

# Intrarticular Sodium Hyaluronate for the Treatment of Osteoarthritis of the Knee. A Retrospective Review of 45 Patients

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## ABSTRACT

Intrarticular Hyaluronic Acid was administered to 45 patients with various grades of osteoarthritis in the knee. Following 3 fortnightly injections, these patients were reviewed at 6 weeks and 3 months with regard to their knee pain. We found that most patients (84.4%) had decreased knee pain following these injections. Patients who had severe grade osteoarthritis based on knee radiographs before the injections were less likely to have pain reduction compared to those with milder grade osteoarthritis. Only 4 (8.9%) patients showed no improvement and were subsequently considered for surgery. Many patients did not require any further treatment (24.4%) and the remaining were given analgesia (64.4%) to aid in their pain. One patient required another course of this injection. There were no complications recorded in this study. We concluded that intrarticular Hyaluronic Acid is an easy and safe method to treat osteoarthritis. The short-term outcome with regard to knee pain is good in patients with milder grades of osteoarthritis.

## Key Words:

*Osteoarthritis, Knee, Sodium Hyaluronate, Pain, Radiograph*

## INTRODUCTION

Osteoarthritis (OA) is a common cause of knee pain especially in the elderly. It can affect all joints. However, when it affects the weight bearing joints (e.g., knees, hips), morbidity rates are higher. Occasionally it occurs following trauma or an autoimmune disease. Its effects vary from no impact upon daily activities to being severely disabled and housebound. While there are many modes of non-surgical treatment, none are regarded as superior. Many surgeons give patients the option of analgesia, physiotherapy and/or behavioural modification before considering knee replacement<sup>1</sup>. This is more important if the patient is younger where the expectation is higher and the patient is likely to outlive the implant. Patients who are very old with other comorbidities are also excellent candidates for non surgical methods of treatment<sup>2</sup>. The high cost of having a

knee replacement is another reason to consider intraarticular injections.

Hyaluronic acid is a natural complex sugar of the glycosaminoglycan family and is a long-chain polymer containing repeating disaccharide units of Na-glucuronate-N-acetylglucosamine. There are many commercially available forms of HA. Most are a viscous solution consisting of a high molecular weight (500,000–730,000 daltons) fraction of purified natural sodium hyaluronate in buffered physiological sodium chloride. The sodium hyaluronate is extracted from rooster combs. HA is administered by intrarticular injection into the joint. HA has been regarded both as a joint lubricant and as a mediator for cartilage repair<sup>3,4</sup>. It is simple to administer and can be given on an outpatient basis. It is a much less costly treatment alternative than joint replacement surgery<sup>5</sup>. Complications occur infrequently<sup>6,7</sup>. Researchers have demonstrated that HA slows down the progression of joint space narrowing<sup>8</sup>.

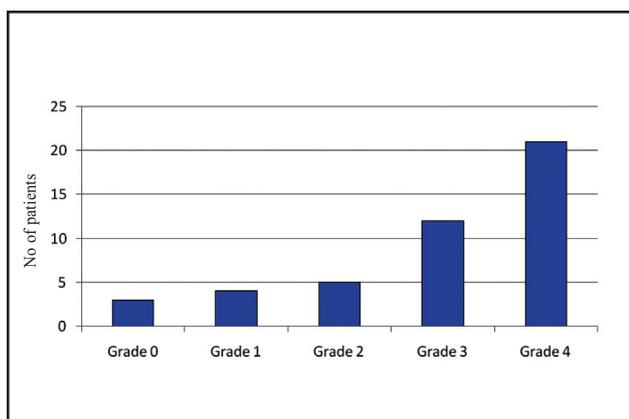
Although results are encouraging overall, patient outcomes are not uniform. Outcomes ranged from fully satisfied patients to those who do not see any obvious benefit. While history and clinical examination are important, these are subjective and vary from patient to patient. We wanted to see if the severity of osteoarthritis on radiographs alone could predict the final outcome for these patients in the short term.

## MATERIALS AND METHODS

This is a retrospective review involving 50 sequential patients seen in a private orthopaedic clinic. They comprised of patients who had primary OA of the knee. The severity of the initial pain was recorded using a visual analogue score (VAS). Each of these patients had 3 courses of intrarticular HA. This injection was given into the affected knee once every 2 weeks. These patients were then reviewed at 6 weeks and at 3 months following the final injection. The following patients were excluded from the study: patients who has OA secondary to trauma, those who did not return for follow up

**Table I:** Severity of osteoarthritis based on radiographs before initiating treatment

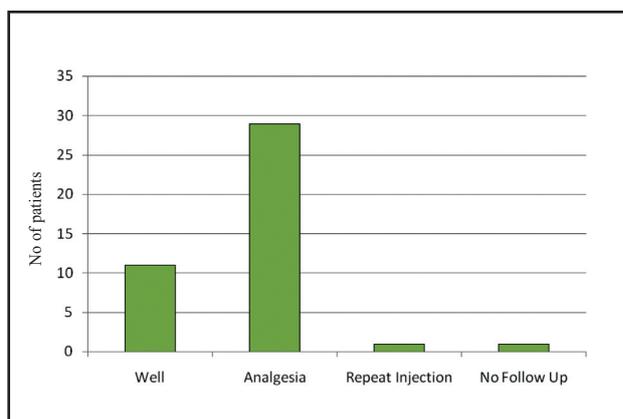
| Grade of OA | Number of patients |
|-------------|--------------------|
| Grade 4     | 21                 |
| Grade 3     | 12                 |
| Grade 2     | 5                  |
| Grade 1     | 4                  |
| Grade 0     | 3                  |



**Fig. 1:** Severity of osteoarthritis in based on radiographs before starting the treatment.

**Table II:** Outcomes at 3 months following completion of HA treatment (3 doses, given once every two weeks)

| Outcome of Knee Pain at 3 months | Percentage of patients |
|----------------------------------|------------------------|
| Satisfied with pain reduction    | 26.2%                  |
| Requires additional analgesia    | 69.0%                  |
| Required another course          | 2.4%                   |
| Lost to follow up                | 2.4%                   |



**Fig. 2:** Final outcome observed 3 months following completion of the 3 doses of HA.

at 3 months post final injection, patients who had other medications injected into the knee joint, and those who did not have a proper anterior-posterior and lateral view radiographs of the injected knee. Also excluded were those patients with previous knee surgery and those with ligament instability of the knee joint being studied. This led to 5 patients being excluded.

The data collected included demographic characteristics, severity of OA as noted from radiographs using the Kellgren-Lawrence Radiographic Grading Scale (Grade 0 to Grade 4), complications, pain reduction (based on VAS) and the need for other forms of treatment following injection.

## RESULTS

There were 45 patients in this study, 17.8% (8) males and 82.2% (37) females. The youngest patient was 28 years old and the oldest was 91 years. The mean age of the patients was 60.7 years. Most of the patients had grade 4 (46.7%) OA on radiographs (Table I). Those with grade 3 OA were the next most common group with 26.7%. Patients who had moderate to severe grades of OA (grade 3 and 4) comprised 73.3% of the total number of patients.

Thirty-eight (84.4%) patients indicated that there was definite pain reduction while only 7 (8.9%) patients denied any improvement. Three (6.7%) patients were unable to tell whether or not there was any improvement; these patients

were reported as having shown no improvement. There were no reported complications (local reaction, allergic conditions, fever or infection) in this series.

Table II shows the final outcome of the patients at 3 months. 11 (26.9%) patients were fully satisfied with the procedure and did not require any further treatment. The majority of the patients (69%) required occasional analgesia. One patient required a repeat injection and one patient was lost to follow up.

## DISCUSSION

Intraarticular HA is not a new treatment for OA. Many studies have shown that it is helpful in reducing the signs and symptoms of OA<sup>6, 11-14</sup>. In the current study, subjects were reviewed at 6 weeks because maximal benefit of the injection is seen at this time, according to previously published reports<sup>10</sup>. A repeat follow up at 3 months ensured that results were maintained.

Patients were grouped according to severity of OA as seen on their radiographs. Those in groups 0, 1 and 2 were considered to have mild OA. Those in groups 3 and 4 were considered to have severe OA. There were 12 (26.7%) patients with mild OA and 33 (73.3%) patients with severe OA. A paired t-test was done to compare these two groups. There was a significant difference in the outcome for patients with milder OA of the knee ( $p < 0.026$ ) compared to those

with severe OA grades. All patients except one had good improvement in the mild OA group following one course of intrarticular injection. This finding has been reported in other studies<sup>15</sup>.

It appears that patients under 50 years of age fared better. However this may be due to the fact that many (24.4%) had milder grades of OA grades compared to older patients. Most of these patients (42.1%) did not need any further treatment and were discharged from follow up.

There were 4 patients who did not have any improvement in terms of pain relief following the injections. Of these, 3 had severe grades of OA. These patients required regular follow up with analgesia and were subsequently considered for surgery. There were no complications noted during or after knee replacement.

We did not have any control group in this study. This is a duly noted limitation. The study period of 3 months provided that only short term outcomes were reported.

## CONCLUSION

Most patients with OA of the knee will have pain reduction in the short term from intrarticular HA. Patients with milder grades of OA have better pain reduction from intrarticular HA compared to those with severe grades of OA.

## ACKNOWLEDGEMENT

Dr. Maria Lee Hooi Sean, Anaesthetist, Sultanah Aminah General Hospital and Head of the Clinical Research Centre for reviewing this article and suggesting changes.

## REFERENCES

1. Snibbe JC, Gambardella, RA. Treatment options for osteoarthritis. *Orthopedics*, 2005; 28(2 Suppl): 215-20.
2. Aggarwal A, Sempowski, IP. Hyaluronic acid injections for knee osteoarthritis. Systematic review of the literature. *Can Fam Physician*, 2004; 50: 249-56.
3. Guidolin DD, Ronchetti IP, Lini E, Guerra D, Frizziero L. Morphological analysis of articular cartilage biopsies from a randomized, clinical study comparing the effects of 500-730 kDa sodium hyaluronate (Hyalgan) and methylprednisolone acetate on primary osteoarthritis of the knee. *Osteoarthritis Cartilage*, 2001; 9(4): 371-81.
4. Meloni F, Milia F, Cavazzuti M, Doria C, Lisai P, Profili S, et al, Clinical evaluation of sodium hyaluronate in the treatment of patients with sopraspinus tendinosis under echographic guide: Experimental study of periarticular injections. *Eur J Radiol*, 2008; 68(1): 170-3.
5. Turajane T, Labpiboonpong V, Maungsiri S. Cost analysis of intra-articular sodium hyaluronate treatment in knee osteoarthritis patients who failed conservative treatment. *J Med Assoc Thai*, 2007; 90(9): 1839-44.
6. Adams ME, Lussier AJ, Peyron JG. A risk-benefit assessment of injections of hyaluronan and its derivatives in the treatment of osteoarthritis of the knee. *Drug Saf*, 2000; 23(2): 115-30.
7. Uthman I, Raynauld JP, Haraoui B. Intra-articular therapy in osteoarthritis. *Postgrad Med J*, 2003; 79(934): 449-53.
8. Jubb RW, Piva S, Beinat L, Dacre J, Gishen P. A one-year, randomised, placebo (saline) controlled clinical trial of 500-730 kDa sodium hyaluronate (Hyalgan) on the radiological change in osteoarthritis of the knee. *Int J Clin Pract*, 2003; 57(6): 467-74.
9. Toh EM, Prasad PS, Teanby D. Correlating the efficacy of knee viscosupplementation with osteoarthritic changes on roentgenological examination. *Knee*, 2002; 9(4): 321-30.
10. Roman JA, Chismol J, Morales M, Donderis JL. Intra-articular treatment with hyaluronic acid. Comparative study of Hyalgan and Adant. *Clin Rheumatol*, 2000; 19(3): 204-6.
11. Kotz R, Kolarz G. Intra-articular hyaluronic acid: Duration of effect and results of repeated treatment cycles. *Am J Orthop*, 1999; 28(11 Suppl): 5-7.
12. Bunyaratavej N, Chan KM, Subramanian N. Treatment of painful osteoarthritis of the knee with hyaluronic acid. Results of a multicenter Asian study. *J Med Assoc Thai*, 2001; 84 Suppl 2: 576-81.
13. Huskisson EC, Donnelly S. Hyaluronic acid in the treatment of osteoarthritis of the knee. *Rheumatology (Oxford)*, 1999; 38(7): 602-7.
14. Frizziero L, Govoni E, Bacchini P. Intra-articular hyaluronic acid in the treatment of osteoarthritis of the knee: Clinical and morphological study. *Clin Exp Rheumatol*, 1998; 16(4): 441-9.
15. Turajane T, Tanavaree A, Labpiboonpong V, Maungsiri S. Outcomes of intra-articular injection of sodium hyaluronate for the treatment of osteoarthritis of the knee. *J Med Assoc Thai*, 2007; 90(9): 1845-52.