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

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Introduction:
Complaints of knee pain secondary to early osteoarthritis are extremely common and may account for up to 30% of visits to orthopaedic surgeons in the United States. Primary osteoarthritis has been classified as a progressive ‘wear and tear’ disorder, with reported prevalence of 25% to 30% in patients forty-five to sixty-five years of age (1), and more than 85% in patients older than sixty-five (2). Recent Appropriate Use Criteria (AUC) from the American Academy of Orthopaedic Surgery (AAOS) evaluates the multidisciplinary use of anti-inflammatory injections, for pain relief, physical therapy, NSAIDs, tramadol, intraarticular corticosteroids, and arthroscopic loose body removal or partial meniscectomy in carefully selected patients (4). However, due to the uncertainty of evidence based recommendations, many anesthesiologists exist between guidelines from different governing agencies. Traditionally, orthopedic surgeons and other physicians in general believe in a combination of pharmacological and nonpharmacological treatments, in an attempt to improve patient function, quality of life, and decrease pain.

Due to the proposed inflammatory changes in early osteoarthritis, 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 Food and Drug Administration label for IA injection. These are methylprednisolone acetate, triamcinolone acetate, triamcinolone hexacetonide, and dexamethasone. Although multiple trials have been carried out on the use of corticosteroid injections, the literature is inconclusive and with mixed results (3.8). Despite patient self-reported improvements from IA corticosteroid injections, a recent Cochrane review from 2006 (9) found no 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 published by the American Academy of Orthopaedic Surgeons (10) reported palpation-guided IA Knee Injection (AKI) at the superolateral patellar (SLP) portal to be the most accurate and consistent of the anterolateral joint line (ALJL) portal to be the least accurate at 70%

Abstract:
Background: Complaints of knee pain secondary to early osteoarthritis may account for up to 30% of visits to orthopaedic surgeons in the United States. Primary osteoarthritis has been classified as a progressive ‘wear and tear’ disorder, with reported prevalence of 25% to 30% in patients forty-five to sixty-five years of age (1), and more than 85% in patients older than sixty-five (2). Recent Appropriate Use Criteria (AUC) from the American Academy of Orthopaedic Surgery (AAOS) evaluates the multidisciplinary use of anti-inflammatory injections, for pain relief, physical therapy, NSAIDs, tramadol, intraarticular corticosteroids, and arthroscopic loose body removal or partial meniscectomy in carefully selected patients (4). However, due to the uncertainty of evidence based recommendations, many anesthesiologists exist between guidelines from different governing agencies. Traditionally, orthopedic surgeons and other physicians in general believe in a combination of pharmacological and nonpharmacological treatments, in an attempt to improve patient function, quality of life, and decrease pain.

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

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

A simple randomization was used to decrease selection bias as patients were selected in an alternating fashion in accordance to the SLP/LP sites. Each patient was the first patient eligible for study received superolateral patellar injection, the second patient received anterolateral joint line injection, etc. A total number of sixty six patients were recruited with thirty patients in each study group. Eligible patients were initial visit to our outpatient clinics evaluated for knee osteoarthritis with Knee Evaluation and Radiographic Assessment of Knee Osteoarthritis (Kerato) scores. The majority of patients had a clinically significant improvement in VAS scores as compared to their initial visit (VAS 4.06, SD 1.41) at final follow up visit (VAS 2.28, SD 1.14). Twenty-four patients were lost to follow up with a total of 34 patients included in the analysis. Ten patients were lost to follow up with a total of 50 patients at completion of the study with date of average age of 60.2(10.8) years (range 39 to 79 years). None of the patients had a knee injury on the side that had been injected through an ALJL knee site and 20 patients were included in the SLP injection site. No significant difference in age or sex between groups was noted upon randomization of patients.

Injection site pain measured with visual analog scale was grade of 2.2(1.93) in patients injected through the AL portal compared to 4.07(1.66) on the SLP portal. Furthermore when classifying significant pain as more than 50 of the visual analog scale, 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 total scores and Visual Analog Scale (VAS) scores can be considered reliable and comparable.

The minimal clinically important difference (MCID) score is a term used to describe the smallest amount of change that is considered meaningful by patients or caregivers. The MCID-VAS was the standard deviation of the means. Patients achieving a change in WOMAC greater than the MCID-VAS were considered to have had a clinically important difference.

Data was recorded in Excel (version 14.4.2), 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.

Discussion:
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 the study with date of average age of 60(10.8) years (range 39 to 79 years). None of the patients had a knee injury on the side that had been injected through an ALJL knee site and 20 patients were included in the SLP injection site. No significant difference in age or sex between groups was noted upon randomization of patients.

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ARTÍCULOS ORIGINALES / ORIGINAL ARTICLE

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. Primary osteoarthritis has been classified as a progressive “wear and tear” condition affecting joints with reported prevalence of 25% to 30% in patients forty-five to sixty-five years old and more than 85% in patients older than sixty-five (3). Recent Appropriateness Criteria (AUC) from the American Academy of Orthopedic Surgery (AAOS) evaluates the multiple multimodal, nonpharmacological treatment options for improving disease symptoms. Recommendations for interventions include pharmacological programs, physical therapy, NSAIDs, tramadol, intraarticular injection therapies, and arthroscopic loose body removal or partial meniscectomy in carefully selected patients (4.5). However, due to the uncertainty of evidence based recommendations, many practitioners seek to exist between guidelines from different governing agencies. Traditionally, orthopedic surgeons and other physicians in general believe in a combination of pharmacological and nonpharmacological conditions 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, knee pain control, and improvement of function (6.7). Currently there are five injectable corticosteroids with Food and Drug Administration (FDA) label for IA injection. These are: methylprednisolone acetate, triamcinolone hexacetonide, and dexamethasone. Although multiple trials have been carried out on the use of corticosteroid IA injection, results have been inconclusive and with mixed results (8.9). Despite patient self-reported improvements from corticosteroid injections, a recent Cochrane review from 2006 (9) failed to find evidence of functional improvement at any follow up 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 of reported palpation-guided IA Knee Injection (IAKI) at the superolateral patellar (SLP) portal to be the most accurate with a mean accuracy rate of 90% and anterolateral joint line (ALJL) portal to be the least accurate at 70% (10-12). However, the author’s experience suggests patients improve irrespective of the site with better pain control, which may suggest poor accuracy reported in said studies. It is therefore the aim of this study to evaluate the efficacy of IA knee injections in reducing pain and improving function in early primary 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 IA knee injections in reducing pain and improving function in patients with early primary osteoarthritis utilizing different entry sites. Patients were contacted initially at the author’s outpatient clinics during their previously scheduled appointments. An institutional review board (IRB) approved all additional clinical and physical exam. Study follow up ended at the time of the study.

Methods:
The study was carried out as an open-label, randomized controlled trial designed to compare the efficacy of IA knee injections in reducing pain and improving function in patients with early primary osteoarthritis utilizing different entry sites. Patients were contacted initially at the author’s outpatient clinics during their previously scheduled appointments. An institutional review board (IRB) approved all additional clinical and physical exam. Study follow up ended at the time of the study.

A simple randomization was used to decrease selection bias as patients were selected in an alternating fashion in accordance to their 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 positive results in our previous studies. The minimal clinically important difference (MCID) for WOMAC and VAS scores was calculated from a change to 27.5(27.17) at the end of the study. The MCID-VAS was therefore considered to have had a clinical important difference.

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 age of 60.2(10.8) years (range 39 to 79 years). Eighteen of 50 patients had been injected through an ALJL knee site and 20 patients were included into the SL portal group.

Injection site pain measured with Visual Analog Scale (VAS) was reported at an average of 22.1(29.63) in patients injected through the AL portal compared to 45.0(33.56) on the SL portal. Furthermore, when classifying significant pain as more than 50 of the VAS, we find evidence that 29% of patients classified it as an important change. A statistically significant difference was noted with 23% of patients classified worse functional and pain outcomes with the SL sites respectively (p=0.214).

Conclusion:
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 improvement of 80% with a VAS score of 50.40 on the AL with a statistically significant difference to the SL sites (p=0.01).

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Discussion:
The current published data and our experience suggests that Intra-Articular corticosteroids 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 mediators, 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 the patient’s 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 comparisons with other modalities of the anti-inflammatory effects of the medications on the affected joints.

Disclosures:
The authors certify that they have no affiliations with or involvement in any organization or entity with a 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.

References:

Resumen:
Introducción: Las quejas de dolor de rodilla secundarias a osteoartritis corresponden a aproximadamente un 30% de las visitas a un médico primario. Debido al mecanismo inflamatorio propuesto como patofisiología de la artritis crónica, las inyecciones intraarticulares de corticosteroides 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 tanto el fin de este estudio evaluar la eficacia de las inyecciones intraarticulares de triamcinolona hexacetonide con esteroides en manejo de dolor y mejoría de función en pacientes con artritis de rodilla temprana; y si la palpación guiada 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 WOMAC y escalas de dolor de 0 a 100. Resultados: Los pacientes que recibieron inyecciones intraarticulares de esteroides tuvieron mejorías cuantificables con un cambio promedio de una desviación estándar en WOMAC y escalas de dolor. La mayoría de los pacientes tuvo una mejoría clínicamente significativa en valor 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 costos al comparar con otras modalidades obteniendo buenos resultados en nuestra población de pacientes de artritis de rodilla temprana.
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 per-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 injection a promising 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 the patient’s 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 needle placement based on 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 for early changes in the idiopathic osteoarthritis patient.

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