III of primary osteoarthritis knee were taken in the study group. Patients who did not cooperate to receive intervention, patients with secondary osteoarthritis knee, who had history of allergy to any component of viscosupplementation, patients with grade I and IV osteoarthritis knee, with gross knee instability, patients who received intraarticular injection in the last one year, and patients having contraindications of intraarticular injection were excluded from the study. Visual analogue scale pain and fifty feet walk time were the primary outcome measures. After taking clearance from the institutional ethical committee, patients were selected based on the inclusion and exclusion criteria, and the baseline assessment was done on the parameters. The selected patients were divided into two groups randomly. Written informed consent was taken from all patients before interventions. One group received intraarticular injection of steroid (depot methylprednisolone 40 mg) and another group received intraarticular injection of steroid plus HMW hyaluronate in a single sitting.

Injections were administered under strict aseptic condition. After administering injections, the patients assessed at an interval of 6 weeks (visit-2) and 12 weeks (visit-3) using the parameters mentioned above. The results have been analyzed according to the standard statistical methods to fulfill the aims and objectives of the study.

Discussion: A majority of patients were females with a mean age of 56.26 years with standard deviation 10.364. Most of the patients had K–L grade III osteoarthritis knee with mean body mass index (BMI) 22.60 and with standard deviation 1.708. Visual analogue scale pain and fifty feet walk time improved in both groups in all visits, but the difference of improvement between groups was not statistically significant.

Keywords: Comparative study, High molecular weight hyaluronate, Intraarticular injection, Osteoarthritis knee, Steroid, Viscosupplementation.

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Introduction

Osteoarthritis (OA) knee is a degenerative joint disease and becomes much more common in the aged.[1,2] Osteoarthritis is the most prevalent articular disease in adults aged 65 years and older and now affects up to 6% of the population, accounting for up to 20% of consultations at the primary care level and is a leading cause of disability at work.[3] Corticosteroid injection should be considered for patients with the knee OA who continue to have pain despite acetaminophen, particularly if they are at particular risk for renal dysfunction.[4] For knee OA patients, corticosteroid injection can be potentially used in conjunction with a course of viscosupplementation (hyaluronate containing solution). Viscosupplementation is FDA approved for patients with the knee OA who continue to have pain despite regular dosage of a simple analgesic such as acetaminophen and nonpharmacologic therapy.[5] After extensive search, it is noted that there is a lack of research on comparative study between effectiveness of intraarticular injection of steroid and steroid plus HMW hyaluronate in primary osteoarthritis knee. Therefore, this project is an attempt to find out the comparison of effectiveness between intraarticular steroid and steroid plus HMW hyaluronate (combined group) in primary osteoarthritis knee.

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Aims and Objectives

To compare the effectiveness of intraarticular injection of steroid and steroid plus high molecular hyaluronate in primary osteoarthritis knee.

Materials and Methods

Institutional Ethical Committee Clearance has been taken and individual informed consent was taken from the patients to be included in the study. The study was conducted in the Department of Physical Medicine and Rehabilitation, Institute of Post-Graduate Medical Education and Research and Seth Sukhlal Karnani Memorial Hospital, Kolkata, and extended from December 2010 to May 2012, and 30 subjects with primary osteoarthritis knee who attended the OPD were included in each group. For the purpose of sample size calculation, pain in VAS was considered as the primary outcome measure. It was a single-blind randomized parallel group study. All patients with primary osteoarthritis knee, i.e., OA with no identifiable etiology or predisposing cause of grade II and grade III of Kellgren–Lawrence (K–L) grading system of radiological classification for the knee OA, were included in the study (K–L grading system includes grade I—unlikely narrowing of joint space with possible osteophytes, grade II—possible narrowing with small osteophytes, grade III—definite joint space narrowing with moderately sized osteophytes and some sclerotic areas, and grade IV includes severe joint space narrowing with multiple large osteophytes and marked sclerosis). Patients who were excluded from the study were those who did not want to participate in the study, patients with grade I and grade IV OA knee, patients having secondary osteoarthritis knee, who are allergic to viscosupplementation, with gross knee instability, with joint prosthesis, patients having contraindication of intraarticular injection, and patients who received intraarticular injection in the knee joint in the last one year.

Parameters studied:

- Pain in VAS
- 50 feet walk time (in seconds).

Study Technique

After taking clearance from the Institutional Ethical Committee, the patients were selected for intervention as per the inclusion and exclusion criteria. The selected patients were examined and assessed at baseline (visit 1) first and the study parameters are measured. The selected patients were divided into two groups randomly. One group received intraarticular injection of methylprednisolone and another group received intraarticular injection of methylprednisolone plus HMW hyaluronic acid in the knee joint. The injections were administered in strict aseptic condition. After the intervention, the patients were assessed at the interval of 6 weeks (visit 2) and 12 weeks (visit 3) using the study parameters. The results have been analyzed according to the standard statistical methods to fulfill the aims and objectives of the study.

Intervention

All patients were educated regarding joint protection and lifestyle modification and all patients were advised exercises for OA knee. All patients were instructed to perform range of motion of the knee exercises and to perform 3–5 sets of 8–12 repetitions per set per knee of quadriceps setting exercises as well as 3–5 sets of 8–12 repetitions per set of wall slides. Only paracetamol 1 g was advised as analgesic on as and when required basis with a maximum tablets of two a day. For intraarticular injection, written informed consent was taken from each and every patient. Forty (40) mg of methylprednisolone was given in symptomatic knee under aseptic condition (for steroid group of patients). For combined group, first 40 mg of methylprednisolone was injected under aseptic condition followed by injection of 6 mL of HMW hyaluronate under aseptic condition in the same sitting in the symptomatic knee. Before injecting any drug, aspiration was attempted under aseptic condition and the fluid was aspirated as much as possible. All injections were administered blindly by a single person following standard techniques as mentioned in the text books of Physical Medicine and Rehabilitation by Joel A Delisa.

Results

Data have been summarized by usual description statistics such as mean and standard deviation (SD) for numerical variables that are normally distributed, and median and interquartile range for those that are not. Numerical variables compared between groups by paired *t* test as variables were normally distributed. Changes from baseline to end of the study have been assessed by paired sample *t* test for parametric variables. Categorical variables are compared between groups by Chi-square test or Fisher's exact test as appropriate.

Demographics

Sex

As Tables 1 and 2 exhibit, there is a majority of females in both study groups.

Age

Figures 1 and 2 reflect the frequency bars of the two study groups. The mean age over both groups is 56.2 years (Table 3).

BMI

Figures 3 and 4 reflect the frequency bar charts of BMI for both groups which are comparable. Table 4 shows the mean BMI over both groups is 22.6.

Radiological Grading

Figures 5 and 6 show the frequency chart of the radiological grading (Kellgren–Lawrwnce) for both groups. Grade III has a preponderance in both groups.

Table 1: Descriptive statistics for sex distribution in steroid group (S = steroid group)

		SEX_S			
		Frequency	*Percent*	*Valid percent*	*Cumulative percent*
Valid	Male	9	36.0	36.0	36.0
	Female	16	64.0	64.0	100.0
	Total	25	100.0	100.0	

Table 2: Descriptive statistics for sex distribution in combined group (SH = combined group)

		SEX_SH			
		Frequency	*Percent*	*Valid percent*	*Cumulative percent*
Valid	Male	7	28.0	28.0	28.0
	Female	18	72.0	72.0	100.0
	Total	25	100.0	100.0	

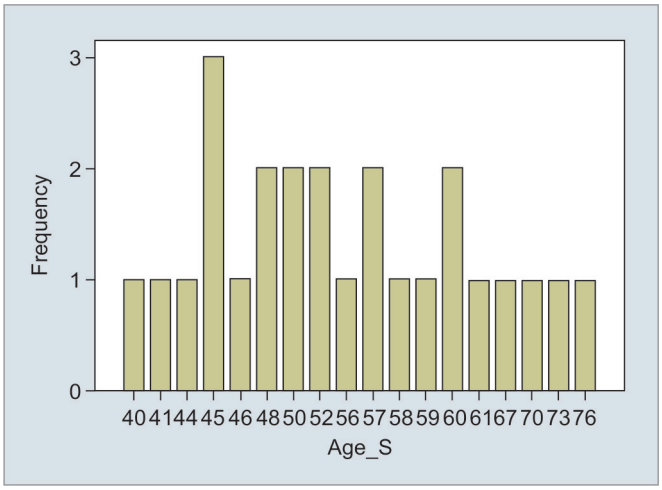

Fig. 1: Descriptive statistics for age distribution in steroid group

Fig. 2: Descriptive study for age distribution in combined group

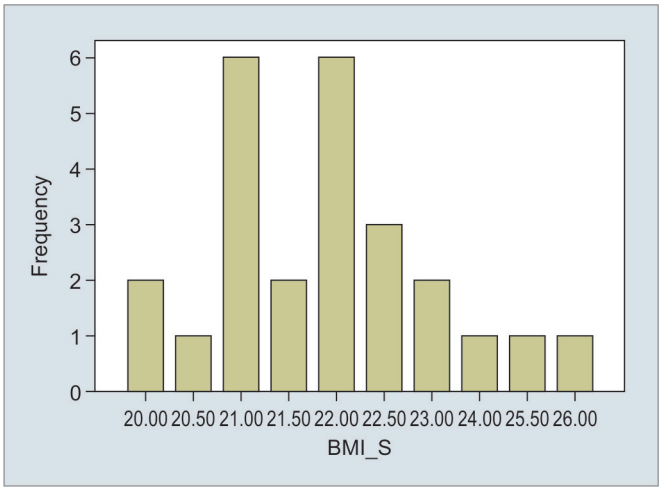

Fig. 3: Descriptive statistics for BMI (body mass index) in steroid group

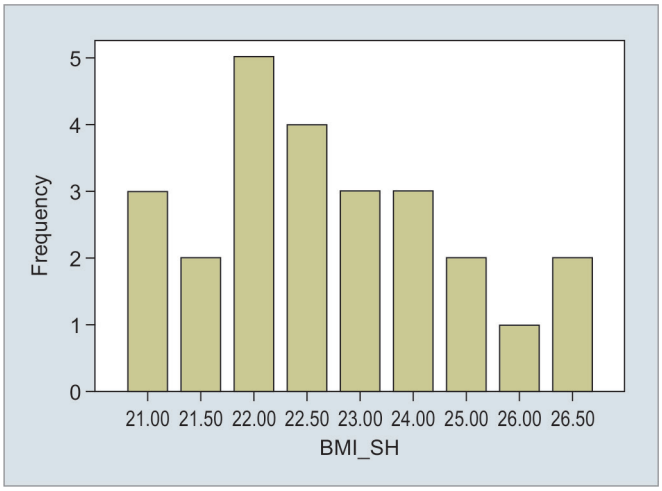

Fig. 4: Descriptive statistics for BMI in combined group

Table 3: Mean age for both groups

Age		
Mean	*N*	*Std. deviation*
56.2600	50	10.36440

Table 4: Mean BMI

BMI		
Mean	*N*	*Std. deviation*
22.6000	50	1.70832

VAS

Table 5 shows VAS for pain improved significantly from first visit to second visit and from first to third visit, but from second to third visit, though improvement was there but that was not statistically significant.

Table 6 shows that similar to steroid group, from second to third visit, there was no significant improvement, but from first to second and from first to third visit, there was statistically significant improvement of VAS pain in combined group.

Table 7 shows VAS pain in both groups improved in every visit, i.e., before interventions (V1) and after interventions (V2 and V3), but there was no statistically significant difference of improvement between groups.

Table 8 shows that fifty feet walk time significantly improved from baseline to second visit and from baseline to third visit, but the improvement was not statistically significant from second to third visit.

Table 9 shows that fifty feet walk time improved significantly from first to second and from first to third visit in combined group, but no statistically significant improvement was seen from second to third visit.

Table 10 shows that fifty feet walk time improved in both groups in every visit, but difference of improvement was not statistically significant between groups.

Dropout

Thirty patients participated in each group, but on subsequent follow-up, five patients in each group failed to attend the department for follow-up, so in total, ten patients were dropped out from the study.

Adverse Effects

No adverse effect occurred in any patient.

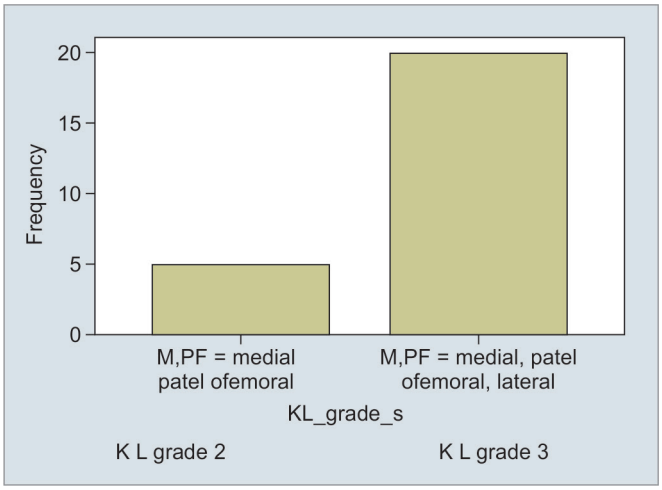

Fig. 5: Descriptive statistics for Kellgren–Lawrence grade in steroid group (K–L = Kellgren–Lawrence)

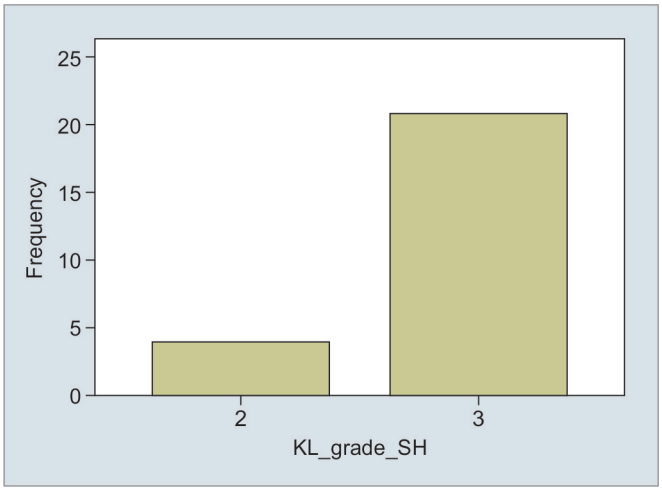

Fig. 6: Descriptive statistics for K–L grade in combined group (II = medial, patellofemoral III = medial, patellofemoral, lateral)

Table 5: Paired sample *t* test for VAS pain of steroid group for all visits

		Paired differences				
					95% confidence interval of the difference	
		Mean	*Std. deviation*	*Std. error mean*	*Lower*	*Upper*
Pair 1	PAIN_VAS_V1_S–PAIN_VAS_V2_S	1.72000	1.59478	0.31896	1.06171	2.37829
Pair 2	PAIN_VAS_V2_S–PAIN_VAS_V3_S	0.92000	1.18743	0.23749	0.42985	1.41015
Pair 3	PAIN_VAS_V1_S–PAIN_VAS_V3_S	2.64000	2.28910	0.45782	1.69510	3.58490

Table 6: Paired sample *t* test for VAS pain of combined group for all visits

		Paired differences				
					95% confidence interval of the difference	
		Mean	*Std. deviation*	*Std. error mean*	*Lower*	*Upper*
Pair 1	PAIN_VAS_V1_SH–PAIN_VAS_V2_SH	2.24000	2.18480	0.43696	1.33816	3.14184
Pair 2	PAIN_VAS_V2_SH–PAIN_VAS_V3_SH	1.60000	2.27303	0.45461	0.66174	2.53826
Pair 3	PAIN_VAS_V1_SH–PAIN_VAS_V3_SH	3.84000	2.52784	0.50557	2.79656	4.88344

Table 7: Paired sample *t* test for VAS pain for between group comparison in all visits

		Paired differences				
					95% confidence interval of the difference	
		Mean	*Std. deviation*	*Std. error mean*	*Lower*	*Upper*
Pair 1	PAIN_VAS_V1_S–PAIN_VAS_V1_SH	0.72000	2.74651	0.54930	−0.41370	1.85370
Pair 2	PAIN_VAS_V2_S–PAIN_VAS_V2_SH	1.24000	3.25679	0.65136	−0.10434	2.58434
Pair 3	PAIN_VAS_V3_S–PAIN_VAS_V3_SH	1.92000	3.96779	0.79356	0.28218	3.55782

Table 8: Paired sample *t* test for fifty feet walk time of steroid group for all visits

		Paired differences				
					95% confidence interval of the difference	
		Mean	*Std. deviation*	*Std. error mean*	*Lower*	*Upper*
Pair 1	FIFTY_FT_WT_V1_S–FIFTY_FT_WT_V2_S	2.52000	2.00250	0.40050	1.69341	3.34659
Pair 2	FIFTY_FT_WT_V2_S–FIFTY_FT_WT_V3_S	1.04000	1.48549	0.29710	0.42682	1.65318
Pair 3	FIFTY_FT_WT_V1_S–FIFTY_FT_WT_V3_S	3.56000	2.59936	0.51987	2.48704	4.63296

Table 9: Paired sample *t* test for fifty feet walk time of combined group for all visits

		Paired differences				
					95% confidence interval of the difference	
		Mean	*Std. deviation*	*Std. error mean*	*Lower*	*Upper*
Pair 1	FIFTY_FT_WT_V1_SH–FIFTY_FT_WT_V2_SH	3.36000	3.82840	0.76568	1.77971	4.94029
Pair 2	FIFTY_FT_WT_V2_SH–FIFTY_FT_WT_V3_SH	1.68000	2.01494	0.40299	0.84827	2.51173
Pair 3	FIFTY_FT_WT_V1_SH–FIFTY_FT_WT_V3_SH	5.04000	4.33474	0.86695	3.25071	6.82929

Table 10: Paired sample *t* test for fifty feet walk time for between-group comparison in all visits

		Paired differences				
					95% confidence interval of the difference	
		Mean	*Std. deviation*	*Std. error mean*	*Lower*	*Upper*
Pair 1	FIFTY_FT_WT_V1_S–FIFTY_FT_WT_V1_SH	−1.28000	7.26590	1.45318	−4.27922	1.71922
Pair 2	FIFTY_FT_WT_V2_S–FIFTY_FT_WT_V2_SH	−0.44000	7.64897	1.52979	−3.59734	2.71734
Pair 3	FIFTY_FT_WT_V3_S–FIFTY_FT_WT_V3_SH	0.20000	7.04746	1.40949	−2.70905	3.10905

Discussion

The effectiveness of intraarticular injection of steroid[6] and HMW hyaluronate in primary osteoarthritis knee has been studied and claimed for a long time,[7] and there are many studies which compared the effectiveness of the two in primary osteoarthritis knee.[8,9] There is a lack of studies which compared the effectiveness of intraarticular injection of steroid and steroid plus HMW hyaluronate in primary osteoarthritis knee. This study showed that in primary osteoarthritis knee, a majority of patients were females as shown in Tables 1 and 2, and it is prevalent in older population with a mean age of 56.26 years as shown in Figures 1, 2 and Table 3. Obesity is an important factor which leads to escalation of cartilage degeneration, though in this study the mean BMI (body mass index) was 22.60 as shown in Figures 3, 4 and Table 4. A majority of the patients had Kellgren–Lawrence radiological grading III of OA knee as shown in Figures 5 and 6. Grade I and grade IV patients were not included in the study, as most of the grade I patients do not have significant pain and other discomforts, so detection of improvement could not be understood and comparison with other group would not be appropriate, and in grade IV patients, it is very difficult to administer injection intraarticularly as the joint space is greatly impaired with the presence of subchondral sclerosis in K–L grade IV osteoarthritis knee.

Statistical analysis of primary outcome measures showed that VAS pain improved significantly from baseline visit to second visit and from baseline visit to third visit, and the improvement from second to third visit was not statistically significant in both the groups as shown in Tables 5 and 6. There was no statistically significant difference of improvement of VAS pain between two groups in each visit as depicted in Table 7. Analysis of fifty feet walk time also revealed similar kind of results. Statistically significant improvement of fifty feet walk time was seen from first to second and first to third visit, but improvement of second to third visit was not statistically significant in both the groups as shown in Tables 8 and 9. There was no statistically significant difference of improvement of fifty feet walk time between the groups in each visit as depicted in Table 10. Onset of improvement of pain could not be determined as most of the patients could not remember the time of onset; also, the duration of pain could not be determined as the final follow-up was at 12th week. So, future research can be designed to study those. No adverse reaction occurred in any patient which suggests that both the treatment options are safe if not otherwise contraindicated.

Limitations

The study had several limitations as follows:

Sample size was small in each group and no control group was taken. It was a short-term study as the final follow-up was at 12 weeks, so it was not possible to know the treatment effects after 12 weeks postinjection. Initial frequent follow-up and statistical analysis were not done, so this study has a limitation to conclude about the immediate postinjection effect. Image-guided interventions such as ultrasound or C-arm can be considered in future for further research.

Conclusion

Both intraarticular injection of steroid and steroid plus HMW hyaluronate are effective in primary osteoarthritis knee in terms of reduction of pain and fifty feet walk time, and also, no treatment option is statistically significantly better than the other after six and twelve weeks postinjection.

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