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Ahmed Zohair Elsaied Hegazy

Resident, Department of Orthopedic Surgery, Faculty of Medicine, Tanta University, Tanta, Egypt

Ashraf Atef Mahmoud

Professor, Department of Orthopedic Surgery, Faculty of Medicine, Tanta University, Tanta, Egypt

Mohamed Osama Ramadan

Assistant Professor of Orthopedic Surgery, Orthopedic Surgery Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Ahmed Mostafa Elsharkawy Lecturer, Department of Radio-Diagnosis, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding Author: Ahmed Zohair Elsaied Hegazy Resident, Department of Orthopedic Surgery, Faculty of Medicine, Tanta University, Tanta, Egypt

Ultrasound-guided intra-articular hyaluronic acid injection in hip osteoarthritis

Ahmed Zohair Elsaied Hegazy, Ashraf Atef Mahmoud, Mohamed Osama Ramadan and Ahmed Mostafa Elsharkawy

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Abstract

Purpose: The purpose of this work was to investigate the efficiency of intra-articular injection of hyaluronic acid (HA) under ultrasound (US) guidance as a symptomatic treatment of hip osteoarthritis (OA).

Methods: This prospective clinical work was performed on 21 individuals aged more than 35 years old, both sexes, with clinical criteria of OA hip, failed medical treatment for pain after one month using nonsteroidal anti-inflammatory drugs (NSAIDs) for primary hip OA and secondary hip arthritis in avascular necrosis and Kellgnen-lawrence criteria I – II – III classification of hip OA. All patients in the study were subjected to radiological investigations (x-ray pelvis antro-posterior view) showing both hips. **Results:** Cases were categorized into excellent group (n = 17) and good group (n = 4). The results were significantly affected by age, weight, and BMI and pre procedural times of NSAID consumption /day and not affected by sex, height, comorbidities, laterality, Kellgnen-lawrence criteria. NSAID consumption had been substantially decreased in the excellent group than good group. The number of patients who required NSAID and NSAID intake, In comparison to baseline, the amount of individuals with pain, the Harris Hip Score (HHS) and the visual analogue scale (VAS), had all been considerably reduced at the three- and six-month scores.

Conclusions: injection of HA intra-articular via ultrasound-guided is an effective and safe treatment for manifested hip OA.

Keywords: Hip osteoarthritis, hyaluronic acid, ultrasound, intra-articular injection

Introduction

Osteoarthritis is a generally prevalent chronic joint condition marked by disintegration and softening of articular cartilage. It causes symptoms including stiffness in the morning, pain, and diminished functioning that, especially in older people, may impact their general wellbeing and quality of life^[1]. The main objective of treatment for people with hip OA is still to reduce their pain. Osteoarthritis is routinely treated with non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics, which are regarded as standard care for the condition.

Unluckily, numerous individuals either cannot take NSAIDs or have severe, often fatal, adverse effects from these medications, including gastrointestinal bleeding and ulceration^[2].

It has already been demonstrated that local corticosteroid injections are beneficial for alleviating hip OA-related pain. Local infection and irritation of soft tissue at the sites of injection, pain aggravation, and septic arthritis are all significant warning signs. The *in vitro* corticosteroids and local anesthesia chondrotoxicity on human chondrocyte populations is a crucial factor to take into account ^[3]. Hyaluronan or derivatives of it are used in viscosupplementation, which tries to alleviate symptoms by reestablishing the physiological characteristics of the synovial fluid ^[4].

Repeated disaccharide units of glucuronic acid and N-acetylglucosamine make up hyaluronan preparations, which are viscous solutions obtained from bacterial fermentation or extracts of rooster comb. several products with varying concentrations and molecular weights are being utilized in therapeutic settings and have received approval in several nations worldwide ^[5].

Due to dilutional impacts, abnormal hyaluronan synthesizing, and free radical destruction, the molecular weight and concentrations of hyaluronic acid are lowered in the osteoarthritic fluid.

As a result, the affected joints lack the biologic and mechanical qualities that HA typically provides ^[6].

Visco-supplementation is a therapeutic method that mimics the benefits of hyaluronate in healthy joints by injecting it into an osteoarthritic joint. This kind of treatment may postpone the need for a complete hip replacement in order to restore the biologic characteristics of normal HA^[7]. While intra-articular HA often takes longer to take impact than intra-articular steroids, the therapeutic benefit of intra-articular injections of HA seems to continue longer, and repeated administration cycles may be helpful in the long-term treatment of this chronic condition^[8]. Intra-articular injections of HA have recently acquired acceptance in the management of this pathological disease due to their beneficial properties (pain relief and improved joint functionality) and lack of significant adverse effects^[1].

The aim of this work was to investigate the effectiveness of intra-articular injection of HA under ultrasound guidance as a symptomatic treatment of hip osteoarthritis.

Patients and Methods

This prospective clinical work was performed on 21 individuals aged greater than 35 yrs. old, both sexes, with clinical criteria of OA hip, failed medical treatment for pain after one month using non-steroidal anti-inflammatory drugs for primary hip OA and secondary hip arthritis in avascular necrosis and Kellgnen-lawrence criteria I – II – III classification of hip OA.

The study was done from January 2022 to January 2023, and Tanta University Hospitals' Ethical Committee has given its ethical approval. All patients provided written permission after being fully briefed.

Exclusion criteria were patient under anti-coagulant therapy, previous hip surgery, skin infection at site of injection, collapse of femoral head on antro-posterior radiograph, mobility impairment disorder (stroke-hemiplegia) and classification of hip OA by Kellgnen-lawrence criteria IV.

Each individual was given a comprehensive medical history, clinical assessment, and radiological studies [X-ray pelvis Antroposterior view showing both hips].

Injection material and technique: HA, single 4 ml (60 mg) of HA 1.5% sodium salt solution for injection intra-articular used once.

The participant was evaluated while lying on his back with a minor internal rotation of the hip (15-20). A linear transducer US probe (Z60 US System, Mindray, North America) was utilized. An anterior parasagittal strategy, lateral to the femoral blood vessels, has been employed to scan the hip joint. Pre-procedure imagery were typically taken, and after that, the individual was ready for the surgery. The individual was covered with medical pad or a sterile towels prior to the injection.

Sterile method was employed: Betadine was used to disinfect the patient's anterior hip and groin region before sterile US gel was placed over the cleaned area just above the intended site of injection. By directing the US transducer towards the most lateral part of the femoral neck, where the joint capsule could be seen, the hip joint was visible in long axis view. Once the ideal site had been found and the femoral head-neck juncture could clearly be seen.

Then local anaesthesia is injected deeply along the track to the joint as seen by the US transducer to make sure that the needle of the syringe containing the local anaesthesia is in the same direction planned to inject HA, then The needle and syringe are separated and needle is left as a landmark for the spinal needle after that is used to inject HA as the local anaesthesia needle is removed immediately before the insertion of the spinal needle.

At that point, a 9-cm-long, 22-gauge spinal needle, or 18gauge cannula is used either by anterior or lateral approach under complete aseptic measures in the same site and direction of the local anaesthesia needle, bevel up, 1 cm away from the US transducer's distal end. The HA was injected and seen reaching the joint's capsule after the needle was at the proper location inside the capsule.

The needle was withdrawn when the injection was finished while keeping vision intact. A little bandage was put on after the needle was taken out, and the individual was then made mobile.

Follow up measures: NSAID consumption is calculated by counting how many days per month the individual consumed these medications in the preceding month.

Delta Harris hip score is used in this process as a measurement tool. The Harris hip score (HHS) is a joint-specific score that includes 10 questions covering the areas of function, pain, physical activity, deformity, and hip range of motion. It must be submitted by both the patient and their physician. The HHS was first introduced for the purpose of evaluating the functional results of post-mold arthroplasty for post-traumatic arthritis.

The HHS is being utilized to assess functional outcome following intracapsular femur neck fractures and per trochanteric fractures of the hip ^[9]. The validated subjective assessment for chronic as well as acute pain is the visual analog scale (VAS). A handwritten marking on a line 10 cm long that shows the transition between "no pains" and "worst pain" was used to record scores. Taking 15 meters to walk. Indivisible hip OA pain was measured using a scale that included five subgroups: spontaneous, throughout the day, at night, when walking, and while bearing weight. Follow up of the cases was every 3 months for 2 times (to be total 6 months).

Statistical analysis

SPSS v26 (IBM Inc., Chicago, IL, USA) was used for the statistical analysis. Histograms and the Shapiro-Wilks test have been employed to assess the normality of the data distribution. Using an unpaired Student's t-test, quantitative parametric factors were provided as mean and standard deviation (SD) to contrast among the two groups. Interquartile range (IQR) and the median were used to show and analyze quantitative non-parametric information, respectively. When applicable, qualitative parameters were analyzed using the Fisher's exact test or Chi-square test and provided as frequency and percentage (%). Statistical significance was defined as a two-tailed P value < 0.05.

Results

Patients were further divided into 2 categories: excellent group (n = 17) and good group (n = 4). There were no poor or fair cases found.

Age, weight, body mass index (BMI) and nonsteroidal antiinflammatory drugs (NSAID) consumption were significantly lower in excellent group than good group. Sex, height, comorbidities, laterality and Kellgnen-lawrence criteria classification were insubstantially difference among the two groups. Table 1

 Table 1: Characteristics, comorbidities, laterality, Kellgnen-lawrence criteria classification and pre procedural NSAID consumption of the studied patients

		Good group (n=4)	Excellent group (n=17)	P value
Age (years)		62.18±7.038	56.75±2.217	0.011*
	Male	2 (50%)	6 (35.29%)	0.596
Sex	Female	2 (50%)	11 (64.71%)	0.586
Weight (Kg)		82.75±4.5	74.47±5.62	0.013*
Height (m)		1.67 ± 0.035	1.65±0.037	0.663
BMI (Kg/m ²)		28.81 ± 1.66	27.07±1.45	0.048*
DM		0 (0%)	5 (29.41%)	0.214
Hypertension		0 (0%)	3 (17.65%)	0.364
Autoimmune disease		1 (25%)	5 (29.41%)	0.861
	Right	3 (75%)	8 (47.06%)	0.283
Hip affected	Left	0 (0%)	7 (41.18%)	0.154
	Bilateral	1 (25%)	2 (11.76%)	0.721
	Ι	1 (25%)	4 (23.53%)	0.921
Kellgnen-lawrence criteria	II	2 (50%)	7 (41.18%)	
-	III	1 (25%)	6 (35.29%)	
Pre- procedural NSAID consumption		3 (75%)	15 (88.24%)	0.496
Times of NSAID consumption /day		2.8±1.41	1.49 ± 1.047	0.047*

Data are presented as mean \pm SD or frequency (%). DM: diabetes mellitus. BMI: body mass index. NSAID: nonsteroidal anti-inflammatory drugs. *: statistically significant as P value<0.05.

The number of injections were one in all patients 21(100.0%). The number of injections were 60 mg / 4ml in all patients 21(100.0%). US probe used was deep (3 Mhz) in 18 (85.7%) patients and superficial (12 Mhz) in 3 (14.3%) patients. 4 (19.05%) patients had pain, 3 (14.3%) patients had low grade fever and 1(4.8%) patient had synovitis. Table 2

Table 2: Number of injections, US probe type of hip osteoarthritis and Complications in the studied patients

		N=21
Number of injections	One (60 mg / 4ml)	21(100.0%)
Type of US meho	Superficial (12 Mhz)	18(85.7%)
Type of US probe	Deep (3 Mhz)	3(14.3%)
	Pain	4(19.05%)
Complications	Low grade fever	3(14.3%)
	Synovitis	1(4.8%)

Data are presented as frequency (%). US: ultrasound.

The number of patients who required NSAID and NSAID intake were significantly lower at 3 and 6 months contrasted to baseline and were comparable between 3 and 6 months. VAS was substantially decreased at 3 months and 6 months contrasted to baseline and was substantially lower at 6 months

contrasted to 3 months. Harris Hip Score was substantially higher at 3 months and 6 months contrasted to baseline and was significantly higher at 6 months contrasted to 3 months. Table 3.

Table 3: Post procedural NSAID, VAS and HHS	consumption in the studied patients
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	Baseline	3 months	6 months	P value	
Number of patients required NSAID	18 (85.71%)	6 (28.57%)	3 (14.29%)	<0.001*	P1<0.001* P2 <0.001* P3=0.453
Number of tablets used per day	2.19±1.03	0.43±0.51	0.33±0.48	<0.001*	P1<0.001*
	0 – 3	0 - 1	0 - 1		P2 <0.001* P3=0.162
NSAID intake (days)	16.19±8.4	4.05±6.7	2.19±4.69	<0.001*	P1<0.001* P2 <0.001* P3=0.305
VAS	6.14±1.15	3.33±1.11	2.14±1.35	<0.001*	P1<0.001* P2 <0.001* P3=0.003*
HHS	43.43±10.83	79.9±2.9	92.67±3.84	<0.001*	P1<0.001* P2 <0.001* P3=0.003*

Data are presented as frequency (%) or mean \pm SD. VAS: visual analogue scale. NSAID: nonsteroidal anti-inflammatory drugs. HHS: Harris Hip Score. *: statistically significant as P value<0.05, P1: p value among baseline and 3 m, P2: p value between baseline and 6 m, P3: p value between 3 m and 6 m.

how many people were in pain, pain during the day, spontaneous pain, pain throughout walking, pain at night, pain weight-bearing, and 15-meter walking time were substantially various across the three measurements (p<0.001). Number of individuals who had pain, pain during the day, spontaneous-pain, pain throughout walking, pain at night, pain weight-

bearing, and 15-meter walking time had been substantially lower at 3 months and 6 months contrasted to baseline and was substantially lower at 6 months contrasted to 3 months. Kellgnen-lawrence criteria was insignificantly different among baseline, 3 months and 6 months. Table 4

		Baseline (n=21)	3 months (n=21)	6 months (n=21)	P value	
Number of patients had pain		21 (100%)	11 (52.38%)	4 (19.05%)	<0.001*	P1<0.001* P2<0.001* P3=0.050*
Pain during the day		64.8±12.4	38.5 ± 22.4	21.7±19.6	<0.001*	P1<0.001*
		51-84	10-76	10-69		P2 <0.001* P3<0.001*
Spontaneous pain		56.3±7.9	28.6±20.6	20±11.79	<0.001*	P1<0.001*
		41-69	8 - 61	10-55		P2 <0.001* P3=0.028*
			37.1±17.9	29±18.7	<0.001*	P1<0.001*
Pain during walking		52-80	19-74	13-83		P2 <0.001* P3<0.001*
		64.8±7.2	36.5±18.4	18.4±9.2		P1<0.001*
Pain at night		52-78	19 - 74	10-42	<0.001*	P2 <0.001* P3=0.04*
		65.9±8.1	36.9±23.4	24.9±7.5		P1<0.001*
Pain weight bearing		53-75	15-70	12-42	<0.001*	P2= 0.004* P3<0.001*
		18.8±3.2	12.7±4	9.3±2.8		P1<0.001*
15-meter walking time (min)		14-24	6-20	5-16	<0.001*	P2 <0.001* P3=0.003*
Kellgnen- Lawrence criteria	Ι	5 (24%)	6 (29%)	6 (29%)		
	II	9 (43%)	10 (48%)	11 (52%)	0.879	
	III	7 (33%)	5 (24%)	4 (19%)		

Data are presented as frequency (%) or mean \pm (SD). *: statistically significant as P value<0.05, P1: p value between baseline and 3 m, P2: p value between baseline and 6 m, P3: p value between 3 m and 6 m.

Case 1

Male patient aged 47 years old, presented with bilateral hip pain, that increase with activity, of two years duration, kellgnen-Lawrence 3, diabetic on oral controlled and hypertensive, no autoimmune disease, BMI: 25, height: 1.64 m, weight:72 kg, failed medical treatment more than one month by NSAIDs. Injected by US guided using superficial probe (12 MHz) with HA "Hyalone 60mg/4ml" once.

For 6 months follow up period: NSAIDs consumption decreased from 3 tablets/day to 0-1 tablet/day. VAS from 7 to 3. Pain during day, 15-meters walking distance, weight bearing, night significantly decreased. HHS from 65 to 90. No major complication was found. Kellgnen-Lawrence criteria insignificantly different. Figure 1

Case 2

Male patient aged 55 years old, presented with bilateral hip pain, more on left side that increase with activity, of three years duration, kellgnen-Lawrence 3, not diabetic nor hypertensive, patient has been on steroids for 1.5 years for pain stopped 2 months before injection, BMI: 28.3, height: 1.7 m, weight: 82 kg, failed medical treatment more than one month by NSAIDs. Injected by US guided using superficial probe (12 MHz) with HA "Hyalone 60mg/4ml" once.

For 6 months follow up period: NSAIDs consumption decreased from 3 tablets/day to 1 tablet/day. VAS from 7 to 1. Pain during day, 15-meters walking distance, weight bearing, night significantly decreased. HHS from 26 to 95. No major complication was found. Kellgnen-Lawrence criteria insignificantly changed. Figure 2

Discussion

The second-largest joint that OA most often affects is the hip joint. Hip OA is more common as people become older and overweight. Those who perform less physical exercise are similarly more likely to have it ^[10].

In this investigation, the lateral circumflex femoral arteries and other minor arteries that were to be avoided were located using Doppler imaging. It was important to do a Doppler examination throughout every treatment since the anatomic position of these smaller veins varied from individual to individuals, particularly in those who received blood-thinning medications.

Micu *et al.*^[11] enlisted individuals with hip OA who had not responded to standard of care treatment, which is consistent with our findings. They discovered that compared to the blind method, ultrasound-guided intra-articular injections (USGIAI) are being shown to be more effective and safer. Similar to this, Parisi *et al.*^[12] treated a group of individuals with knee OA by injecting HA into the joint under US guidance. They demonstrated that the US offers an alternate method for ensuring precise needle positioning and also has a number of important benefits.

Additionally, Berkoff *et al.* ^[13] shown that US is a commonly utilized imaging technique to assess musculoskeletal disorders and uses high-frequency sound waves to image soft tissues and bony structures. US-guided intra-articular knee injections result in better clinical results and are less expensive.

Additionally, Sibbitt *et al.* ^[14] reported that clinical musculoskeletal specialists are increasingly using sonographic needle guiding during standard office injection treatments.

Our findings showed that, following intra-articular injection of HA, VAS score was substantially reduced at 3 months and 6 months in follow-up contrasted with baseline and was substantially reduced at 6 months contrasted to 3 months.

Nouri et al. ^[10] randomized clinical study involving individuals with grade 2 and 3 hip OA is consistent with our findings. They discovered that the VAS score in the group receiving HA injections was substantially reduced at 2 months and 6 months contrasted with baseline, as well as at 6 months contrasted to 2 months. Similar findings were made by Micu et al. [11] who discovered that pain as measured by the VAS score considerably and gradually declined from the beginning up to 3 and 6 months. Micu et al.'s research [15] on individuals suffering from KLC II and III hip OA included giving them HA-USGIA three times in a row on a weekly basis. They discovered that from baseline to 3 and 6 months, correspondingly, the pain as measured by the VAS score exhibited a considerable and gradual reduction. Moreover, Parisi et al. ^[12] found that pain VAS scores, was significantly reduced at 6 months after treatment with US-guided joint HA injection in the management of OA in knee compared to baseline. Similarly, Dallari et al. [16] performed a randomizedcontrolled work on 111 individuals with OA in the hip, (KLG) 1 to 4. They found that VAS score was significantly lower in follow-up following intra-articular injection of HA at 2 months and 12 months contrasted to baseline and was substantially lower at 12 months contrasted to 2 months.

In our results, Harris Hip Score (HHS) was substantially greater at 3 and 6 months in follow-up after intra-articular injection of HA contrasted to baseline and was substantially higher at 6 months contrasted to 3 months.

In line with our findings, Nouri *et al.* ^[10] showed that HHS was substantially higher in follow-up after intra-articular injections of HA at 2 months and 6-month period contrasted to baseline and was substantially higher at 6 months contrasted to 2 months. Similarly, Abate and Salini. ^[11] Enlisted twenty individuals with moderate to severe hip OA. They found that HHS was significantly higher in follow-up after intra-articular injections of HA at 3 months and 6-month period contrasted to baseline and was substantially higher in follow-up after intra-articular injections of HA at 3 months and 6-month period contrasted to a months. Moreover, Dallari *et al.* ^[16] found that HHS was substantially greater at 12-month period and 6 months contrasted to baseline and was significantly greater at 12 months.

In our results, the number of patients who required NSAID and NSAID intake were significantly lower in follow up after intra articular injection of HA at 3 months and 6 months compared to baseline and were significantly lower at 6 months than 3 months.

In agreement with our results, Micu *et al.* ^[11] found that in follow-up after intra-articular injections of HA, a significantly

lower in number of individuals who required NSAID and NSAID intake at 3 months from baseline. Similarly, Alberto *et al.*^[17] conducted a work on individuals with hip OA, intraarticular injections of HA. They showed that NSAID intake was significantly lower in follow-up after intra-articular injections of HA at 3 and 6 months contrasted to baseline and were significantly lower at 6 months than 3 months. Additionally, Migliore *et al.*^[18] conducted double-blind, prospective, 6 months randomised study of 42 individuals with hip OA. HA was administered twice (once a month) under US guidance. They found patients who required NSAID and NSAID intake was substantially lower at 3- and 6-month period versus baseline.

In our results, number of individuals who suffered pain, pain during the day, spontaneous pain, pain throughout walking, pain at night, pain bearing weight, and 15-meter walking time were significantly lower in follow-up after intra-articular injections of HA at 3 months and 6 months contrasted to baseline and was substantially lower at 6 months contrasted to 3 months.

In line with our findings, Micu *et al.* ^[11] revealed that pain were substantially lower at 3 months and 6 months contrasted to baseline and was substantially lower at 6 months contrasted to 3 months. Additionally, Dallari *et al.* ^[16] revealed that number of individuals who had pain were substantially lower at 6 months and 12 months contrasted to baseline and was substantially lower at 12 months contrasted to 2 and 6 months.

In our results, complications of studied cases were (19.05%) patients had pain, (14.3%) patients had low grade fever and (4.8%) patients had synovitis. No major complications in follow up after intra-articular injections of HA were demonstrated in the studied patients.

These results were also observed by Micu *et al.*^[11] who found that no major complications were found in the studied patients during treatment and the follow-up period after intra articular injection of HA. Similarly, Micu *et al.*^[15] found that there was no relevant complications in the studied patients during treatment and the follow-up period after intra articular injection of HA. Additionally, Koh *et al.*^[19] and Dallari *et al.*^[16] found that no septic complications were reported in the studied patients during treatment and the follow-up period after intra articular injection of HA. Additionally, Koh *et al.*^[19] and Dallari *et al.*^[16] found that no septic complications were reported in the studied patients during treatment and the follow-up period after intra-articular injections of HA.

Limitations: Quite a tiny study size, and no control group receiving no therapy was included. Single-center research. We were unable to rule out the likelihood that some of these individuals got further care. The follow-up period of six months was rather short.

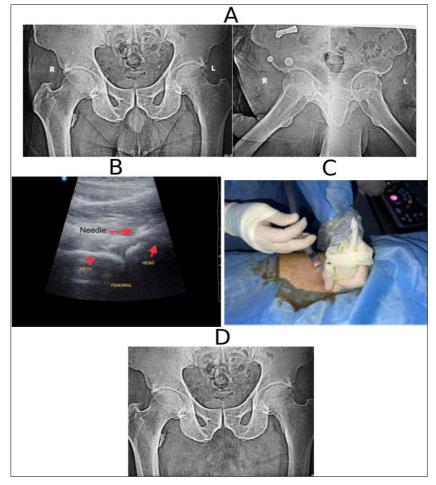


Fig 1: (A): Plain x-ray before the injection showing the osteoarthritis hip kellgnen-Lawrence grade 3 with multiple osteophytes, narrowing of joint space. (B): Ultrasound showing head neck junction. (C): Injection method of "hyalone 60mg/4ml" ultrasound guided. (D): Follow up x-ray after 6 months with insignificant change

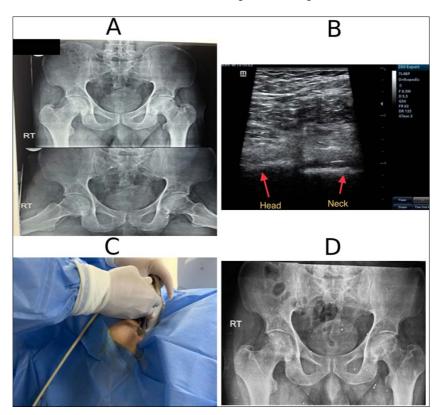


Fig 2: (A): Plain x-ray before the injection showing the osteoarthritis hip kellgnen-Lawrence grade 3 with multiple osteophytes, narrowing of joint space. (B): Ultrasound showing site of injection at head neck junction. (C): Injection method of "hyalone 60mg/4ml" ultrasound guided. (D): Follow up x-ray after 6 months with insignificant change

Conclusions

The intra-articular injections of HA under US guidance is an efficient and secure treatment for a symptomatic hip OA as observed through lower NSAID consumption, VAS score and Harris Hip Score with no major complications were found.

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