



Original Article

Pharmacological Effects of Hyaluronic Acid on Osteoarthritis of Knee Joint

Md. Enamul Haque,¹ Md. Ariful Haque,² Samil Uddin Ahmed,³ Md. Habibul Hasan,⁴
 Md. Zafar Imam,⁵ Md. Abdul Awal⁶

Abstract

This longitudinal type of prospective study was carried out the clinical outcome of intra-articular Hyaluronic Acid injection in the management of mild to moderate osteoarthritis of knee joint. The sample size was 78 which was selected purposively. Partially structured questionnaire was used to collect data from the respondents by face-to-face interview. All efforts were made to collect data accurately. For open questions, the respondents were asked in such a manner way so that they could speak freely and explain their opinion in a normal and neutral way. Regarding age in group distribution of the respondents it was found that majority (47.4%) were in the age group of more than 61 years. The man monthly family income was 215431.21 ± 16898.112 Taka. About 41.0% were overweight, 14.1% had hypertension, 80.8% had multiple symptoms of osteoarthritis in knee joint, 94.87% had restricted range of motion. It was identified that 92.31% relieved pain by injections, 60.25% had satisfactory feeling after injections. The relationship between age group of the respondents was statistically significant ($p < 0.05$; $p < 0.01$) with side effect of injection, pain relief after injection, feeling of patients after injection. The relationship between BMI of the respondents was statistically significant ($p < 0.05$; $p < 0.01$) with pain relief after injection, feeling of patients after injection. The relationship between complications of injection was statistically significant ($p < 0.05$; $p < 0.01$) with systemic diseases of the respondents.

Key words: Hyaluronic Acid, Osteoarthritis, Knee joint.

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Introduction

A clinical syndrome of joint pain with multifactorial etiopathogenesis is known as Osteoarthritis (OA), which is categorized by a sort of steady loss of osteophyte formation, articular cartilage, inflammation of the joint and subchondral bone remodeling and one this syndrome, OA causes pain and loss of function leading to be a major source of disability. Among the topmost ten causes of disability across the

world, it is the common form of joint disease worldwide. OA has been turned into an important financial burden for the global economy and arose itself as the foremost public health problem in pace with the aging of the population and growing obesity.²

A common joint disease is Knee osteoarthritis (OA), which affects 240 per 100,000 people in the US every year. Knee OA is one of the five principal causes of disability among non-

¹ Assistant Professor, Department of Ortho-Surgery, Rajshahi Medical College & Hospital, Rajshahi, Bangladesh.

² Associate Professor, Institute of Biological Sciences, University of Rajshahi.

³ Consultant, Ortho-Surgery

⁴ Junior Consultant, Ortho-Surgery, Rajshahi Medical College Hospital, Rajshahi.

⁵ Senior Consultant, Ortho-Surgery, Modernized District Hospital, Joypurhat

⁶ Assistant Professor, Department of Public Health, Varendra University, Rajshahi.

institutionalized adults because of its affecting on the quality of the individual's life. Due to absence from work and for early retirement, it bears a major socioeconomic impact, whereas about 40% of adults with knee OA state their health to be poor or impartial. Estimation shows losses between \$3.4 and \$13.2 billion per year caused for job-related issues. There are varieties of treatment options for knee OA considering the severity of the disease. In order to control symptoms, modifications of simple analgesia and lifestyle are sufficient for mild cases. Knee replacement is a treatment for advanced stages of the disease. Knee replacement helps to alleviate pain and restore physical function as well as it is safe and cost effective.³

Intra-articular injections are used for knee pain caused due to moderate OA. With a view to managing acute flare-ups of the disease, an injection is widely used, which is steroid-based and has a combination with a local anesthetic. A common occurrence in OA is to alleviate pain due to synovitis, and their accomplishment depends on the powerful anti-inflammatory provided in the joint, which is also referred to as hyaluronate or hyaluronan. HA is a naturally found large viscoelastic glycosaminoglycan molecule that originated in cartilage and synovial fluid.⁴ Traumatic vigor dissipation, shock preoccupation, defensive coating of the articular cartilage surface, and lubrication are the properties included there.⁵ Anti-inflammatory effects have been shown on cells in vitro^{6,7}, and chondrocyte apoptosis in OA is slowed down by modifying the process of cartilage matrix degradation and binding CD44 and ICAM-1 receptors.⁴ The patients with knee OA have a reduction in concentration and the molecular weight of HA in the synovial fluid.^{8,9} Intra-articular HA injections are considered to reinstate the viscoelasticity of synovial HA, and the protective functions grown naturally in the joint since the viscoelasticity of synovial fluid and HA concentration and integrity are proportional to each other. In spite of in-vitro studies having a sound principle and being promising^{6,7} clinical studies have been less conclusive on the efficacy of HA in dealing with osteoarthritic knee pain.

Compared with a placebo, it is suggested by some studies to bear an effect¹⁰, while no clear benefit is suggested by other studies.^{11,12} Moreover, some studies conclude with HA having no additional benefit compared to much inexpensive substitute of corticosteroid injections¹³ whereas it may have a prolonged effect than corticosteroids, suggested by others.^{10,14}

Being focused on relief of symptoms and retention or improvement of function, treatment for knee OA is conducted¹⁵. In the case of OA with topical analgesics, primary pharmacological options are required those including symptomatic slow-acting drugs¹⁶⁻¹⁸ in addition to exercise, physiotherapy, and weight loss.¹⁹ Oral nonsteroidal anti-inflammatory drugs (NSAIDs) should be considered if symptoms continue.¹⁶ More offensive options like intra-articular (IA) injections may be specified ensuing oral therapy¹⁶, and it may include some benefits like minimal adverse events (AEs), amplified bioavailability, and abridged systemic exposure.²⁰ Lubrication and elastic shock absorption are provided naturally by Hyaluronic acid (HA), which is a usual long-chain polymer with repetition of disaccharide units.²¹⁻²³ Pain relief, improved function, and reduced stiffness are the benefits reported in favor of supplemental HA injections²⁴⁻²⁷ despite the fact that conceivable apparatuses of action for HA have not been fully explained.^{28,29}

Materials and Methods

It was a longitudinal type of prospective study at the Department of Orthopedic Surgery, Rajshahi Medical College Hospital, Rajshahi, from January 2018 to December 2020. All the patients with mild to moderate osteoarthritis of knee joint attending Rajshahi Medical College Hospital, Rajshahi, Dolphin Clinic, Kadirganj, Rajshahi and Medicare diagnostic center, Puthia, Rajshahi during the study period were included in this study. A purposive sampling technique was used, and the total sample size was 78. Data were collected from the study patients by face-to-face interview through a partially structured questionnaire. Baseline information on some selected socio-demographic and biological characteristics of the

respondents and information regarding mild to moderate osteoarthritis was collected. All efforts were made to collect data accurately. For open questions, the respondents were asked in such a manner so that they could speak freely and explain their opinion in a normal and neutral way. No leading questions were asked. Mobility scale (WOMAC) scoring was recorded in the concerned portion of the questionnaire. The study protocol was approved by the ethical committee of the Institute of Biological Sciences of the University of Rajshahi. The permission of the authority of

Rajshahi Medical College Hospital, Rajshahi, Dolphic Clinic, Kadirganj, Rajshahi and Medicare Diagnostic Centre, Puthia, Rajshahi was taken before starting the study. The aim and objectives of the study, along with its procedure, risks, and benefits of the study, were explained to the respondents in easily understandable language, and then informed consent was taken from each participant. Then it was assured that all information and records would be kept confidential, and the procedure would be used only for research purposes.

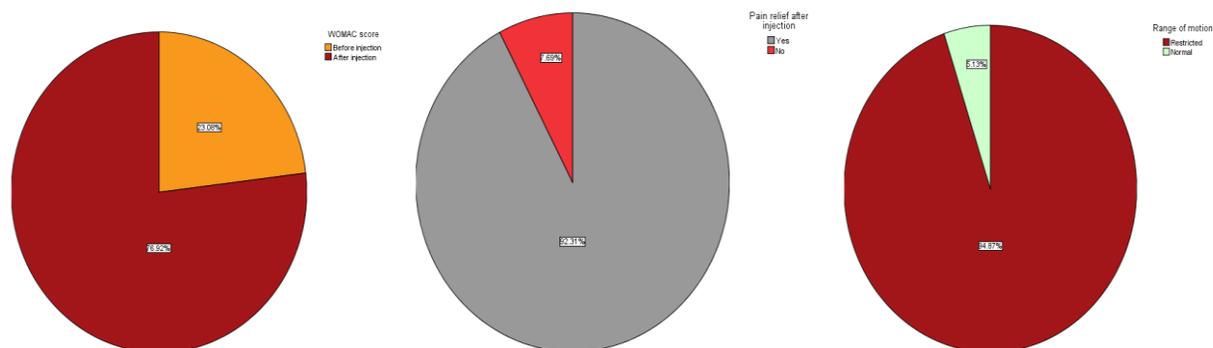
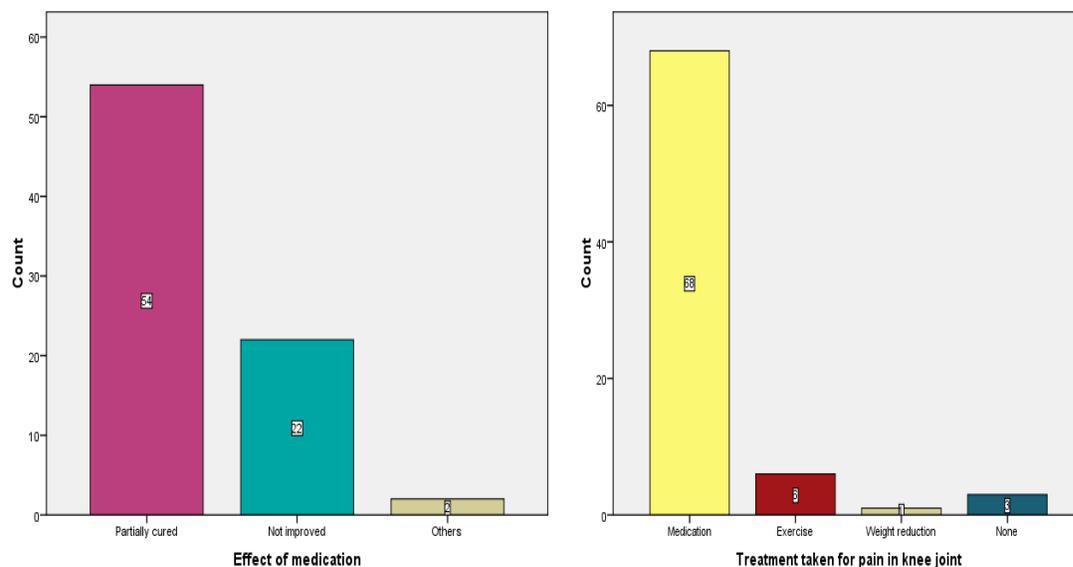
Results

Table 1 shows the relationship between the age group of the respondents and the side effects of injections. About 100.0%, 84.8%, and 94.6 % of the respondents who were in the age group of <50 years, 50-60 years, and 61+ years had no side effects of the injection, respectively. About 100.0%, 87.9%, and 94.6 of the respondents who were in the age group of <50 years, 50-60 years, and 61+ years relieved pain after injections, respectively.

About 50.0%, 51.5%, and 70.3% of the respondents who were in the age group of <50 years, 50-60 years, and 61+ years were satisfied after injections, respectively. About 87.5%, 91.7%, 96.9%, and 85.7% of the respondents having undernutrition, normal-nutrition, overweight, and obese relieved pain after injections, respectively. About 62.5%, 37.5%, 65.6%, and 85.7% of the respondents who had undernutrition, normal nutrition, overweight and obese had satisfactory feelings after injections, respectively. About 100.0% of the respondents who had up to 4.1 mmol/L RBS were fully satisfied after injections, 62.8%, 50.0%, and 65.0% of the respondents who had RBS 4.2-7.5 mmol/L, 7.6-10.5 mmol/L, and >10.5 mmol/L were satisfied after injections respectively. About 94.3%, 76.5% and 100.0% of the respondents who had pain <3 years, 3-5 years, and >5 years respectively had no side effect of the injection respectively. It was originated that 54 of the respondents had been cured partially as the effect of medication, 22 respondents had no improvement, and two respondents had other conditions. Regarding the WOMAC score, it was found that 76.92% of the respondents' condition after injection, and 23.08% had this condition before injection. Regarding pain relief after injection, it was found that 92.31% of the respondents relieved pain after injection, and 7.69% did not get relief after injection. Regarding the range of motion, it was found that 94.87% of the respondents had a restricted range of motion, and 5.13% had it normal.

Table 01: Distribution of the respondents by their different characteristics

Variables	Group	Side effects of injections			χ^2_{value}	P-value
		Yes N (%)	No N (%)			
Age group	<50 Years	0 (0.0)	8 (100.0)	2.907	0.005	
	50-60 years	5 (15.2)	28 (84.8)			
	61+ years	2 (5.4)	35 (94.6)			
Duration of knee joint pain	<3 years	3 (5.7)	50 (94.3)	5.910	0.005	
	3-5 years	4 (23.5)	13 (76.5)			
	>5 years	0 (0.0)	8 (100.0)			
Pain relief after injections						
Age group	<50 Years	Yes N (%)	No N (%)	1.851	0.005	
	50-60 years	8 (100.0)	0 (0.0)			
	61+ years	29 (87.9)	4 (12.1)			
BMI	Under Nutrition (<18.50)	35 (94.6)	2 (5.4)	2.072	0.005	
	Normal nutrition (18.50-26.99)	7 (87.5)	1 (12.5)			
	Overweight (27.00-29.99)	22 (91.7)	2 (8.3)			
	Obese (30.00+)	31 (96.9)	1 (3.1)			
Feeling after injections						
Age group	<50 Years	Not Satisfactory	Satisfactory	Satisfied	5.358	0.005
	50-60 years	0 (0.0)	4 (50.0)	4 (50.0)		
	61+ years	4 (12.1)	17 (51.5)	12 (36.4)		
BMI	Under Nutrition (<18.50)	1 (2.7)	26 (70.3)	10 (27.0)	14.148	0.001
	Normal nutrition (18.50-26.99)	0 (0.0)	5 (62.5)	3 (37.5)		
	Overweight (27.00-29.99)	2 (8.3)	9 (37.5)	13 (54.2)		
	Obese (30.00+)	1 (3.1)	21 (65.6)	10 (31.2)		
RBS (mmol/L)	Up to 4.1	2 (14.3)	12 (85.7)	0 (0.0)	8.90	0.005
	4.2-7.5	0 (0.0)	0 (0.0)	1 (100.0)		
	7.6-10.5	2 (4.7)	27 (62.8)	14 (32.6)		
	>10.5	3 (21.4)	7 (50.0)	4 (28.6)		
		0 (0.0)	13 (65.0)	7 (35.0)		



Discussion

This longitudinal type of prospective study was carried out to find out the clinical outcome of intra-articular Hyaluronic Acid injection in the management of mild to moderate osteoarthritis of knee joints. The age group of this study revealed that 47.4% were more than 61 years age group, 42.3% were 50-60 years age group and 10.3% were less than 50 years age group. The mean age group was 60.97 ± 8.150 years (Table 01). Neogi T was found most of the respondents were more than 55 years of age.² It was invented that 41.0% of the respondents were overweight, 30.8% were in a normal nutrition state, 17.9% were obese, and 10.3% were undernutrition. The mean BMI was 25.60 ± 4.197 BMI (Table no. 01). Being overweight had a great influence on osteoarthritis

in women, and it increased with their weight.¹⁰ It was observed that 55.1% of the respondents had RBS of 4.2-7.5 mmol/L, 25.6% had >10.5 mmol/L, 17.9% had 7.6-10.5 mmol/L, and 1.3% had Up to 4.1 mmol/L. The mean RBS of the respondents was 9.0074 ± 3.621 mmol/L (Table 01). Among osteoarthritis patients, a vital role is played by diabetes for responding to the hyaluronic acid injections. Poor response is observed in the majority of diabetic patients.³⁰ It was recognized that 62.8% of the respondents took <6 months of medication, 23.1% took 6-12 months, and 14.15 took >12 months of medication. The mean duration of taking medication was 5.173 ± 4.03 Years (Table 01). Conservative treatment did not cure the pain in the knee joint in the long run.³¹ Regarding the range of motion, it was found that 94.87% of the respondents had a restricted

range of motion, and 5.13% had it normal (Figure no. 5). Regarding pain relief after injection, it was found that 92.31% of the respondents relieved pain after injection, and 7.69% did not get relief after injection (Figure no. 4). In another study, most (71.9%) of the respondents relieve pain after injections.³² Regarding WOMAC score, it was found that 76.92% of the respondents' condition after injection and 23.08% had this condition before injection (Figure no. 3). Improvements in WOMAC subscales are not shown by the participants after initiating hyaluronic acid injections. (aching/pain: 0.50; 95% CI: -0.11 to 1.11, arduousness: -0.07; 95% CI: -0.38 to 0.24, and operative: 0.49; 95% CI: -1.34 to 2.32).³⁰ Better improvement is observed among the patients in the MMP group compared to the patients in the AM group considering the total index score of WOMAC index total score, pain score, stiffness score, and Lequesne index total score over the full follow-up period (all $P < 0.01$).³³ It was originated that 54 of the respondents had been cured partially as the effect of medication, 22 respondents had no improvement, and two respondents had other conditions (Figure no. 2). It was brought into being that 47 of the respondents had a satisfactory attitude after injections, 26 respondents were fully satisfied, and five respondents were not satisfied (Table no. 01). The relationship between the age group of the respondents and side effects of injections status was found statistically significant ($p < 0.05$) [Table no. 1]. The relationship between the age group of the respondents and pain relief after injection status was found statistically significant ($p < 0.05$) [Table no. 1]. The relationship between the age group of the respondents and the feeling of patients after injection was found statistically significant ($p < 0.05$) [Table no. 1]. It was revealed that pain increase with age and if untreated for a long time.³⁴ The relationship between the BMI group of the respondents and pain relief after injection was found statistically significant ($p < 0.05$) [Table no. 1]. The relationship between the BMI group of the respondents and the feeling of patients after injection was found statistically highly significant ($p < 0.01$) [Table no. 1]. Pottie P *et al.* found that obesity is associated with

osteoarthritis.³⁵ The relationship between the RBS group of the respondents and the feeling of patients after injection was found statistically significant ($p < 0.05$) [Table no. 1]. The relationship between the duration of knee joint pain and side effects of injections was found statistically significant ($p < 0.05$) [Table no. 1].

Conclusion

Viscosupplementation for symptomatic osteoarthritis of the knee is a newly available option. Experience with this treatment is growing as it becomes more widespread among orthopedic surgeons and rheumatologists. Family physicians with the inclination and skills to perform intra-articular injections may also consider this as an option for use in their patients with symptomatic knee osteoarthritis. Although study results are not definitive, data do exist suggesting long-term efficacy in a significant number of patients. Future indications may expand to other joints and other forms of arthritis. So this study might open a new era in ameliorating the suffering of the people and will provide evidence for the most clinically-effective and cost-effective approach to manage mild to moderate osteoarthritis of knee joints in Bangladesh.

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Corresponding Author:
Dr. Md. Enamul Haque
Assistant Professor
Department of Ortho-Surgery
Rajshahi Medical College
Rajshahi-6205, Bangladesh
E-mail: enamul67ortho@gmail.com