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Physical Medicine

A PROSPECTIVE INTERVENTIONAL STUDY TO ASSESS THE CLINICAL EFFICACY OF VISCO-SUPPLEMENTATION ON KNEE OSTEOARTHRITIS IN A TERTIARY CARE CENTER OF NEW DELHI

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ABSTRACT Osteoarthritis, also known as degenerative joint disease, is the most common type of musculoskeletal disease and is a leading cause of disability among the elderly. In our present study we have included symptomatic primary OA knee patients and treated them with 3 intra articular doses of high molecular weight sodium hyaluronic acid. It was found that the intake of rescue analgesic (paracetamol) as well as the supra-patellar circumference has decreased in between baseline and other follow up visits (45, 90 and 180 days) but the effect diminished in between the 3rd and 4th follow up. Similarly, there was significant improvement in fifty feet walking time from baseline to other subsequent visits but the entire gain in walking speed was within the first 45 days. The Health Assessment Questionnaire (HAQ), published in 1980 by the Stanford Arthritis Center, is among the first patient reported outcome (PRO) instruments and is also the most cited and employed PRO instruments till date, particularly but not exclusively in the rheumatic disease literature. As before there is significant decrease in HAQ score from baseline to all other subsequent visits, but there is a plateauing of effect in between 3-6 month.

KEYWORDS :

INTRODUCTION

In 1951, hydrocortisone was introduced and popularized for intra-articular administration.Steroid injections may provide short term pain relief and have an anti-inflammatory effect on the affected joint but not more than 3 injections are recommended in a year.[1] In search of an intra articular product with more biological plausibility to rectify the basic pathology behind osteoarthritis, researchers started utilizing Hyaluronic acid since the 1960's for joint injury related OA in horses. Preliminary human clinical studies were performed in the early seventies using the non-inflammatory fraction of hyaluronic acid (NIF-Na HA) and in 1987 Japan and Italy pioneered in first clinical use in human being. Gradually clinical use started in Canada in 1992 and Europe in 1995. United States Food and Drug Administration (FDA) approved injection Hyaluronic Acid in 1997.[2]

Hyaluronic acid is the major constituent of 1-2 µm layer on the surface of articular cartilage in association with aggrecans and link proteins; as a liquid phase matrix element HA also circulates in the synovial space rendering the unique viscoelastic property of synovial fluid, which is otherwise a simple plasma dialysate.[3] Visco-supplementation with HA allows for restoration of the elasto-viscous properties of synovial fluid, although other mechanism must exist. The actual period that the injected HA product stays within the joint space is in the order of hours to days, but the clinical efficacy is often in the order of months (up to 6 months).[4]

In a systemic review of 9 Randomized controlled trials' (RCT's) done by Ayral X in 2001, HA was found to be more effective than placebo for pain in 8 out of 9 studies. 3 RCT's also showed improved function as well as reduced need for intra-articular steroid injection over the study period of 1 year. 5 RCT's suggested similar benefit of HA and steroid at 1 month, but with superiority of HA after a few months.[5]

In the largest metaanalysis to date, the Cochrane Collaboration undertook a systematic review of the evidence for visco-supplementation in 2005. A total of 63 RCT's were examined and the authors concluded that for patients with OA knee, visco-supplementation with either hyaluronan or hylan products, there was an 11% to 54% improvement in pain and a 9% to 15% improvement in function compared to baseline at the 5 to 13 week post injection period.[6]

Aims and objectives of the present study:

To ascertain the effectiveness of intra-articular injection of Hyaluronic Acid in knee osteoarthritis by assessing the improvement in function and pain (symptomatic efficacy).

METHODOLOGY:

After getting due clearance of the Institutional Review Board we conducted the study in the Outpatient Department of Physical medicine and Rehabilitation, VMMC and Safdarjung Hospital, New Delhi from October 2010 to March 2012. It was a prospective interventional one group pre-test post-test study.

Inclusion criteria:

Patients of both gender in the age group 30-70 years were included after informed consent, only if they had primary knee OA of tibio-femoral joint and pain was at-least > 40mm on a 100 mm VAS scale. Also the pain should have persisted for at least 15 days in the prior month.

Exclusion criteria:

Kellgren-Lawrence Grade IV OA or Secondary OA were excluded from the study as also those patients who had knee surgery within prior 12 months. Also excluded are those who received intra-articular treatment with any product or joint lavage or arthroscopic procedure within prior 6 months or ipsilateral cruciate or collateral ligament injury within past 3 months or having evidence of joint laxity.

Other standard contraindications of intra articular injections (like overlying skin infection or joint infection, history of crystalline arthropathy or inflammatory arthritis, on anticoagulation therapy or allergic to avian protein) as well as contra indication to MRI (e.g. metal implants, claustrophobia) are not included in the study. Those patients who are having some over whelming general condition are excluded also as a standard procedure (like pregnant or nursing mother, morbid obesity, venous or lymphatic stasis or simply unwilling to participate in the study).

Selection of cases

43 consecutive patients with primary OA of the knee as defined by the American College of Rheumatology criteria[7] attending our OPD and satisfying the inclusion and exclusion criteria were taken into the study after informed consent. Thirteen patients dropped out from the study. Consequently, we had a total study population of 30, on whom we did all the requisite assessments and interventions. We recorded the baseline demographic parameters of these patients as well as did some routine baseline investigations.

METHODOLOGY OF INTERVENTION:

All patients enrolled within the study received 3 doses of high molecular weight sodium hyaluronic acid. We used injection containing purified Sodium Hyaluronate with molecular weight of 5.03 x 103 gram/mole (i.e., 5.03 million daltons) obtained from bacterial source viz. Streptococcus zooepidermicus. The content of the pre filled syringes (2.5 ml) was injected intra-articularly in the affected knee/ knees at an interval of 1week with aspiration of any joint effusion (if necessary). The lateral approach of knee injection is most commonly used and is used in this study also.

Any adverse effect (if any) is noted during each injection procedure. Pain killers or other natriceutical medications were not allowed throughout the study period of 6 months, except paracetamol (maximum dose of 2 gm/day), when needed and the patient was asked to keep record of the number of tablets/day. As a general protocol all the patients were encouraged to avoid squatting, lose weight and taught quadriceps strengthening exercises. The exercise regimen was straight leg raising with 6 second holding time, 30 repetitions, one set and done twice daily for six months.

Tools of measurement:

Each patient was evaluated on baseline (day 0), day 45, 90 and 180 in terms of tools of measurement which included:

(1) Symptomatic efficacy parameter i.e., Validated Indian Version of the Health Assessment Questionnaire or modified HAQ score (at each visit). [8,9,10]

(2) Also noted was total number of paracetamol intake over previous one week (at each visit), 50 foot walking time (at each visit) and supra-patellar circumference (at each visit).

Statistical analysis:

Data obtained from the 30 patients who completed the stipulated follow up were compiled and analysed using SPSS version 17.

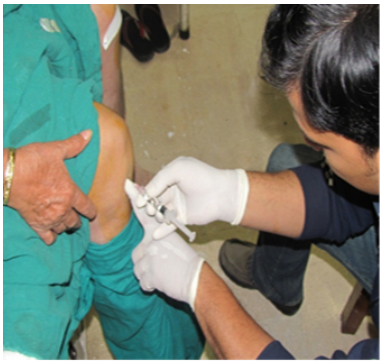
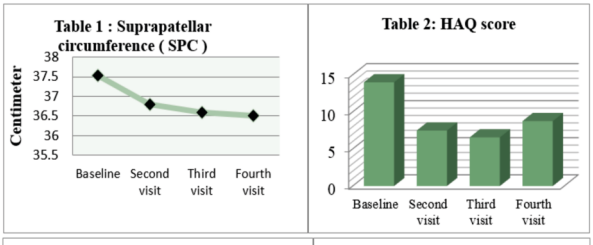


FIGURE 1: INJECTION PROCEDURE

RESULTS:

The supra-patellar circumference (SPC) was measured in each involved knee (n = 55) and the mean values were found to be 37.54 ± 2.293 cm, 36.80 ± 2.204 cm, 36.59 ± 2.143 cm and 36.50 ± 2.143 cm respectively on first, second, third and fourth visit. Thus, there was significant decrease in supra-patellar circumference (and hence in knee swelling also) on second, third and fourth visit (when compared from baseline). But, in between the third and fourth visit there was no real significant change (p = 0.235).



The HAQ (modified Health Assessment Questionnaire) score of each of the 30 patients were recorded and the mean was found to be 14.00 ± 2.816, 7.50 ± 3.246, 6.57 ± 4.108 and 8.77 ± 4.732 respectively. So, there is significant decrease in HAQ score from baseline to all other subsequent visits (p = 0.0001), but in between the third and fourth visit there is significant increase in score (p = 0.0001). Naturally it suggests a plateauing of effect in between 3-6 month.

Each of the 30 patients was made to walk 150 feet in normal speed and then one third of the time taken is noted as the average 50 feet walking time (FFT). The mean values at each visit were found to be 32.17 ± 8.338 seconds, 29.03 ± 6.881 seconds, 28.53 ± 6.469 seconds and 28.93 ± 7.172 seconds respectively. There was significant improvement (p = 0.0001) in FFT from baseline to other subsequent visits. The entire gain in walking speed was within the first 45 days. There was a rather a slight increase in fifty feet walking time between the third and fourth visit, which was statistically insignificant (p =0.216).

The amount of paracetamol (PCM) intake over the last week by each of the 30 patients was enquired at each visit to make an indirect assessment of pain. The mean PCM intake was 7.40 ± 3.692, 1.57 ± 1.455, 0.63 ± 1.066 and 1.03 ± 1.129 at baseline, second, third and fourth visit respectively. There was a definite decrease of PCM intake from baseline to all subsequent visits (p = 0.0001), but between the third and fourth visit there was a significant increase in PCM intake (p = 0.012).

DISCUSSION:-

The National Institute for Health and Care Excellence (NICE) guidelines for knee OA proscribes against injecting articular hyaluronate injections in knee. The Osteoarthritis Research Society International guideline [11,12] concludes that hyaluronic acid have uncertain efficacy in knee OA. The American College of Rheumatology guidelines for the treatment of OA did not make recommendations regarding the use of hyaluronic acid injections for either knee or hip.[13] Even without any significant recommendation from international guidelines, intra articular hyaluronic acid is still popular among both clinicians and patients due to its mode of delivery to a large extent.[14]

Our present study aims to assess the efficacy of intra articular hyaluronic acid in symptomatic osteoarthritis patients on few quantifiable parameters and scales. The supra-patellar circumference, fifty feet walking time, health assessment questionnaire and paracetamol intake are some parameters which are direct measures of symptomatic improvement of the patient and hence utilized in our study.

The supra-patellar circumference (an indirect measure of sub-clinical knee effusion) showed a significant decrease at the end of the study, which corroborates well with the existing literature. [15,16]

Similarly, fifty feet walking time significantly improved from baseline in our study like that noted by Cihat Ozturk et al. even after one year of treatment Ozturk C, et al.[17] Also, Roy D Altman and Ronald Moskowitz in their study observed modest changes favorable to HA in respect of time to perform 50 feet Walk test, knee range of motion and effusion.[18]

Vajara Phiphobmongkol et al. in their study over 31 patients of Thai origin showed a decreasing trend of paracetamol consumption from baseline to the final follow up at six months.[19] JJ Scali et al in his study also reported that only 5% patients took paracetamol at the end of study, compared from 40% at baseline. In our study paracetamol consumption decreased from average 7.40 tablets per week at the beginning to 1.03 tablets per week at the end of trial.[16]

The Health Assessment Questionnaire (HAQ), published in 1980 by the Stanford Arthritis Center, is among the first patient reported outcome (PRO) instruments and is also the most cited and employed PRO instruments till date, particularly but not exclusively in the rheumatic disease literature.[9] A prospective multicentric trial done in Italy by Foti C et al over 1266 patients documented improvement in HAQ score which was very statistically significant. Our study also showed a significant improvement in HAQ over time from baseline and the effect was maintained for at least six months. [20]

CONCLUSION:

From our study we can draw conclusions that Injection Hyaluronic Acid is a safe and effective treatment for OA knee. The beneficial effect of visco-supplementation reaches peak at 3 months and is maintained up to 6 month. Visco-supplementation improves walking speed of a patient, reduces his dependence upon analgesics, decreases clinical and sub-clinical knee effusion and improves the patients subjective wellbeing (as measured via HAQ)

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