Research Article

Efficacy and Treatment Response of Intra-articular Corticosteroid Injections in Patients With Symptomatic Knee Osteoarthritis

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Abstract

Introduction: Intra-articular corticosteroid injections are often used for short-term pain relief in patients with knee osteoarthritis (OA). This study investigates the efficacy of intra-articular corticosteroid injections in patients with symptomatic knee OA and factors that affect treatment response.

Methods: This prospective, multicentered cohort study had 100 participants with radiographic evidence of knee OA enrolled. Participants received one corticosteroid injection into the affected knee and were evaluated before the injection (baseline) and at 3 weeks, 6 weeks, 3 months, and 6 months after the injection.

Results: Participants' Visual Numeric Scale and Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores improved at all time points except for the Visual Numeric Scale score at 6 months, compared with baseline scores ($P < 0.001$). Participants with Kellgren-Lawrence grade 1 or 2 OA saw clinical improvement in the WOMAC scores at all time points, compared with the baseline score ($P < 0.01$). Compared with all other subgroups, obese patients with Kellgren-Lawrence grade 3 or 4 OA had significantly worse WOMAC scores at baseline, 6 weeks, and 3 months ($P < 0.01$ and $P < 0.01$, respectively).

Discussion: Our findings validate previously established guidelines for nonsurgical management of knee OA and suggest that intra-articular corticosteroid injections may be an acceptable short-term management option in patients unwilling or unable to undergo surgical treatment. Obesity and OA severity affect the efficacy of intra-articular corticosteroid injections.

Conclusion: Patients receiving intra-articular corticosteroid injections had improved pain and function. Clinicians should expect less improvement in patients with obesity and/or advanced arthritis. Clinical benefits of intra-articular injections in these patients are less predictable.

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Osteoarthritis (OA) is a common chronic disease, affecting nearly 52.5 million people or 22.7% of the population in the United States.[1] It is one of the most common causes of pain and disability among the elderly.[2] Knee OA is the most prevalent form of OA, with symptoms occurring in 13% of women and 10% of men aged >60 years.[3,4]

Nonsurgical treatments include activity modification, bracing, physical therapy, intra-articular injections, and oral anti-inflammatory medications. Intra-articular injections can include hyaluronic acid, platelet-rich plasma, stem cells, and corticosteroids. The American Academy of Orthopaedic Surgeons (AAOS) 2013 clinical practice guideline strongly recommended against the use of hyaluronic acid injections and did not recommend for or against growth factor or platelet-rich plasma injections in patients with symptomatic knee OA.[5]

Intra-articular corticosteroid injections have been widely used for short-term pain relief since the 1950s.[6] Their use is indicated by the American College of Rheumatology for short-term pain relief that interferes with daily life.[6-10] Few side effects have been reported.[7-10] However, the AAOS found only four placebo comparison studies evaluating pain relief beyond 4 weeks that met the rigorous study selection criteria of the AAOS 2013 clinical practice guideline.[5,11-14] Thus, evidence regarding the use of intra-articular corticosteroids for the management of symptomatic knee OA was determined to be inconclusive.[5] Furthermore, no conclusions could be made about the duration of pain relief or functional improvement. Prior studies have found that the beneficial effects of intra-articular corticosteroid injections can last anywhere from 2 to 24 weeks.[12,15] The purpose of this study was to investigate the efficacy of intra-articular corticosteroid injections in the management of symptomatic knee OA and to identify factors that affect treatment response.

Methods

After the study was approved by our Institutional Review Boards, study participants were prospectively enrolled across two academic centers from February 2013 through December 2014. Participants were aged ≥40 years, had radiographic evidence of knee OA, and had previously undergone unsuccessful treatment with anti-inflammatory medication and/or acetaminophen for pain relief. Exclusion criteria included previous intra-articular injection into the affected knee within 6 months, previous total knee arthroplasty or unicompartmental arthroplasty of the affected knee, narcotic pain medication use, pregnancy, systemic disease diagnosis (eg, rheumatoid arthritis, systemic lupus erythematosus), metabolic disease diagnosis (eg, Paget disease), or pain disorder (eg, fibromyalgia, complex regional pain syndrome). Patients who declined to participate received equivalent levels of care.

Participants were recruited at the time of the intra-articular corticosteroid injection. At the baseline visit, participants received one intra-articular injection of 1 mL of triamcinolone 10 mg and 4 mL of 1% lidocaine without epinephrine into the affected knee through an anterolateral portal with the knee bent in 90° of flexion. Two board-certified and fellowship-trained orthopaedic surgeons (E.G.M. and E.L.S.) performed all injections. Participants who received bilateral intra-articular injections (n = 11) were asked to complete a separate survey for each knee. Surveys were administered before the injection (baseline) and again at 3 weeks, 6 weeks, 3 months, and 6 months after the injection. The following demographic data were collected at baseline: age at time of consent, height, weight, smoking status, symptom duration, gout presence, and Kellgren-Lawrence OA grade ≥1 based on radiographs obtained within 1 year of study initiation. The Kellgren-Lawrence OA grade was radiographically determined by two board-certified orthopaedic surgeons (E.G.M. and E.L.S.).[16] Body mass index (BMI) was calculated as the weight in pounds divided by the height in inches squared and multiplied by 703 $(kg/m^2)/(lb/in^2)$.[17]

Standardized patient-reported questionnaires were administered at each time point and included the Western Ontario and McMaster Universities Arthritis Index (WOMAC) score, the Medical Outcomes Study 36-Item Short Form (SF-36), and the Visual Numeric Scale (VNS) for pain.[18,19] Knee pain, function, and stiffness were assessed using the 24-item WOMAC questionnaire. General health status was assessed with the SF-36 questionnaire. Study data were collected and managed using REDCap (Research Electronic Data Capture),[20] which is a secure, web-based application that is designed to support data capture for research studies, providing an intuitive interface for validated data entry, audit trails for tracking data manipulation and export procedures, automated export procedures for seamless data downloads to common statistical packages, and procedures for importing data from external sources. Patients had the option to complete surveys by phone, mail, or REDCap. Study participants independently submitted

Table 1

Patient Demographics

| Variable	Total No. of Patients	Mean (SD) or Number	Minimum	Maximum
Age (yr)	100	61.2 (8.5)	43.7	80.4
Height (in)	94	66.2 (3.9)	57.0	75.0
Weight (lb)	94	194.7 (48.1)	112.0	359.0
Body mass index	94	31.2 (7.0)	20.6	51.5
<30 kg/m^2		49 (52.1%)	NA	NA
≥30 kg/m^2		45 (47.9%)	NA	NA
Smoking status	100			
No		91 (91.0%)	NA	NA
Yes		9 (9.0%)	NA	NA
Drug abuse status	100			
No		100 (100%)	NA	NA
Yes		0 (0%)	NA	NA
Kellgren-Lawrence osteoarthritis grade	96			
1		28 (29.2%)	NA	NA
2		28 (29.2%)	NA	NA
3		29 (30.2%)	NA	NA
4		11 (11.5%)	NA	NA
Symptom duration (yr)	81	4.2 (7.8)	0.0	47.0
Baseline WOMAC scores				
Pain	97	8.2 (3.8)	0.0	16.0
Stiffness	98	3.7 (1.6)	0.0	7.0
Physical function	98	24.8 (12.8)	0.0	63.0
Total	98	36.7 (17.3)	1.0	85.0
Baseline Visual Numeric Scale score	96	5.5 (2.1)	1.4	10.0
Baseline SF-36 domain scores				
Physical functioning	100	50.0 (25.3)	0.0	100.0
Physical role functioning	100	61.3 (40.1)	0.0	100.0
Bodily pain	98	48.6 (22.3)	0.0	100.0
General health perceptions	100	69.9 (21.6)	0.0	100.0
Vitality	98	57.0 (20.0)	15.0	100.0
Social role functioning	98	73.3 (25.6)	12.5	100.0
Emotional role functioning	97	25.8 (38.6)	0.0	100.0
Mental health	98	77.7 (15.3)	28.0	100.0

NA = not applicable, WOMAC = Western Ontario and McMaster Universities Arthritis Index

surveys distributed via REDCap, whereas study personnel entered data into REDCap from surveys returned by mail or completed over the phone.

Informed consent was obtained from 144 English-speaking participants. The attrition rate reflected 31 patients (21.5%), including 2 participants who underwent knee surgery (knee arthroscopy or total knee ar-throplasty) before the completion of the study, 25 participants who were lost to follow-up, and 4 participants who did not meet the study criteria because of a systemic disease diagnosis (ie, rheumatoid arthritis). Thirteen patients received bilateral injections and were removed from the study post hoc. Therefore, 100 patients were included in the study for analysis.

The primary outcome variable was overall WOMAC score, with a range of zero to 85. Higher scores represent higher levels of pain, disability, and/or stiffness. The 3-month measure was chosen as the primary time point of interest for power analysis purposes. Secondary outcomes were the SF-36 and VNS scores. Sample size calculations were based on a paired

Figure 1
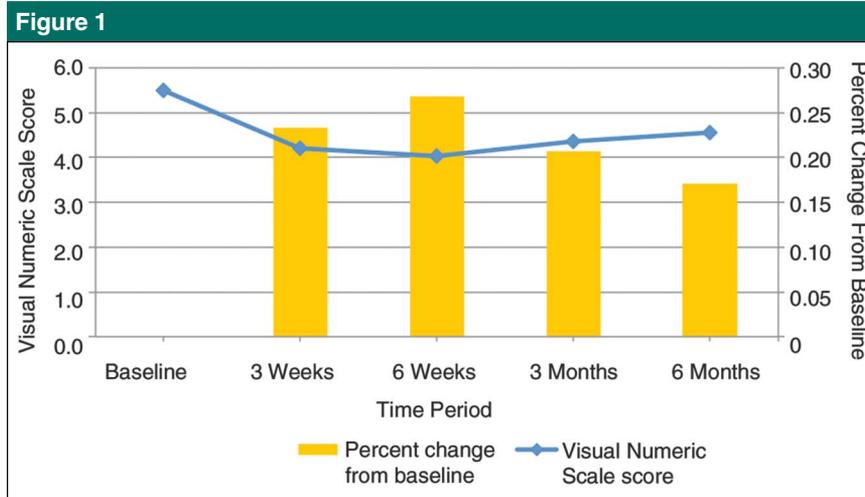
Line and bar graphs showing Visual Numeric Scale (VNS) scores for pain in study participants over time. Mean VNS scores are represented by the blue line graph; the percentage change from baseline is represented by the yellow bar graph. A VNS score of zero indicates no pain; a score of 10 indicates severe pain.

Student *t*-test analysis of change in WOMAC scores from baseline to 3 months. We determined that 82 patients needed to be enrolled, assuming 80% power and two-sided α equal to 0.05. Thus, our enrollment target was a minimum of 100 patients to account for a 15% attrition rate.

Overall summary statistics of patient characteristics and baseline patient-reported outcome measures were calculated in terms of means and standard deviations for continuous variables and frequencies and percentages for discrete variables. Multiple generalized estimating equation[9] models were used to examine the longitudinal trend of mean patient-reported outcome measures (WOMAC, including subscales and total score; VNS for pain; and SF-36 domains) from baseline to 6 months postintervention, while controlling for missing data at follow-ups. A final generalized estimating equation model was built to examine the longitudinal change of total WOMAC over time while controlling for the effect of obesity (defined as BMI ≥30 kg/m²) and OA grade, as well as the

interaction of those factors across time. Reported *P* values from all pairwise comparisons were adjusted with the Bonferroni technique. Statistical significance was defined as $P < 0.05$.

In addition to statistical significance, the minimal clinically important difference (MCID) was assessed for the WOMAC and VNS scores. For the VNS, an MCID of 27.9% reduction (raw change divided by baseline score and multiplied by 100) or a decrease of 1.7 points was used for this study.[21] Based on prior studies, the WOMAC cutoff we used for the MCID was 21.7%.[11,22,23] All analyses were performed using SPSS version 22.0 (IBM).

Results

In total, 100 patients were included in this study. The mean age was 61.2 years (SD, 8.5 years; range, 43.7 to 80.4 years). Patient characteristics, including demographic information and baseline patient-reported outcome measures, are shown in Table 1. Overall, study participants reported

a statistically significant reduction in pain according to the VNS at all follow-up time points relative to the baseline score except at 6 months. Pain was reduced by 23.9%, 26.9%, 20.7%, and 17.1% at 3 weeks, 6 weeks, 3 months, and 6 months, respectively ($P < 0.05$, except at 6 months, for which $P = 0.114$) (Figure 1). However, pain reduction did not reach clinical significance at any of these time points (MCID, 27.9%).

WOMAC subscale scores for pain, stiffness, and physical function had clinically and statistically significant improvements over time with respect to the patients' mean baseline scores ($P < 0.05$ for all comparisons) (Table 2). The total WOMAC scores at 3 weeks, 6 weeks, 3 months, and 6 months improved 34.0%, 37.6%, 34.4%, and 40.2%, respectively, relative to the baseline score, all of which were statistically and clinically significant ($P < 0.001$; MCID, 21.7%) (Figure 2). Reported changes in the eight domains of the SF-36 are reported in Table 3. Physical health domains had considerable improvements from baseline. Significant improvements from the baseline were seen at 3 weeks and 6 weeks for physical functioning ($P = 0.048$ and $P = 0.002$, respectively), at all time points (3 weeks, 6 weeks, 3 months, and 6 months) for physical role functioning ($P = 0.025$, $P = 0.013$, $P = 0.043$, $P = 0.014$, respectively), and at all time points for bodily pain ($P = 0.005$, $P = 0.001$, $P = 0.008$, $P = 0.001$, respectively). However, no significant improvements were found in any of the mental health domains at any time point ($P > 0.05$).

Main effects of patient age, smoking status, and history of drug use were not significantly associated with the total WOMAC score ($P > 0.05$). After adjustment for BMI and OA grade, the overall WOMAC score decreased in terms of both statistical significance and clinical relevance at each time point with respect to the

Table 2

Changes in Western Ontario and McMaster Universities Arthritis Index and Visual Numeric Scale Scores Over Time

Outcome Measure	Time	Mean (SD)	95% Confidence Interval	P Value[a]	Change From Baseline	Percent Change From Baseline[b]
Visual Numeric Scale	Baseline	5.5 (2.1)	5.1-5.9			
	3 weeks	4.2 (2.4)	3.7-4.8	**0.002**	−1.3	23.9%
	6 weeks	4.0 (2.4)	3.5-4.6	**<0.001**	−1.5	26.9%
	3 months	4.4 (2.4)	3.8-4.9	**0.013**	−1.2	20.7%
	6 months	4.6 (2.5)	4.0-5.2	0.114	−1.0	17.1%
WOMAC pain	Baseline	8.2 (3.8)	7.4-8.9			
	3 weeks	5.1 (3.7)	4.3-5.9	**<0.001**	−3.1	37.9%
	6 weeks	4.6 (3.6)	3.7-5.4	**<0.001**	−3.6	44.3%
	3 months	5.0 (3.4)	4.2-5.8	**<0.001**	−3.2	39.1%
	6 months	4.4 (3.7)	3.4-5.3	**<0.001**	−3.9	46.9%
WOMAC stiffness	Baseline	3.7 (1.6)	3.4-4.0			
	3 weeks	2.7 (1.7)	2.3-3.1	**<0.001**	−1.1	27.4%
	6 weeks	2.4 (1.8)	2.0-2.8	**<0.001**	−1.3	35.1%
	3 months	2.9 (1.9)	2.5-3.3	**0.001**	−0.9	22.2%
	6 months	2.5 (1.8)	2.0-2.9	**<0.001**	−1.2	33.5%
WOMAC physical function	Baseline	24.8 (12.8)	22.1-27.2			
	3 weeks	16.4 (12.3)	13.7-19.1	**<0.001**	−8.4	33.9%
	6 weeks	15.9 (12.7)	13.0-18.9	**<0.001**	−8.9	35.9%
	3 months	16.1 (12.1)	13.3-19.0	**<0.001**	−8.7	35.0%
	6 months	15.1 (12.7)	12.0-18.3	**<0.001**	−9.7	39.1%
WOMAC total	Baseline	36.7 (17.3)	32.9-39.8			
	3 weeks	24.2 (17.0)	20.4-28.0	**<0.001**	−12.4	34.0%
	6 weeks	22.9 (17.6)	18.8-27.0	**<0.001**	−13.8	37.9%
	3 months	24.0 (16.8)	20.2-27.9	**<0.001**	−12.6	34.4%
	6 months	21.9 (17.6)	17.6-26.3	**<0.001**	−14.7	40.2%

WOMAC = Western Ontario and McMaster Universities Arthritis Index
[a] Bold type indicates statistical significance at $P < 0.05$.
[b] Minimal clinically important difference is defined as 27.9% reduction (raw change divided by baseline score and multiplied by 100) for VNS and 21.7% reduction for WOMAC. None of the values in this column meets these criteria.

baseline WOMAC score ($P < 0.001$). Patients with BMI ≥30 kg/m² experienced clinically relevant WOMAC score improvements of 35%, 33%, 32%, and 40%, respectively, at 3 weeks, 6 weeks, 3 months, and 6 months. Patients with BMI <30 kg/m² had similar clinically relevant relative score improvements of 37%, 44%, 40%, and 32%, respectively, at 3 weeks, 6 weeks, 3 months, and 6 months (Table 4). Both the patients with worse OA (ie, Kellgren-Lawrence grade 3 or 4) and the patients with milder OA (ie, Kellgren-Lawrence grade 1 or 2) experienced clinically relevant WOMAC score improvements (35%, 30%, 23%, and 26% versus 36%, 46%, 48%, and 48% at

3 weeks, 6 weeks, 3 months, and 6 months, respectively) (Table 4). When BMI (<30 kg/m² versus ≥30 kg/m²) and OA grade (grade 1 or 2 OA versus grade 3 or 4 OA) were combined, all groups had clinically relevant WOMAC score improvement at all time points, except obese patients with severe OA grade (BMI ≥30 kg/m² with Kellgren-Lawrence grade 3 or 4) at the 3-month follow-up point (15%).

Figures 3 and 4 demonstrate that overall WOMAC scores improved over time for most time points regardless of BMI and OA grade. However, obese participants (BMI ≥30 kg/m²) had worse WOMAC scores on average at every follow-up time point, compared with nonobese

participants (BMI <30 kg/m²), but this difference was statistically significant only at baseline, 6 weeks, and 3 months and not at 6 months ($P = 0.003$, 0.010, 0.003, and 0.009, respectively). Baseline WOMAC scores also significantly differed between the obese and nonobese participants ($P < 0.0001$). Participants with grade 3 or 4 OA had no significant difference at any time point compared with participants with grade 1 or 2 OA except at 3 months, where WOMAC scores were significantly worse for the group with grade 3 or 4 OA ($P = 0.004$). Using the statistical model that we generated, we found that obese patients with more severe OA had the worst total WOMAC

Figure 2
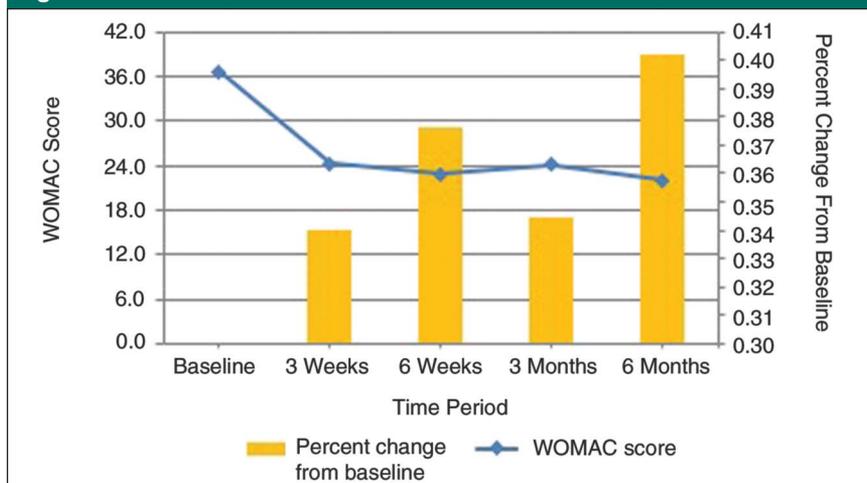
Line and bar graphs showing Western Ontario and McMaster Universities Arthritis Index (WOMAC) total scores calculated as the sum of the WOMAC subscores for pain, stiffness, and physical function in study participants over time. Mean WOMAC scores are represented by the blue line graph; the percentage change from baseline is represented by the yellow bar graph.

Discussion

Intra-articular corticosteroid injections are a common nonsurgical management option for patients with osteoarthritic knees. Corticosteroid intra-articular injections were recommended for short-term pain relief in patients with OA in a 2008 AAOS clinical practice guideline on the treatment of OA of the knee.[24] However, this recommendation was based on only four articles in the literature with adequate power and study design.[11-14] This AAOS clinical practice guideline was updated in 2013 and noted that the published data on the use of intra-articular corticosteroid injections for the treatment of knee OA were "inconclusive" and that the treatment was no longer "recommended," as had been previously stated in 2008.[5]

scores at baseline, 6 weeks, and 3 months, compared with patients in other combined WOMAC and BMI categories (Table 5 and Figure 5).

Our results show that intra-articular corticosteroid injections significantly improve knee pain, stiffness, and function in patients with symptomatic knee OA, regardless of patient BMI or Kellgren-Lawrence OA grade. Compared with baseline measures, VNS pain reduction was statistically significant at all follow-up points except at 6 months postinjection and did not reach the cutoff of 27.9% improvement to be considered clinically relevant. Patients experienced pain reduction of 23.9%, 26.9%, 20.7%, and 17.1% at the 3-week, 6-week, 3-month, and 6-month follow-up time points, respectively. Interestingly, these patients had both statistically significant and clinically relevant score improvement in all WOMAC categories ($P < 0.001$), including WOMAC pain. A comparison of total WOMAC scores between baseline and all follow-up time points showed improvement at 3 weeks, 6 weeks, 3 months, and 6 months of 34.0%, 37.6%, 34.4%, and 40.2%, respectively, which reached the cutoff for clinical

relevance of 21.7%. Although we found clinically relevant and statistically significant improvements in WOMAC scores after intra-articular corticosteroid injections in both obese and normal BMI patients, obese patients had significantly poorer WOMAC total scores on average at all time points compared with nonobese patients, and this difference was statistically significant at baseline, 6 weeks, and 3 months ($P = 0.003$, $P = 0.010$, $P = 0.009$, respectively). Also, both the patients with high Kellgren-Lawrence grades and the patients with low Kellgren-Lawrence grades experienced clinically relevant improvement in WOMAC total scores; however, the WOMAC total scores remained worse at each time point for patients with higher-grade OA (Kellgren-Lawrence grades 3 or 4) compared with those with lower-grade OA (Kellgren-Lawrence grades 1 or 2), and this difference was significant at 3 months postinjection ($P = 0.004$).

Our results validate previously established guidelines for nonsurgical management of knee OA. Furthermore, the results suggest that intra-articular corticosteroid injections are an acceptable short-term treatment option for patients unwilling or unable to proceed with surgical intervention.[7,11,13,14,25] The results revealed that certain patient factors, such as obesity and OA severity, affect the efficacy of intra-articular corticosteroid injections. Understanding these factors can help guide discussions about expectations with patients regarding nonsurgical pain management. Although obese patients experienced improved pain relief and function, their overall scores were higher than those of nonobese patients at all assessment intervals. These findings are consistent with the AAOS guidelines, which recommend weight loss to reduce the risk of the development of

Table 3

Medical Outcomes Study 36-Item Short Form Score Changes Over the Study Period for the Study Population

SF-36 Domain	Time	Mean (SD)	P Value[a]	Change From Baseline[b]	Percent Change From Baseline
Physical functioning	Baseline	50.0 (25.3)	N/A	N/A	N/A
	3 weeks	60.8 (25.5)	**0.048**	−10.872*	21.8%
	6 weeks	64.2 (23.9)	**0.002**	−14.225*	28.5%
	3 months	60.5 (25.1)	0.070	−10.502	21.0%
	6 months	62.0 (27.8)	0.052	−12.081	24.2%
Physical role functioning	Baseline	61.3 (40.1)	N/A	N/A	N/A
	3 weeks	42.2 (42.6)	**0.025**	19.069*	31.1%
	6 weeks	40.9 (40.7)	**0.013**	20.372*	33.3%
	3 months	43.3 (40.8)	**0.043**	17.917*	29.3%
	6 months	39.8 (42.5)	**0.014**	21.477*	35.1%
Bodily pain	Baseline	48.6 (22.3)	N/A	N/A	N/A
	3 weeks	60.7 (22.4)	**0.005**	−12.034*	24.7%
	6 weeks	63.1 (22.7)	**0.001**	−14.452*	29.7%
	3 months	60.0 (21.2)	**0.008**	−11.344*	23.3%
	6 months	63.9 (24.8)	**0.001**	−15.262*	31.4%
General health perceptions	Baseline	69.9 (21.6)	N/A	N/A	N/A
	3 weeks	71.2 (17.9)	>0.999	−1.248	1.8%
	6 weeks	70.2 (19.1)	>0.999	−0.278	0.4%
	3 months	70.9 (18.3)	>0.999	−1.008	1.4%
	6 months	71.4 (21.6)	>0.999	−1.439	2.1%
Vitality	Baseline	57.0 (20.0)	N/A	N/A	N/A
	3 weeks	60.6 (18.6)	>0.999	−3.543	6.2%
	6 weeks	60.5 (20.4)	>0.999	−3.500	6.1%
	3 months	61.8 (19.1)	>0.999	−4.759	8.3%
	6 months	63.2 (20.7)	0.601	−6.190	10.9%
Social role functioning	Baseline	73.3 (25.6)	N/A	N/A	N/A
	3 weeks	78.0 (21.0)	>0.999	−4.627	6.3%
	6 weeks	79.1 (22.8)	>0.999	−5.712	7.8%
	3 months	79.7 (20.5)	0.732	−6.325	8.6%
	6 months	81.2 (19.9)	0.304	−7.812	10.7%
Emotional role functioning	Baseline	25.8 (38.6)	N/A	N/A	N/A
	3 weeks	18.3 (33.1)	>0.999	7.440	28.9%
	6 weeks	18.9 (33.6)	>0.999	6.854	26.6%
	3 months	16.0 (28.1)	0.567	9.773	37.9%
	6 months	20.5 (33.2)	>0.999	5.260	20.4%
Mental health	Baseline	77.7 (15.3)	N/A	N/A	N/A
	3 weeks	79.6 (14.4)	>0.999	−1.876	2.4%
	6 weeks	80.5 (15.1)	>0.999	−2.816	3.6%
	3 months	80.3 (15.1)	>0.999	−2.596	3.3%
	6 months	79.9 (15.8)	>0.999	−2.214	2.8%

N/A = not applicable, SF-36 = Medical Outcomes Study 36-Item Short Form
[a] Bold type indicates statistical significance at $P < 0.05$.
[b] Asterisk indicates a statistically significant change from baseline.

OA.[5] Our results suggest that weight loss may also help maximize the benefits of intra-articular corticosteroid injections. Furthermore, patients with severe knee OA experienced less pain relief and functional improvement than did those with less severe OA. Understanding these factors may be useful to clinicians when counseling patients about optimal treatment options.

Despite improvement in WOMAC scores, obese patients experienced more pain and functional deficits than did their nonobese counterparts, both before and after treatment. This finding is consistent with those of previous studies, suggesting an association of increased BMI not only with increased chronic musculoskeletal pain but also with increased chronic pain in general.[26-28] This phenomenon can be caused by several factors. Increased body weight places more mechanical load on knee joints, thereby causing more

Table 4

Relative Improvement of Western Ontario and McMaster Universities Arthritis Index Total Score Based on Body Mass Index and Kellgren-Lawrence Grade Categories

Time Point	Body Mass Index		Kellgren-Lawrence Grade	
	<30 kg/m²	≥30 kg/m²	1 or 2	3 or 4
3 wk	37%	35%	36%	35%
6 wk	44%	33%	46%	30%
3 mo	40%	32%	48%	23%
6 mo	32%	39%	48%	26%

Figure 3
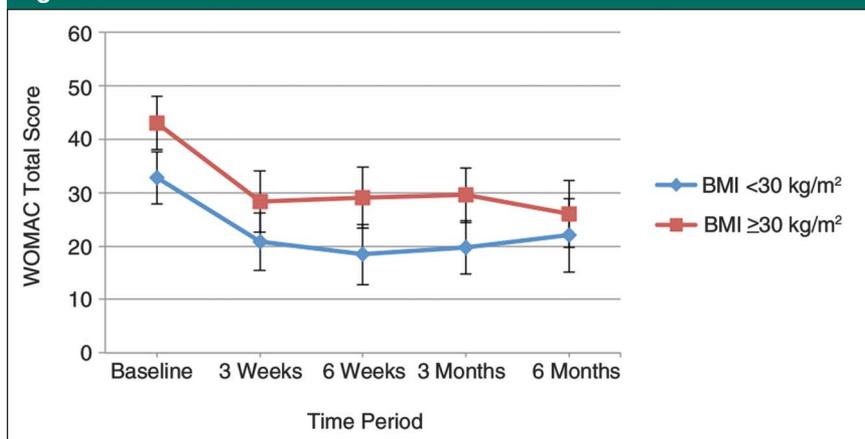
Line graph showing Western Ontario and McMaster Universities Arthritis Index (WOMAC) total scores over time in study participants with body mass index (BMI) <30 kg/m² and study participants with BMI ≥30 kg/m². Error bars indicate 95% confidence intervals.

Figure 4
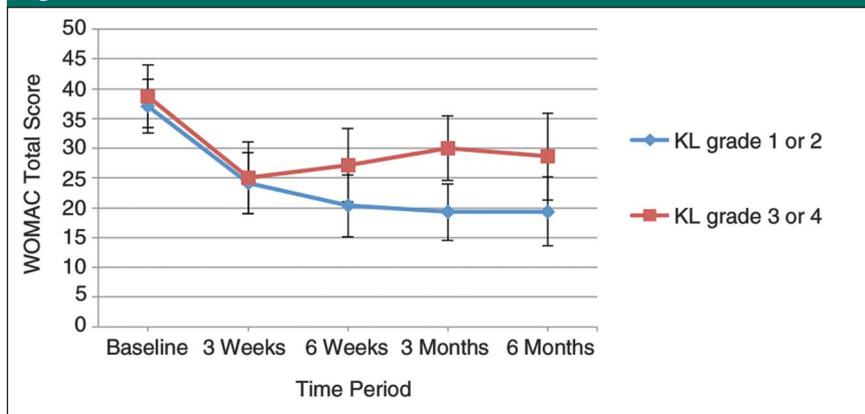
Line graph showing Western Ontario and McMaster Universities Arthritis Index (WOMAC) total scores for study participants with Kellgren-Lawrence (KL) grade 1 or 2 osteoarthritis and study participants with KL grade 3 or 4 osteoarthritis. Error bars indicate 95% confidence intervals.

knee pain in obese patients than in nonobese patients.[29,30] Obesity is also associated with decreased physical activity, which can lead to decreased muscle strength. Muscle weakness has been shown to worsen joint pain.[31,32] Decreased physical activity can also lead to inadequate resistance exercise; such exercise has been shown to decrease pain and to increase physical function in patients with knee OA.[33-35] Obesity can also cause pain through inflammation. Adipose tissue can release adipo-cytokines, such as leptin, adipo-nectin, and resistin, which can cause pain because of joint degeneration or local pro-inflammatory effects.[36,37]

Interestingly, even though obese patients had significantly worse WOMAC scores than nonobese patients had at most time points (baseline, 6 weeks, and 3 months), the differences in WOMAC total scores at the 3-week and 6-month marks were not statistically significant. This finding suggests that obese patients experienced more improvement than nonobese patients experienced in all WOMAC categories in the first 3 weeks and 6 months after treatment. Similar patterns have been seen in a study of the management of back pain by epidural steroid injections in adults with degenerative lumbar spinal stenosis, in which obese patients experienced greater improvement at earlier postinjection time points, compared with nonobese patients.[38] Morbidly obese patients (BMI ≥40 kg/m²) have also been found to have greater reductions in pain at 12 months after total hip arthroplasty than nonobese patients (BMI <30 kg/m²) have.[39] The reason for these findings is unclear. One possible explanation of the greater pain relief experienced by obese patients may be their lower level of physical activity along with the anti-inflammatory effects of the treatment.[38] The

Table 5

Results of Statistical Modeling With Tests of Overall Effects[a]

Variable 1	Variable 2	Variable 3	Estimate (95% Confidence Interval)	P Value[b]
Time (versus baseline)				
3 weeks	—	—	−13.5 (−21.1, −6.0)	<**0.0001**
6 weeks	—	—	−14.4 (−22.0, −6.7)	<**0.0001**
3 months	—	—	−14.2 (−20.5, −7.9)	<**0.0001**
6 months	—	—	−14.1 (−20.7, −7.6)	<**0.0001**
BMI group factor	—	—	8.5 (5.0, 12.0)	<**0.0001**
Osteoarthritis grade 3 or 4 (versus osteoarthritis grade 1 or 2)	—	—	5.8 (2.3, 9.3)	**0.001**
BMI*Time				
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Baseline	—	10.7 (3.8, 17.7)	**0.003**
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	3 weeks	—	7.5 (−0.4, 15.4)	0.063
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	6 weeks	—	10.7 (2.5, 16.8)	**0.009**
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	3 months	—	9.7 (2.5, 16.9)	**0.009**
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	6 months	—	4.1 (−5.3, 13.4)	0.387
Osteoarthritis grade*Time				
Grade 3 or 4 (versus grade 1 or 2)	Baseline	—	1.2 (−5.7, 8.2)	0.726
Grade 3 or 4 (versus grade 1 or 2)	3 weeks	—	1.0 (−6.9, 8.9)	0.805
Grade 3 or 4 (versus grade 1 or 2)	6 weeks	—	6.9 (−1.2, 14.9)	**0.028**
Grade 3 or 4 (versus grade 1 or 2)	3 months	—	10.7 (3.5, 17.9)	**0.004**
Grade 3 or 4 (versus grade 1 or 2)	6 months	—	9.2 (−0.1, 18.5)	0.052
BMI*osteoarthritis grade*time				
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 1 or 2	Baseline	8.9 (−0.1, 17.8)	0.052
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 3 or 4	Baseline	12.6 (2.0, 23.3)	**0.021**
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 1 or 2	3 weeks	4.3 (−5.9, 14.6)	0.400
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 3 or 4	3 weeks	10.6 (−1.4, 22.6)	0.082
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 1 or 2	6 weeks	3.8 (−6.6, 14.2)	0.471
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 3 or 4	6 weeks	17.6 (5.3, 30.0)	**0.006**
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 1 or 2	3 months	2.9 (−6.6, 12.5)	0.540
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 3 or 4	3 months	16.5 (5.7, 27.3)	**0.003**
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 1 or 2	6 months	1.7 (−9.8, 13.2)	0.768
BMI ≥30 kg/m^2 (versus BMI <30 kg/m^2)	Grade 3 or 4	6 months	6.4 (−8.2, 21.0)	0.384

BMI = body mass index
[a] Variables and P values were as follows: time ($P < 0.001$), BMI ≥30 kg/m^2 ($P < 0.001$), Kellgren-Lawrence osteoarthritis grade 3 or 4 ($P = 0.002$), BMI*time ($P < 0.001$), osteoarthritis grade*time ($P = 0.007$), BMI*osteoarthritis grade*time ($P = 0.004$).
[b] Bold type indicates statistical significance at $P < 0.05$.

AAOS clinical practice guideline of 2013 did not recommend hyaluronic acid as an intra-articular injection to treat the symptoms of knee OA, citing strong evidence.[5] Similarly, the use of biologic injection was deemed inconclusive by the AAOS.

In our study, participants with lower Kellgren-Lawrence grades exhibited greater improvement in WOMAC scores, compared with participants with higher Kellgren-Lawrence grades. This finding is consistent with results of previous studies.[40,41] This finding may be attributable to a variety of factors. First, pain associated with OA is the result of anatomic changes within the joint. Cartilage is aneural, but the subchondral bone, periosteum, osteophytes, periarticular ligaments, muscle, synovium, and joint capsule all have rich innervation.[42] Intra-articular corticosteroids relieve pain by controlling inflammation and, in experimental models, have been shown to reduce the presence of synovitis and inflammation.[12,43] However, in knees in which more severe anatomic changes have already occurred, the anti-inflammatory effects of intra-articular

Figure 5
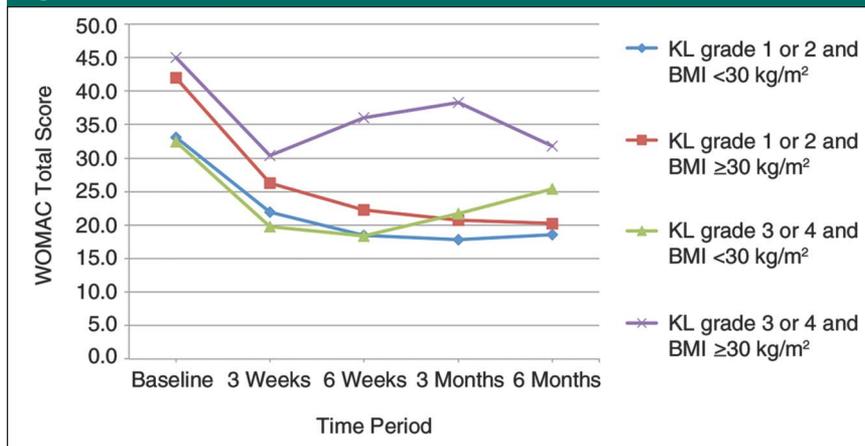
Line graph showing WOMAC total scores in study participants in a combined model of Kellgren-Lawrence (KL) osteoarthritis grade and body mass index (BMI) categories.

corticosteroids are less likely to be effective. Another possible explanation is that chronic pain syndrome has developed in patients with more advanced OA. Persistent nociceptive pain is associated with central neurogenic sensitization. This sensitization amplifies peripheral pain signals, leading to chronic pain syndrome, which is unlikely to improve with intra-articular corticosteroid injections.[42]

The results of the SF-36 show that the general health perception and mental health domains were not improved by intra-articular corticosteroid injection. Results did reveal the considerable effect of pain on mental and physical health. Further research is necessary to understand the mental health comorbidities associated with OA. Some studies suggest that alternative OA treatments, such as viscosupplementation, provide greater duration of relief, compared with corticosteroid injections.[5] Studies also suggest that certain clinical factors are associated with longer-term benefits of injection.[11,13,41,44] Such factors include aspiration of substantial effusion before injection and noninflammatory characteristics of the knee observed via

ultrasonography. Additional comparison studies are needed to determine optimal nonsurgical management of symptomatic knee OA.

Limitations of this study include the lack of a corresponding placebo arm and an attrition rate of 21.5%. It is possible that the benefits of treatment were the result of the placebo effect. Additional research comparing intra-articular corticosteroid injections and intra-articular saline injections should be performed to assess the role of the placebo effect on reported symptom eradication. Additional evidence of the efficacy of intra-articular corticosteroid injections in the short-term relief of OA pain, ideally in unbiased and adequately powered randomized controlled trials, is needed. Although our power analysis controlled for the attrition rate, it is possible that participants who did not benefit from the treatment were less likely to complete future surveys, which may have resulted in selection bias.

Conclusion

Patients with symptomatic knee OA who received intra-articular injec-

tions of triamcinolone and lidocaine demonstrated improved pain and function for up to 6 months post-injection. Patients with BMI ≥ 30 kg/m^2 or Kellgren-Lawrence OA grades of 3 or 4 had worse WOMAC scores overall, compared with other patients. Patients with more severe OA experienced a smaller response to treatment than did patients with less severe OA.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 11, 12, 14, 25, 40, and 41 are level I studies. References 1, 2, 13, 16, 18, 19, 21-23, 28, 31, 35, 38, and 39 are level II studies. Reference 27 is a level III study. Reference 29 is a level IV study.

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