Research Article

Clinical Improvement of osteoarthritic knee pain by adding intra-articular steroid Injection to viscosupplementation

Ahmed Latteef Al-Shamari ***FIBMS***

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Address for Correspondence:
Dr.Ahmed Latteef Al-Shamari Lecturer at Dept. of Surgery, College of Medicine / Al-Mustansiriya University. Orthopedic surgeon at Al-Yarmook Teaching Hospital.

Abstract

Background: Intra-articular injections have been used for many years to treat painful joint disorders, especially by means of injecting crystalline suspensions of long-duration corticosteroids. Viscosupplementation, which is a relatively new intervention, consists of injection of exogenous hyaluronic acid into joints in order to treat osteoarthritis of knee joint.

Patients and Methods: A prospective cohort study was conducted in a private orthopedic clinic in Baghdad from March 2013 to the end of September 2014, where it enrolled a total of fifty six (56) patients of middle ages, ranging from 39 to 64 years, classified as either grade II or III according to Kellgren and Lawrence radiographic criteria. Intra-articular injection of two drugs (a long acting steroid drug, then hyaluronic acid) were given locally in one or both knee joints with one week apart. To evaluate the effect of therapy, current study group patients were assessed by Visual Analogue Scale (VAS) after 1 week, and after 4-8 weeks from the beginning of the therapeutic trial.

Results: more than two-third of cases were women (a ratio of 2.1:1), with age group of 50- 59 years old. No statistical correlation was found between Visual analogue scale (VAS) and radiographic grading (i.e. Kellgren and Lawrence radiographic criteria). Significant statistical difference ($P<0.05$) was shown in patients receiving intra-articular corticosteroids after week "1" of therapy, and a slightly better effect after adding hyaluronic acid on week "4" regarding the VAS scale of pain for radiographic grade II patients. Radiographic grade III patients showed a significant statistical correlation in VAS after week (4) of therapy for both moderate and severe classes.

Conclusion: Intra-articular injections of both corticosteroids and hyaluronic acid with one week apart appear to give clinical improvement better than using Intra-articular injection of hyaluronic acid alone.

Key words: VAS, intra-articular injection, knee joint, long-term steroids, hyaluronic acid.

INTRODUCTION

Osteoarthritis (OA) of knee is a common progressive joint disorder that can cause pain and disability in the elderly . With an estimated incidence rate of 240 per 100,000 person-years (1), it is a major public health problem in western countries and often results in early retirement and joint replacement. In the absence of effective disease modifying medical interventions for knee OA, treatments are primarily symptomatic in nature, often including intra- articular injections of a corticosteroid or hyaluronic acid (2).

Osteoarthritis is pathologically characterized by focal areas of damage to articular cartilage at load- bearing areas associated with new bone formation at joint margins, changes in subchondral bone, variable degrees of mild synovitis, joint space thickening due to cartilage loss, osteophyte formation, and joint capsule thickening (3).

Currently, treatments do not target cure, but rather are forms of palliative management involving physical, pharmacologic, and surgical approaches. In particular, intra- articular (IA) injection based treatments, such as, hyaluronic acid (HA), steroid, and others, are designed to manage associated pain (1).There are more than 50 methods for treating knee OA, the main treatment options include: non pharmacological management, pharmacological management, use of intra-articular injections and surgical treatments (4).

Intra-articular injections have been used for many years to treat osteoarthritis of knee joint by means of injecting crystalline suspensions of long-duration corticosteroids. Viscosupplementation, which is a relatively new intervention, consists of injection of exogenous hyaluronic acid into joints in order to treat osteoarthritis (5).Hyaluronic acid is a polysaccharide that is produced naturally by type B cells of the synovial membrane. Its molecules, of high molecular weight, form a high-viscosity solution that serves both as a lubricant and as a shock absorber. Viscosupplementation has short-term efficacy due to its pain-relief effect, but it is also considered to be a drug that modifies the course of osteoarthritis, with benefits within a period lasting for between six months and a few years. It is believed that the long-term results from hyaluronic acid are due to its modulating mechanism of action, especially through its interaction with the CD44 receptors of synoviocytes (6, 7).Most placebo-controlled studies demonstrate clinical improvement within two to five weeks after the intra-articular injection of hyaluronic acid. In comparing Viscosupplementation with intra-articular injection of corticosteroids, the most recent data suggest that over the first four weeks, intra-articular corticosteroids seem to be relatively more effective against pain. From the fourth week onwards, the two approaches have equal efficacy, but after the eighth week, hyaluronic acid has greater efficacy (6). Visual Analogue Scale (VAS) measures a patient's pain intensity or other features. Pain scales are based on self-report, observational (behavioral), or physiological data. Self-report is considered primary and should be obtained if possible. Pain scales are available for neonates, infants, children, adolescents, adults, seniors, and persons whose communication is impaired. Pain assessments are often regarded as "the 5th Vital Sign (8, 9).

General roles of intra-articular knee injection :

The best approach to a knee injection is the path of least obstruction and maximal access to the synovial cavity, which could be supero-lateral, supero-medial, or antero-medial/ antero-lateral. Ultrasound guidance in intra-articular knee injections may improve accuracy and the likelihood of directing medication into the joint space (10).Plain radiography is recommended to better assess the bony anatomy of the individual knee joint. The knee injection site can be selected based the patient's bony anatomy and can be marked via the tip of a retracted ballpoint pen prior to sterile preparation. The superolateral approach into the suprapatellar pouch might provide a better and more reliable route of entry into the knee joint than the superomedial or anteromedial/anterolateral approaches (11).

The concept of the triangle with reasonable accuracy was also reported, in which one line is drawn from the apex of the patella (the apex of the triangle) to the lateral pole of the patella and another line is drawn from the apex to the medial upper pole of the patella, resulting in an inverted triangle. The base of the triangle forms the upper border of the patella. The lateral line of the triangle is then marked at the midpoint, where the needle can be inserted and directed into the intra-articular knee joint (12).

Superolateral Knee Injection

For the superolateral approach, the patient lies supine with the knee almost fully or fully extended with a thin pad support underneath the knee to facilitate relaxation. The clinician's thumb is used to gently rock then stabilize the patella while the needle is inserted underneath the supralateral surface of patella, aimed toward the center of the patella, and then directed slightly posteriorly and inferomedially into the knee joint (figure 4) (11).

Superomedial Knee Injection

For the superomedial approach, the patient lies supine with the knee almost fully or fully extended with a thin pad support underneath the knee to facilitate relaxation. The clinician's thumb is used to gently rock and then stabilize the patella while the needle is inserted underneath the supramedial surface of patella, aimed toward the center of the patella, and then directed slightly posteriorly and inferolaterally into the knee joint (10).

Anteromedial/Anterolateral Knee Injection

For the anterolateral and anteromedial approaches, the patient can sit or lie supine with the knee flexed 90° to better expose the intra-articular surface to facilitate ease of needle entry into the joint space.

The sterile needle can be inserted lateral or medial to the patellar tendon for the anterolateral or anteromedial approach (figure 3), respectively, approximately 1 cm above the tibial plateau, and directed 15-45° from anterior knee surface vertical midline toward the intra-articular joint space (12).

PATIENTS AND METHODS

This study is a prospective cohort study; it was conducted in a private orthopedic clinic in Baghdad from March 2013 to the end of September 2014, where it enrolled a total of fifty six (56) patients of middle ages, ranging from 39 to 64 years, with known osteoarthritis of the knee joints diagnosed both clinically and by radiological features, and classified as either grade II or III according to Kellgren and Lawrence radiographic criteria (figure 1).

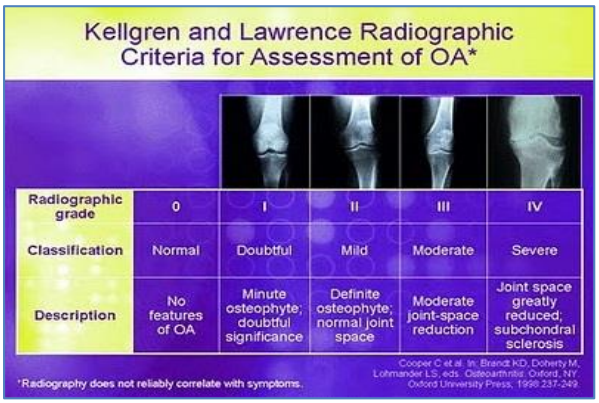

Figure 1. Kellgren and Lawrence radiographic criteria

Among these patients, 38 were females while 18 were males with a ratio of about (2.1: 1). Another group of 42 patients- a control group- were involved in this study, who were having the same medical condition but managed with hyaluronic acid injection alone.

Intra-articular injection of two drugs (a long acting steroid drug, then hyaluronic acid) were given locally in one or both knee joints with one week apart to avoid pseudo septic arthritis when we inject both of them at same time . To evaluate the effect of therapy, current study group patients were assessed by Visual Analogue Scale (VAS) after 1 week, and after 4-8 weeks from the beginning of the therapeutic trial.

Total scores range from 0 to 10 (based on a scale of 0 to 2 for five items), with a higher score indicating more severe pain (0="no pain" to 10="severe pain") were used for calculating Visual Analogue Scale, as shown in figure (2) (10).

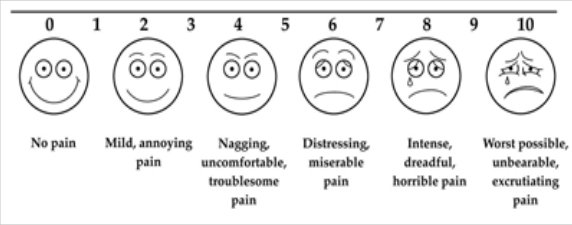

Figure 2. Visual analogue scale of pain (VAS).

A 18-21-gauge needle was used for knee injections with a 3-4 mL syringe . For injections, needle gauge should be based on medication viscosity, a higher-gauge needle may increase the resistance in pushing the medication while minimizing discomfort. For sterilization, either iodine or hexachlorodine scrub was used. For anesthesia, lidocaine or an ethyl chloride spray should were used (12).

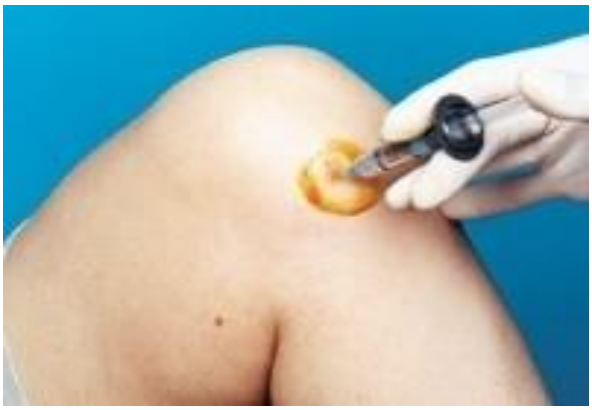

Figure 3. One method for injecting a knee joint. The patient is lying supine on the examination table with the left knee flexed to 90 degrees. The injection site is marked by the barrel of a pen along the medial joint line, palpable just medial to the inferior pole of the patella. The femur is to the left, and the tibia is to the right.

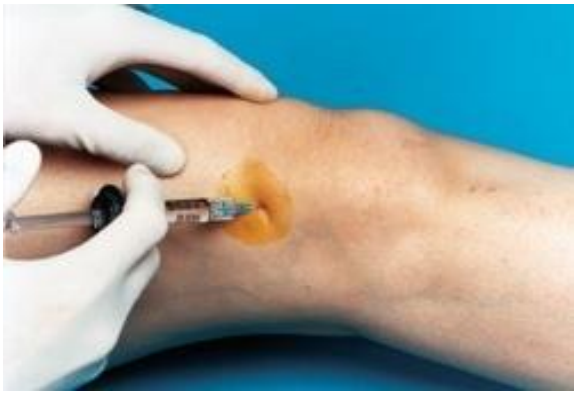

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Figure 4. Alternative method for injecting a knee joint. The patient is lying supine on the examination table with the right knee extended. The injection site is marked along the superolateral corner of the patella. The needle is angled slightly toward the underside of the patella. The femur is to the left, and the tibia is to the right.

Base line data about subjects were obtained from their history and clinical examination, a previously arranged questionnaire was used for this purpose. Statistical analysis was performed using statistical package for social sciences program version 18 (SPSS V.18, Chicago, USA). Chi- square test was used to test the association between discrete variables. All P values used were asymptotic and two sided. Findings with P value less than 0.05 were considered significant.

RESULT

Among patients enrolled in this study, females were 38 and males were 18 - with a ratio of about (2.1 : 1). The sex distribution is shown in figure (5).

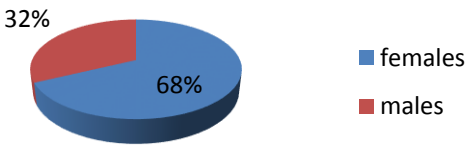

Figure 5. The distribution of study cases according to sex.

The age distribution of current study cases is shown in Table (1). About 61% of osteoarthritis patients' group in current study (i.e. 34 patients) were in the (50- 59) years age group.

Among study group cases, 36 patients (64.3%) were following the therapeutic regimen exactly as advised, and both injections with one week apart were taken. Twelve patients (21.4%) were taking both injections but with varying periods (>1- 4 weeks) apart. Only 8 patients (14.3%) were receiving the first steroid injection and absent during follow up so they are excluded from this study. Figure (6) show the compliance of current study patients in regard to therapy regimen.

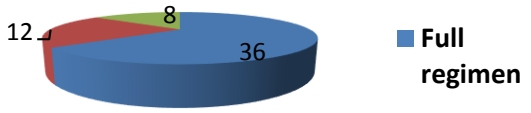

Figure 6.The distribution of cases according to patient compliance to therapy.

The study group patients were distributed in table (2), according to Kellgren and Lawrence radiographic criteria for assessment.

Twenty five (25) patients of study group were under grade II, the remaining (31) cases were under grade III. The distribution of study group and control group cases according to the visual analogue scale (VAS) is illustrated in figure (7). Most of cases (about 79%) were distributed on 3- 8 points of VAS scale. The relation between VAS and radiographic grading of current cases before therapy, and whom have had full therapeutic regimen, is illustrated in table (3). Non- significant statistical correlation was found. One week after injection of the first drug (i.e. the long acting steroid) and before the second injection of hyaluronic acid, the correlation between VAS and grade II of current cases showed a significant statistical difference with moderate pain- study group cases ($P < 0.05$), as illustrated by table (4). After 4-8 weeks of therapeutic trial, table (5) shows that the correlation of VAS with grade II of current cases still showed a significant correlation between VAS and moderate pain- study group cases with P value <0.05. Other VAS classes showed a non- significant statistical correlation in regard to group II cases. The relation between VAS and grade III, one week after injection of the first drug (i.e. the long acting steroid) and before the second drug injection, is shown in table (6). The relation between VAS and grade III of current cases showed non- significant statistical correlation. In table (7), the correlation between VAS and grade III, 4-8 weeks after starting therapy shows a significant statistical difference in both moderate pain and severe pain classes of study group compared with the control group.

Table 1. The distribution of current study cases according to age groups.

Age group	Patients		Control		Total	
	Females	***Males***	***Females***	***Males***	***Females***	***Males***
30- 39 years	***1*** *(3%)*	- *(0%)*	***1*** *(3%)*	***1*** *(8%)*	***2*** *(3%)*	***1*** *(3%)*
40- 49 years	***4*** *(11%)*	***2*** *(11%)*	***5*** *(17%)*	***2*** *(15%)*	***9*** *(13%)*	***4*** *(13%)*
50- 59 years	***24*** *(63%)*	***10*** *(56%)*	***16*** *(55%)*	***7*** *(54%)*	***40*** *(60%)*	***17*** *(25%)*
60- 69 years	***9*** *(24%)*	***6*** *(33%)*	***7*** *(24%)*	***3*** *(23%)*	***16*** *(24%)*	***9*** *(29%)*
Total	***38*** *(100%)*	***18*** *(100%)*	***29*** *(100%)*	***13*** *(100%)*	***67*** *(100%)*	***31*** *(100%)*

Table 2. Distribution of cases according to Kellgren and Lawrence criteria.

Groups	*Grade II*			*Grade III*			*Total*
	Full regimen	***>1 week apart***	***Single injection***	***Full regimen***	***>1 week apart***	***Single injection***	
Study group	***15*** *(27%)*	***3*** *(5%)*	***7*** *(12.5%)*	***21*** *(37.5%)*	***9*** *(16%)*	***1*** *(2%)*	***56*** *(100%)*
Control group	***20*** *(48%)*			***22*** *(52%)*			***42*** *(100%)*

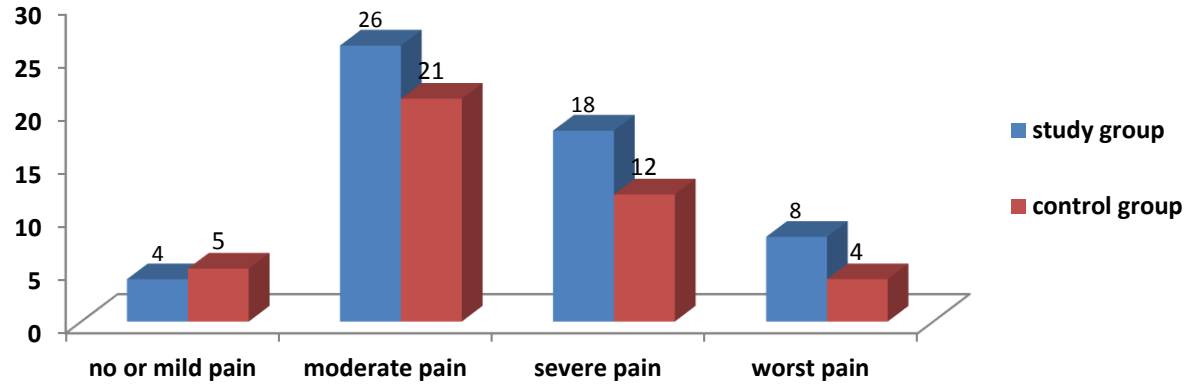

Figure 7.The distribution of study group cases & control cases according to Visual Analogue Scale (VAS).

Table 3. The relation between radiographic grading and VAS before therapy.

Visual analogue scale (VAS)	Grade II		Grade III		Odds ratio	P- value
	S	**C**	**S**	**C**		
Mild or no pain	2	4	1	1	0.5	0.67
Moderate pain	8	10	10	12	0.96	0.95
Severe pain	4	5	8	7	0.7	0.67
Worst pain	1	1	2	2	1	1.00
Total	15	20	21	22	0.79	0.59

S=study group , C=control group.

Table 4. The relation between grade II and VAS before and after one week of Rx.

Visual analogue scale (VAS)	Grade II before Rx		Grade II after 1 week of injection		Odds Ratio	P- value
	S	**C**	**S**	**C**		
Mild or no pain	2	4	10	6	0.3	0.22
Moderate pain	8	10	1	10	8.0	0.045*
Severe pain	4	5	2	3	1.2	0.87
Worst pain	1	1	0	1	∞	0.39
Total	15	20	15	20	1	-

**** Significant / S=study group , C=control group.***

Table 5.The relation between grade II and VAS before and after 4-8 weeks of Rx.

Visual analogue scale (VAS)	Grade II before Rx		Grade II after 4-8 weeks of injection		Odds Ratio	P- value
	S	**C**	**S**	**C**		
Mild or no pain	2	4	15	9	0.3	0.19
Moderate pain	8	10	0	8	∞	0.02*
Severe pain	4	5	0	2	∞	0.24
Worst pain	1	1	0	1	∞	0.39
Total	15	20	15	20	1	-

**** Significant / S=study group , C=control group.***

Table 6.The relation between grade III and VAS before and after one week of Rx.

Visual analogue scale (VAS)	Grade III before Rx		Grade III after 1 week of injection		Odds Ratio	P- value
	S	**C**	**S**	**C**		
Mild or no pain	1	1	5	4	0.8	0.88
Moderate pain	10	12	9	10	0.9	0.9
Severe pain	8	7	6	6	1.1	0.86
Worst pain	2	2	1	2	2	0.66
Total	21	22	21	22	1	-

S=study group , C=control group.

Table 7. The relation between grade III and VAS before and after 4-8 weeks of Rx.

Visual analogue scale (VAS)	Grade III before Rx		Grade III after 4-8 weeks of injection		Odds Ratio	P- value
	S	**C**	**S**	**C**		
Mild or no pain	1	1	20	5	0.25	0.33
Moderate pain	10	12	1	10	8.3	0.036*
Severe pain	8	7	0	6	∞	0.02*
Worst pain	2	2	0	1	∞	0.36
Total	21	22	21	22	1	-

**** Significant / S=study group , C=control group***

DISCUSSION

Viscosupplementation remains a controversial OA treatment option, especially because of the delayed onset of pain and functional improvement. Adding corticosteroids to the procedure could speed the relief of symptoms owing to its fast mechanism of action. It is approved that the addition of steroid to viscosupplementation 1) improve first-week pain and function compared with viscosupplementation alone, 2) diminish adverse effects of viscosupplementation alone (13).

This study was done for the patients who refuse the surgery, and in those who have been used all other pharmacological and non pharmacological measures with failure of relieving knee pain. Some patients at first refuse the intra-articular injection but finally they accept as they need anything to get rid of their pain.

Most of cases which selected in this study are middle to elderly age group, two thirds of them are female and one third are male. This is because OA is a disease that progresses over time and culminates in the destruction of articular cartilage and joints. Thus, with an increasing elderly population the treatment of knee osteoarthritis has become a major healthcare issue. It has been shown that women are more severely impacted by knee osteoarthritis. Differences in knee anatomy, kinematics, previous knee injury, and hormonal influences may play a role. Sex difference with respect to osteoarthritis presentation, treatment, and the allocation of resources also exists (3, 4).

In general, women present for treatment in more advanced stages of osteoarthritis and have more debilitating pain than their male counterparts. In addition, healthcare providers are more likely to recommend total joint arthroplasty for their male patients. Understanding how and why these gender differences occur is instrumental in formulating an inclusive strategy for combating osteoarthritis in the future (4, 14).

In current study we found that there is no correlation between radiological finding and clinical symptoms-according to visual analogue scale of pain (VAS)-although only the Kellgren and Lawrence grade 2 and 3 were chosen as grade 1 should be treated at first by general measures and oral analgesia while grade 4 need surgical intervention.

Knee pain was improved in grade 2 and 3 when we started use steroid injection specially at first 1-4 weeks but after 4-8 weeks the hyaluronic acid become more effective and last long i.e. there is significant improvement when adding steroid to viscosupplementation rather than use hyaluronic acid injection alone and this result was agreed with studies by Ozturk and col¬leagues, who performed a 1 year, randomized, single blind trial of 40 patients with knee

OA (15), and also by de Campos and colleagues, who found nearly the same results when enrolled 104 patients with knee osteoarthritis and randomized them to receive either a single intra-articular injection of hylan GF-20, or a single intra-articular injection of hylan GF-20 plus triamcinolone hexacetonide, and asses them according to visual analogue scale (VAS). They found that the addition of triamcinolone hexacetonide improves first-week symptom and functional scores of viscosupplementation, but not beyond (13).

Bannuru and colleagues compare the efficacy of intra-articular hyaluronic acid with corticosteroids for knee osteoarthritis (OA) by selecting randomized trials that reported effects of intra-articular hyaluronic acid versus corticosteroids on knee OA. They found From baseline to week 4, intra-articular corticosteroids appear to be relatively more effective for pain than intra-articular hyaluronic acid. By week 4, the 2 approaches have equal efficacy, but beyond week 8, hyaluronic acid has greater efficacy. Understanding this trend is useful to clinicians when treating knee OA (2).

Conclusion

Intra-articular injections of both corticosteroids and hyaluronic acid with one week apart appear to give a clinical improvement better than using Intra-articular injection of hyaluronic acid alone. Understanding this trend is useful to clinicians when treating knee Osteoarthritis (OA).

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