

# International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958  
P-ISSN: 2706-6630  
IJOS 2021; 7(2): 506-512  
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[www.orthopaper.com](http://www.orthopaper.com)  
Received: 12-02-2021  
Accepted: 17-03-2021

**Dr. Amit Dhond**  
Associate Professor, Department  
of Orthopedics, D.Y. Patil  
Hospital and Research Centre,  
Nerul, Navi Mumbai, India

**Dr Parth Agarwal**  
Senior Registrar, Department of  
Orthopedics, D.Y. Patil Hospital  
and Research Centre, Nerul,  
Navi Mumbai, India

**Dr Suraj Sharma**  
PG Resident, Department of  
Orthopedics, D.Y. Patil Hospital  
and research Centre, Nerul, Navi  
Mumbai, India

**Dr Abhishek Dubey**  
PG Resident, Department of  
Orthopedics, D.Y. Patil Hospital  
and research Centre, Nerul, Navi  
Mumbai, India

**Corresponding Author:**  
**Dr Abhishek Dubey**  
PG Resident, Department of  
Orthopedics, D.Y. Patil Hospital  
and research Centre, Nerul, Navi  
Mumbai, India

## To study results of articular triamcinolone versus hyaluronic acid injection in osteoarthritis of knee

**Dr. Amit Dhond, Dr. Parth Agarwal, Dr. Suraj Sharma and Dr. Abhishek Dubey**

**DOI:** <https://doi.org/10.22271/ortho.2021.v7.i2g.2670>

### Abstract

**Purpose:** To decide efficacy of TA vs HA in osteoarthritic patients. Most treatment modalities provide symptomatic relief but intra articular injections with TA and HA probably have the potential of altering the course of the disease.

**Methods:** 60 subjects attending the study scheduled to be given the defined intra articular injection were enrolled as per the study selection criteria.

**Results:** Mean age of cases in TA group was 57 years while it was 58.5 years for cases in HA group ( $p=0.322$ ). Mean VAS score was comparable between TA and HA group at baseline ( $p=0.313$ ). After 1 week of intra-articular injection, pain reduction was more in TA group as compared to HA ( $p<0.05$ ). However, the results were comparable from week 3 onwards ( $p>0.05$ ). By the end of 1 year, VAS score was comparable to baseline in TA group ( $p=0.81$ ) while it was still significantly lower than baseline in HA group ( $p<0.05$ ). Incidence of complications were comparable between two groups with flare ups seen in 13.3% and 6.7% cases of TA and HA group respectively. Acute synovitis developed in 3.3% and 6.7% cases of TA and HA group while 1 case (3.3%) of HA group developed Haemarthrosis.

**Conclusion:** Study shows difference between the 2 intervention groups is the duration of effectiveness. TA mitigates pain faster than HA but the effect of HA is more sustained. Thus HA appears to be superior in duration of pain relief when compared to TA while pain relief is faster with TA.

**Keywords:** articular triamcinolone versus, hyaluronic acid injection, knee

### Introduction

Osteoarthritis (OA) of the knee is a common medical condition that is often seen in general practice and causes considerable pain and immobility. OA refers to a clinical syndrome of joint pain with multifactorial etiopathogenesis that is characterized by the gradual loss of articular cartilage, osteophyte formation, subchondral bone remodeling, and inflammation of the joint [3]. In addition to the consequences for the patient, osteoarthritis forms a considerable burden for society because of its chronic course and the high costs of its intervention [3, 6, 14].

The risk factors include genetics, female gender, trauma, age and obesity [16]. The most common symptoms of osteoarthritis are progressive pain, which is intermittent and mild at first, but grows more chronic and debilitating over time. The pain is usually mitigated by rest and deteriorated by movement in patients [2]. Joints that are more likely to be affected are knees, spine and hips. Osteoarthritis is often asymmetric [12]. The common medicines that are administered to patients with osteoarthritis are acetaminophen, nonsteroidal anti-inflammatory drugs, tramadol, narcotic analgesics and corticosteroids. Other treatment alternatives such as glucosamine sulfate, chondroitin and methyl sulfonylurea methane are also used for this disease [9]. Current treatments such as the use of oral steroids and non-steroidal anti-inflammatory drugs are not satisfactory due to their significant side effects and poor therapeutic results. For this reason, attempts have been made to find novel methods.

Intra-articular corticosteroid injection is inexpensive and leads to short-term improvement (4-8 weeks) in knee osteoarthritis resonances. Conversely, injections of hyaluronic acid is more expensive, but it helps achieve long-term improvement of symptoms. Total replacement of hip, knee or shoulder joint is recommended for patients with chronic pain and joint dysfunction, despite maximum medical therapy.

Hyaluronic acid provides softening, adhesive and elastic properties for synovial fluid, which improves joint function. In osteoarthritis, the concentration and molecular weight of hyaluronic acid is reduced by 33-50% due to elevated levels of pro-inflammatory cytokines, free radicals and proteases. Given the effect of hyaluronic acid on joint function due to its lubricant properties and intra-articular reduction of this substance in patients with OA, the articular injection of hyaluronic acid has been proposed as a new treatment of osteoarthritis [13]. Peyron was one of the first to apply this procedure for the treatment of rheumatoid synovitis to more than 336 patients in 1993 [7].

Although the injection of hyaluronic acid or triamcinolone is widely used to alleviate the symptoms of knee osteoarthritis, few studies have compared the effectiveness of these two procedures. Each year, many reconstructive surgeries are performed on knees around the world but only a fraction of patients are satisfied with these surgical procedures and most prefer drug therapies.

There are not many documented studies testing the effectiveness of HA with triamcinolone in India. In this scenario, the present study was conducted to compare the effectiveness of hyaluronic acid and triamcinolone for the treatment of primary osteoarthritis of knee.

### Methodology

Written informed consent was taken from each patient before the injection process. Demographic and baseline pain and

function data was collected using validated instruments. The patient's fasting blood sugar and complete blood count was done to exclude diabetes and active infections or eosinophilia.

### Inclusion Criteria

- All cases of OA grade 1 and grade 2 on Kellgren and Lawrence scale
- All cases of age included from 40 – 65 years.

### Exclusion Criteria

- OA cases of grade 3 and grade 4.
- Any systemic comorbidities like Diabetes, active infections or eosinophilia

### Injection Procedure

- The Group A was given inj. Triamcinolone single dose (1ml 40mg triamcinolone + 5ml 1% lidocaine)
- The Group B was given 6ml of inj. hyaluronic acid
- The injection was administered in the operation theatre with all aseptic precautions. All injections were given by lateral mid patellar approach. (Figure 1)
- All patients received a standardized post-injection protocol of analgesic (Tab. Paracetamol 1000mg) OD for 5 days and ice fomentation.
- All injections were prepared and administered by the primary investigator.



**Fig 1:** Injection Through lateral parapatellar approach

At 1 week, 3 week, 6 weeks, 6 months and 1 year post intra-articular injection:

Clinical examination for evaluation of pain (by VAS scale) and other complications. During the follow up period, patients were instructed about the exercises of the knee.

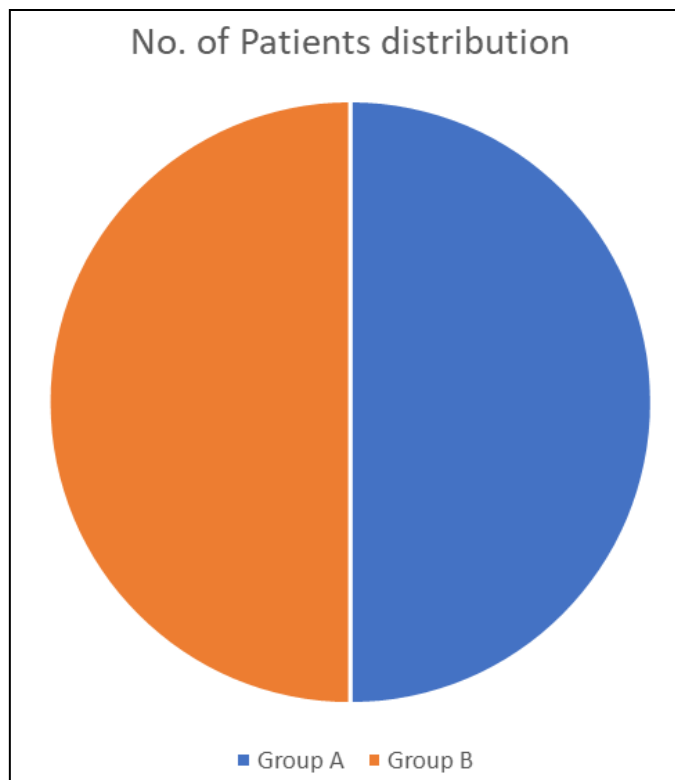
### Results

A total of 60 consecutive cases of grade I and II osteoarthritis

of knee (as per Kellgren and Lawrence grading) were randomly divided into two groups (Figure 2) using simple randomisation technique into Group A & B. Mean age of cases in Triamcinolone group was 57 years while it was 58.5 years for cases in hyaluronic acid group (p=0.322) (Figure 3). Overall female predominance was seen in present study with 75% females to 25% males (Table 2). Total of 43.3% cases were working, 31.7% were retired and 25% were homemakers

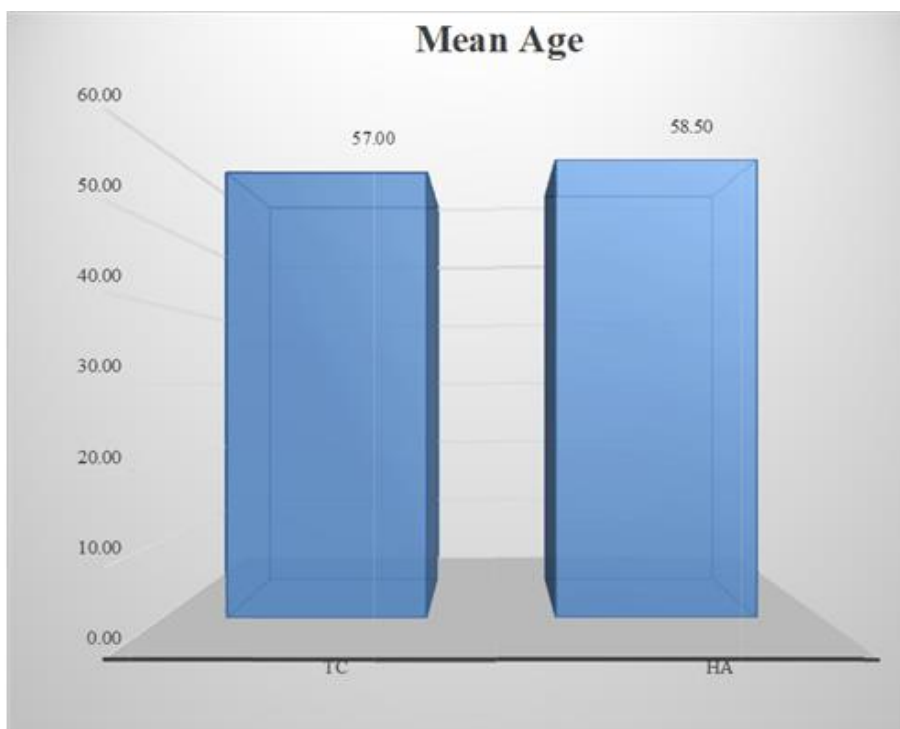
(p=0.56) (Table 3). History of smoking was given by 8.3% cases, with no difference between the two groups (p=1.0) (Table 4). Out of total 60 cases, 38.3% were in Osteoarthritis grade I while remaining 61.7% were in Osteoarthritis grade

II (Kellgren & Lawrence grading) (Table 5). Right side was slightly more involved than left side, with 58.3% cases of right knee OA as compared to 41.7% cases of left side OA (Table 6).



**Fig 2:** Number of Patients Distribution

**Group A** – Intra-articular injection of hyaluronic acid and; **Group B** – Intra-articular injection of Triamcinolone



**Fig 3:** Mean Age distribution of study subjects

Mean VAS score was comparable between triamcinolone and hyaluronic acid group at baseline (7.15 vs 7.52; p=0.313). After 1 week of intra-articular injection, pain reduction was more in triamcinolone group as compared to HA (5.01 vs

5.76;  $p < 0.05$ ) (Table 7). However, the results were comparable from week 3 onwards ( $p > 0.05$ ). By the end of 1 year, VAS score was comparable to baseline in triamcinolone group (7.11 vs 7.15; p=0.81) while it was still significantly

lower than baseline in HA group (6.43 vs 7.52;  $p < 0.05$ ). Incidence of complications were comparable between two groups with flare ups seen in 13.3% and 6.7% cases of triamcinolone and HA group respectively (Table 8). Acute

synovitis developed in 3.3% and 6.7% cases of triamcinolone and HA group while 1 case (3.3%) of HA group developed Haemarthrosis.

**Table 1:** Group Distribution of Study subjects

Variables	Group	N	Mean age	SD	p-value
Age	TC	30	57.00	9.10	0.322
	HA	30	58.50	8.30	

Group	N	%
Triamcinolone (TC)	30	50.0%
Hyaluronic acid (HA)	30	50.0%
Total	60	100.0%

**Table 2:** Distribution of Study sub jects as per Gender

Gender	Group		Total
	TC	HA	
Male	8	7	15
	26.7%	23.3%	25.0%
Female	22	23	45
	73.3%	76.7%	75.0%
Total	30	30	60
	100.0%	100.0%	100.0%

p- value - 1.0

**Table 3:** Distribution of Study subjects as per Occupation

Occupation	Group		Total
	TC	HA	
Housewife	8	7	15
	26.7%	23.3%	25.0%
Retired	11	8	19
	36.7%	26.7%	31.7%
Working	11	15	26
	36.7%	50.0%	43.3%
Total	30	30	60
	100.0%	100.0%	100.0%

p- v alue - 0.56

**Table 4:** Distribution of Study subjects as per Smoking history

Smoking	Group		Total
	TC	HA	
Yes	2	3	5
	6.7%	10%	8.3%
No	28	27	55
	93.3%	90.0%	91.7%
Total	30	30	60
	100.00%	100.00%	100.00%

p-value – 1.0

**Table 5:** Distribution of Study subjects as per Osteoarthritis grade

OA Grade	Group		Total
	TC	HA	
I	12	11	23
	40.0%	36.7%	38.3%
II	18	19	37
	60.0%	63.3%	61.7%
Total	30	30	60
	100.00%	100.00%	100.00%

p-value – 1.0

**Table 6:** Distribution of Study subjects as per Laterality

Laterality	Group		Total
	TC	HA	
Right	17	18	35

	56.7%	60.0%	58.3%
Left	13	12	25
	43.3%	40.0%	41.7%
Total	30	30	60
	100.0%	100.0%	100.0%

**Table 7:** Mean VAS score comparison among study groups

VAS Score	Group	N	Mean	SD	p- value
Baseline	TC	30	7.15	2.01	0.313
	HA	30	7.52	2.17	
1 week	TC	30	5.01	2.22	<0.05
	HA	30	5.76	1.79	
3 week	TC	30	4.98	2.33	0.39
	HA	30	5.21	1.91	
6 week	TC	30	6.20	2.11	0.07
	HA	30	5.01	1.79	
6 months	TC	30	6.69	2.03	0.14
	HA	30	5.88	1.99	
1 year	TC	30	7.11	2.12	0.29
	HA	30	6.43	2.37	

**Table 8:** Distribution of Study subjects as per Incident Complications

Complications	Group		Total	p- value
	TC	HA		
Flare ups	4	2	6	0.67
	13.3%	6.7 %	10.0%	
Acute Synovitis	1	2	3	1.00
	3.3%	6.7 %	5.0%	
Haemarthrosis	0	1	1	1.00
	0.0%	3.3 %	1.7%	
Muscle Pain	1	1	2	1.00
	3.3%	3.3%	3.3%	

## Discussion

Osteoarthritis is a chronic disabling disease with morbidity and pain. Knee is a weight bearing joint frequently affected by degenerative processes which cause much disabilities. There are a few diseases modifying medical therapies for this disease condition. While primary treatment goals in knee OA include pain reduction improvement and improvement of joint mobility and function. Decreasing the progression of disease is an important secondary goal. Recent meta-analysis studies have argued that pharmacological interventions, to treat knee OA with oral NSAIDs, is inferior to intra-articular injections (Bannuru *et al.* 2015) [3]. Intra-articular injection of visco supplementation with hyaluronic acid (HA) is a conservative intervention which is frequently administered with the hope of achievement of both primary and secondary therapeutic goals (Strand *et al.* 2015) [15].

Corticosteroids are other medications used as non expensive pain modifying intra-articular injections (Bellamy *et al.* 2006) [4]. These two categories of intra-articular injections need to be clinically evaluated comparatively to assign their indications, contra-indications, cost-benefits and hence, to find their solid location in the algorithmic approach to the treatment of OA.

Askari A *et al.* [1] in their study observed similar results with pain score before intervention in corticosteroid group was  $7.1 \pm 2.01$  same as Hyaluronic acid group  $7.5 \pm 2.17$  ( $p < 0.313$ ). In corticosteroid group, pain at end of first month significantly decreased to  $5.69 \pm 2.33$  ( $p < 0.01$ ). At the end of second month, pain increased to  $5.90 \pm 2.33$  but it was significantly lower than pain before intervention ( $p < 0.01$ ). At end of third month, pain score increased to  $6.56 \pm 2.15$  and it was not statistically different with primary pain ( $P = 0.200$ ). In Hyaluronic acid group at end of first month, pain

significantly decreased to  $6.63 \pm 2.03$  ( $p < 0.01$ ). Unlike corticosteroid, at end of second month, pain continued its decreasing to  $6.43 \pm 2.01$  ( $p < 0.01$ ). At end of third month, pain score increased to  $6.70 \pm 2.01$  but it was significantly lower than primary pain ( $p < 0.05$ ).

Bannuru *et al.* [5] studied the effectiveness of corticosteroid injections and hyaluronic acid in reducing the symptoms of knee osteoarthritis, concluding that corticosteroid was more effective in reducing symptoms in short-term (2 weeks) whereas in long terms (8 weeks) hyaluronic acid was proved to be more effective than corticosteroids in relieving symptoms.

In a study by Creamer *et al.* [8] on the effect of hyaluronic acid and placebo on increasing the generation of proteoglycans and reducing symptoms of osteoarthritis, it was concluded that hyaluronic acid had no effect on increasing the generation of proteoglycan but it mitigated symptoms in the long term.

Present study aimed to compare the effectiveness of intra-articular hyaluronic acid and triamcinolone for the treatment of primary osteoarthritis of knee. A total of 60 consecutive cases of grade I and II osteoarthritis of knee (Kellgren and Lawrence grading) randomly divided into one of the following two groups (30 each) using simple randomization. (Figure 2).

Follow up was maintained at 1 week, 3 week, 6 weeks, 6 months and 1 year post intra-articular injection for evaluation of pain and Other complications.

Mean age of case in steroid group was 57 years while it was 58.5 years for cases in hyaluronic acid group ( $p < 0.322$ ). Overall female predominance was seen in present study with 75% females to 25% males. In present study, Mean VAS score was comparable between triamcinolone and hyaluronic acid group at baseline ( $7.15$  vs  $7.52$ ;  $p < 0.313$ ). After 1 week of

intra-articular injection, pain reduction was more in triamcinolone group as compared to HA (5.01 vs 5.76;  $p < 0.05$ ). However, the results were comparable from week 3 onwards ( $p > 0.05$ ). By the end of 1 year, VAS score was comparable to baseline in triamcinolone group (7.11 vs 7.15;  $p = 0.81$ ) while it was still significantly lower than baseline in HA group (6.43 vs 7.52;  $p < 0.05$ ). The results showed that intra-articular triamcinolone injection provide faster pain relief but the effect does not sustain beyond 6 months while more sustained pain relief is provided by hyaluronic acid.

Our results are in accordance with previous studies, who also observed that effectiveness of pain reduction was more durable in HA group compared to Corticosteroids (Leighton *et al.* 2014, Askari *et al.* 2016 and Bannuru *et al.* 2009) [1,5,11]. The similarity of efficacy of Hyaluronic acid(HA) and Triamcelonone acetate (TA) is encouraging since HA is, as far as is known, not subject to any of the theoretical risks that are associated with intra-articular steroids [10]. meta-analysis indicates that Intraarticular CS is more effective on pain relief than intraarticular HA in short term (up to 1 month), while HA is more effective in long term (up to 6 months) [17]. By adhering to the joint cartilage, HA may protect the cartilage from CS erosion, improving the safety of CS application [18].

In a similar study by Askari A *et al.* [1], mean age of corticosteroid group was 57 years and that of hyaluronic acid group with 58.5 years respectively. In corticosteroid group 82.6% and in hyaluronic acid group 87.3% were females.

In present study, Incidence of complications were also comparable between two groups with flare ups seen in 13.3% and 6.7% cases of triamcinolone and HA group respectively. Acute synovitis developed in 3.3% and 6.7% cases of steroid and HA group while 1 case (3.3%) of HA group developed Haemarthrosis. Similarly Ray *et al.*, Leighton *et al.* [11], Askari *et al.* [1] and Bannuru *et al.* [5] also observed no difference between the two groups with regards to incident complications. These findings showed that both hyaluronic acid and triamcinolone were safe for intra-articular use in osteoarthritis cases.

To summarize, it is argued that the most important difference between the two interventions is the duration of effectiveness. Having compared to triamcinolone, Hyaluronic acid is suggested to be superior in the duration of pain relief.

## Conclusion

Present study results showed that most important difference between the two intervention groups is the duration of effectiveness. Triamcinolone mitigates pain faster than hyaluronic acid but the effect of hyaluronic acid is more sustained. Thus hyaluronic acid appears to be marginally superior in the duration of pain relief when compared to triamcinolone while pain relief is faster with triamcinolone. As osteoarthritis (primary osteoarthritis) of knee is a common disease affecting large number of patients of variable demographic and racial backgrounds, a more widespread study is required for a more conclusive outcome.

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