International Journal of Research in Medical Sciences
Gantait K et al. Int J Res Med Sci. 2021 Jun;9(6):1731-1734
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20212243

Original Research Article

Efficacy and safety of single dose of Non-animal stabilized hyaluronic acid intraarticular injection for knee Primary osteoarthritis: a pilot study at Midnapore Medical college in West Bengal

Kripasindhu Gantait*, Kalimujjaman Molla, Akshaya Elango

Department of Medicine, Midnapore Medical College, Mindapore, West Bengal, India

Received: 30 March 2021
Revised: 10 May 2021
Accepted: 11 May 2021

***Correspondence:**
Dr. Kripasindhu Gantait,
E-mail: gkripasindhu@yahoo.in

ABSTRACT

Background: Hyaluronic acid is a commonly prescribed intra-articular (IA) therapy for knee primary osteoarthritis (OA). In India majority of population lives in rural areas having limited resources and socio-cultural biodiversity. Their personal, socio-cultural and occupational habits vary and need to be addressed. The primary outcome measure was pain of knee joint reduction after therapy and follow up visit. Secondary outcomes were therapy related adverse events (AEs).
Methods: Population (n=20) are selected from rural areas of age range 40 to 60 years having poor economic background and daily labour by profession. Participants with diabetes and cardic illness and BMI ≥30 were excluded. All participants were having grade- 2 B/L knee OA with mild effusion and fulfill the ACR classification criteria. Each participant was assessed on Visual analog scale (VAS) pain and Composite indian functional knee assessment scale (CIFKAS) at the end of three months of therapy and statistical analysis was done.
Results: Among the 20 participants 11 were female, 9 were male. The mean (mean±S.D.) of BMI and duration of disease was 23.6±2.73 and 4±2.08 respectively. Pearson correlation coefficient calculated for pain during physical activity/ pain during functional ADL activity, ability to perform physical activity/ ability to perform ADL activity and social function and emotional function score were 0.634/0.701, 0.731/0.687 and 0.566/0.607 respectively which indicates that they are highly correlated.
Conclusions: A single dose of IA NASHA is effective and safe in reducing pain and functional disability in patients with primary OA of knee.

Keywords: Knee osteoarthritis, Functional disability, CIFKAS, NASHA

INTRODUCTION

Knee osteoarthritis (OA) is the leading cause of chronic disability mainly affecting the elderly population, but may appear as early as 35 years of age. It is characterized by a range of disorders of clinical and pathological outcome resulting in structural and functional abnormalities and reduced functional performance abilities.[1-4] Osteoarthritis is a common disorder. It is estimated that approximately four per cent of the world's current population is affected by osteoarthritis. Knee pain is the most frequently reported peripheral joint complaint in community-based studies worldwide and has been found to be present in 5-13% of adult populations in Asia by the 'Community Oriented Programme for the Control of Rheumatic Diseases' (COPCORD) studies.[5-8] Its prevalence estimated in India, Thailand, Malaysia, Shanghai, and Philippines is approximately 13.2%, 12.5%, 9.3%, 10.9%, and 5% respectively. The male:female ratio was 2.7%:6%, 9.4%:10.9% and 8.5%:12.3% for the Chinese, Malaysians

and Indians respectively.[7] One of the nonsurgical options for the symptomatic management of OA is intra-articular injection of hyaluronic acid (HA), also referred to as visco-supplementation. HA is a vital component of synovial fluid for lubrication and shock absorption in joints. OA is characterized by a decrease in HA concentration in the synovial fluid as the disease progresses, leading to a reduction in visco-elastic properties.[8] NASHA is highly purified non-animal stabilized hyaluronic acid.[9] The patho-physiological mechanism in primary OA is believed to be failure of an otherwise normal joint because of excessive load.[10] Strengthening of quadriceps and hamstring muscles reduces pain and disability in OA knee.[11] Kellgren and Lawrence grading scale for osteoarthritis.[12] (Table 1).

Table 1: Radiological grading scale of osteoarthritis.

Grade	Radiological findings
0	Normal
1	doubtful joint space narrowing and possible osteophytic lipping
2	definite osteophytes and possible joint space narrowing
3	moderate multiple osteophytes, definite narrowing of joint space and some sclerosis and possible deformity of bone ends.
4	large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends

Table 2: ACR clinical classification criteria for osteoarthritis of the knee.

ACR clinical classification criteria
Pain in the knee
+
AND one of the following
Over 50 years of age.
Less than 30 minutes of morning stiffness.
Crepitus on active motion and osteophytes

The CIFKAS is a tri-dimensional therapist administered and self-reported questionnaire (individual performance based) assessment instrument.[14] The instrument is divided into three major domains of functional performance. The first is the pain domain which assesses each knee separately and includes severity of pain during physical and functional Activities of daily living (ADL) activity. The second is the functional disability domain measuring the functional disability status during physical and functional ADL activity. The third i.e. psychosocial domain measures the psychosocial impact of disability on functional performance and socio-cultural integration.

Aim of this study was to measure the efficacy of single dose intra-artcular injection NASHA for pain reduction of knee primary osteoarthritis and also find out its adverse events.

METHODS

The study was conducted in the Rheumatology unit and the department of General Medicine of Midnapore Medical College and Hospital situated in Paschim Medinipur district of West Bengal. This study was conducted for period of six months from September 2019 to March 2020.

This is a longitudinal observational, institution based, single centre study. The study was approved by the Institutional Ethics Committee of the Hospital. Written and informed consent was taken from each of the study subjects.

Twenty patients with Grade 2 primary OA of knee fulfilling the ACR 1986 criteria attending the rheumatology outpatient of Midnapore Medical College, West Bengal, were included. Exclusion criteria included associated comorbid conditions, such as stroke, heart disease, diabetes and vascular diseases, patients with inflammatory disease of joints like rheumatoid arthritis, recent knee trauma patients with body mass index (BMI) >30.

Each participant was assessed on Visual analog scale (VAS) pain and Composite Indian Functional Knee Assessment Scale (CIFKAS) at baseline and end of three months of therapy.

Descriptive and inferential statistical analysis was done. The Mean±S.D. and Pearson correlation coefficient were calculated for using statistical package for social sciences (SPSS) Statistics.

RESULT

Among the 20 participants 11 were female, 9 were male. The mean age of study population was 52±6.52 (mean±S.D.) where minimum was 40 years and maximum was 60 years. The mean (mean±S.D.) of BMI and Duration of disease was 23.6±2.73 and 4±2.08 respectively (Table 3).

Table 3: Baseline characteristics of participants (n=20).

Character	Mean ± SD (n=20)
Male:female	9 :11
Age	52±6.52
Duration of disease	4±2.08
BMI	23.6±2.73

Mean±S.D. score for pain before and after therapy on VAS were 8.56±1.15 and 3.1±2.34 respectively and pearson correlation coefficient was calculated and showed positive correlation (Table 4).

Pearson correlation coefficient calculated for pain during physical activity/ pain during functional ADL activity ,

ability to perform physical activity/ ability to perform ADL activity and social function and emotional function score were 0.634/0.701, 0.731/0.687 and 0.566/0.607 respectively which indicates that they are highly correlated (Table 5).

Table 4: VAS knee pain score before (B) and after (A) therapy (n=20).

	Mean±SD	Pearson correlation coefficient (r)
B	8.56±1.15	0.821
A (End of three months of therapy)	3.1±2.34	

Table 5: CIFKAS before (B) and after (A) therapy (n=20).

		Mean±SD	Pearson correlation coefficient (r)
Pain domain IA	B	4.62±0.6	0.634
	A (at 3 months of therapy)	1.62±1.25	
IB	B	4.50±0.51	0.701
	A (at 3 months of therapy)	1.5±1.40	
Functional domain IIA	B	4.68±0.47	0.731
	A (at 3 months of therapy)	1.68±1.25	
IIB	B	4.62±0.61	0.687
	A (at 3 months of therapy)	1.59±1.26	
Psychosocial domain IIIA	B	3.98±0.68	0.566
	A (at 3 months of therapy)	1.76±1.35	
IIIB	B	4.1±0.7	0.607
	A (at 3 months of therapy)	1.8±1.41	

Table 6 summarizes the number of participants who experienced therapy related AEs and type of AEs after receiving single dose of IA- NASHA.

Table 6: Therapy related adverse events in participants (n=20).

Participants experiencing a therapy related AEs [N (%)]	Type of therapy related AEs [N (%)]
5 (25%)	Arthralgia -2 (10%) Joint swelling -1 (5%) Injection site pain -2 (10%)

DISCUSSION

Among the 20 participants 11 were female, 9 were male. The mean age of study population was 52±6.52 (mean±S.D.) where minimum was 40 years and maximum was 60 years. The mean (mean±S.D.) of BMI and Duration of disease was 23.6±2.73 and 4±2.08 respectively. High BMI as a risk factor for developing OA of knee was observed by Blagojevic et al.[15] In our study, 73.6% of participants fall under normal BMI. As our study had a small sample size, we could not observe the relationship of BMI and OA severity. In a study conducted by Huskisson et al on safety and efficacy of IA HA, 100 patients with OA knee were given five doses of HA weekly.[16] Primary efficacy criteria were pain on walking measured with VAS and Lequesne index. At the end of 5 weeks, there was significant difference in favour of HA against placebo (p=0.087). In our study, we observed improvements in both VAS and CIFKAS scores from the baseline to the end of 3 month. Similar findings were also observed by Leopold et al.[17] With this study, it was possible to demonstrate the effectiveness of IA administration of NASHA with regards to pain and function in patients suffering from OA. The very low incidence of side effects and the safety of HA will make it suitable for the treatment of OA in elderly patients who cannot tolerate NSAIDs or for whom they are contraindicated. To evaluate the long-term effects of HA, studies with longer follow-up periods are suggested.

The limitations of the study are non-blinding and shorter follow-up.

CONCLUSION

From the current study, it was found that single dose of IA NASHA is effective in reducing pain and disability in patients with primary OA of knee at end of 3 months. A larger sample size with longer period of follow-up will be necessary to see if the improvement is maintained for longer term.

ACKNOWLEDGEMENTS

Authors would like to thank the support of Medical Superintendent of Midnapore Medical College, West Bengal, India and we are also grateful to the participants for their cooperation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Millward-Sadler SJ, Wright MO, Lee H. Integrin-regulated secretion of interleukin 4: A novel pathway of Mechano-transduction in human articular Chondrocyte. J Cell Biol. 1999;145(1):183-9.
2. Hurley MV. The role of muscle weakness in the pathogenesis of osteoarthritis. Rheum Dis Clin North Am. 1999;25(2):283-98.
3. Hurley MV. Muscle dysfunction and effective rehabilitation of knee osteoarthritis: what we know and what we need to find out. Arthritis Rheum. 2003;49(3):444-52.
4. Sharma L. Proprioceptive impairment in knee osteoarthritis. Rheum Dis Clin North Am. 1999;25(2):299-314.
5. Dixon J, Howe TE. Quadriceps force generation in patients with osteoarthritis of the knee and asymptomatic participants during patellar tendon reflex reactions: an exploratory cross-sectional study. BMC Musculoskeletal Disorders. 2005;6:46.
6. Chaiamnuay P, Darmawan J, Muirden KD. Epidemiology of rheumatic disease in rural Thailand: a WHO-ILAR COPCORD study. Community Oriented Programme for Control of Rheumatic Disease. J Rheumatol. 1998;25(7):1382-7.
7. Manek NJ, Lane NE. Osteoarthritis: current concepts in diagnosis and management. Am Fam Physician. 2000;61(6):1795-804.
8. Wen DY. Intra-articular hyaluronic acid injections for knee osteoarthritis. Am Fam Physician. 2000;62(3):565-70.
9. Boettger MK, Kümmel D, Harrison A, Schaible HG. Evaluation Of Long-Term Antinociceptive Properties Of Stabilized Hyaluronic Acid Preparation (NASHA) In An Animal Model Of Repetitive Joint Pain. Arthritis Research and Therapy. 2011;13(4):R110.
10. Goldring MB, Goldring SR. Articular cartilage and subchondral bone in the pathogenesis of osteoarthritis. Ann N Y Acad Sci. 2010;1192:230-7.
11. Al-Johani AH, Kachanathu SJ, Ramadan Hafez A, Al-Ahaideb A, Algarni AD, Alroumi MA et al. Comparative study of hamstring and quadriceps strengthening treatmentsin the management of knee osteoarthritis. J Phys Ther Sci. 2014;26(6):817-20.
12. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16:494-502.
13. R Altman, G Alarcon, D Appelrouth. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheumatism. 1991;34(5):505-14.
14. Veerapen K, Asokan RN, Rathakrishnan V. Clinical and radiological profile of symptomatic knee osteoarthritis in Malaysia. APLAR J Rheumatol. 2004;7(2):97-107.
15. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. Osteoarthritis Cartilage. 2010;18(1):24-33.
16. Huskisson EC, Donnelly S. Hyaluronic acid in the treatmentof osteoarthritis of the knee. Rheumatology (Oxford). 1999;38(7):602-7.
17. Leopold SS, Redd BB, Warme WJ, Wehrle PA, Pettis PD, Shott S. Corticosteroid compared with hyaluronic acid injections for the treatment of osteoarthritis of the knee a prospective, randomized trial. J Bone Joint Surg Am. 2003;85(7):1197-203.

Cite this article as: Gantait K, Molla K, Elango A. Efficacy and safety of single dose of Non-animal stabilized hyaluronic acid (NASHA) intraarticular injection for knee Primary osteoarthritis: a pilot study at Midnapore Medical college in West Bengal. Int J Res Med Sci 2021;9:1731-4.