

Evaluation of Intra – Articular Hyaluronic Acid Injection in Primary Osteoarthritis of Knee

Dr Janak Rathod¹, Dr Vikram Jasoliya², Dr Mitesh Patel³, Dr Divyaprakash Sharma⁴

¹Additional Professor & HOU, SMIMER Hospital, Surat, India

²Assistant Professor, SMIMER Hospital, Surat, India

^{3,4}Junior Resident, SMIMER Hospital, Surat, India

1. Introduction

Primary osteoarthritis of knee is the most common disease and the leading cause of disability in middle age and elderly. It is characterized by progressive loss of articular cartilage, marginal new bone formation, pain aggravated by activity and stiffness after a period of immobility. Age and obesity are the most predictive risk factors of osteoarthritis affects people mostly over the age of 40 years.

Synovial fluid present in all synovial joints contain hyaluronic acid. It not only provides painless movements and shock absorbing properties, but also nourishment to the articular cartilage. In osteoarthritis, there is reduction in the viscoelasticity of synovial fluid secondary to a decrease in the molecular weight and concentration of hyaluronic acid which reduces the shock absorbing effect. It leads to painful and restricted movement of the affected joint.

2. Aims & Objectives

To assess the efficacy of intra – Articular Hyaluronic acid injection in primary osteoarthritis of knee joint.

- 1) To relief of pain
- 2) Improvement in function the knee joint.

Diagnosis criteria

The following of radiological features were considered evidence of osteoarthritis knee:

- 1) Narrowing of joint space associated with sclerosis of subchondral bone.
- 2) The formation of the osteophyte on the joint margins.
- 3) Small pseudocystic areas with sclerotic wall situated usually in the subchondral bone.

Laboratory test is not indicated except to evaluate for the other diseases or to monitor potential adverse effects from pharmacotherapy

Ahlaback classification of knee osteoarthritis

It is the most widely used classification scheme

- Grade 1: narrowing of the joint space
Grade 2: Obliteration of joint space
Grade 3: Minor bone attrition (less than 5 mm)
Grade 4: Moderate bone attrition (5–10 mm)
Grade 5: Major bone attrition, often with subluxation (Lateral translocation of the tibia at least 5 mm in weight bearing radiographs) and lateral arthrosis.

Hyaluronic Acid in Joint

HA is especially found in various forms of cartilage but none more than the hyaline cartilage. Hyaline cartilage covers the ends of the long bones where articulation occurs and provides a cushioning effects for the bones. The hyaline cartilage has been called the gristle cartilage because its resistance to wear and tear.

Hyaluronic Acid in Synovial Fluid

HA is responsible for the viscoelastic quality of the synovial fluid which acts as both a lubricant and the shockabsorber.

Mechanism of Action of intra articular Hyaluronic Acid

Although the predominant mechanism of hyaluronic acid is unknown, in vitro & in vivo and clinical studies demonstrate, various physiological effect of exogenous hyaluronic acid.

HA coats the surface of articular cartilage and shares space deeper in the articular cartilage among collage fibrils and sulfated PGs. In this respect, HA probably protects the cartilage and blocks the loss of PGs from the cartilage matrix into the synovial space, maitaning the normal cartilage matrix. Similarly, HA may also help prevent invasion of inflammatory cells into the joint space.

In acute & chronic inflammatory processes of the joint, the size of HA molecules decreases at the same time as the number of cells in the joint space increases.

In synovial fluid from knee joints in OA, concentrations of HA, glycosaminoglycans, and keratin sulfate are lower than in synovial fluid from normal knee joints. The pro – inflammatory cytokines IL-1 and TNF -alpha stimulate the expression of HA synthetase, which may contribute to the frag-mentation of HA under inflammatory conditions. Exogeneous HA may facilitate the production of newly synthesizes HA. Higher MW agents stimulated the synthesis of HA more than lower MW formulations and an optimal concentrations was noted for each MW. HA in the synovial fluid binds to chondrocytes via the CD44 receptors, supporting a role for HA in healthy cartilage. The primary means of retention and anchoring of PG aggregates to chondro – cytes is the CD44 HA receptors. CD44 adhesion to HA has also been shown to mediate chondro- cyte proliferation and function.

Hyaluronan and Nociception

Relief of knee pain from OA with HA in clinical studies may be due to the effects of HA on nerve impulses and

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nerve sensitivity. HA may have direct or indirect effects on substance P, which can be involved in pain. Since substance P interacts with excitatory amino acids, PGs, And nitric – oxides, the effect of HA on these factors can indirectly affect the pharmacology of substance p. Additionally, HA has been shown to inhibit an increased vascular permeability induced by Substance P.

Molecular and cellular effects of Hyaluronan

Many effects of exogenous HA on the extracellular matrix, inflammatory mediators, and immune cells have been reported invitro studies. The influence of HA on these factors may contribute to cartilage protection in osteoarthritis.

After giving HA to patients we have examined the patient at different intervals with “**THE WESTERN ONTARION AND MCMASTER UNIVERSITIES INDEX (WOMAC) – 1982**”

Patients and Methods

Sample size – 300 patients
 Duration – October 2017 to October 2018

Inclusion Criteria

- 1) Patient suffering from primary Osteoarthritis
- 2) Patients of OA having persistant pain form more than 1 month despite use of conservative therapy.
- 3) Radiological grade 1 -2 Osteoarthritis
- 4) Patient willing for study

Exclusion Criteria

- 1) Grade 3-5 changes in X – Ray (Ahlback Grade)
- 2) Fixed flexion Deformity
- 3) Secondary OA (post infection, neoplasm, trauma, Pagets disease.)
- 4) Uncontrolled DM
- 5) Allergy to hypersensitivity of drug
- 6) Significant joint effusion
- 7) Pregnancy and lactation.

Technique

Patient is explained about the disease and about the complete procedure along with benefits and risks associated with the procedure. Procedures was done in minor operation theatre. After written consent, cleaning and draping of the skin was done, thoroughly with betadine and spirit. Local anaesthesia is given at the entry of injection after lignocaine sensitivity test.

a) Patient supine with knee extended –

Lateral mid – patellar and medial – patellar injection is administered with the lower extremity extended on examination table. The needle is advanced transversely between the articular surface of the patella- femoral joint at midpoint of patella. By this technique intra articular HA injection was given in 80 % pt with OA Knee

b) Patient with sitting with knee flexed –

Anterolateral and anteromedial injection is given with patient’s leg hanging over the side of the examination table with the knee flexed to approximately 90 degrees. Injection

site is selected inferior to patella one finger breadth proximal to joint surface and either medial or lateral to patellar tendon. The needle is directed obliquely toward the inter – condylar notch. By this technique IAHA injection was given 20 % with primary osteoarthritis.

With the 21 G 1.5” needle entry is made in joint by either of the methods mentioned above. If needle tip touches the bone the needle tip is redirected. Aspiration is done to make sure that the needle is inside the joint cavity. After aspiration, full contents of the syringe were injected inside the joint. Bandage was applied at injection site. Knee was moved for some time. So that the drug spread uniformly in the knee joint.

Drug Used – Sodium Hyaluronate solution 1%
Each prefilled syringe of 2 ml contains 20 mg sodium hyaluronate

Post injection Management

- 1) Oral antibiotics were giver for 3 days
- 2) Analgesics was given for the period of 3 days
- 3) Patients were advised to take local cold application
- 4) Mobilization was started immediate after the injection
- 5) Qudriceps exercises were started after injections

Schedule and follow up

Each intra – articular injections was given once for 3 consecutive weeks. Injection was given in the selected same site at each consecutive time. Follow up was done on 2nd, 4th, 6th month and final follow up at 1 year on OPD or telephonic conversation.

Evaluation

Patient was evaluated finally according to WOMAC score at 6 Months and 1 year.

3. Observations and Results

At the start of the study total 300 patients who mate inclusion criteria were enrolled but we could follow 270 patients regularly at 2nd, 4th, 6th months i.e. nearly 90 % of total patients. The reasons for loss to follow up in 30 patients were no relief in symptoms after the 1st injection in 12 patients, increase knee pain & swelling at injection site 8 patients, cost of 3 injections not affordable for 5 patients, and some personal problems of patients.

The study was designed to follow up the patients up to 1 year but due to time constraints we were able to follow 140 patients only. Hence in the present study for analysis purpose we studied 270 cases up to 6 months and 140 patients up to 1 year.

Baseline Characteristics of Patients

Character of patients		Participants
Mean Age		52.4
Female Male ratio		1.4:1
Duration OA		3.1 years
Osteoarthritis	Rt knee	165(55%)
	Left knee	135(45%)
Ahlback grade (grade1)		218(73%)
(grade 2)		82(27%)

Age distribution

Age Group	Frequency	Percent
40 -49	117	39.4%
50 -59	110	36.70%
60 -69	61	20.20%
70 – 80	12	3.70%
Total	300	100%

Sex Distribution

Sex	Frequency	Percent
Male	127	42.30%
Female	173	57.70%
Total	300	100.00%

Duration of Pain

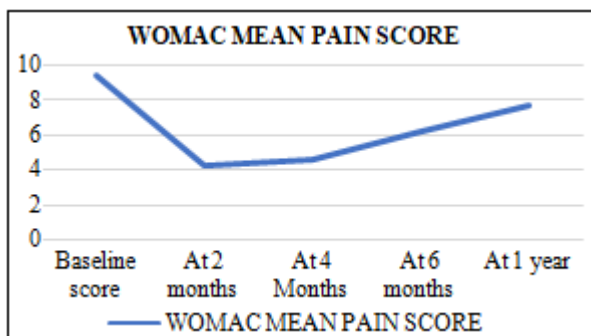
Duration of pain	Frequency	Percent
1 -5 years	254	84.90%
6 – 10 years	43	14.10%
>10 years	3	1.0%
Total	300	100.00%

Ahlback Grading of involved knee

Radiological Grade	Involved Knee
Grade 1	218
Grade 2	82
Total	300

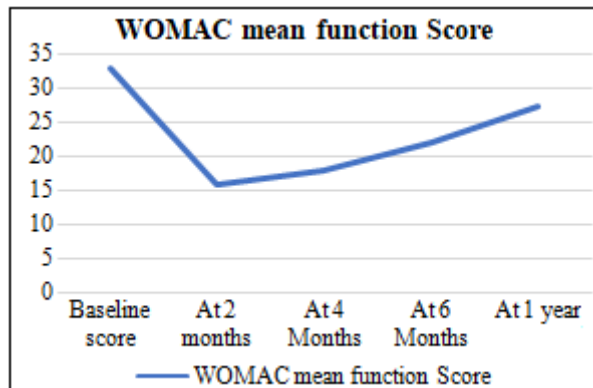
Means of the pain Relief score of WOMAC indices of patients

Duration of follow up	WOMAC mean pain score	SD(+/-)
Baseline Score	9.4	2.9
At 2 Months	4.2	2.1
At 4 months	4.6	2.1
At 6 Months	6.2	2.1
At 1 year	7.7	2.1



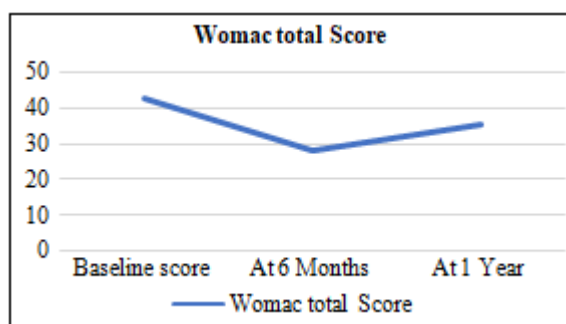
Means of the function scores of WOMAC indices of Patients

Duration of Follow up	WOMAC mean function score	Sd(+/-)
Baseline score	32.9	9.7
At 2 months	15.7	2.8
At 4 Months	17.8	5.1
At 6 Months	21.9	6.3
At 1 Year	27.4	6.1



Means of total scores of WOMAC indices of Patients

Duration of follow up	WOMAC Total Score	SD(+/-)
Baseline score	42.4	12.1
At 6 months	28.1	8.1
At 1 year	35.2	8.2



Complications

Non Specific effusion of knee joint was amongst 2 patients (0.7%). 30 (10%) patients were found to have increase knee pain and swelling at injection site who left the study.

4. Summary and Conclusions

4.1 Summary

- 1) **Age distribution** – Patients of primary osteoarthritis belonged to age group between 40-80 years and mean age was 52.4
- 2) **Sex Distribution** – There was a female preponderance in our patients with female to male ratio of 1.4:1
- 3) **Duration of pain** – mean duration of pain was 3.1
- 4) **Ahlback grade of involved knee** : Distribution of early osteoarthritis of knee according to ahlback grade. Patients with grade 1 are more than the grade 2
- 5) **Pain relief** – Mean WOMAC pain score improvement in patients at 6 months was 34% and continued for 1 year
- 6) **Functional improvement** – Mean WOMAC function score improvement in patients was 33% improvement at 6 months which continued for 1 year
- 7) **Total WOMAC Score** : Mean total WOMAC Score improvement at 6 months was 34% improvement which lasted for 1 year
- 8) **Complications** : Only 0.7% of patients were found to have non septic effusion of knee joint and 30 (10%) patients were found to have increase knee pain and swelling at injection site.

4.2 Conclusion

Present study documented the effect of intra articular injection of Hyaluronic Acid not only in reducing pain but it increases the functional outcome in patient with primary knee osteoarthritis in Ahlback radiological Grade 1 & 2. Once a week with three consecutive injections reduces pain and improves function which last upto 6 months – 1 year and hyaluronic acid have no serious adverse events apart from increase pain over injection site for few days, swelling of knee joint after injection.

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