THERAPEUTIC EFFICACY OF INTRA-ARTICULAR NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) IN THE TREATMENT OF INFLAMMATORY ARTHRITIS

TIME FOR AWARENESS & ESTABLISHING A ROLE IN ARTHRITIS PATIENT CARE IN 2023 AND BEYOND

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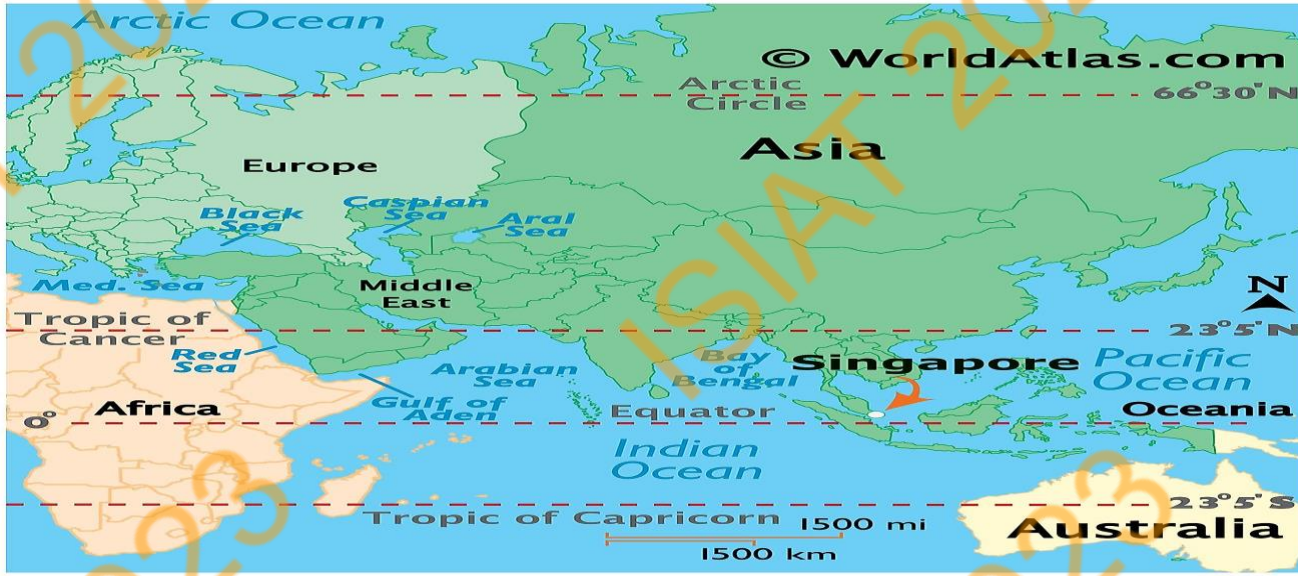
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Arctic Circle
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Middle East
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Red Sea
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Singapore
Pacific Ocean
Africa
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Equator
Oceania
Indian Ocean
23°5'S
Tropic of Capricorn
1500 mi
1500 km
Australia

INTRA-ARTICULAR NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

- **Inflammatory arthritis** is encountered very often in daily clinical practice. Whereas most clinicians are aware of intra-articular (IA) steroid injections, few are aware of the utility of IA nonsteroidal anti-inflammatory drugs (NSAIDs) in the treatment of such painful conditions.
- This presentation serves to review the current literature regarding the usage of IA NSAIDs in clinical practice and its utility, efficacy and potential is summarised.

Lisbon

3-5 October 2019

INTRA-ARTICULAR NSAIDs THERAPY

- ✓IA NSAIDs have been used since **1995** in the post-operative setting and then in various clinical settings of knee osteoarthritis and other inflammatory joint disorders.
- ✓The IA NSAIDs used reported in the literature include **ketolorac, piroxicam and pareocoxib (Dynastat)**.
- ✓I will summarise the experimental publications and clinical studies on IA NSAIDs.
- ✓Summarised presentations of my experiences with the usage of IA Ketorolac, IA Piroxicam and IA Pareocoxib will also be presented, including interesting case reports.
- ✓A review of reported literature up to 2023 on the usage of IA NSAIDs in the treatment of osteoarthritis will also be presented.

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EC ORTHOPAEDICS
Review Article

Intraarticular Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in the Treatment of Inflammatory Arthritis: Establishing a Role in Arthritis Patient Care Today

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Received: September 18, 2019; **Published:** October 18, 2019

Abstract

Inflammatory arthritis is very commonly encountered in clinical practice and is on the rise due to inflammatory osteoarthritis (OA) and gouty arthritis from an aging population (inflamaging) and increasing prevalence of metabolic syndrome. Common therapeutic options used to manage the pain and inflammation includes oral non-steroidal anti-inflammatory drugs (NSAIDs), oral steroids, intramuscular (IM) NSAIDs and intraarticular (IA) steroid injections. Due to the limitations of IA steroids, the use of IA NSAIDs represents a useful therapeutic alternative in many patients with inflammatory arthritis, especially in those who recur after

WHY INTRA-ARTICULAR NSAIDs THERAPY?

- THE CLINICAL NEED:
  - SOME PATIENTS DO NOT WANT STEROID INJECTIONS (SHARED DECISION MAKING)
  - DIABETIC PATIENTS WITH HYPERGLYCAEMIA
  - STEROID SENSITIVITY OR ADVERSE REACTIONS
  - RECURRENT OR PERSISTENT JOINT INFLAMMATION DESPITE IA STEROID INJECTIONS
  - EFFECT OF STEROIDS (EG METHYPREDNISOLONE) ON CHONDROCYTE CELLS VIABILITY/CHONDROTOXICITY
  - LONG TERM EFFECTS OF REPEATED TRIAMCINOLONE INJECTIONS – MRI STUDIES SHOWED CARTILAGE VOLUME LOSS AFTER 2 YEARS.

Intra-articular Corticosteroid Injections in the Hip and Knee: Perhaps Not as Safe as We Thought?

- Andrew J. Kompel, Oct 15 2019https://doi.org/10.1148/radiol.2019190341

Adverse Joint Events after IACS Injections in Knee and Hip Joints

Adverse Event	Hip	Knee	Both Joints
No. of injections	307	152	459
RPOA 1	21 (7)	5 (3)	26 (6)
RPOA 2	2 (0.7)	1 (0.7)	3 (0.7)
ON	3 (1)	0	3 (0.7)
SIF	4 (1)	0	4 (0.9)
Total adverse joint events	30 (10)	6 (4)	36 (8)

Note.—Data are number of events, and data in parentheses are percentages. IACS = intra-articular corticosteroid; ON = osteonecrosis; RPOA 1 = rapid progressive osteoarthritis type 1; RPOA 2 = rapid progressive osteoarthritis type 2; SIF = subchondral insufficiency fracture.

WHY INTRA-ARTICULAR NSAIDs THERAPY?

- BEING A PATIENT-ORIENTED AND SOLUTION-OREIENTED PHYSICIAN AND RHEUMATOLOGIST…I ASKED MYSELF THIS QUESTION

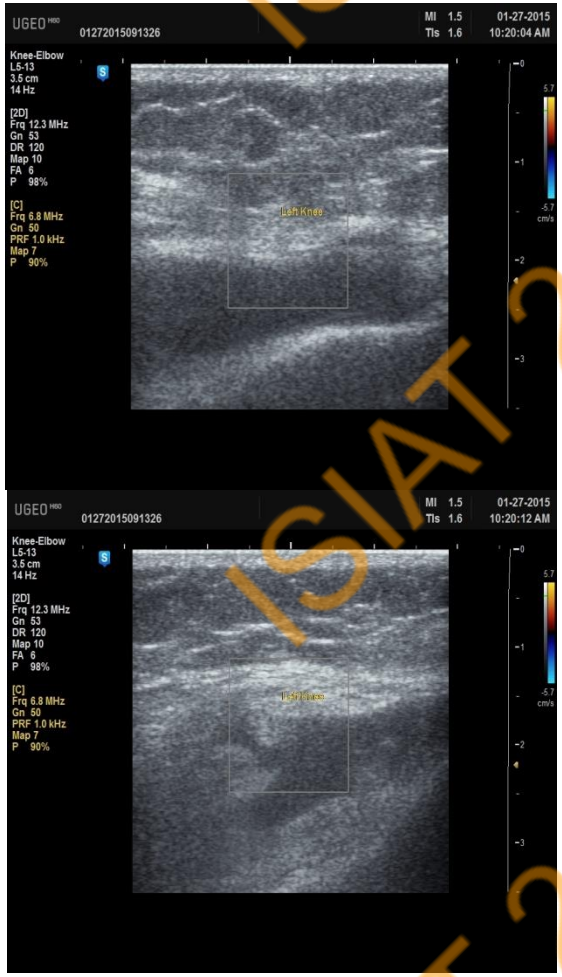
"IN THOSE CLINICAL SCENERIOS, CAN IA NSAIDs BE AN ALTERNATIVE INTRA-ARTICULAR THERAPY???"

Illustrative Case Example 1:

- AKH, 75/CHI/F with chronic left knee pain, worsened after fall 3 months ago, resulting to left knee effusion.
- Ultrasound of the left knee showed Effusion 3+, Synovitis 2+ and Osteophytes. (Figure 1-2)
- **Left knee aspiration was done and IA ketorolac 30mg was given.**

➢ She was reviewed a week later and the left knee pain improved.

Follow-up viscosupplementation with IA hyaluronic acid (HA) Orthovisc was given.



Experimental studies of intra-articular NSAIDs joint injection

There have been several studies done in rats model of induced osteoarthritis with IA ketorolac, piroxicam and parecoxib, the first and only cyclooxygenase-2 (COX-2) inhibitor available and IA ketorolac and lornoxicam in the rabbit knee joint.

The use of I/A ketorolac has been studied in animal models and shown to have no detrimental effects on the joints [9,10]. The local tolerability of lornoxicam after single and repeated IA administration into the rabbit knee joint did not show signs of toxicity to the bone or chondrotoxicity [11].

Su., *et al*. in their study also showed the safety of repeated I/A ketorolac and Hyaluronic Acid (HA) injections over a 4-week period [12]. There were no pharmacokinetics interaction or toxicity seen. This was also confirmed by a similar study using IA piroxicam in the rats OA model [13].

In terms of efficacy, IA piroxicam administration showed significant reduction in the rat knee swelling, corresponding to the reduction of prostaglandin E2 levels in the joint. Both IM and IA piroxicam led to rapid rise in the plasma piroxicam concentration, but the systemic bioavailability of piroxicam was relatively lower compared to that after IM injection, indicating that the IA route provided a higher piroxicam concentration in the local tissue [13]. Hence the therapeutic effect of IA administration was more effective in terms of reduction in joint swelling and inflammatory levels compared to IM route. In the study with IA parecoxib, the excitatory amino acids levels were significantly reduced and they were accompanied with suppression of synovial inflammation and a significant inhibition of cartilage degeneration in the anterior cruciate ligament-transected knee in rats [14].

And in the studies where IA NSAIDs were combined with HA administration, there were no pharmacokinetic interactions, but on the other hand, the anti-inflammatory and anti-nociceptive efficacies of IA piroxicam were synergistically increased upon co-treatment with HA in the rat OA knee model [15].

The positive experimental studies have underlined the basis of the good outcome experience that have been seen in clinical practice. When administered locally, high concentrations of NSAIDs can be achieved at the site of cell injury with a better outcome and local administration can lead to clinical benefits such as use of lower doses, lower subsequent systemic exposure and a reduced frequency of adverse events [16].

INTRA-ARTICULAR NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

- **Experimental studies** of IA NSAIDs have shown no chondrotoxocity but good pharmacokinetic and pharmacodynamic efficacy and amelioration of inflammation in rat and rabbit OA models.
- IA ketorolac injection in rat OA model to be efficacious and has synergistic effects when combined with hyaluronic acid (HA)injection.
- Other studies in IA pareocoxib have also shown good clinical outcome, and superior to IM NSAIDs.
- Higher concentration of local NSAIDs at the site of cellular injury, which is more effective and has less systemic toxicity and adverse effects!

Regul Toxicol Pharmacol. 2019 Mar;102:79-89. doi: 10.1016/j.yrtph.2019.01.011. Epub 2019 Jan 3.

Pharmacokinetics and four-week repeated-dose toxicity of hyaluronic acid and ketorolac combination following intra-articular administration in normal rats

Su Hwan Kim [1], Ki Wan Park [1], Jong Min Kim [1], Myoung Jin Ho [2], Hyung Tae Kim [2], Seh Hyon Song [1], Jeong Hoon Kim [1], Myung Joo Kang [3]

Affiliations + expand

PMID: 30611819 DOI: 10.1016/j.yrtph.2019.01.011

Abstract

Intra-articular (IA) injection of hyaluronic acid (HA) in combination with nonsteroidal anti-inflammatory drugs, such as ketorolac (KL), have been clinically investigated to provide more rapid and profound pain relief in patients with osteoarthritis. However, its safety, local tolerance, and potential for pharmacokinetic interaction have not been assessed. In this study, the pharmacokinetics and toxicity of a combination of HA and KL were evaluated in normal rats following four-week repeated-dose injection. Rats received HA or KL alone at 4 mg/kg or 16 mg/kg, respectively, or HA/KL combination at 4/4 mg/kg, 4/8 mg/kg, or 4/16 mg/kg on a weekly basis. The rats exhibited temporal, reversible changes in hematology, serum chemistry, and urinalysis caused primarily by KL treatment. No deleterious effects were observed on the joint following repeated IA HA/KL administration, which showed only minimal to mild levels of temporary inflammatory

CLINICAL USAGE OF INTRA-ARTICULAR NSAIDs INJECTION THERAPY:

- IA ketorolac usage was first reported in 1995 for post-operative pain relief following outpatient knee arthroscopy.
- Since then, IA ketorolac injection in several clinical studies have been shown to be efficacious and as good as corticosteroids, and has synergistic effects when combined with hyaluronic acid (HA)injection.
- Other studies in IA oxicam and pareocoxib have also shown good clinical outcome, and superior to oral NSAIDs.

INITIAL CLINICAL EXPERIENCES AND PRESENTATIONS WITH IA NSAID INJECTIONS:

- **16TH SSR-MSR WORKSHOPS IN RHEUMATOLOGY, AUG 2015, SINGAPORE –**
  - INTRARTICULAR PIROXICAM AS A NOVEL THERAPUETIC APPROACH FOR THE TREATMENT OF INFLAMMATORY ARTHRITIS: AN INITIAL REPORT OF 60 PATIENTS
- **49th Singapore-Malaysia Congress of Medicine 2015 –**
  - EFFICACY AND SAFETY OF INTRARTICULAR KETOROLAC IN THE TREATMENT OF INFLAMMATORY ARTHRITIS – A REPORT OF THE INITIAL EXPERIENCE WITH 40 PATIENTS
- **AUSTRALIA RHEUMATOLOGY ASSOCIATION (WITH RHPA) 2016 ANNUAL SCIENTIFIC MEETING, DARWIN, AUSTRALIA.**
  - **INTRARTICULAR DYNASTAT STUDY**

EFFICACY AND SAFETY OF INTRA-ARTICULAR INJECTION OF CYCLOOXYGENASE-2 INHIBITOR PARECOXIB IN THE TREATMENT OF INFLAMMATORY ARTHRITIS – A FIRST REPORT OF THE INITIAL EXPERIENCE WITH 60 ASIAN PATIENTS

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OBJECTIVES

While oral and intra-muscular non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in the treatment of arthritis pain, they are sometimes ineffective and associated with side effects. Intra-articular (IA) non-cyclooxygenase 2 (COX-2) selective NSAIDs usage namely ketolorac and piroxicam have been reported by us in treatment of inflammatory arthritis.[1,2] The use of IA COX-2 inhibitor Pareocoxib has only been reported in experimental animal setting.[3]

COX-2 is induced in chondrocytes when exposed to cytokines like interleukin 1B, and show increased prostaglandin E2 production. The production of excitatory amino acids (EAA) like glutamate and aspartate is also increased. Parecoxib, a water soluble prodrug of the oral formulation of valdecoxib, is approximately 20,000fold more potent against COX-2 than COX-1.(Figure 1) It is the first and only injectable COX-2 inhibitor available. It is rapidly metabolized into the active form, with peak plasma valdecoxib concentration occurring between 30min and 3.5 hour. Parecoxib reduced EAA, suppressed synovial inflammation, and inhibited cartilage degeneration.[3]

We are the first to report our experience in 60 Asian patients who were treated with IA parecoxib for the management of inflammatory arthritis.

METHODS

IA Parecoxib has been offered in our clinic for patients with inflammatory arthritis since April 2015. Those patients who received IA Parecoxib between April 2015 to December 2015 were identified. Their records were reviewed with reference to the arthritis diagnosis, treatment and response to therapy and follow-up. The data were collated and analyzed. Dosage was Pareocoxib 40mg per joint injected.

RESULTS

60 patients were reviewed. Age range: 27-84 years. Male - 20, Female - 40; Racial distribution: 47 Chinese, 3 Malay, 10 Indian. Diagnosis: Inflammatory Osteoarthritis (OA) 67% , Rheumatoid Arthritis (RA) - 13, Gouty Arthritis- 4, Reactive arthritis -1, Spondyloarthritis - 2 . 37 patients had previous treatment with steroids. 83.3% of patients had synovitis on ultrasound. Joints injected – 77 Knees; 5 Ankles; 1 Wrist and 1 Shoulder. Treatment summary: IA Pareocoxib 40mg was given in 37 joints and in 35 other injections, it was combined with steroids, viscosupplementation (VS), and/or methotrexate (MTX). (See Table 1) The VS used included Synvisc, Orthovisc, Healvis, and Arthromac. Response rate: 30% complete recovery; 70% improvement; 11 had recurrent joint inflammation. There was no adverse events or allergic reactions noted. Mean duration of response and follow-up ranged from 1 month to 9 months.

Table 1: Treatment summary: IA Pareocoxib either given alone or in combination

TREATMENT	NO OF INJECTIONS:
PAREOCOXIB ONLY	37
PAREOCOXIB + STEROIDS	8
PAREOCOXIB + VISCOSUPPLEMENTATION	23
PAREOCOXIB + STEROIDS + VISCOSUPPLEMENTATION	2

PATIENT EXAMPLE 1

RBD, a 37-year-old Malay man, who has a history of recurrent gouty knee arthritis since 2011. He had previous treatment with intra-articular steroids injections in 2014 every 2-3 months. In 2015, he had recurrent knee inflammation since Jan, for which IA prednisolone and IA brufencon were given in Jan and March. Uric Acid level was high at 11.3mg/dl despite febuxostat. He had persistent knee pain and required IA ketolorac 30mg and IA piroxicam 20mg injection. Ultrasound of Right knee showed effusion 3+ and synovitis 2+ and aspiration of 30 mls fluid done. IA piroxicam 20mg and betasol 1ml were given. He had left knee pain and swelling 1 week later and had similar knee aspiration and injection done.(Figure 2,3). 2 weeks later in May 2015, he had similar attacks of knee inflammation for which IA Pareocoxib 40mg were given to both knees. He had weekly IA Pareocoxib injections into both knees for 3 weeks until the knee synovitis and effusion subsided. For the 2nd half of the year, he required an additional 3 more injections for control of his gouty flares due to noncompliance and dietary indiscretion.

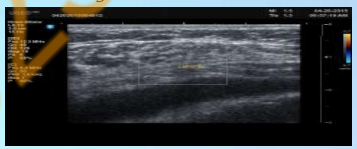

Figure 2: Ultrasound showing left knee effusion

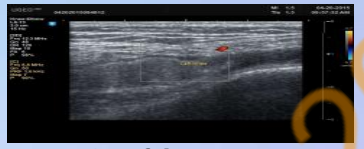

Figure 3: Left knee synovitis and tophi. DP+ve

PATIENT EXAMPLE 2

TAP, 70-year-old Chinese lady, with a long standing history of RA and Multi-joint OA, presented with recurrent left knee pain and swelling. She had Right TKA, and on IV Actemra for control of RA. She has a history of multiple drug allergies and intolerance, including vioxx, arcoxia, celebrex, voltaren, sulindac, anarex, and DMARDs like methotrexate, sulphasalazine, and mycophenolate. She had IA betamethasone injection to the right knee in 3/15 and had recurrent pain in 5/15. Ultrasound left knee (Fiqure 4) showed synovitis and effusion, for which she was given IA Pareocoxib 40mg and Arthromac 3% (Sodium hyaluronate).She did not have any adverse reaction to IA Pareocoxib and was well for 2 months.

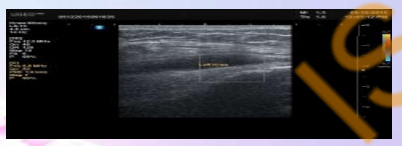

Figure 4: Ultrasound left knee showing synovitis and effusion.

PATIENT EXAMPLE 3

KP, a 63-year-old Indian male taxi-driver, with a history of inflammatory OA knees and gout, presented with bilateral knee pain and swelling in Jan'15. He had bilateral knee aspiration and IA Betamethasone into both knees followed by 2 serial IA hyaluronic acid injections into both knees 1 week apart. In April, he presented again with knee stiffness, and was noted to have left knee effusion (Figure 5). He had left knee aspiration followed by IA Pareocoxib 40mg into the left knee joint. On follow-up 9 months later, he was noted to be well and his left knee symptoms have improved by 85%.

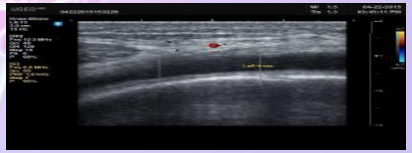

Figure 5 showing left knee effusion on ultrasound. DP+

CONCLUSIONS

IA Parecoxib is a useful and safe therapeutic modality for the treatment of inflammatory arthritis with over 90% response rate.

IA Pareocoxib can be recommended for use in the following settings:

1. Persistent or recurrent inflammatory joint pain despite IA steroid injection.
2. Those who are allergic or intolerant of oral NSAIDs.

INTRA-ARTICULAR PARECOXIB INJECTION FOR THE TREATMENT OF INFLAMMATORY ARTHRITIS FOLLOWING TOTAL KNEE ARTHROPLASTY A REPORT OF 8 ASIAN PATIENTS

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AIM:

Inflammatory arthritis following total arthroplasty (TKA) is not uncommonly encountered in clinical practice, and presents as a diagnostic and therapeutic challenge. While usage of intra-articular NSAIDs injection has been used by the authors in the treatment of inflammatory arthritis, it's usage in the clinical setting of post TKA has never been reported. The aim of this study is the make the first report of the therapeutic efficacy of intra-articular (IA) Parecoxib injection in the treatment of inflammatory arthritis following TKA in Asian patients. Parecoxib is a COX-2 selective NSAID available for parental usage, and it's use in the therapy of inflammatory arthritis is also presented in this conference.

METHODS:

All patients who presented to the clinic from April 2015 to January 2018 with post TKA inflammatory arthritis were reviewed and analysed with reference to the patients' demographics, clinical presentations, diagnoses and treatment outcomes. All patients had their diagnosis confirmed with ultrasound and diagnostic knee aspiration were done in an aseptic technique. All patients had IA Parecoxib 40mg injected into the knee joint for the treatment of the inflammatory arthritis, and follow-up review done.

RESULTS:

A total of 8 female patients were reviewed. Racial distribution: 4 Chinese, 2 Malay, 2 Indians. Age range: 63-86 years (Mean of 69 years). Background Diagnoses: Rheumatoid Arthritis (RA) – 4, Inflammatory Osteoarthritis (OA) – 4. Bilateral TKA – 3 patients; Right TKA – 4; Left TKA – 1.

Classification of Causes of Post TKA effusion	No. of Patients
IRA (Increased activity of RA)	3
NS (Nonspecific Synovitis)	4
DI (Deep Infection)	1

Duration of TKA : 1-10 years (Mean of 5.8 years). Mean duration of symptoms: 9 days (Range 2-30 days): All had knee pain, 7 had knee swelling, and 1 felt feverish. Ultrasound knee showed effusion and synovitis in all 8 patients. 4 had +ve Power Doppler signals. 1 patient had MRI knee which showed synovitis and effusion. Knee Fluid analysis showed leukocytes and erythrocytes in all patients. 2 had uric acid crystals. 1 had Gram-ve Bacilli, and fluid culture grew E. Coli.

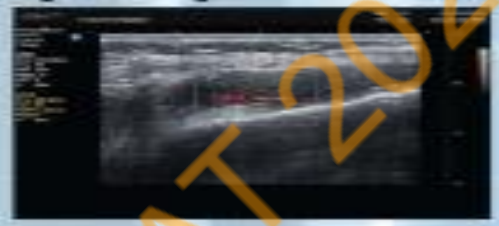
All 8 patients responded to IA Parecoxib with reduction in pain and swelling. 7 had 1 knee injected and 1 had both knees injected. The knee with DI had 4 injections of Parecoxib over 3 weeks.

Duration of follow-up and benefit ranged from 2 weeks to 5 months. No adverse effects were encountered.

PATIENT EXAMPLE 1:

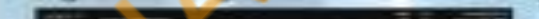
Mdm R, a 72-year-old Indian lady with RA and OA knee, had left TKR in Dec'14. In Nov'15, she presented with 1 month history of left knee pain. Ultrasound showed Effusion 3+, Synovitis 2+, Power Doppler +ve. (Figure1 and 2)

Fig. 1 showing knee effusion



Left Knee Aspiration was done aseptic technique and 20mls of yellow fluid was removed. Joint Fluid FEME: RBC 80-85 HPF; WBC2-3HPF; Micro-organisms – Nil. IA Parecoxib 40mg was given without any complications.

Fig. 2 showing synovitis



Diagnosis: IRA. She was reviewed a

PATIENT EXAMPLE 2:

Mdm AL, a 66-year-old Chinese with multi-joint OA and RA, had right TKR in 2005. She was feverish and had right knee pain and swelling for 1 week's duration. She had right knee effusion. Ultrasound showed Effusion3+, Synovitis 2+ and +ve Power Doppler. (Figure 5,6) Aseptic knee aspirate showed 8mls of yellowish pus. IA Parecoxib 40mg was given together with IA Ceftriaxone 500mg and Gentamicin 80mg. Knee Fluid FEME showed pus cells 3+, Gram-ve Bacilli. Fluid C/S was E Coli, sensitive to Ceftriaxone and Gentamicin. Diagnosis: DI. She was reviewed on the 3rd day and was given a 2nd course of IA Parecoxib 40mg and Ceftriaxone 1g. A repeat knee aspirate showed C/S negativity! And she improved with reduction of the knee pain and swelling. She was given IA Parecoxib 40mg weekly into her right knee for another 2 weeks, with almost complete resolution of her knee pain. The patient being adamant on only outpatient therapy was treated with IV and oral antibiotics for 4 weeks. The CRP reduced from 71.5 mg/L to 14 mg/L.

World Journal of Clinical Cases

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World J Clin Cases 2019 December 6; 7(23): 3971-3979

DOI: 10.12998/wjcc.v7.i23.3971

ISSN 2307-8960 (online)

ORIGINAL ARTICLE

Observational Study

Comparison of intra-articular injection of parecoxib *vs* oral administration of celecoxib for the clinical efficacy in the treatment of early knee osteoarthritis

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Author contributions: Lu L and Huang XW contributed to study

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of the institutional database was performed for International Classification of Diseases Ninth Revision

Table 4 Comparison of inflammatory cytokine levels in the synovial fluid in the three groups before and after treatment

Group	Case	IL-6 (pg/mL)		TNF-α (pg/mL)		IL-10 (pg/mL)	
		Before	After	Before	After	Before	After
Group A	37	418.7 ± 27.8	384.1 ± 25.0[b]	3.66 ± 0.38	3.03 ± 0.28[b]	5.47 ± 0.32	6.04 ± 0.49[b]
Group B	37	415.7 ± 28.2	212.6 ± 23.4[b]	3.53 ± 0.47	2.07 ± 0.33[b]	5.52 ± 0.30	7.46 ± 0.44[b]
Group C	36	412.7 ± 37.1	137.8 ± 29.0[b]	3.56 ± 0.53	1.45 ± 0.26[b]	5.42 ± 0.43	8.72 ± 0.60[b]
F value		0.34	871.17	0.70	275.41	0.87	246.74
P value		0.715	< 0.001	0.497	< 0.001	0.422	< 0.001

[b]Comparison of interleukin-6, Tumor necrosis factor-α and interleukin-10 levels for each group before and after treatment, significant differences were found ($P < 0.001$). Data are presented as mean ± SD of pg/mL. IL-6: Interleukin-6; TNF-α: Tumor necrosis factor-α; IL-10: Interleukin-10.

ARTICLE HIGHLIGHTS

Research background

Oral non-steroid anti-inflammatory drugs (NSAIDs) are often used for the treatment of osteoarthritis. However, in elderly people, oral NSAIDs have certain side-effects especially in the incidence of adverse gastrointestinal reactions and cardiovascular risk. Meanwhile, the compliance with long-term use of NSAIDs is low in early osteoarthritis.

EVIDENCE-BASED PRACTICE

HELPDESK ANSWERS

Are intra-articular NSAID injections as effective as intra-articular corticosteroid injections for the treatment of knee osteoarthritis?

Place, Chris MD; Tischler, Ryan DO

Author Information

Evidence-Based Practice 22(10):p 14-15, October 2019. | *DOI:* 10.1097/EBP.0000000000000296

Open Access

Original Article

Intra-Articular Injection of Methyl Prednisolone With Ketorolac

Pak Armed Forces Med J 2021; 71 (3): 819-22

COMPARISON OF INTRA-ARTICULAR METHYLPREDNISOLONE AND KETOROLAC INJECTIONS IN IMPROVING RANGE OF MOTION FOR DIFFERENT SHOULDER JOINT DISORDERS

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Combined Military Hospital Mangla/National University of Medical Sciences (NUMS) Pakistan, *Combined Military Hospital Jhelum/National University of Medical Sciences (NUMS) Pakistan, **Combined Military Hospital Quetta/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To compare the efficacy of intra-articular injection of methyl prednisolone with ketorolac for improvement in range of motion in various shoulder joint disorders.

Study Design: Quasi-experimental study.

Place and Duration of Study: Departments of Internal and Rehabilitation Medicine, Combined Military Hospital Mangla, from Nov 2018 to May 2019.

Methodology: Through non-probability consecutive sampling, patients with shoulder disorders were enrolled in the study and divided into two groups. Group A received intra articular corticosteroid injection and group B received intra-articular Ketorolac injection. Outcome was measured in terms of improvement in shoulder range of motion.

Results: A total of 60 patients were selected, 40 (66.7%) male and 20 (33.3%) female. 30 (50%) patients had adhesive capsulitis, 24 (40%) had rotator cuff syndrome and 6 (10%) had impingement syndrome. 24 patients received methyl prednisolone acetate injection while 36 received ketorolac injection. There was no significant difference in the mean gain in flexion, extension, abduction, internal or external rotation between both groups (p=0.224, p=0.261, p=0.884, p=0.238, and p=0.584 respectively).

Conclusion: There was no significant difference in efficacy of corticosteroid and ketorolac when injected intra-articularly in shoulder joint disorders.

Keywords: Intraarticular injections, Methylprednisolone, Ketorolac, Shoulder joint.

INTRODUCTION

Shoulder joint has unique dynamics. This function is attributed to its ball and socket nature. Tasks such as prehensile function of hand, reach, and exploration of surroundings are basic for survival. The extensive ranges of motion of shoulder joint enable these

luding various metabolic/endocrine disorders e.g. diabetes mellitus, neurologic disorders e.g. stroke, cardiac diseases, heart surgery, and malignancy[1,2].

Shoulder joint disorders are the thirdcommonest kind of musculoskeletal disorders. The incidence of shoulder pain reporting in primary care per year is

THE JOURNAL OF ARTHROPLASTY
AAHKS AMERICAN ASSOCIATION OF HIP AND KNEE SURGEONS

JOINT PRESERVATION | VOLUME 36, ISSUE 2, P416-422, FEBRUARY 2021

Intra-articular Injections of the Hip and Knee With Triamcinolone vs Ketorolac: A Randomized Controlled Trial

Kevin Jurgensmeier, BS • Darin Jurgensmeier MD • Derek E. Kunz, MD • Peter G. Fuerst, PhD • Lucian C. Warth, MD • Steven B. Daines, MD

Published: August 21, 2020 • DOI: https://doi.org/10.1016/j.arth.2020.08.036 •

Abstract

Background

Clinicians commonly utilize intra-articular injections to treat symptomatic primary arthritis. Steroid injections are common yet have immune-modulating effects and can alter gene expression

Original Research

Effect of Intra-articular Ketorolac Versus Corticosteroid Injection for Knee Osteoarthritis

A Retrospective Comparative Study

Jianda Xu,* MD, PhD, Yuxing Qu,*† MD, PhD, Huan Li,†‡ MS, Aixiang Zhu,§ MS, Tao Jiang,* MD, PhD, Zheng Chong,* MD, PhD, Bin Wang,* MD, PhD, Pengfei Shen,* MD, PhD, and Zikang Xie,* MD, PhD

Investigation performed at Changzhou Traditional Chinese Medical Hospital, Nanjing University of Traditional Chinese Medicine, Changzhou, China

Background: Intra-articular corticosteroid injections have been widely used and are considered a mainstay in the nonoperative treatment of symptomatic knee osteoarthritis (OA). However, their increased use can have negative implications, including chondral toxicity and a high risk of infections. As a result, nonsteroidal anti-inflammatory drugs have been considered as an alternative.

Purpose: To determine the pain relief and safety of ketorolac versus a corticosteroid to supplement an intra-articular sodium hyaluronate injection for the treatment of symptomatic knee OA.

Study Design: Cohort study; Level of evidence, 3.

Methods: A total of 84 patients with unilateral symptomatic knee OA receiving 5 weekly injections were enrolled in this retrospective study. Group A (n = 42) received 3 weekly intra-articular corticosteroid injections (0.5% lidocaine, 25 mg of triamcinolone acetonide, and 25 mg of sodium hyaluronate, followed by 2 weekly injections of 0.5% lidocaine and 25 mg of sodium hyaluronate) using Kellgren–Lawrence grading. Visual analog scale (VAS) was the primary outcome measure. A query

The Journal of Arthroplasty 31 (2016) S293–S297

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Allied Health

Economic Impact of Ketorolac vs Corticosteroid Intra-Articular Knee Injections for Osteoarthritis: A Randomized, Double-Blind, Prospective Study

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ARTICLE INFO

Article history:
Received 1 December 2015
Received in revised form
4 May 2016
Accepted 6 May 2016
Available online 18 May 2016

ABSTRACT

Background: Knee osteoarthritis is a disabling disease that costs billions of dollars to treat. Corticosteroid gives varying pain relief and costs $12 per injection, whereas ketorolac costs $2 per injection, per institutional costs. The aim of this study was to compare ketorolac with corticosteroid based on pain relief using patient outcome measures and cost data.

Methods: A total of 35 patients were randomized to ketorolac or corticosteroid intra-articular knee injection in a double-blind, prospective study. Follow-up was 24 weeks. Osteoarthritis was evaluated using Kellgren–Lawrence grading. Visual analog scale (VAS) was the primary outcome measure. A query

Patient Presentation of the Efficacy of IA Pareocoxib For Recurrent Knee Inflammation due to Gouty Arthritis

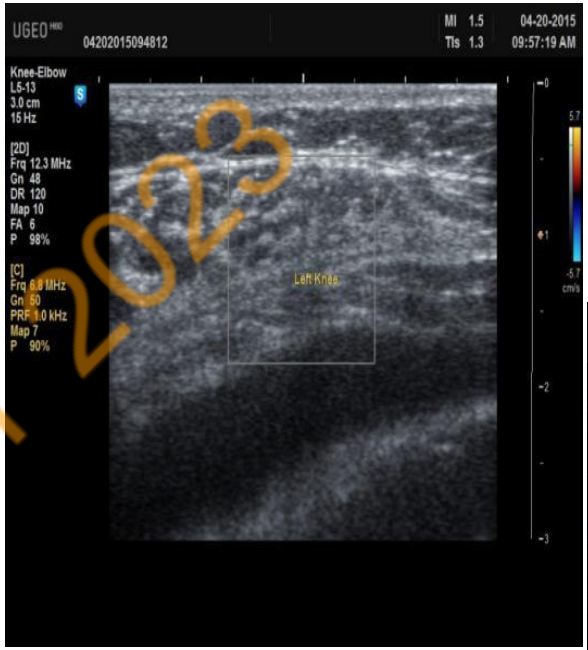
- RBD, a 37-year-old Malay man, who has a history of recurrent gouty knee arthritis since 2011.
- He had previous treatment with intra-articular steroids injections in 2014 every 2-3 months, due to gouty flares from non-compliance.
- In 2015, he had recurrent knee inflammation since Jan, for which IA prednisolone and IA betamethasone were given in Jan and March. Uric Acid level was high at 11.3mg/dl despite febuxostat.

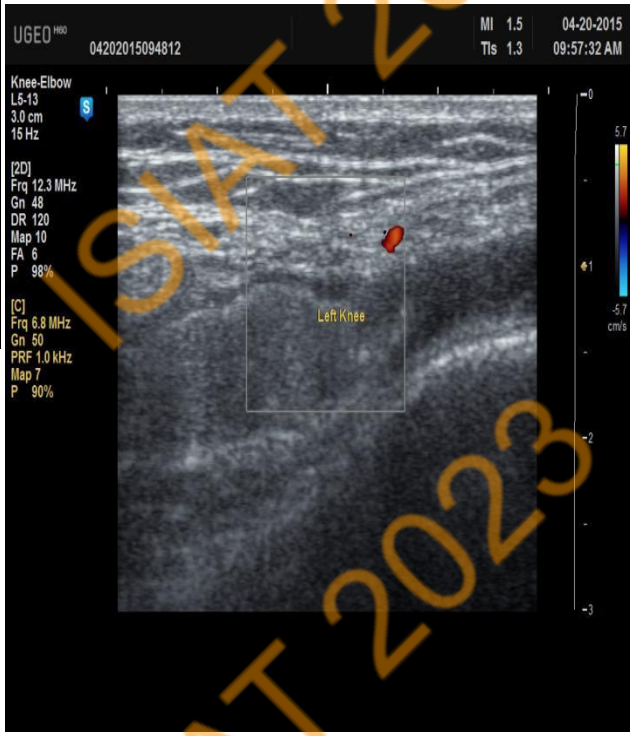
Efficacy of IA Pareocoxib For Recurrent Knee Inflammation due to Gouty Arthritis

- He had persistent bilateral knee pain and required IA ketolorac 30mg and IA piroxicam 20mg injection.
- Few weeks later, he had recurrent knee inflammation.
- Ultrasound of Right knee showed effusion 3+ and synovitis 2+ and aspiration of 30 mls fluid done.
- IA piroxicam 20mg + betamethasone 1ml combination IAT were given with resolution.
- He had left knee pain and swelling 1 week later and had similar knee aspiration and injection done.

Efficacy of IA Pareocoxib For Recurrent Knee Inflammation due to Inflammatory Arthritis

- 2 weeks later in May 2015, he had similar attacks of knee inflammation for which IA Pareocoxib 40mg were given to both knees.
- He had weekly IA Pareocoxib 40mg injections into both knees for 3 weeks until the knee synovitis and effusion subsided. He was well for the next few mths.





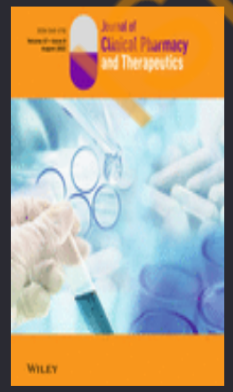
SUCCESSFUL USAGE OF IA NSAID IN PATIENTS WHO ARE ALLERGIC TO ORAL NSAIDs

- ESM,67/CHINESE/MAN WITH H/O OF GOUT AND OA KNEE.
- **ALLERGIC TO ORPHENARINE, NAPROXEN, DICLOFENAC K(CATAFLAM) WITH PERIORBITAL EDEMA**
- 6/3/23 PRESENTED WITH SEVERE LEFT KNEE PAIN AND SWELLING FOR 3 DAYS AFTER A URTI.
- KNEE ASPIRATION DONE AND **IAT WITH TRIAMCINOLONE 40MG + PAREOCOXIB 40MG + TRAMADOL 25MG**.
- FLUID +VE FOR MSU CRYSTALS
- NO REACTION TO IA PAREOCOXIB (DYNASTAT)
- 1 WEEK LATER, FULL RESOLUTION OF INFLAMMATORY ARTHRITIS

SUCCESSFUL USAGE OF IA NSAID IN PATIENTS WHO ARE ALLERGIC TO ORAL NSAIDs

- **8/9/23** PRESENTED WITH SUDDEN ONSET OF LEFT KNEE PAIN AND EFFUSION.
- KNEE ASPIRATION DONE AND **IAT WITH TRIAMCINOLONE 40MG + PAREOCOXIB 40MG + TRAMADOL 25MG**.
- RESPONDED WELL AND HAD NO REACTION TO IA PAREOCOXIB (DYNASTAT). FLUID TEST –VE FOR MSU CRYSTALS
- **25/9/23** PRESENTED WITH RECURRENT LEFT KNEE EFFUSION FOR 3 DAYS AFTER A MINOR TWIST FOLLOWING EXERCISE.
- KNEE ASPIRATION DONE AND **IAT DYNASTAT 40MG + CONJURAN POLYNUCLEOTIDE 2ML GIVEN WITH FULL RECOVERY.**

Details



Journal of Clinical Pharmacy and Therapeutics
Volume 47, Issue 8
Aug 2022
Pages i-iv, 1091-1298

ARTICLE

Pharmacokinetics, safety and efficacy of intra-articular non-steroidal anti-inflammatory drug injections for the treatment of osteoarthritis: A narrative review

View article page

Daniel J. Selig, Adrian T. Kress, Isaiah M. Horton, Jeffrey R. Livezey, Eliot J. Sadik, Jesse P. DeLuca

CITE | Check for updates

Received: 24 March 2022 | Accepted: 31 March 2022
DOI: 10.1111/jcpt.13669

REVIEW ARTICLE

Journal of Clinical Pharmacy and Therapeutics
WILEY

Pharmacokinetics, safety and efficacy of intra-articular non-steroidal anti-inflammatory drug injections for the treatment of osteoarthritis: A narrative review

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Abstract

What is known and Objective: Osteoarthritis (OA) is a common cause of joint disease and activity limitation in adults. Common therapies to treat OA-related pain are oral and topical non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articular (IA) corticosteroids. However, prolonged courses of oral NSAIDs are associated with systemic adverse effects and repeat IA corticosteroid injections may cause cartilage degeneration. IA NSAIDs may be an alternative therapy possibly minimizing systemic side effects while maintaining efficacy. Therefore, we sought to summarize the pharmacokinetics, safety and efficacy of IA NSAIDs to help providers make a more informed decision on the use of IA NSAIDs.

Methods: We searched the National Library of Medicine Database with terms "intraarticular and nsaid", yielding 1032 results. Only traditional formulations of NSAIDs were considered for inclusion. Animal studies were included if animals were healthy or if the method of arthritis induction was a reasonable model of osteoarthritis. Human studies were included if humans were healthy or if the primary disease studied was osteoarthritis of a large joint. Of 1032 results, 31 research articles met the inclusion criteria and were summarized in this review.

Results and Discussion: We found that single doses of IA NSAIDs provided far less total systemic and synovial exposure compared to a one week course of oral NSAIDs,

Intra-Articular NSAIDs Might Be Future OA Treatment

by U.S. Medicine | Dec 12, 2022

BETHESDA, MD — Are intra-articular non-steroidal anti-inflammatory drugs a viable option for treatment of osteoarthritis in adults?

A new study from Walter Reed National Military Medical Center, the Uniformed Services University of the Health Sciences, both in Bethesda, MD, and Georgetown University School of Medicine in Washington, DC, sought to answer that question.

"Osteoarthritis (OA) is a common cause of joint disease and activity limitation in adults. Common therapies to treat OA-related pain are oral and topical non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articular (IA) corticosteroids," according to the article in The Journal of Clinical Pharmacy and Therapeutics. "However, prolonged courses of oral NSAIDs are associated with systemic adverse effects and repeat IA corticosteroid injections may cause cartilage degeneration. IA NSAIDs may be an alternative

WHY INTRA-ARTICULAR NSAIDs THERAPY?

- BEING A PATIENT-ORIENTED AND SOLUTION-OREIENTED PHYSICIAN AND RHEUMATOLOGIST…I ASKED MYSELF THIS QUESTION

"IN THOSE CLINICAL SCENERIOS, CAN IA NSAIDs BE AN ALTERNATIVE INTRA-ARTICULAR THERAPY???"

The answer is

CONCLUSIONS

- IA NSAIDs have a definitive role in the treatment of inflammatory arthritis, and represents an additional armamentarium available to IA therapist taking care of patients with **severe and recurrent joint inflammation.**
- **It's use can be administered in those who are unable to take steroid injections, or refuse steroids, or allergic or intolerant to oral NSAIDs.**
- IA NSAIDs can be combined with IAHA with synergistic effect
- IA NSAIDs can be used in the **post-arthroscopic setting** and **post-knee arthroplasty synovitis** with good results.
- I propose that IA NSAIDs can be used as a first or second line IA anti-inflammatory agent for the effective treatment of the painful, inflamed joints.