Does Injection Site Matter? A Randomized Controlled Trial to Evaluate Different Entry Site Efficacy of Knee Intra-articular Injections

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Abstract:

Background: Complaints of knee pain secondary to early osteoarthritis may account for up to 30% of visits to primary care physicians. Due to the proposed inflammatory changes in early osteoarthritis, intra-articular injections of corticosteroids (IACS) have been considered as an option for disease progression modification, pain control, and improvement of function. However, some studies have suggested poor accuracy rates of IA injections depending on the entry site chosen. It is therefore the aim of this study to evaluate the efficacy of IA knee corticosteroid injection in reducing pain and improving function in patients with early osteoarthritis and whether the low accuracy rates reported with the Anterolateral joint line injection site translate to worse functional and pain outcome measures as compared to Suprapatellar lateral injections. Materials and Methods: The study was carried out as an open-label, randomized controlled trial with 60 sequential patients recruited. Simple randomization separated groups into anterolateral joint line or suprapatellar lateral injection sites. Improvements were measured with WOMAC and VAS scores after injection of Lidocaine and steroid solution. Results: Patients receiving IACS injections had a measurable improvement in self-reported outcomes as evidenced by standard deviation change in WOMAC and VAS scores. The majority of patients had a clinically significant improvement in VAS scores as compared to their initial measures with a notable amount of patients improving significantly as well on their WOMAC scores, irrespective of the injection site chosen. Conclusions: We have therefore continued the use of palpation-guided intra-articular knee injections in an effort to reduce costs as compared to other injection modalities with positive results in our osteoarthritis patients.

Introduction:

Complaints of knee pain secondary to early osteoarthritis are extremely common and may account for up to 30% of visits to primary care physicians,(1,2). Primary osteoarthritis has been classified as a progressive "wear and tear" degenerative condition with reported prevalence of 25% to 30% in patients forty five to sixty-five years of age and more than 85% in patients older than sixty-five (3). Recent Appropriate Use Criteria (AUC) from the American Academy of Orthopedic Surgery (AAOS) evaluates the multiple nonsurgical conservative modalities for improving disease symptoms. Recommendations include self-management programs, physical therapy, NSAIDs, tramadol, intraarticular (IA) corticosteroids, and arthroscopic loose body removal or partial meniscectomy in carefully selected patients (4,5). However, due to the uncertainty of evidence based recommendations, many inconsistencies exist between guidelines from different governing agencies. Traditionally, orthopedic surgeons and other physicians in general believe in a combination of pharmacological and non-pharmacological treatment options to improve patient function, quality of life, and decrease pain.

Due to the proposed inflammatory changes in early osteoarthritis, IA injections of corticosteroids have been considered as an option for disease progression modification, pain control, and improvement of function (6,7). Currently there are five injectable corticosteroids with a Food and Drug Administration label for IA injection. These are methylprednisolone acetate, triamcinolone acetate, betamethasone acetate, triamcinolone hexacetonide, and dexamethasone. Although multiple trials have been carried out on the use of corticosteroid injections, most have been inconclusive and with mixed results (3,8). Despite patient self-reported improvements with IA corticosteroid injections, a recent Cochrane review from 2006 (9) failed to find evidence of functional improvement at any follow time-point in patients who received IA corticosteroid injections.

In addition to the inconclusive evidence, multiple studies suggest different accuracy rates of IA knee injections depending on the anatomic site chosen for injection. A recent systematic review of the literature reported palpation-guided IA Knee Injection (IAKI) at the superolateral patellar (SLP) portal to be the most accurate at greater than 93% and anterolateral joint line (ALJL) portal to be the least accurate at 70%

(10-12). However, the author's experience suggests patient improved outcomes despite the poor accuracy reported in said studies. It is therefore the aim of this study to evaluate the efficacy of IA knee corticosteroid injection in reducing pain and improving function in patients with early osteoarthritis and whether the low accuracy rates reported with the ALJL injection site translate to worse functional and pain outcome measures.

Materials and Methods:

The study was carried out as an open-label, randomized controlled trial designed to compare the efficacy of intra-articular knee corticosteroid injections in controlling pain and improving function in patients with early primary osteoarthritis changes utilizing different entry sites. Patients were contacted initially at the author's outpatient clinics during their previously scheduled appointments. The institutional review board (IRB) approved this study. All patients gave the informed consent prior being included into the study.

A simple randomization was used to decrease selection bias as patients were selected in an alternating fashion in accordance to clinic appointment time (eg., first patient eligible for study received superolateral patellar injection, second patient received anterolateral joint line injection, etc). A total number of sixty patients were recruited with thirty patients in each study group. Eligible patients were initial visitors to our outpatient clinics evaluated for knee osteoarthritis with Kellgren and Lawrence Grade 1 to Grade 3 radiographic evidence of knee arthritis. Our inclusion criteria included, no previous knee injections, persistent pain in the knee resulting in the clinic visit, significant pain on visual analog pain of more than 4 out of 10, and failure of other non-surgical interventions such as exercise and analgesics. Exclusion criteria included advanced osteoarthritis surgery, hemorrhagic effusions, use of warfarin or antiplatelet therapy, presence of systemic infection, uncontrolled diabetes mellitus, history of previous injections, and patients with any degenerative knee condition other than primary osteoarthritis.

Once patient was included in the study, demographic questionnaire, visual analog scale, and WOMAC (Western Ontario and McMaster Universities) scores were calculated and recorded. A 5-ml syringe with 1 ml of Triamcinolone acetate (40mg/ml) and 4 ml of Lidocaine 1% solution was injected into selected injection site. Immediately after injection, a pain analog scale questionnaire was given for quantification of pain in relation to site. After completion of the appointment, a 4-week follow up visit was given, as is the author's usual protocol with previous knee injection. On this second visit, the same pain analog scale (0-100) was provided and a WOMAC follow up questionnaire performed in addition to usual clinical history and physical exam. Study follow up ended at this follow up.

The WOMAC score consists of twenty-four items divided into three subscales including pain, stiffness, and physical function. We used a 5-point Likert-type scoring format for analysis. Final scoring on a basis of nighty six possible points suggests total disability secondary to arthritis. Higher scores indicate worse pain, stiffness, and functional limitations. Due to the fact that assessment is subjective, initial and final values will not be compared within different patients to decrease risk of response bias. However, changes in WOMAC scores and Visual Analog Scale (VAS) scores can be considered reliable and comparable.

The minimal clinically important difference (MCID) score is a statistical model that attempts to elucidate the significance of changes in scores measured by statistical instruments when compared to clinically significant changes. The MCID is therefore an estimate of the minimum amount of change a patient would need to overcome in an outcome to classify it as an important change. A distribution-based MCID score was calculated using the standard deviations of the means. Patients achieving a change in WOMAC or VAS scores were considered to have had a clinically important difference13.

Data was recorded in Excel (version 14.4; Microsoft) and analyzed in XLSTAT. Differences in recorded 2-group data were determined with the t test and chi-squared for comparisons of proportions, with significance at the $P<0.05$ level.

Results:

A total of 60 patients were recruited in this study as per the inclusion criteria. Ten patients were lost to follow up with a total of 50 patients at completion of study date with an average age of 60.2(10.8) years (range 39 to 79 years). At cut off date, 30 patients had been injected through an ALJL knee site and 20 patients were injected through a SLP site. No significant difference in age or sex between groups was noted upon randomization of patients.

Injection site pain measured with VAS was reported at an average of 22.1(29.83) in patients injected through the AL portal compared to 45.0(33.56) on SL portal ($p=0.015$). Furthermore, when classifying significant pain as more than 50 of 100 on the VAS, a notable yet not statistically significant difference was noted with 23% of patients compared to 40% on the AL versus the SL sites respectively ($p=0.214$).

The ALJL group had initial VAS scores of 73.93(17.92) that changed at final follow up to an average of 42.33(16.80) with a MCID-VAS of 86% (26 out of 30 patients). The SLP site had an average VAS of 59.43(18.47) with a change to 27.5(27.17) at the end of the study. The MCID-VAS was calculated at 80% (16 out of 20 patients). No significant difference

Discussion:

The current published data and our experience suggests that Intra-Articular corticosteroid injections are a safe treatment option for patients with good results and positive patient outcomes. However, it has remained unclear whether these results are secondary to disease modification by the injected agents, natural disease progression or just part of the anti-inflammatory effects of the medications on the affected joints.

Our data suggest that patients receiving IACS injections have a measurable improvement in self-reported outcomes as evidenced by standard deviation change in WOMAC and VAS scores. The majority of patients in both treatment groups had a clinically significant improvement in VAS scores as compared to their initial measures with a notable amount of patients improving significantly as well on their WOMAC scores. The improvement noted was irrespective of the injection site chosen. No significant difference was noted assuming an intra-articular injection versus a peri-articular injection as per injection site. It is suggested therefore that assuming an accuracy rate as previously reported, the effect of the injection is not necessarily dependent on the placement of the medication within the knee capsule.

It is known that corticosteroids affect the local cellular environment by modulation of cell inflammatory mediators3, therefore making the application of corticosteroids to the general area of the inflammatory process an efficacious way to treat the underlying symptomatology of the disease.

As a secondary outcome measure, it was noted that although pain scores and functional outcomes improved significantly over an early follow-up in both treatment modalities, there was a significant difference in the needle-stick pain comparing superolateral with anterolateral injection sites. Although this cannot be attributed necessarily to a benefit of one injection site over the other, it does serve as an indication for the authors that the palpation-guided injection site should be chosen in accordance with experience injecting and not based on intra-articular injection accuracy rates as to decrease the patient's initial perceived pain.

As a conclusion, we have continued the use of palpation-guided intra-articular knee injections in an effort to reduce costs as compared to other injection modalities with positive results in our osteoarthritis patients. These medications have shown a safe therapeutic index and improved patient quality of life measures after injection. They continue to be part of the arsenal available against early changes in the idiopathic osteoarthritis patient.

Disclosures:

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Ethical Standards:

All patients gave the informed consent prior being included into the study. All procedures performed in the study were in accordance with the ethical standards of the IRB and with the Helsinki declaration and its later amendments or comparable ethical standards.

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Resúmen:

Introducción: Las quejas de dolor de rodilla secundarias a osteoartritis temprana corresponden a aproximadamente un 30% de las visitas a un médico primario. Debido al mecanismo inflamatorio propuesto como patofisiología de la artritis temprana, las inyecciones intraarticulares de corticoesteroides han sido consideradas como una opción para modificar la progresión de la condición, manejo de dolor y mejoría de función del paciente. Sin embargo, algunos estudios han sugerido resultados sub-óptimos dependiendo del lugar escogido para inyección. Es por lo tanto el fin de este estudio evaluar la eficacia de las inyecciones intraarticulares de rodilla con esteroides en manejo de dolor y mejoría de función en pacientes con artritis temprana; y si la pobre exactitud reportada con la inyección anterolateral articular se traduce a peores resultados

al compararlos con inyecciones laterales suprapatelar. Materiales y Métodos: El estudio fue llevado a cabo como un estudio controlado aleatorio abierto con 60 pacientes secuenciales reclutados. Los grupos aleatorios se separaron de usando distribución sencilla en grupos de inyección suprapatelar lateral y anterolateral articular. Las mejorías se midieron con valores WOMAC y escalas de dolor de 1 al 100. Resultados: Los pacientes que recibieron inyecciones intraarticulares de esteroides tuvieron mejorías cuantificables con un cambio en promedio de una desviación estándar en WOMAC y escalas de dolor. La mayoría de los pacientes tuvo una mejoría clínicamente significativa en valores de dolor y en las escalas WOMAC, irrespectivo del lugar de inyección escogido. Conclusión: Hemos continuado el uso de inyecciones intraarticulares guiadas por palpación en un esfuerzo para reducir costos al compararlos con otras modalidades obteniendo buenos resultados en nuestra población de pacientes de artritis de rodilla temprana.