

The duration of response to intra-articular steroid injections in patients with osteoarthritis of the knee: a single centre's experience

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Abstract

Background: The burden of Osteoarthritis (OA) is huge, with a sizable proportion of patients that have failed the analgesic treatment and are not candidates for surgery or have refused surgery. Intraarticular corticosteroid injections (IASI) are considered standard of care for pain relief and control of local inflammation in this category of OA patients. However, there is a wide variation in the duration of response to steroid injections. This study was designed to determine the duration of response to IASI in patients with osteoarthritis of the knee in our environment.

Methods: Fifty-four patients aged between 30 and 80 years who have been diagnosed with osteoarthritis using the American College of Rheumatology criteria and have met the inclusion criteria were enrolled in the study and were given intra-articular steroid injections to the knee. Their responses were assessed using visual analogue scale (VAS) score, Western Ontario, and McMaster Universities Osteoarthritis Index (WOMAC) score at 2, 4 and 12 weeks. The patients were classified as responders if there was a fifty percent improvement in the WOMAC scores and a fifty percent

reduction in the VAS score and non-responders if there is less than fifty percent improvement in the WOMAC score and less than fifty percent reduction in the VAS score.

Results: Fifty-two patients completed the study; 78.4% and 100% of these had good WOMAC and VAS responses respectively at 2 weeks but this proportion gradually reduced to 47.9% and 56.3% for WOMAC and VAS respectively at 3 months.

Conclusion: Intra-articular steroid injections provide sustained response in patients with osteoarthritis of the knee who have failed analgesic therapy and are not candidates for total knee replacement for up to three months and the response decreases with advancing age.

Key words: Intra-articular steroid injection (IASI). Osteoarthritis. Duration of response.

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Introduction

Osteoarthritis (OA) is by far the most usual form of joint disease throughout the world.¹ It is strongly associated with older age; some studies estimate that over 80% of people ≥ 55 years of age have osteoarthritis of at least one joint.² OA affects the hips, knees, spine, hands, and feet. Knee OA is the most important because of the high prevalence of pain and disability it causes in older adults, with resultant increase in healthcare resource utilization particularly in terms of joint replacements.^{1,2}

Hydrocortisone was introduced for intra-articular injection in 1951.³ Since then, vast experience has confirmed the value of this agent and of other corticosteroid injections for combating pain and inflammation when injected into the joint in patients with inflammatory arthropathies. However, its use in osteoarthritis has been fraught with controversies. Early studies in mice, rats, and rabbits suggested that multiple corticosteroid injections might alter cartilage protein

synthesis and consequently damage the cartilage.³ These deleterious effects curbed early enthusiasm for intra-articular corticosteroid therapy in osteoarthritis. Subsequent reviews found that, the knee joints of patients who received multiple intra-articular injections of steroids showed no significant evidence of destruction or accelerated deterioration.^{4,5} A detailed study of intra-articular steroid injections in monkeys also showed no appreciable joint damage, suggesting that primates' joints respond differently to those of rodents.⁶ Most authorities now consider intra-articular corticosteroid therapy for osteoarthritis of considerable value when used appropriately and judiciously.^{3,4,7-10}

The duration of response to intra articular steroid injection varies greatly. Corticosteroid injection into the knee for management of osteoarthritis have been shown to be statistically and clinically significant at reducing pain in the short term.^{2,11-14} However, the exact duration of pain relief varies. A systematic review of level 1 studies published in 2009, found that corticosteroid injections for management of pain related to osteoarthritis of the knee showed statistically and clinically significant pain relief at 1 week after injection but the benefit was not significantly better than placebo beyond 1 week.² A Cochrane Review update in 2015 supported this result by concluding that the clinical benefits of intra-articular steroid knee injections

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remained unclear 1 to 6 weeks after injection because of low quality of evidence.¹¹ No evidence of clinical benefit was found 6 months after patients received an injection. Studies on this topic are variable, resulting in a lack of high-quality, high powered, placebo-controlled prospective randomized trials. The 2015 Cochrane Review graded the quality of evidence as “low,” which was defined as having little confidence in the results due to the discordant methods and the small sample sizes used in the studies.¹¹ Data from published trials indicate, however, that there is significant variation in both the magnitude and duration of response to steroid injections. As an example, the magnitude of pain improvement measured using a visual analogue scale (VAS) on a 0-100 scale varied between a mean change of 16.2 and 35.7 mm, while the duration of pain relief varied between 1 and 8 weeks.^{1,15} Although the explanation for the wide range in response is unknown, we endeavored to offer information on the magnitude and duration of response to IASI in our environment in this research.

Material and Methods

Fifty-four patients visiting the Jos University Teaching Hospital, Jos Plateau state from October 2019 to October 2020 were included in the study by simple convenient sampling. Informed consent was obtained from the patients at the time of enrollment, and the study was approved by the ethics committee of Jos University Teaching Hospital. The inclusion criteria were patients who were 30 to 80 years of age, with a diagnosis of OA based on the American College of Rheumatology (ACR) clinical classification criteria¹⁶ with or without radiological support and who were not responding to conventional treatment of OA such as NSAIDs, acetaminophen and physiotherapy for more than 3 months. Exclusion criteria included known hypersensitivity to Depo Medrol 40mg and 2% Lidocaine.

Relevant history, physical examination (body mass index and detailed musculoskeletal examination) and knee radiograph was obtained from the subjects and data entered. Prior to administration of intra-articular steroid injection (IASI) visual analogue scale (VAS) score,¹⁶ Western Ontario, and McMaster Universities Osteoarthritis Index (WOMAC) score¹⁷ were measured for each subject. Under proper aseptic conditions, 40 mg methylprednisolone acetate mixed with 2 % lignocaine was injected into the symptomatic knee, and patients were advised to observe 24-hour bed rest at home before returning to their pre-IASI activity and were not placed on any form of physiotherapy, acetaminophen and

NSAIDs. VAS and WOMAC were re-calculated at 2 weeks, 4 weeks, and 3 months post IASI administration. Subjects who had improvement in WOMAC score of 50 % or more compared to the baseline before IASI were considered responders, and those with less than 50% improvement from their initial WOMAC score were regarded as non-responders. Similarly, 50% or more reduction in VAS score was categorized as responders, and less than 50 % reduction was categorized as non-responders.

The data was entered into excel sheet which was subsequently exported into Statistical Package for the Social Sciences version 23.0. for analysis. Univariate analysis of the socio-demographic characteristics of the patient were done, and the basic descriptive statistics were presented in frequency and percentages. Quantitative variables were described using mean and standard deviation while qualitative variables were described using frequencies, proportions, charts, and tables. Proportions were compared by calculating χ^2 with Yates correction or by Fisher exact test. The WOMAC score was transformed to a dichotomous variable of responders and non-responders which include the partial responders, VAS response was already in the dichotomous variable state.

Results

A total of fifty-two patients who met the inclusion criteria were recruited for the study; four patients were lost to follow up, giving an attrition rate of 15.4%. About 95% of the patients were above the age of 40 years old with a mean age of 53.5 years. There was a predominance of females with a male to female ratio of 3:7. Table 1

WOMAC and VAS responses were 78.4 percent and 100 percent for the first two weeks and then gradually decreased to 47.9 percent and 56.3 percent for the second and third weeks, respectively. (Table 2)

Following IASI treatment for three months using WOMAC score, age was found to be associated with outcome. As age increases, the percentage of patients with a poor outcome response increases from zero percent at 40 years to 85.7 percent at 79 years with a statistically significant P value of .003. At three months, 73.3 percent of non-alcoholics had a poor response, but 83.3 percent of alcoholics had a good response. This relationship was statistically significant, with a P value of 0.001. There is statistically significant correlation with sex, with a P value of 0.016, 64.7% of females had a poor response while 78.6 percent of males had good response (Table 3).

Table: 1 Socio-demographic Characteristics

Variable	Frequency (%)
Age (Years)	
<40	2(4.2)
40-59	32(66.7)
60-79	14(29.2)
Mean ± SD	53.5±10.1
Sex	
Male	14(29.2)
Female	34(70.8)
Education	
Primary	17(35.4)
Secondary	21(43.8)
Tertiary	10(20.4)
Occupation	
Business	4(8.3)
Civil servant	15(31.3)
Housewife	15(31.3)
Lecturing	2(4.2)
Trading	12(25.0)
BMI	
Normal	6(12.5)
Overweight	16(33.3)
Obese	24(54.2)
Systemic Hypertension	24(50.0)
Hepatitis B positive	4(8.3)
Hepatitis C positive	13(27.1)
History of alcohol ingestion	18(37.5)
History of smoking	6(12.5)

Discussion

Osteoarthritis is a degenerative joint disorder, which is a public health burden since it is one of the most common joint diseases all over the world and a common presentation in most outpatient clinic. It is strongly associated with age, and extremely common in older people. The mean age of subjects in the present study is in keeping with well-known age-related prevalence of osteoarthritis peaking at about age 60 years.^{1,18} The male to female ratio in the present study is similar to the female preponderance recognized globally.¹

The results of the present study have been replicated in other studies, which have demonstrated that corticosteroid injections into the knee for the therapy of osteoarthritis are statistically and clinically significant in lowering pain in the short term.^{2,11-14} However, the exact duration of pain relief remains a controversy. A systematic review published in 2009 of level 1 studies found that corticosteroid injections for management of pain related to osteoarthritis of knee showed statistically and clinically significant pain relief at 1 week after

Table:2 The Response to Intra-Articular Steroid Injections

Response	Total	Percent
WOMAC 2 weeks		
Non-responders	10	21.6
Responders	38	78.4
6 weeks		
Non-responders	11	22.9
Responders	37	77.1
3 months		
Non-responders	25	52.1
Responders	23	47.9
VAS 2weeks		
Non-responders	0	0.0
Responders	48	100.0
6 weeks		
Non-responders	9	18.8
Responders	39	81.3
3 months		
Non-responders	21	43.8
Responders	20	56.3

injection.² There seemed to be some benefit in the short-term after 1 week, but the data was not statistically significant compared with placebo. A Cochrane Review update in 2015 supported this result by concluding that the clinical benefits of intra-articular steroid knee injections remained unclear after 1 to 6 weeks injection because of low quality of evidence.¹¹ No evidence of clinical benefit was found 6 months after patients received an injection. Studies on this topic are variable, and a lack of high-quality, high powered, placebo-controlled prospective randomized trials exists; the 2015 Cochrane Review graded the quality of evidence as "low," which was defined as having little confidence in the results due to the discordant studies based on small studies.¹¹ Individual patient variables and severity of arthritis may affect the efficacy of injections. Recently, a group of 100 patients who got a steroid injection for symptomatic knee osteoarthritis reported better WOMAC and Visual Numeric Scale scores at 3, 6, 12, and 24 weeks following injection, except for the Visual Numeric Scale score at 24 weeks, as compared to baseline values.¹² The duration of response to intra articular steroid injection varies greatly. The present study shows that intra articular steroid injection is effective in the management of patient with osteoarthritis of the knee joint, this is also in keeping with several studies which supports its use.^{4,7,10} This study showed that IASI was effective in reducing pain in the first two weeks. Most patients had improvement in their pain scores on both scales in the first two weeks post

Table 3 Association between background characteristics and Outcome at the end of study Based on WOMAC

Characteristics	Outcome		Total	χ ²	P-value
	Poor	Good			
Age					0.003F*
<40	0(0.0)	2(100.0)	2(4.2)		
40-59	13(40.6)	19(59.4)	32(66.6)		
60-79	12(85.7)	2(14.3)	14(29.2)		
Sex					0.016Y*
Male	3(21.4)	11(78.6)	14(29.2)		
Female	22(64.7)	12(35.3)	34(70.8)		
Education					0.845F
Primary	9(52.9)	8(47.1)	17(35.4)		
Secondary	12(57.1)	9(42.9)	21(43.8)		
Tertiary	4(40.0)	6(60.0)	10(20.4)		
Occupation					0.060F
Business	0(0.0)	4(100.0)	4(8.3)		
Civil servant	7(46.7)	8(53.3)	15(31.3)		
Housewife	10(66.7)	5(33.3)	15(31.3)		
Lecturing	0(0.0)	2(100.0)	2(4.2)		
Trading	8(66.7)	4(33.3)	12(25.0)		
BMI					0.362
Normal	2(33.3)	4(66.7)	6(12.5)		
Overweight	7(43.8)	9(56.3)	16(33.3)		
Obese	16(61.5)	10(38.5)	26(54.2)		
Systemic Hypertension					>0.999Y
Yes	13(54.2)	11(45.8)	24(50.0)		
No	12(50.0)	12(50.0)	24(50.0)		
Hepatitis B					>0.999Y
Yes	2(50.0)	2(50.0)	4(8.3)		
No	23(52.3)	21(47.7)	44(91.7)		
Hepatitis C					0.261Y
Yes	9(69.2)	4(30.8)	13(27.1)		
No	16(45.7)	19(54.3)	35(72.9)		
Alcohol					<0.001Y*
Yes	3(16.7)	15(83.3)	18(37.5)		
No	22(73.3)	8(26.7)	30(62.5)		
Smoking					0.156Y
Yes	1(16.7)	5(83.3)	6(12.5)		
No	24(57.1)	18(42.9)	42(87.5)		

*Statistically significant, Y Yates correction and F Fischer exact test

IASI, and at six weeks post injection using WOMAC was 77.1% and VAS 81.3%, and about half the number of participants still maintained good pain control at 3 months, with a WOMAC 47.9% and a VAS score of 56.3%. More patients in this study had sustained pain control at 3 months compared to subjects in the Pakistan study, where about 16.1% of the subject had about 50%

Using VAS score only age and alcoholic status had a significant association with outcome. (Table 4)

Table 4 Association between Demographic and Outcome at the end of study Based on VAS

Characteristics	Outcome		Total	χ ²	P-value
	Poor	Good			
Age					0.029F*
<40	0(0.0)	2(100.0)	2(4.2)		
40-59	11(34.4)	21(65.6)	32(66.6)		
60-79	10(71.4)	4(28.6)	14(29.2)		
Sex					0.093Y
Male	3(21.4)	11(78.6)	14(29.2)		
Female	18(52.9)	16(47.1)	34(70.8)		
Education					0.567F
Primary	9(52.9)	8(47.1)	17(35.4)		
Secondary	9(42.9)	12(57.1)	21(43.8)		
Tertiary	3(30.0)	7(70.0)	10(20.4)		
Occupation					0.097F
Business	0(0.0)	4(100.0)	4(8.3)		
Civil servant	6(40.0)	9(60.0)	15(31.3)		
Housewife	10(66.7)	5(33.3)	15(31.3)		
Lecturing	0(0.0)	2(100.0)	2(4.2)		
Trading	5(41.7)	7(58.3)	12(25.0)		
BMI					0.921
Normal	2(33.3)	4(66.7)	6(12.5)		
Overweight	7(43.8)	9(56.3)	16(33.3)		
Obese	12(46.2)	14(53.8)	26(54.2)		
Systemic Hypertension					>0.999Y
Yes	10(41.7)	14(58.3)	24(50.0)		
No	11(45.8)	13(54.2)	24(50.0)		
Hepatitis B					>0.999Y
Yes	2(50.0)	2(50.0)	4(8.3)		
No	19(52.3)	25(56.8)	44(91.7)		
Hepatitis C				0.738	0.390Y
Yes	7(53.8)	6(46.2)	13(27.1)		
No	14(40.0)	21(60.0)	35(72.9)		
Alcohol					0.009Y*
Yes	3(16.7)	15(83.3)	18(37.5)		
No	18(60.0)	12(40.0)	30(62.5)		
Smoking					0.322Y
Yes	1(16.7)	5(83.3)	6(12.5)		
No	20(47.6)	22(52.4)	42(87.5)		

*Statistically significant, Y Yates correction and F Fischer exact test

reduction in pain up to the 3 months using WOMAC and about 38.7% had more than 50% reduction in pain using VAS.¹ It is clearly obvious, there is a large variation in both extent and duration of response to steroid

injections, this study looked at the socio-demographic profile to determine if there is any relationship with response to IASI at 3 months. It found an association with 50% reduction in pain at 3 months using both the WOMAC and VAS score. The variables of socio-demographic profile which showed relationship are age, sex, and alcohol. The association with age and status of alcohol consumption was significant for both WOMAC and VAS scores while sex is only significant with WOMAC score. The relationship with age is inverse as the good response decreased with increasing age, this is like the finding in the Pakistan study which showed a negative correlation with age, indicating that a patient presenting with a greater age will show lesser response to IASI according to VAS.¹ In the same vein, we found out that alcoholics responded better than non-alcoholics using both WOMAC and VAS score, the reason for this is not known, but it could be because more of the alcoholics are of the younger age group. However, after running a logistic regression, none of the variables identified could predict the response at 3 months. Most studies including large systemic reviews have not found factors that could predict response at 3 months.^{4,14}

Considering the foregoing, intra-articular steroid injection, as recommended by the American College of Rheumatology, is a valuable tool in the treatment of osteoarthritis of the knee in patients who have failed to respond to non-steroidal anti-inflammatory drugs and are not candidates for total knee replacement.

There are certain limitations to our study, it's a single centre experience and cannot represent the whole population. We are unable to compare blind vs. ultrasound-guided injection technique in Intra-articular steroid injection.

Conclusion.

We conclude that intra-articular steroid injections provide sustained response in patients with osteoarthritis of the knee who have failed analgesics and are not candidates for total knee replacement for up to three months and the response decreases with advancing age.

References

1. Fatimah N, Salim B, Raja EU, Nasim A. Predictors of response to intra-articular steroid injections in patients with osteoarthritis of the knee joint. *Clin Rheumatol.* 2016;35(10):2541-2547.
2. Hepper CT, Halvorson JJ, Duncan ST, M. Gregory AJ, Dunn WR, Spindler KP. The Efficacy and Duration of Intra-articular Corticosteroid Injection for Knee Osteoarthritis: A Systematic Review of Level I Studies. *J Am Acad Orthop Surg.* 2009;17(10):638-646.
3. Neustadt DH. Intra-articular injections for osteoarthritis of the knee. *Cleveland Clinic Journal of medicine.* 2006;73(10):897.
4. Balch H, Gibson J, El-Ghobarey A, Bain L, Lynch M. Repeated corticosteroid injections into knee joints. *Rheumatology.* 1977;16(3):137-140.
5. Keagy RD, Keim HA. Intra-articular steroid therapy: repeated use in patients with chronic arthritis. *Am J Med Sci.* 1967;253(1): 45-51.
6. Gibson T, Burry HC, Poswillo D, Glass J. Effect of intra-articular corticosteroid injections on primate cartilage. *Ann Rheum Dis.* 1977;36(1):74-79.
7. Raynauld JP, Buckland-Wright C, Ward R, et al. Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2003;48(2): 370-377.
8. Mankin HJ, Conger KA. The acute effects of intra-articular hydrocortisone on articular cartilage in rabbits. *J Bone Joint Surg Am.* 1966;48(7):1383-1388.
9. Zuckner J, Machek O, Caciolo C, Ahern AM, Ramsey R. Intra-articular injections of hydrocortisone, prednisolone, and their tertiary-butylacetate derivatives in patients with rheumatoid arthritis and osteoarthritis. *J Chronic Dis.* 1958;8(5):637-644.
10. Letters F. Hydrocortisone and osteoarthritis. *JAMA.* 1959;170:1451.
11. Juni P, Hari R, Rutjes AW, et al. Intra-articular corticosteroid for knee osteoarthritis. *Cochrane Database Syst Rev.* 2015(10):Cd005328.
12. Matzkin EG, Curry EJ, Kong Q, Rogers MJ, Henry M, Smith EL. Efficacy and Treatment Response of Intra-articular Corticosteroid Injections in Patients With Symptomatic Knee Osteoarthritis. *J Am Acad Orthop Surg.* 2017;25(10):703-714.
13. Maricar N, Parkes MJ, Callaghan MJ, et al. Structural predictors of response to intra-articular steroid injection in symptomatic knee osteoarthritis. *Arthritis Res Ther.* 2017;19(1):88.
14. Maricar N, Callaghan MJ, Felson DT, O'Neill TW. Predictors of response to intra-articular steroid injections in knee osteoarthritis--a systematic review. *Rheumatology (Oxford).* 2013;52(6):1022-1032.
15. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken).* 2012;64(4):465-474.
16. Crichton N. Visual analogue scale (VAS). *J Clin Nurs.* 2001;10(5):706-706.
17. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol.* 1988;(12):1833-40.
18. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis.* 2014;73(7):1323.