

## COMPARISON OF VARIOUS INTRA-ARTICULAR CORTICOSTEROIDS IN KNEE OSTEOARTHRITIS MANAGEMENT

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### ABSTRACT

**Objective:** To compare the intra-articular injections of Methylprednisolone (MP) and Triamcinolone (TC) in relieving mean pain and mean functional improvement in osteoarthritis (OA) knees management.

**Study Design:** Randomized clinical trial.

**Place and Duration of Study:** Outpatient department of Rehabilitation Medicine of Combined Military Hospital Peshawar, from Jan 2016 to Jun 2016.

**Material and Methods:** Two hundred and forty cases with OA knees were selected and randomly divided into two groups of 120 each. Cases of group 'I' and 'II' were injected with MP and TC respectively. Mean visual analogue score VAS score for pain and mean Lequesne Functional Index Score (LFS) for functional status were evaluated at 6th post-injection week.

**Results:** Mean age of group I was  $55.05 \pm 2.053$  where as that of group II was  $54.84 \pm 2.082$ . Group I had 47 (39%) males and 73 (61%) females. Group II had 48 (40%) males and 72 (60%) females. Group I had significantly less mean VAS as compared to group II ( $9.34 \pm 1.858$  vs  $11.38 \pm 1.954$ ) ( $p < 0.001$ ) and less mean LFS ( $9.34 \pm 1.858$  vs  $11.38 \pm 1.954$ ) ( $p < 0.001$ ) after six weeks of injection. MP had significantly better results in patients of 56-60 years of age and male patients because of comparatively less mean VAS and LFS scores ( $p < 0.001$ ).

**Conclusion:** MP is superior to TC in relieving pain and functional improvement in OA knees management.

**Keywords:** Corticosteroids, Knees, Knee Joint, Methylprednisolone, Osteoarthritis, Triamcinolone.

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### INTRODUCTION

Osteoarthritis (OA) is a gradually progressing, but active disease of articular cartilage degeneration, presenting with symptoms of joint pain, stiffness, and limitation of movement<sup>1,2</sup>. Knee OA is a common progressive problem, affecting mainly persons over 40 years of age<sup>3</sup>. It is harshly painful, often chronic and affects work and social activities due to stiffness and immobility<sup>4,5</sup>.

The goals of management of OA are to control pain principally, minimize disability and improve the quality of life<sup>6-8</sup>. The major pharmacologic modalities used are NSAIDs, opioid analgesics, intra-articular corticosteroids, intra-articular hyaluronic acid and colchicine<sup>9-10</sup>.

Intra-articular corticosteroids provide sufficient pain relief by inhibiting prostaglandin synthesis and controlling local inflammation by decreasing the activity of collagenase and other destructive enzymes<sup>11,12</sup>. These have been reported to slow down cartilage catabolism and osteophyte formation<sup>13</sup>. Consequently, intra-articular corticosteroids is a common management strategy, as recommended by American Rheumatology College<sup>14,15</sup>. Various corticosteroids like Methylprednisolone (MP) and Triamcinolone (TC) have been used with variable success rates<sup>2,4,5</sup>.

A recent international study compared the results of pain relief and functional improvement after intra-articular injections of single doses of TC and MP. Both TC and MP provided adequate pain relief and functional improvement in the patients with knee OA. It concluded that MP was more effective steroid as compared to TC until the sixth week<sup>2</sup>.

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This study was principally aimed to find out better intra articular corticosteroid in our local setup, which not only relieves pain and reduces disability in OA knees quickly, thus enabling the person to return to routine activity with little discomfort; As well as keeping the person maximally functional for a longer duration of time.

## PATIENTS AND METHODS

This randomized clinical trial were carried out in the out-patient department of Rehabilitation Medicine of Combined Military Hospital (CMH) Peshawar (tertiary care hospital) from Jan 2016 to Jun 2016. Both male and female patients of 50-60 years of age, having OA knees meeting clinical ACR criteria (regardless of duration), visual analogue score (VAS) for pain  $\geq 5$ , Lequesne Functional Index Score (LFS)  $\geq 12$  at presentation were enrolled by consecutive sampling. All patients suffering from septic arthritis, diabetes mellitus, chronic renal failure, bleeding disorders, peripheral vascular disease, hypersensitivity to MP and TC, and those using immunosuppressive drugs and systemic steroids were excluded from study to avoid confounding factors. Permission from hospital ethical committee was obtained. After explaining the procedure and associated complications in detail, a written informed consent was taken from every patient included in the study. No financial burden was incurred on the study participants.

Using WHO sample size calculator, sample size calculated was 120 patients in each group. Two hundred forty patients were selected and randomly divided into two equal groups of 120 each by lottery method. In group I, the patients were injected MP whereas in group II, the patients were injected TC. All the patients undergone intra articular corticosteroid injection in pain clinic at CMH Peshawar as outdoor patients, under strict asepsis. One ml (40mg) of MP/ TC and 4 ml of 1% plain bupicaine were injected into the cavity via anterolateral approach after ensuring negative aspiration. An adhesive dressing was applied and the patients were

advised to apply ice to the injection site to minimize pain and inflammation. They were given cap Amoxicillin 500 mg thrice daily and tab mefenamic acid as required for three days. They were instructed to avoid weight bearing & unnecessary physical activity for the next 48 hours, as well as to look for signs of infection e.g. erythema, warmth, or swelling at the site of injection, or systemic signs like fever and chills. All patients had regular weekly reviews and were assessed at the end of 6 weeks following the procedure to analyze the improvement in the degree of pain and functional status respectively. Each patient was asked to rate the pain perception on a VAS of 1-10. The functional state was assessed as per LFS. Data for each patient was recorded on a follow up performa.

All collected data were analyzed using Statistical Package for Social Sciences (SPSS) version 22. Mean and standard deviation were calculated for quantitative variables like age, VAS and LFS scores in both groups. The qualitative variables like gender of both groups were presented in terms of percentages and frequencies. Mean VAS and LFS scores of both groups were compared by applying independent sample t-test. Effect modifiers like age and gender were controlled by stratification. Post stratification independent sample t-test was applied. A  $p$ -value  $\leq 0.05$  was considered statistically significant.

## RESULTS

Two hundred and forty cases (120 in each group) were analyzed statistically. None of the subjects dropped out, or lost at any point during the study. The age distribution ranged from 51-59 years in the study. Mean age was  $55.05 \pm 2.053$  and  $54.84 \pm 2.082$  in groups I and II respectively. There were 150 (62%) cases in age group of 51-55 years and 90 (38%) were in group of 56-59 years. Ninety Five (40%) patients were males and 145 (60%) were females. Group I had 47 (39%) males and 73 (61%) females, whereas group II had 48 (40%) males and 72 (60%) females. Mean Pre-Injection VAS Scores were  $7.41 \pm 0.912$  and  $7.48 \pm$

0.820, whereas mean pre-injection LFS Scores were  $15.96 \pm 1.717$  and  $16.53 \pm 1.528$  in groups I and II respectively.

While analyzing mean VAS scores after 6 weeks of injection, group I ( $3.94 \pm 0.99$ ) had less pain as compared to the group II ( $5.09 \pm 1.202$ ) with statistically significance ( $p < 0.001$ ). Similarly,

age ( $p < 0.001$ ). MP had significantly better results in patients of 56-60 years of age because of comparatively less mean pain and functional disability scores.

Similarly, MP had significantly better results in male patients ( $p < 0.001$ ) because of comparatively less mean pain and functional

**Table-I: Post-Injection Mean VAS & Mean LFS scores.**

Variable	MP (n=120)	TC (n=120)	p-value
VAS after 6 weeks	$3.94 \pm 0.99$	$5.09 \pm 1.202$	<0.001
LFS after 6 weeks	$9.34 \pm 1.858$	$11.38 \pm 1.954$	<0.001

**Table-II: Comparison of Mean VAS and LFS in stratified data (age groups).**

Category	Age Groups	Study Group	N	Mean $\pm$ SD	p-value
Mean VAS Score	51-55 Years	MP	76	$4.01 \pm 0.973$	<0.001
		TC	74	$4.93 \pm 1.253$	
	56-60 Years	MP	44	$3.82 \pm 1.018$	<0.001
		TC	46	$5.35 \pm 1.079$	
Mean LFS Score	51-55 Years	MP	76	$9.41 \pm 1.805$	<0.001
		TC	74	$11.07 \pm 2.135$	
	56-60 Years	MP	44	$9.23 \pm 1.963$	<0.001
		TC	46	$11.89 \pm 1.509$	

**Table-III: Comparison of Mean VAS and LFS in stratified data (gender groups).**

Category	Age Groups	Study Group	N	Mean $\pm$ SD	p-value
Mean VAS Score	Male	MP	47	$3.68 \pm 1.086$	<0.001
		TC	48	$4.79 \pm 1.429$	
	Female	MP	73	$4.11 \pm 0.891$	<0.001
		TC	72	$5.29 \pm 0.985$	
Mean LFS Score	Male	MP	47	$8.47 \pm 1.804$	<0.001
		TC	48	$10.81 \pm 2.447$	
	Female	MP	73	$9.90 \pm 1.676$	<0.001
		TC	72	$11.76 \pm 1.439$	

while analyzing mean LFS Score after 6 weeks of injection, group I ( $9.34 \pm 1.858$ ) had less functional disability as compared to the group-II ( $11.38 \pm 1.954$ ) with statistically significance ( $p < 0.001$ ) (table-I). As mean pain and functional status scores were less (less disability) after MP than TC, MP was significantly better than TC in relieving pain until 6 weeks after injection in OA knees.

Data was stratified into age and gender groups and the mean VAS and LFS scores in this stratified data along-with their comparison is shown in table-II & III. There was significant difference in the mean VAS and LFS scores for MP and TC inpatients of 51-55 and 56-60 years of

disability scores.

## DISCUSSION

OA knee is a common disabling problem owing to agonizing pain and limitation of functional activity. Its optimal treatment modality is expected to be technically easy to perform and cheap outpatient procedure, which can effectively reduce pain and improve function and quality of life<sup>1-2</sup>. Intra-Articular corticosteroid injection is such an ideal procure with excellent results and is recommended as a part of the ACR protocol for OA knee management<sup>13</sup>. It is generally preferred as last non-operative modality in cases, when the other conventional modalities have failed<sup>4-6</sup>. Several studies have

revealed effective pain relief and functional improvement with different corticosteroids<sup>7</sup>; two commonly used are MP and TC.

Few international studies have compared MP and TC in terms of pain relief and improvement in functional status<sup>2,4,5</sup>, whereas a local pilot study<sup>14</sup> has studied the effects of only TC in the management of OA knees. Thus, this RCT has compared these most important outcomes after injections of MP and TC in 240 patients until 6 post-injection weeks. Mean VAS Scores of MP & TC were  $3.94 \pm 0.99$  and  $5.09 \pm 1.202$  respectively with statistical difference ( $p < 0.001$ ). Similarly mean LFS Scores of MP & TC were  $9.34 \pm 1.858$  and  $11.38 \pm 1.954$  respectively with statistical difference ( $p < 0.001$ ). Thus, MP was significantly better than TC in relieving pain and improving functional status until 6 weeks after the injection.

Yavuz *et al*<sup>2</sup> compared the efficacy of placebo and MP, TC & betamethasone in OA knees. The comparison of only TC and MP after 6th post injection week revealed that mean VAS scores were  $5.2 \pm 1.2$  and  $4.3 \pm 1.4$  with significant difference ( $p = 0.009$ ), and mean LFS scores were  $11.3 \pm 3.4$  and  $10.1 \pm 3.1$  after TC and MP injections respectively with no significant difference ( $p = 0.524$ ). Thus, MP was statistically more effective analgesic as compared to TC until the sixth week. A similar study done by Shikhar and colleagues<sup>4</sup> observed a significantly better VAS score after MC as compared to TC after 4 weeks ( $p = 0.016$ ). However, both had nearly same efficacy at 8 & 12 weeks. MC was significantly better than TC in terms of functional improvement, due to significantly better WOMAC Score at 8 ( $p = 0.011$ ) and 12 ( $p = 0.02$ ) weeks. On overall results, MC was concluded to be better than TC.

An RCT by Jain *et al*<sup>3</sup> also concluded that MP provides more immediate and prolonged improvement in pain, stiffness, and function of joint as compared to TC. The study by Pyne<sup>15</sup> revealed that both TC and MP showed significant pain relief at week 3 ( $p < 0.01$ ) but only MP showed significant pain relief at week 8 ( $p < 0.05$ ). There was no significant difference between the two

agents in functional improvement at either 3 or 8 weeks. Godwin *et al*<sup>9</sup> in asystematic review concluded that intra-articular corticosteroid injection results in clinically and statistically significant reduction in pain of OA knee 1 week after injection. No study showed beneficial effect of TC beyond 1 week. MP, however, showed a continuing beneficial effect for 3 weeks. At the same time, systematic reviews by Hepper *et al*<sup>6</sup> and Jüni *et al*<sup>11</sup> showed TC to be more effective in pain reduction than other corticosteroids in OA knees.

Thus, our study when analyzed in context of these supporting studies implies that MP is superior to TC in relieving pain and improving functional status in the management of OA knees until 6 weeks after the injection. However, other variables like predisposing factors (e.g. trauma, obesity & excessive physical activity), severity of disease at presentation, duration of disease and radiological grade of OA before treatment bring out the need for further long-term controlled trials, giving detailed information about the efficacy of MP & TC.

## CONCLUSION

MP is superior to TC in relieving pain and functional improvement in OA knees management.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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