Original Research Paper

Volume - 11 | Issue - 03 | March - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Physical Medicine

EFFECTIVENESS OF INTRA-ARTICULAR HYALURONIC ACID INJECTION IN FUNCTIONAL IMPROVEMENT OF PATIENTS WITH KNEE OSTEOARTHRITIS.

Dr Firdaus Kamal Associate Professor, Deptt of Physical Medicine & Rehabilitation IPGME&R, Kolkata

Dr Vasundhara Ghosal* Assistant Professor, Deptt of Physical Medicine & Rehabilitation IPGME&R, Kolkata. *Corresponding Author

ABSTRACT **Objective:** The functional improvement with intra-articular hyaluronic acid injection single dose in knee OA is limited. The aim was to assess the therapeutic efficacy of intra-articular hyaluronic acid injection in knee Osteoarthritis. **Method:** Sixty four (64) Patients with Osteoarthritis (OA) knee were selected between February 2016 and December 2018 in this prospective study. These patients had failed to respond adequately to conservative treatment comprising pain medicines and therapeutic exercise and other rehabilitative measures. Functional scoring as per WOMAC and VAS for pain at rest and during walking was documented. Patients received one injection of 6 ml hyaluronic acid (Hylan G-F 20). Baseline characteristic were taken and they were reviewed 6 months post-injection. Use of only paracetamol, when required was allowed for concomitant analgesia. **Results:** The mean age of the patients was 58 ± 5 years; mean duration of symptoms 5.4 ± 1.5 years and mean body mass index (BMI) 27.15 kg/m2. All the patients were available at final follow-up. The resting and walking VAS pain significantly improved from baseline after the injection (45 from 70 and 51 from 82, respectively). There was significant improvement of pain and disability based on the WOMAC scores. Adverse events were recorded and included local pain and swelling, mild redness, and/or effusion in the knee. The beneficial effects stayed till 6 months.**Conclusions:** Intra-articular injection of hyaluronic acid appeared to be therapeutic efficacious and safe for the treatment of osteoarthritis of the knee. The pain relief and functional improvement lasts for up to 6 months. The procedure is tolerated well and associated with very few local adverse events. Better patient compliance was also noted. The need for concomitant analgesia is reduced.

KEYWORDS : Hyaluronic Acid, Knee Osteoarthritis, Visco-supplimentation,

INTRODUCTION:

Osteoarthritis is the most common chronic joint disorder in the elderly mostly affecting the weight bearing joints of the lower limbs particularly the knees[1]. It is characterized by progressive deterioration and loss of articular cartilage and by reactive new bone formation at the joint margins [2]. Clinical manifestations include slowly developing joint pain, stiffness, and joint enlargement with limitations of motion. Knee osteoarthritis results from mechanical and idiopathic factors that alter the balance between degradation and synthesis of HA in synovial fluid and articular cartilage and subchondral bone.

There are several options for treating osteoarthritis of the knee including conservative (analgesics, physiotherapy/ physical modalities, weight-relieving braces, intra-articular injections of steroid, Hyaluronic acid, platelet rich plasma) and surgical (osteotomy, arthroplasty) treatment.

Hyaluronic acid (HA) is a linear, long-chain, unbranched, hydrophilic, high molecular weight muco-polysaccharide forming a critical constituent component of the synovial fluid and of cartilage. In patients with osteoarthritis, synovial hyaluronic acid is depolymerized and cleared at higher rates than in normal individuals [2], leading to deterioration of joint cartilage and synovial fluid characteristics etc and manifesting clinically as pain and loss of function. Hence, intraarticular viscosupplementation with HA may restore normal biochemical properties/ characteristics in various joint structures, resulting in improved pain control and function [3].

Viscosupplementation is FDA approved for patients with knee OA who continue to have pain despite pharmacological agents including NSAIDS and interleukin-1 inhibitors etc [4] and non-pharmacologic therapy [5]. Relief of knee pain from OA with HA in clinical studies may be due to the effects of HA on nerve impulses and nerve sensitivity [6] and suppression of inflammatory responses to interleukin-1[7][8]. This is corroborated with clinical trials comparing HA and placebo, where in pain relief was significant with HA [9]. Amelioration of pain is comparable with NSAIDS [10] and even superior to intraarticular corticosteroid [11], lasts longer but takes more time to take effect [10].

The literature on single HA injections is less. The purpose of this study was to evaluate both clinical and functional outcomes with one injection of Hyaluronic injection in patients with osteoarthritis knee.

Materials and Methods:

This prospective clinical trial was approved after Institutional Ethical Committee clearance and individual informed consent (both written and verbal). Patients were enrolled between Feb 2016 and Dec 2018. The study was conducted at outpatient department of Physical Medicine and Rehabilitation of IPGME&R SSKM Hospital, Kolkata. Sixty four patients with Osteoarthritis of knee were selected based on the inclusion criteria were (1) Resting visual analog scale pain of >50 mm and (2) Radiographic evidence for osteoarthritis and at least one of the following three characteristics; Age ≥50yrs, Morning stiffness ≤ 30 min in duration and coarse crepitus on motion (as per American College of Rheumatology guidelines 1986).

All patients had symptomatic knee pain at the tibiofemoral joint and radiographic evidence of osteoarthritis (loss of cartilage thickness, osteophyte formation, subchondral sclerosis, or cysts) [12]. All patients had received conservative treatment for knee pain with unsatisfactory results.

The patients with unilateral osteoarthritis knee were observed after intraarticular HA injection. The painful and functionally limiting knee was studied in patients with bilateral disease (n=45, 70.3%). At entry, the affected knee had radiographic evidence of grade (Kellgren Lawrence) 2-3 osteoarthritis [13]. Unwilling patients and those with grade 4 arthritis, inflammatory joint disease and crystal arthropathy were excluded. Also patients with uncontrolled diabetes mellitus, uncontrolled hypertension, coagulopathy, skin infections around knee joint, allergy to viscosupplementation, arthroplasty and those who had received previous intraarticular HA or glucocorticoid injection were excluded.

Assessment

Patient details and demographic data were documented at baseline (age, sex, body mass index, comorbidities, and concomitant medications). The WOMAC [14] and VAS pain scores were noted. The WOMAC scores are based on the three subdomains of pain, stiffness, and difficulty in performing daily activities. The visual analog scale (VAS) ranged from 0 to 100 mm, with lower numbers representing less pain and higher numbers representing more pain. The VAS and WOMAC was used as a self-administered questionnaire in accordance with the developers' instructions[14].

Intervention

Hyaluronic acid is supplied as 6ml syringe containing Hylan G-F 20 and was supplied by the Govt of West Bengal free of cost to the patients. Under aseptic precautions, the injections Injection Hyaluronic acid was performed via supero-lateral approach with a 22-gauge needle in minor OT. Patients were instructed to refrain from strenuous activity for a day following the intra-articular injections.

Initial baseline data was documented and a follow up was done at 6 months duration for the study.

RESULTS

Subject Characteristics

Sixty four (64) patients were recruited for the study over a period of 2 years. Study population baseline demographics are given in **Table1**. No patient was lost to follow up. Majority of the patients were females (56.2%). The mean age was 58 ± 5 years. The mean Body mass index 27.15 Kg/m^2.

Outcome

A. Evaluation of visual analog pain scale (VAS).

1. VAS at rest: Visual analog pain scale (VAS) revealed an average score of 70 pre-injection at rest. From this base line, the value dropped to 45
2. VAS after walking: Walking 30 m revealed an average pain score of 82 pre-injection that dropped to 51. **(Please enter Figure 1 here)**

B. The mean WOMAC Pain scores improved from 10.84 ± 1.98 to 5.00 ± 2.15. The mean stiffness score improved from 2.40 ± 1.29 to 1.50 ±1.08. The mean functional score improved from 36.75 ± 5.33 to 32.84 ±6.64. The paired t test showed that mean of all the WOMAC were significantly lower than the first visit ($p<0.01$). **(Please enter Graph 1 here)**

There were no systemic adverse events reported. Local adverse events including pain and swelling at injection site were observed two (2) in injections.

DISCUSSION

Osteoarthritis is the most common form of joint disorder in the elderly and a major source of disability[1]. The prevalence continues to increase as the older adult and obese populations grow [4][9]. More than 50% of patients older than 65 years have radiographic changes in the knee that indicates arthritis [9]. It is characterized by activity related pain and troublesome stiffness. Traditional non-operative treatment of osteoarthritis includes activity modification, weight loss, rehabilitative exercise, nonsteroidal anti-inflammatory medications (NSAIDs), Interleukin -1 and intra-articular injections. All of them have their own advantages and disadvantages. Surgical treatment, in the form of osteotomy and arthroplasty of the hip and knee is usually reserved for severe stages.

Visco-supplementation with HA has gained popularity as a modality for the treatment of osteoarthritis of the knee. The rational for the intraarticular injection of hyaluronic acid is to restore the viscoelasticity of synovial fluid by providing exogenous HA thus helping to augment the flow of synovial fluid, normalize the synthesis and inhibit the degradation of endogenous hyaluronic acid, and relieve joint pain [9][16]. The properties of biocompatibility and a prolonged half-life within the synoviumare added advantages[15].

The literature supports the use and efficacy of HA even though AAOS hasn't recommended for or against it. Many randomized controlled studies have demonstrated a longer-term effect in pain control with HA injections compared with corticosteroids [17] and placebo [18][19]. Hyaluronic acid has approximately a 1% incidence of side effects per injection. The most common side effects are local reactions of the knee such as swelling, pain, and increased warmth. This type of reaction typically lasts for 1 to 2 days [3] which is similar to that of our study. With proper patient selection and injection technique, these injections are a viable treatment option for patients with early symptomatic knee OA. The group receiving the hyaluronic acid also had a significantly reduced need for treatment at 1 year [19].

CONCLUSION:

The results of this study show that intraarticular injection of hyaluronic acid has a significant effect on functional outcome and reduction of osteoarthritic knee pain. Possibly due to the disease modifying effect of the drug, the symptom relief is seen upto 6 months. Careful selection of the patient is important to achieve satisfactory results. Significantly better response to injection is seen in early OA (Grade 2) is than in advanced arthritis. Advancing age and obesity seems to be unfavorable variables for symptomatic improvement. The procedure was associated with few local adverse events as the injection site and decreases pill count for analgesics. Both rest pain and activity related pain seems to improve with HA injection which is similar to previous studies[20]. The need for long-term study cannot be over emphasized. So, we can conclude that single injection of hyaluronic acid injections in osteoarthritis of knee seems to be an effective option. The lesser hospital visits and procedures is another advantage.

Table 1: Demographic Characteristic

Parameter Category	Number and percentage
Total number of Patients	64
Age	
Mean (SD)	58 (±5)
Range	50 to 70
Gender	
Female	36 (56.2%)
Male	28 (43.7%)
Body Mass Index (kg/m2)	
Mean (SD)	27.15
Radiological Grading (Kellgren Lawrence Classification)	
Grade I	0
Grade II	38 (59.37%)
Grade III	26 (40.62%)
Grade IV	0

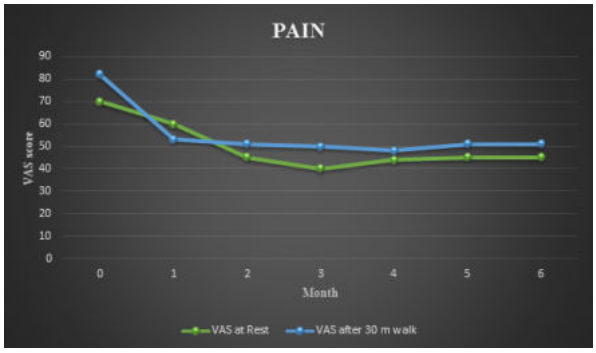
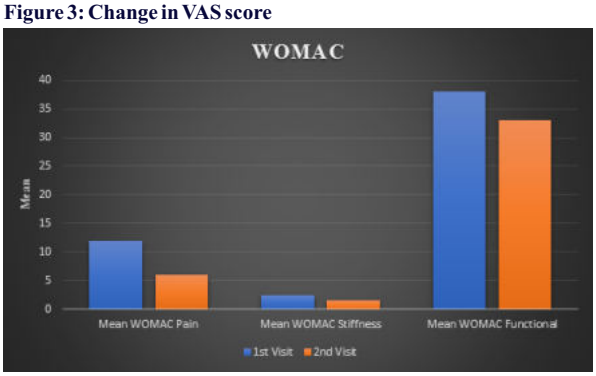


Figure 3: Change in VAS score



Graph 1: Change WOMAC Score

REFERENCES

1. Dieppe P: Osteoarthritis. Acta Orthop Scand Suppl 1998;281:2-5
2. EA, B., & Denlinger, J. L. (1993). Viscosupplementation: a new concept in the treatment of osteoarthritis. *J Rheumatol Suppl*, *39*, 3-9.
3. Rydell, N., & Balazs, E. A. (1971). Effect of intra-articular injection of hyaluronic acid on the clinical symptoms of osteoarthritis and on granulation tissue formation. *Clinical Orthopaedics and Related Research (1976-2007)*, *80*, 25-32.
4. Kim RH, Springer BD, Douglas DA. Knee reconstruction and replacement. In: Flynn F, ed. Orthopaedic Knowledge Update. Rosemont, IL: American Academyof Orthopaedic Surgeons; 2011:469-475
5. Stitik, T. P., Kazi, A., & Kim, J. H. (2008). Synvisc®® in knee osteoarthritis. *International Journal of Clinical Rheumatology*, *3*(3), 215.
6. Begg, C., Cho, M., Eastwood, S., Horton, R., Moher, D., Olkin, I., ... & Stroup, D. F. (1996). Improving the quality of reporting of randomized controlled trials: the CONSORT statement. *Jama*, *276*(8), 637-639.
7. Yasui, T., Akatsuka, M., Tobetto, K., Hayaishi, M., & Ando, T. (1992). The effect of hyaluronan on interleukin-1α-induced prostaglandin E 2 production in human osteoarthritic synovial cells. *Agents and actions*, *37*(1), 155-156.
8. Monfort, J., Nacher, M., Montell, E., Vila, J., Verges, J., & Benito, P. (2005). Chondroitin sulfate and hyaluronic acid (500-730 kda) inhibit stromelysin-1 synthesis in human osteoarthritic chondrocytes. *Drugs under experimental and clinical research*, *31*(2), 71-76.
9. Culliford, D. J., Maskell, J., Beard, D. J., Murray, D. W., Price, A. J., & Arden, N. K. (2010). Temporal trends in hip and knee replacement in the United Kingdom: 1991 to 2006. *The Journal of bone and joint surgery. British volume*, *92*(1), 130-135.
10. Adams, M. E., Atkinson, M. H., Lussier, A. J., Schulz, J. I., Siminovitch, K. A., Wade, J. P., & Zummer, M. (1995). The role of viscosupplementation with hylan GF 20 (Synvisc®) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing hylan GF 20 alone, hylan GF 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone. *Osteoarthritis and cartilage*, *3*(4), 213-225.

11. Mamlin, L. A., Melfi, C. A., Parchman, M. L., Gutierrez, B., Allen, D. I., Katz, B. P., ... & Freund, D. A. (1998). Management of osteoarthritis of the knee by primary care physicians. *Archives of family medicine*, *7*(6), 563.
12. Altman, R., Asch, E., Bloch, D., Bole, G., Borenstein, D., Brandt, K., & Wolfe, F. (1986). Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *29*(8), 1039-1049.
13. Kellgren JH, Jeffrey MR, Ball J. The epidemiology of chronic rheumatism. Atlas of standard radiographs of arthritis. Oxford: Blackwell Scientific Publications; 1963.
14. Bellamy N. WOMAC osteoarthritis index users guide. Queensland, Australia: University of Queensland; 2000. p 1-43.
15. Watterson, J. R., & Esdaile, J. M. (2000). Viscosupplementation: therapeutic mechanisms and clinical potential in osteoarthritis of the knee. *JAAOS-Journal of the American Academy of Orthopaedic Surgeons*, *8*(5), 277-284.
16. Lee, S., Park, D., & Chmell, S. J. (2004). Viscosupplementation With Hylan GF 20 (Synvisc)–Pain and Mobility Observations from 74 Consecutive Patients. *The journal of knee surgery*, *17*(02), 73-77.
17. Bellamy, N., Campbell, J., Welch, V., Gee, T. L., Bourne, R., & Wells, G. A. (2006). Viscosupplementation for the treatment of osteoarthritis of the knee. *Cochrane database of systematic reviews*, (2).
18. Dixon, A. S. J., Jacoby, R. K., Berry, H., & Hamilton, E. B. D. (1988). Clinical trial of intra-articular injection of sodium hyaluronate in patients with osteoarthritis of the knee. *Current medical research and opinion*, *11*(4), 205-213.
19. Dougados, M., Nguyen, M., Listrat, V., & Amor, B. (1993). High molecular weight sodium hyaluronate (hyalectin) in osteoarthritis of the knee: a 1 year placebo-controlled trial. *Osteoarthritis and cartilage*, *1*(2), 97-103.
20. Petrella, R. J., DiSilvestro, M. D., & Hildebrand, C. (2002). Effects of hyaluronate sodium on pain and physical functioning in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled clinical trial. *Archives of internal medicine*, *162*(3), 292-298.