

Intra-Articular Corticosteroid Injections to the Temporomandibular Joints Are Safe and Appear to Be Effective Therapy in Children With Juvenile Idiopathic Arthritis

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Purpose: The purpose of this study was to evaluate the safety and efficacy of intra-articular corticosteroid injections (IACIs) of the temporomandibular joint (TMJ) in children with juvenile idiopathic arthritis (JIA) when administered by an oral and maxillofacial surgeon without imaging guidance.

Materials and Methods: This was a retrospective study of children with JIA, seen at a single center, who were selected based on having received IACIs of the TMJ. All subjects received the intervention, which consisted of referral to a single oral and maxillofacial surgeon for TMJ IACI with 5 to 10 mg triamcinolone hexacetonide, under general anesthesia. Primary outcomes assessed in all subjects were the safety of the procedure and efficacy as determined by the change in maximal incisal opening (MIO). In addition, a subset of 31 subjects underwent repeat magnetic resonance imaging of the TMJ, permitting analysis of the change in the acute and chronic findings of arthritis in those patients.

Results: Sixty-three patients (68% female) received 137 IACIs. The mean age for diagnosis of JIA was 8.5 years, and the mean age at presentation for TMJ injections was 10 years. The injections were well tolerated: only 1 patient developed the steroid complication of hypopigmentation, and none developed degeneration or ankylosis. In terms of efficacy, the mean MIO increased from 40.8 ± 0.93 to 43.5 ± 0.90 mm ($P = .001$); in addition, changing the unit of analysis to individual joints, in patients who underwent repeat magnetic resonance imaging examination, 51% of TMJs showed magnetic resonance imaging evidence of improvement of arthritic changes, of whom 18% had complete resolution of TMJ arthritis.

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Conclusions: The results indicate that IACI of the TMJ can be safely performed by experienced oral and maxillofacial surgeons without a requirement for computed tomographic guidance. In addition, these results show that IACI may be effective in the management of TMJ arthritis, although further studies are required.

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Juvenile idiopathic arthritis (JIA) is a chronic rheumatologic disease of children that is characterized by inflammatory synovitis and affects approximately 1 in 1,000 children worldwide.¹ Although involvement of the temporomandibular joint (TMJ) in JIA has been recognized for more than 100 years,² TMJ arthritis is one of the most clinically underappreciated joints because of the paucity of suggestive historical or clinical findings.³ Magnetic resonance imaging (MRI) studies have indicated prevalence rates ranging from 63% to 75%, with the vast majority of patients being asymptomatic.^{4,5} The standard orthopantomogram displays only late changes, and even ultrasound lacks sensitivity for the evaluation of active TMJ arthritis,⁵ whereas MRI with gadolinium contrast and surface coils detects early findings (before bony changes) of inflammation, such as marrow edema, inflammation (enhancement) of the synovium, and joint effusions. Therefore, MRI with contrast is considered the gold standard for diagnosis.⁶

The treatment of TMJ arthritis is controversial. Traditional and more recently developed biologic disease-modifying antirheumatic drugs are often highly effective in the management of JIA in general, but there are minimal data on their specific efficacy in TMJ arthritis in children. The authors previously reported on children receiving systemic immunosuppressive therapy who also required local therapy.⁷ Thus, many practitioners use intra-articular corticosteroid injections (IACIs) of the TMJ. Although the IACI has long been recognized to be safe and effective therapy for more accessible joints,⁸ reports of TMJ bony ankylosis in adults after IACI have led to concerns over the safety of this procedure in children.⁹ In addition, studies in rabbits have reported decreased mandibular growth after IACI of the TMJ.⁶ Nevertheless, several prior studies that have been published in the rheumatology literature have reported the procedure to be safe and effective, with the latter established by the symptomatic relief and improvement in maximal incisal opening (MIO).^{7,10-13} Most of these studies, however, used imaging guidance, which requires prolonged anesthesia and, for computed tomography (CT)-guided injections, exposure to high levels of radiation. One report described IACI of the TMJ in 25 children with JIA as performed by an oral and maxillofacial surgeon (OMS) using general anes-

thesia.¹¹ There are no published guidelines on the management of TMJ arthritis.

At the authors' center, IACIs of the TMJ are performed by an experienced OMS under monitored anesthesia care (MAC), obviating prolonged anesthesia or exposure to radiation. The safety and efficacy of TMJ IACI performed in this manner has yet to be reported. This study tested the hypothesis that IACI of the TMJ performed by an experienced OMS under MAC is safe and effective in the management of JIA. This report describes the results obtained at the authors' center.

Materials and Methods

STUDY DESIGN/SAMPLE

This was a retrospective study of children with JIA, followed at a single center (Children's Hospital of Alabama), who were selected based on having been referred for IACI of the TMJ on at least 1 occasion. Inclusion criteria were the diagnosis of JIA by a pediatric rheumatologist according to validated criteria,¹⁴ identification of TMJ arthritis based on clinical or MRI findings, and referral to an OMS for IACI. The exclusion criterion was a diagnosis other than JIA (eg, systemic lupus erythematosus). All IACIs took place from November 2007 through May 2010. Institutional review board approval was obtained for this study.

INTRA-ARTICULAR CORTICOSTEROID INJECTIONS

All TMJ IACIs were performed by the same experienced OMS (P.D.W.) at the University of Alabama Hospital (Birmingham, AL). All patients were injected under MAC in an outpatient operating room. Triamcinolone hexacetonide (TH) 20 mg/mL (Lek Pharmaceuticals, Inc, Wilmington, NC) was diluted by an equal volume of 1% lidocaine HCl (Xylocaine; AstraZeneca, Wilmington, DE) with 1:100,000 epinephrine, creating TH 10 mg/mL. One or both TMJs were prepped with alcohol gauze, entered with a 23-gauge needle, and injected with 0.5 to 1.0 mL of the diluted TH into the superior joint space, constituting TH 5 to 10 mg. Confirmation of entering into the joint space was noted by translation of the mandible upon injection, without image guidance.

MRI OF THE TMJ

MRIs were performed as described previously.¹² Briefly, using a head coil with the patient's mouth

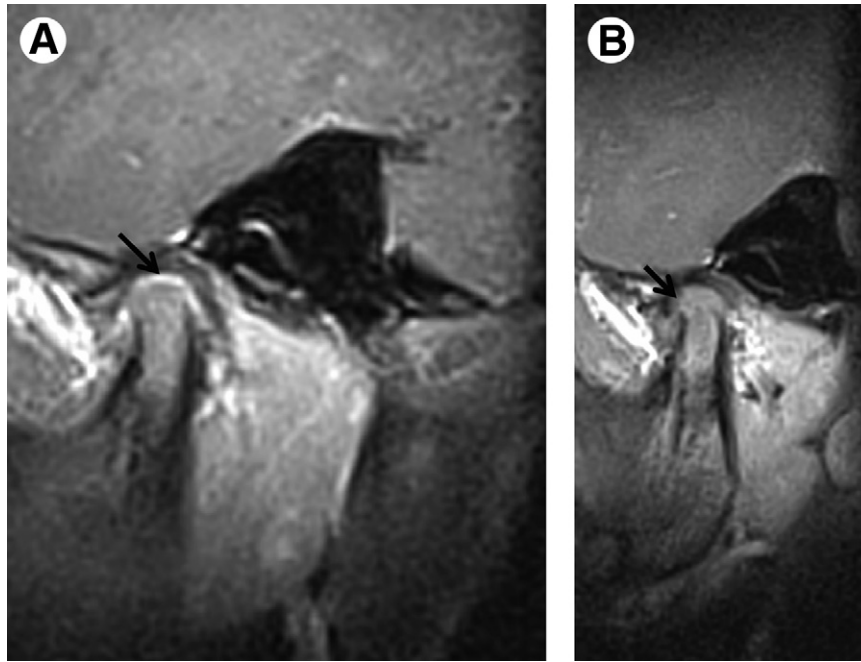


FIGURE 1. T1-weighted fat-saturated sagittal images after gadolinium administration display synovial enhancement (arrow) in the left temporomandibular joint *A*, before intra-articular corticosteroid injection and *B*, resolution after intra-articular corticosteroid injection. *B*, An erosion of the condylar head is present (arrow).

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closed, 2- to 3-mm thick sagittal and coronal T1-weighted and fat-saturated T2-weighted images were obtained, followed by the administration of gadolinium contrast and additional T1-weighted fat-saturated sagittal and coronal images. Acute changes were defined as joint fluid or synovial enhancement, and chronic changes were defined as erosive changes, condylar flattening, or disc displacement (Fig 1). Assessment of whether the MRI was overall improved or worsened was made by the chart reviewers (M.L.S., T.S.) based on the written report.

DATA COLLECTION

Because all patients received IACIs, the primary predictor variable was time. The primary outcome variables were safety of the IACI as assessed by the chart review and efficacy as assessed by measurement of the MIO. In addition, in a subset of patients, follow-up MR images of the TMJ permitted a comparison of MR images before and after IACI. A retrospective chart review was performed that collected demographic information, medication use, MIO before and after IACI, MRI of the TMJ results, and complications of the procedure. MIO was measured by the Therabite Measuring Scale (Atos Medical, West Allis, WI).

DATA ANALYSIS

Descriptive variables were recorded as mean \pm standard deviation. Comparison of MIO values before

and after IACI was performed by a paired *t* test. All analyses were conducted with SPSS 17 (SPSS, Inc, Chicago, IL).

Results

PATIENT POPULATION

Sixty-three patients were included in this study. Their clinical and demographic information is presented in Table 1. Sixty patients (95%) underwent bilateral TMJ IACIs initially, whereas the other 3 patients (5%) had only unilateral injections. Eight patients (13%) underwent reinjection once, and 6 of these injections were bilateral. One hundred thirty-seven injections were performed (60 bilateral injections, 3 unilateral injections, 6 bilateral reinjections, and 2 unilateral reinjections).

SAFETY

This procedure was well tolerated. All patients tolerated the anesthesia, and there were no serious adverse events from the IACI, such as infection, chondrolysis, or ankylosis. Only 3 patients reported postinjection complications, all of which were minor. These consisted of localized swelling 2 days postoperatively in 1 patient, fever 2 weeks postoperatively in another, and 1 instance of skin hypopigmentation at the site of injection noted 10 months after IACI in a third patient.

Table 1. PATIENT CHARACTERISTICS

Age at diagnosis of JIA (yrs), mean \pm SD	8.5 \pm 4.2
Age at diagnosis of TMJ arthritis (yrs), mean \pm SD	9.5 \pm 4.2
Gender, n (%)	
Female	43 (68%)
Male	20 (32%)
Race/ethnicity, n (%)	
Caucasian	54 (86%)
Latino	1 (1.6%)
African-American	8 (13%)
Medicines, n (%)	
None or NSAIDs alone	5 (7.9%)
CSs alone	2 (3.2%)
Conventional DMARDs alone \pm CSs	10 (16%)
Biologic DMARDs alone \pm CSs	5 (7.9%)
Conventional and biologic DMARDs \pm CSs	41 (65%)
MRI findings at baseline, n (%)*	
Normal bilaterally	3 (4.9%)
Acute synovitis only	41 (67%)
Acute and chronic synovitis	16 (26%)
Chronic synovitis only	1 (1.6%)

Abbreviations: CSs, corticosteroids; DMARDs, disease-modifying antirheumatic drugs; JIA, juvenile idiopathic arthritis; NSAIDs, nonsteroidal anti-inflammatory drugs; MRI, magnetic resonance imaging; SD, standard deviation; TMJ, temporomandibular joint.

*Only 61 patients underwent baseline MRI.

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MAXIMAL INCISAL OPENING

Paired pre- and postoperative MIO values were available in 55 patients (Fig 2). Twenty-one patients (34%) presented with a preinjection MIO smaller than 40 mm, which is considered smaller than normal.¹⁵ After injection, this number decreased to 15 patients (27%). The mean preinjection MIO was 40.8 \pm 0.93 compared with 43.5 \pm 0.90 mm after IACI ($P = .001$). Overall, 36 patients (66%) presented an improvement, 15 (27%) showed worsening, and 4 (7.3%) recorded no change.

MRI FINDINGS

Before the procedure, 61 patients underwent MRI of the TMJ; of the other 2, 1 had braces and the other required a pacemaker, so they underwent CT. Of the 122 TMJs imaged by MRI, 100 (82%) of 122 TMJs were found to have evidence of arthritis on the initial MR image. Among the 100 TMJs found to have evidence of arthritis, 80 (80%) had evidence of acute arthritis (joint fluid, synovial enhancement) without chronic changes, 18 (18%) had acute and chronic changes (joint erosions, condylar flattening, disc displacement; Fig 1), and 2 (2%) had only chronic changes. Three of the 4 TMJs evaluated by CT showed evidence of chronic changes; acute arthritis cannot be visualized by CT. Nineteen of the 22 TMJs without

evidence of arthritis on MRI or CT were injected based on patient history and physical examination indicating signs and symptoms of TMJ arthritis. The remaining 3 TMJs were never injected.

Thirty-one patients underwent repeat MRI after a mean interval of 5.3 \pm 5.1 months after injection (range, 0.5 to 23 mo). Within this population of 31 patients, 47 of the 62 TMJs originally showed evidence of acute TMJ arthritis on the preinjection MR image. Of the 15 individual joints that were normal at baseline, all continued to be normal at follow-up. Of the other 47 TMJs, 24 (51%) showed evidence of improvement of arthritic changes, 9 (18%) of which showed complete resolution of acute arthritic changes; 15 (32%) showed evidence of worsening arthritic changes, including new-onset erosions or condylar flattening in 7 (14%); and 8 TMJs (16%) were unchanged. An illustrative example of improvement is shown in Figure 1.

MIO Before and After IACI

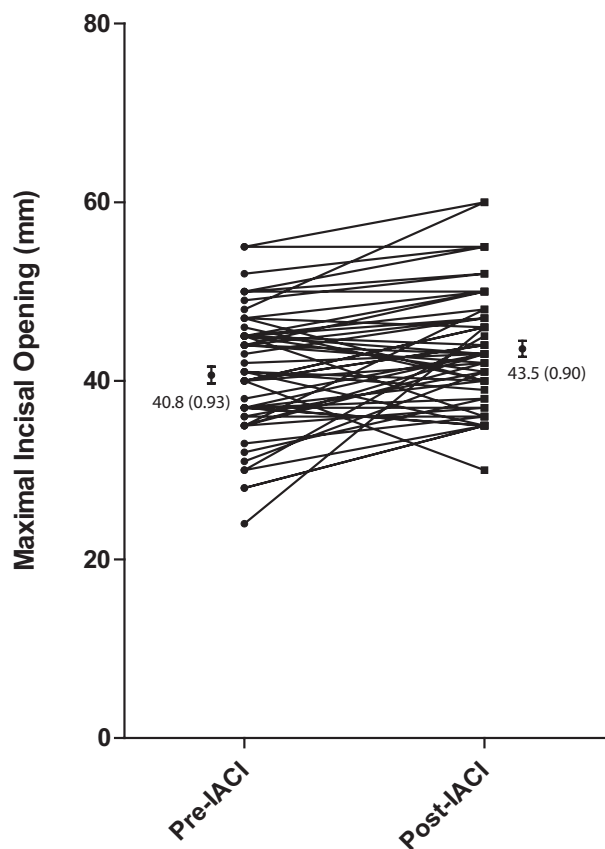


FIGURE 2. Measurements of maximal incisal opening (MIO) in 55 children with juvenile idiopathic arthritis and temporomandibular joint arthritis before and after intra-articular corticosteroid injection (IACI). Numbers represent the maximal incisal opening (standard error of the mean) in centimeters.

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Discussion

The purpose of this study was to evaluate the safety and efficacy of IACI of the TMJ in children with JIA when performed by an experienced OMS using MAC in the absence of imaging guidance. To that end, 63 children with JIA who underwent 137 IACIs were studied. The IACIs were well tolerated, with no serious adverse events and only 3 minor adverse events reported. Overall, the IACIs also appeared to be effective. The MIO increased postoperatively from a mean of 40.8 ± 6.9 to 43.5 ± 6.6 mm ($P \leq .001$); in addition, in the 31 subjects who underwent repeat MRI, 51% of the TMJs showed improved findings, 18% of whom resolved completely, although 32% showed worsening.

The present findings confirm previous reports that IACI of the TMJ can be safely performed in children with JIA^{10-13,16}; moreover, this is the first study to report that the procedure can be performed with MAC in the absence of imaging guidance. This is important for 2 reasons. The first is that the use of imaging guidance and/or general anesthesia prolongs the procedure, thus entailing additional risks. Second, this procedure avoids use of ionizing radiation, the long-term risks of which in pediatric subjects have yet to be fully explored.^{17,18} There were no reports of chondrolysis or ankylosis, as previously reported in adults⁹; the reasons for the safety differences in pediatric and adult subjects are not clear. In addition, there were no reports of decreased mandibular growth, as has been observed in rabbits treated with IACI of the TMJ.¹⁹ The improved safety profile in children compared with laboratory animals illustrates that animal data cannot always be extrapolated to humans, as previously reported in the context of cartilage injury caused by fluoroquinolones.^{20,21}

The present efficacy data also confirm those reported in prior smaller studies, including findings of improvement in TMJ arthritis evidenced by MRI in 48% to 73% and MIO increases ranging from 5 to 7 mm.^{7,11,12} Nevertheless, findings of imaging evidence of improvement in only 51%, with complete resolution in only 18%, may appear disappointing. In fairness, unchanged findings may be considered successful treatment, because conditions such as JIA are normally characterized by an uninhibited progression of arthritic damages.²² In addition, there was a statistically significant increase in the MIO of 2.7 mm, with 66% of patients showing an increase. However, there is clearly room for improvement, and it is unclear whether the increase in the MIO, although statistically significant, is also clinically significant.

The major limitation of this study is the absence of a control group. There are no randomized trials eval-

uating the efficacy of IACI of the TMJ, and in light of the reported benefits of IACIs of other joints⁸ and the potential consequences of untreated inflammation of the TMJ, the authors believe that it would be unethical to withhold therapy. Although the absence of a control group does not cloud the interpretation of the safety data, it does complicate the analysis of efficacy. It could be argued that some of the improvement reported in the present study was due to systemic immunosuppressive therapy, because 90% were on conventional and/or biologic disease-modifying antirheumatic drugs (Table 1). Importantly, the presence of TMJ arthritis despite the use of immunosuppressive therapy at baseline in most cases suggests that this joint may be somewhat refractory to therapy. Other limitations are that the evaluators were not blinded to therapy and that repeat MRI was performed in only 31% of subjects; although the authors wanted to obtain repeat MR images in all subjects, factors beyond their control (scheduling concerns, cost, and perceived risks of sedation or contrast) limited this to 31. Important strengths of the study are that this is one of the largest of its kind ever published and the first to describe the use of IACI of the TMJ under MAC and in the absence of imaging guidance.

In summary, the present study showed that IACI of the TMJ performed by an experienced OMS in the absence of imaging guidance can be safely performed in children with JIA; the procedure also appears to be effective in at least a subset of patients. Future studies may be performed to evaluate different dosages of TH or even different medications, such as intra-articular infliximab.²³ It will also be of benefit to evaluate the outcomes of children diagnosed and treated early in the course of the disease. Long-term data on patient outcomes of importance should be evaluated, because even a partial response may result in important functional benefits.

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