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Original Article

Comparison of Intra-Articular Steroid Injection with Combined Oral Steroid and Intra-Articular Steroid Injection to Treat Patients with Knee Osteoarthritisa

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ABSTRACT

Objective: To evaluate the benefits provided by a short course of low dose oral Prednisolone followed by intra-articular injection of Methylprednisolone to treat osteoarthritis Knee as compared to intra-articular injection of Methylprednisolone and placebo.

Study Design: Quasi-experimental study

Place and Duration of Study: Department of Rehabilitation Medicine, Combined Military Hospital Quetta, Pakistan from Aug to Nov 2023.

Methodology: Ninety nine patients with OA of Knee joint were randomly assigned to 3 groups, Group-A received a short course (14 days) of low dose oral steroids (15 mg Prednisolone) followed by one intra-articular steroid injection (administered two weeks later). Patients in Group-B received intra-articular injection of steroid only and Group-C received intra-articular injection of normal saline. All patients were evaluated using the Western Ontario and McMaster Universities (WOMAC) & Visual Analogue Scale (VAS) score before the treatment and at 2,6,12 and 16 weeks following treatment.

Result: There were significant improvements in both Group-A & Group-B. Particularly, patients in Group-A had significantly superior VAS and WOMAC scores than were seen in groups B and C. The VAS and WOMAC scores remained the same as were pre-treatment in group C. Group-A and B both showed improvement but to different extent with superior results in Group-A till 16 weeks.

Conclusion: The combination of short course of low dose oral steroids with intra-articular steroid injections resulted in significantly superior symptomatic improvement, with sustained lower VAS and WOMAC scores, hence improving quality of life for 16 weeks.

Keywords: Methylprednisolone, Osteoarthritis, Prednisolone.

How to Cite This Article: *Mahboob F, Razzaq S, Ahmad I, Rashid M, Younus U, Shah SH. Comparison of Intra-Articular Steroid Injection with Combined Oral Steroid and Intra-Articular Steroid Injection to Treat Patients with Knee Osteoarthritisa. Pak Armed Forces Med J 2025; 75i1: 121-126. DOI: https://doi.org/10.51253/pafmj.v75i1.11526*

INTRODUCTION

Osteoarthritis is a common and disabling condition that represents a substantial and increasing health burden. Clinically, the knee is the most common site of osteoarthritis, followed by the hand and hip[1].Pain and stiffness are the chief complaints along with reduced physical function. Diagnosis of hip or knee OA can be made on the basis of the history and physical exam. Radiographs portray the severity of structural damage and improve specificity when osteophytes or joint space narrowing are present[2].

One cardinal feature of OA pathogenesis is deranged or increased pro-inflammatory cytokines level. Since inflammation has a major role in pathogenesis of osteoarthritis and pain is a major symptom common therapeutic measures for knee OA are mainly based on the use of oral or local application NSAIDs and oral or intra-articular corticosteroids. Biologic research is now focused on the importance of growth factors in the maintenance of normal tissue structure and tissue lesion repair[3].

This study aimed to explore the anti-inflammatory role of oral steroid in therapeutic management of OA and to investigate the superiority of intra-articular steroid injection following a short course of low dose oral steroid as compared to just intra articular steroid injections for the medical management of symptomatic osteoarthritis knee. We hypothesised that steroid intra-articular injection following a short course of low dose oral steroid

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Received: 21 Jan 2024; revision received: 01 Feb 2024; accepted: 16 Feb 2024

treatment will be more efficacious than the intra-articular steroid injection alone both in the short and long term.

METHODOLOGY

The study protocol was reviewed and approved by the Institutional Ethical Review Board of CMH Quetta Hospital (IERB/14/2023) and study was conducted from Aug 2023 to Nov 2023. Patients were enrolled after consent at the outpatient department of rehabilitation medicine. G Power software was used to estimate sample size, 33 patients were randomly assigned to each of 3 groups

Inclusion criteria: Patients aged 45-75 years who had knee pain and swelling for at least 4 months, OA knee joint classified as Kellgren Lawrence/ K-L grade 2 and 3 on radiographs and BMI ranging from 18-31 were included in the study.

Exclusion criteria: Patients with OA knee joint secondary to trauma/ sepsis , OA Knee joint classified as K-L grade 1 and 4 on radiograph, connective tissue/autoimmune disorders and BMI > 31, were excluded.

Using a random number table, 102 patients were assigned into 3 groups randomly (Figure-I). Patients of Group-A were given, short course of oral Prednisolone 15 mg daily for 14 days before intra-articular injection in lateral tibiofemoral joint through lateral suprapatellar approach of 2 ml of Methylprednisolone (80mg) combined with 3 ml of Bupivacaine, Group-B was given intra-articular injection of 80 mg of Methylprednisolone (2 ml) with 3 ml of Bupivacaine. Group-C received 5 ml of normal Saline as intra-articular knee injection.

VAS & WOMAC scores were used as the primary outcomes. Firstly, knee pain was evaluated with VAS score and patients expressed their pain on a scale of 0-10, with 10 as extreme pain. Secondly, WOMAC total and subscale scores were recorded. Patients were evaluated 5 times; before treatment, at 2nd, 6th, 12th and 16th week following the Intra-articular injection. Categorical variables (OA knee grade, gender) were shown as frequency and continuous variables (age, BMI, pain and function scores) were reflected by standard deviation & mean. For initial VAS and WOMAC scores ANOVA was performed for comparison of the pre-procedure values, for repeated measures, analysis of variance was done for comparing VAS and WOMAC scores at different evaluations. The least significant difference (LSD) test was used for post-hoc analysis to compare the three groups after treatment. SPSS 26.0 software package was used for statistical analysis with p value < 0.05 deemed statistically significant.

RESULTS

102 enrolled patients fulfilled the inclusion criteria. 2 participants were lost from group A, and another from group B. Hence, a total of 99 of the 102 recruited patients were evaluated till 16 weeks post-injection treatment. The gender, age, BMI, osteoarthritis grade, before treatment WOMAC and VAS scores depicted no significant differences on pre-treatment evaluation (Table-I).

Table I - Comparison of Demographic Features (n=99)

Variables	Group-A	Group-B	Group-C	*p*-value
Age (years) (Mean ± Sd),Range	61.58±6.06, (45-70)	61.61±6.75, (45-72)	60.76±5.10, (45-70)	0.258**
Gender (Male:Female)	12:21	19:14	16:17	
BMI (mean ± SD), kg/m2	24.44±1.57	24.42±1.60	23.27±1.98	0.421**
Grade 2	10	13	17	
Grade 3	23	20	16	
VAS (mean ± SD)	6.88±0.99	6.76±1.03	6.82±1.07	0.060**
WOMAC (mean ± SD)				
Pain	14.39±2.14	14.30±2.33	14.30±2.40	0.750**
Stiffness	4.67±0.85	4.45±0.79	3.94±0.64	0.351**
Function	45.06±7.77	44.45±6.60	45.33±6.30	0.120**
WOMAC Total	64.12±10.27	63.21±9.26	63.58±9.71	0.625**

VAS:Visual analogue scale, Western Ontario and McMaster Universities (WOMAC) score, *significant difference (p< 0.05)

Patient's pain was evaluated on a 10-cm scale of VAS and after treatment it reduced to different extent on 2nd week follow-up for all groups but more in Group-A & Group-B.

Repeated measures ANOVA showed significant differences in pain (VAS) for each group (F = 22.154, p=0.005). Post-hoc tests revealed, pain reduction for Group-A was notably superior to Group-B and Group-C. There was a significant difference between Group-

A & B at 2nd , 6th , 12th & 16th weeks (p=0.002, p=0.00,p=0.02,p=0.02) (Table-II) (Figure-II).

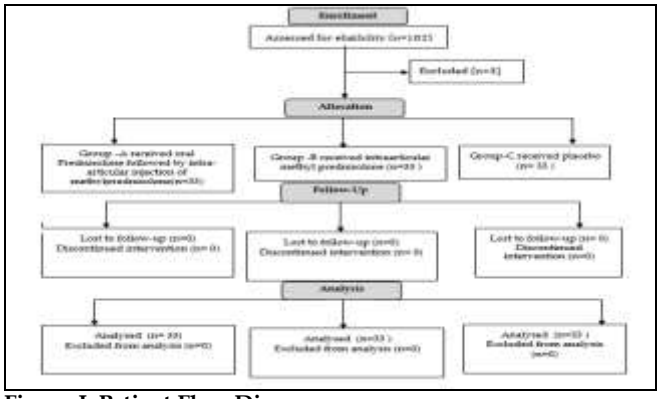

Figure-I: Patient Flow Diagram

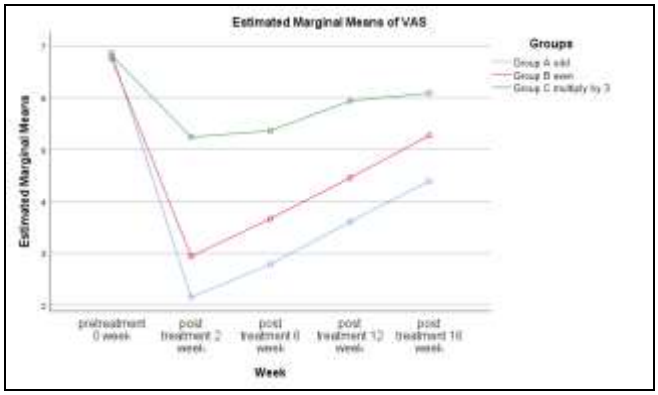

Figure-II

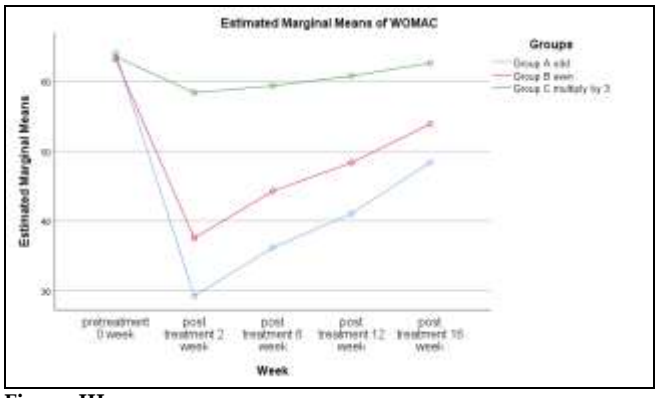

Figure-III

Regarding WOMAC pain subscale; significant improvement was seen in both Group-A & B as compared to the pre-treatment values but Group-A showed significant superiority as compared to Group-Btill 16 weeks and Group-Balso showed better improvement than C till 16th week (p= 0.00). The stiffness subscale of WOMAC expressed significant difference between Group-A and B even at the 12th week but not at 16th week (p=0.005, p =0.285 respectively), the same was true for comparison between Group-Band C at the 12th & 16th week (p = 0.001, p = 0.646, respectively). As for WOMAC function subscale, every group initially showed significant improvement but even Group-A was not significantly better than B at 16th week (p=0.06). Total WOMAC scores expressed significant improvement in Group-A as compared to Group-Beven at 12th and 16th week (p=0.000, p=0.016) (Figure-III) (Table -III).

DISCUSSION

Osteoarthritis (OA) is the most common chronic joint disorder, leading contributor to disability in terms of years lived with disability and is characterized by local inflammation and structural joint damage[4]. In our study, The combination oral and IA steroid injection group was significantly superior to intra-articular steroid group and placebo in both VAS score and WOMAC pain, stiffness and function subscales till 16 weeks post treatment, claiming that the oral steroid combined with intra-articular injections may have additional value. Both intra-articular steroid injection groups showed reduction in clinical efficacy at 16 weeks, still appeared well compared with their initial values, and placebo. Short course of oral low dose steroid administered for 14 days in patients with knee OA was to supress the complicated inflammatory process occurring in all compartments of knee (synovium, cartilage, bone, ligaments, tendons and bursae) by diffuse drug delivery as compared to IA injection. This course led to reduction in tenderness, swelling and stiffness and prepared the joint well for IA injection and was associated with better and longer lasting pain relief. This also eliminated the risk of toxic effect of high dose steroid on cartilage and possibility of septic arthritis, by reducing the number of IA injections for symptomatic relief. As far as we know, no study has endeavoured to measure the therapeutic effect of oral steroid course before giving IA steroid injection for OA knee as compared to direct IA glucocorticoid injection. This novel technique is particularly effective in treatment of mild and moderate OA knee. This regimen offers clinicians with a new treatment option, with fewer injection and effective relief for a longer time. This treatment was found to be cost effective, potent for pain reduction and avoids any immune responses or reactions. OA community is intensely investigating synovial inflammation as we now know more about the cellular and molecular players in

Table II- Visual Analogue Scale (VAS) Scores Mean ± SD (95% CI) for Group-A, Group-B, Group-C (n=99)

Groups	Pretreatment Week	2nd Post Treatment week	6th Post Treatment Week	12th Post Treatment Week	16th Post Treatment Week
A	6.88±0.99**	2.15±0.44*	2.79±0.65*	3.61±0.74*	4.39±0.99*
	(6.51–7.24)	(1.79–2.51)	(2.42–3.14)	(3.24–3.96)	(4.03–4.75)
B	6.76±1.03**	2.94±0.89*	3.67±0.92*	4.45±0.97*	5.27±0.94*
	(6.39–7.11)	(2.57–3.30)	(3.31–4.02)	(4.09–4.81)	(4.91–5.63)
C	6.82±1.07**	5.24±1.37*	5.36±1.45*	5.94±1.45*	6.09±1.33*
	(6.45–7.18)	(4.88–5.60)	(5.00–5.72)	(5.58-6.30)	(5.72–6.45)
p	>0.05**	<0.05*	<0.05*	<0.05*	<0.05*

Table III- WOMAC Scores for Group A, B, C Mean ± SD (95% CI) (n=99)

Variables	Groups	Pre-Treatment Week	Post Treatment Week 2	Post Treatment Week 6	Post Treatment Week 12	Post Treatment Week 16
Pain	A	14.39± 2.15** (13.59–15.19)	5.70±1.64 (4.90-6.49)	7.21±2.04 (6.41 – 8.07)	8.79±2.35 (7.99 – 9.58)	10.27±2.54 (9.47-11.06)
	B	14.30±2.33** (13.50-15.09)	8.03±2.66 (7.23-8.82)	10.12±4.40 (9.32-10.91)	10.97±2.64 (10.17-11.76)	12.27±2.67 (11.47 – 13.06)
	C	14.30±1.40** (13.50-15.09)	12.61±1.51 (11.81-13.40)	12.94±1.54 (12.14 – 13.73)	13.24±1.67 (12.44 – 14.03)	13.97±1.51 (13.17 – 14.76)
	p-value	>0.05**	<0.05*	<0.05*	<0.05*	<0.05*
Stiffness	A	4.67±0.85 (4.42-4.91)	1.30±0.58 (1.05-1.55)	2.09±0.67 (1.84-2.33)	2.61±0.74 (2.35-2.85)	3.52±0.93 (3.26-3.76)
	B	4.45±0.79 (4.20-4.70)	1.82±0.80 (1.57-2.06)	2.58±0.86 (2.33-2.82)	3.12±0.92 (2.87-3.37)	3.73±0.94 (3.48-3.97)
	C	3.79±0.41 (3.69-4.18)	2.79±0.54 (2.63-3.12)	3.18±0.58 (2.96-3.45)	3.76±0.43 (3.51-4.00)	3.82±0.39 (3.57-4.06)
	p-value	<0.05*	<0.05*	<0.05*	<0.05*	<0.05*
Function	A	45.06±7.77** (42.90-47.21)	22.21±5.56 (20.05-24.37)	26.85±8.22 (24.29-29.00)	29.64±6.90 (27.47-31.79)	34.58±9.12 (32.41-36.73)
	B	44.45±6.60** (42.29-46.61)	27.67±7.16 (25.50-29.82)	31.58±6.93 (29.41-33.73)	34.24±7.37 (32.08-36.40)	37.88±7.59 (35.72-40.03)
	C	45.33±3.30** (43.17-47.49)	42.91±3.39 (40.75-45.06)	43.21±3.12 (41.05-45.37)	43.79±3.17 (41.63-45.94)	44.85±3.17 (42.69-47.00)
	p-value	>0.05**	<0.05*	<0.05*	<0.05*	<0.05*
Total	A	64.12±10.27** (61.31-66.93)	29.21±6.80 (26.40-32.02)	36.15±9.40 (33.34-38.96)	41.03±8.90 (38.22-43.84)	48.36±11.33 (45.55-51.17)
	B	63.21±9.26** (60.40-66.02)	37.52±9.63 (34.70-40.32)	44.27±10.31 (41.46-47.08)	48.33±9.93 (45.52-51.14)	53.88±10.40 (51.06-56.68)
	C	63.58±3.71** (60.76-66.38)	58.39±4.00 (55.58-61.20)	59.39±3.63 (56.55-62.17)	60.79±3.71 (57.97-63.59)	62.64±3.93 (59.82-65.44)
	p-value	>0.05**	<0.05*	<0.05*	<0.05*	<0.05*

synovitis , although more in-depth studies are needed to evaluate the role of anti-inflammatory pharmacotherapy for long term relief of symptoms and to halt the disease process[4].

Several OA risk factors, including ageing, obesity, trauma and mechanical loading, play a role in OA pathogenesis, likely by modifying synovial biology[5]. Synovial inflammation is present in the OA joint and has been associated with radiographic and pain progression[4]. One of the most important factors in the pathogenesis of OA is a disturbed cytokine balance in favor of pro-inflammatory cytokines[6]. As far as the treatment of the OA knee is concerned, patient education, weight loss encouragement for overweight patients, exercise, self-efficacy and self-management programs are considered core treatments for hip and knee OA[7]. Unfortunately, no approved disease-modifying drugs exist, and non-operative therapies are associated with only small to moderate benefits and may have serious adverse effects[8].

NSAIDS and glucocorticoids have a vital role in pharmacotherapy of this degenerative joint disease because of their anti-inflammatory and analgesic properties. In latest updated OARSI guidelines, topical NSAIDs were recommended more strongly than all oral analgesics due to a favourable balance of consistent efficacy and minor, transient side effects[9]. Patients unable to take NSAIDs, or who do not respond, can try intra-articular corticosteroid injections, which typically relieve pain for a few weeks[10]. Currently, intra-articular triamcinolone acetonide and MethylPrednisolone are most commonly used to treat KOA[11], former ensures pain relief for more than 12 weeks (12), while later significantly relieves early pain in OA patients, and the efficacy of the local injection of MethylPrednisolone acetate lasted for 24 weeks[13].Several professional guidelines recommend use of IA glucocorticoid injection for patients with knee OA who have not responded to oral or topical analgesics[14]. Clinical trials have demonstrated the short-term effectiveness of IA glucocorticoid injection in reducing moderate to severe knee pain[15,16]. Corticosteroid IA injection have no greater effect on pain than placebo after three months [17] and it may be inferior to physical therapy at one year[18]. In addition, there is a causal association between high dose and the prolonged administration of corticosteroids and the chondrotoxicity[19]. We now need to look for other more potent and long lasting treatment regimen for symptomatic osteoarthritis of knee , that is why we endeavoured in our study to introduce addition of short term low dose oral steroid before IA injection in hope of prolonging its effect of pain relief and improved function.

The findings of our study revealed that the combination of short course of low dose oral steroids with intra-articular steroid injections resulted in significantly superior symptomatic improvement, with sustained lower VAS and WOMAC scores, hence improving quality of life for 16 weeks.There are other studies supportive of use of oral steroids in OA particularly in hand OA. Treatment with 10 mg Prednisolone for 6 weeks is efficacious and safe for the treatment of patients with painful hand osteoarthritis and signs of inflammation[20]. As this is established now that anti-inflammatory medication should be cardinal in management of OA, we capitalized on the same and attempted to formulate a new more potent treatment regimen with established clinical benefits without any significant side effects.

ACKNOWLEDGEMENTS

We are appreciative of the cooperation of all the physical medicine and rehabilitation department assistants who supported us during this study.

LIMITATIONS OF STUDY

results may be biased by treatment allocation, questionnaires and outcomes used in this study needs to be more tangible and reliable. In future studies, larger clinical trials are required to establish our results as well.

CONCLUSION

The treatment regimen of combined short course of low dose oral steroid with intra-articular injection of Methylprednisolone is much superior in improving self-reported pain, stiffness and physical function (VAS and WOMAC scores) in patients of knee osteoarthritis. Additionally, this novel and encouraging therapeutic regimen has better outcome than just intra-articular injection of Methylprednisolone or placebo even after 16 weeks of treatment.

Conflict of Interest: None.

Funding Source: None.

Authors Contribution:

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

FM & SR: Conception, study design, drafting the manuscript, approval of the final version to be published.

IA & MR: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

UY & SHS: Conception, data acquisition, drafting the manuscript, 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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