

Benefit of Intraarticular Corticosteroid Injection Under Fluoroscopic Guidance for Subtalar Arthritis in Juvenile Idiopathic Arthritis

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ABSTRACT. *Objective.* To determine the demographics of subtalar arthritis, the response to intraarticular corticosteroid injection, and the injection complication rate in a clinic sample of children with juvenile idiopathic arthritis (JIA).

Methods. A chart review was performed of all patients at a tertiary medical center who underwent subtalar corticosteroid injection during the past 5 years. Injection of 1 ml of triamcinolone hexacetonide or acetone into the midsubtalar joint was performed using a lateral oblique approach under fluoroscopic guidance. Improvement was defined by enhanced foot inversion and eversion at the following office visit.

Results. Thirty-eight patients underwent 55 subtalar injections during the study period. All 7 JIA subtypes were represented. Thirty-one patients (82%) had subtalar arthritis at time of JIA diagnosis and 32 (84%) had concomitant tibiotalar ankle arthritis. Improvement was observed following 34 (89%) of the initial 38 injections. The mean duration of improvement was 1.2 years (SD \pm 0.9). Twenty patients (53%) developed hypopigmentation or subcutaneous atrophy. This complication was associated with a higher volume of injected corticosteroid per patient weight ($p = 0.02$) and with less efficacious injections ($p = 0.04$).

Conclusion. Subtalar arthritis in children with JIA is common. Similar to other joints, subtalar arthritis responds to corticosteroid injection in approximately 90% of cases and often remains improved for greater than one year. Hypopigmentation and subcutaneous atrophy are frequent complications and are likely related to the dose of injected corticosteroid and possibly the accuracy of needle placement. (First Release Sept 15 2006; J Rheumatol 2006;33:2330–6)

Key Indexing Terms:

JUVENILE IDIOPATHIC ARTHRITIS SUBTALAR JOINT INTRAARTICULAR INJECTIONS
DRUG THERAPY GLUCOCORTICIDS FLUOROSCOPY

Arthritis of the subtalar (talocalcaneal) joint has been reported to be relatively common in children with juvenile idiopathic arthritis (JIA)^{1,2}. Chronic inflammatory arthritis of the subtalar joint can result in significant morbidity, including spontaneous joint fusion or debilitating pain requiring arthrodesis^{3,4}. Either spontaneous subtalar fusion or arthrode-

sis leads to an altered gait with undue stresses placed upon other weight-bearing joints, resulting in further morbidity^{3,5}. Intraarticular corticosteroid injections are a frequently used and proven therapy for a variety of joints in children with JIA⁶⁻¹⁰. Although arthritis of the subtalar joint is not infrequent, this joint is less commonly injected, possibly due to technical difficulty or lack of recognition. Successful injection of the subtalar joint in JIA under fluoroscopic guidance has been described¹, but outcome data are lacking. We determined the demographics of juvenile subtalar arthritis, its response to intraarticular corticosteroids, and the injection complication rate.

MATERIALS AND METHODS

Patients. All patients who met criteria for JIA¹¹ and underwent fluoroscopically guided subtalar intraarticular corticosteroid injection between January 1, 2000, and March 1, 2005, were retrospectively identified using a hospital procedure database, and a chart review was performed. During the study period, patients found to have qualitatively decreased foot inversion or eversion on physical examination were referred for injection as the standard of care at the discretion of their treating physician, in all cases a board-certified pediatric rheumatologist. Patient demographics were collected, including sex, JIA subtype, age at diagnosis of JIA, age at recognition of subtalar arthritis, presence of tibiotalar ankle arthritis, use of disease modifying antirheumatic drugs (DMARD), elapsed time from recognition of subtalar arthritis until injection,

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and antinuclear antibody, rheumatoid factor and HLA-B27 status. Institutional review board approval was obtained prior to the chart review.

Injection procedure. All subtalar injections were performed by 2 pediatric interventional radiologists (AMC or RDK). Adequate intravenous sedation was obtained with a combination of midazolam, fentanyl, and pentobarbital as described⁷. Local anesthesia at the site of injection was provided with bicarbonate buffered 1% lidocaine. A 22-gauge intravenous catheter or 21-gauge venipuncture needle was inserted into the tarsal cavity and directed toward the posterior talocalcaneal joint using a lateral oblique approach under fluoroscopic guidance. Less than one milliliter (ml) of nonionic contrast (Optiray[®] 320, Tyco Healthcare/Mallinckrodt) was injected to confirm needle placement in the subtalar joint (Figure 1). One milliliter of triamcinolone hexacetonide (20 mg/ml) (Aristospan[®], SAB-Pharma Inc.) was then injected, unless the entire volume could not be injected freely. During a time period when triamcinolone hexacetonide was commercially unavailable, the same volume of triamcinolone acetonide (40 mg/ml) (Kenalog[®], Bristol-Myers Squibb) was used instead, as these 2 medications have been shown to have similar per-volume potencies¹². Routine flushing of the needle tract with less than 0.5 ml of bicarbonate buffered 1% lidocaine during the removal of the needle was instituted during the study period. Patients were asked to avoid weight bearing as much as possible for 24 hours following injection, at which time they could resume normal activity.

Outcome measures. Patients were examined before and after the injections by their same treating physician. Improvement was defined as qualitatively enhanced foot inversion and eversion at the first office visit following corticosteroid injection regardless of the elapsed time between injection and examination. Resolution was defined as qualitatively normal foot inversion and eversion, the absence of any subjective complaints of ankle (tibiotalar or talocalcaneal) pain, and the absence of any gait abnormality attributed to the ankle by the treating physician at the first office visit following corticosteroid

injection, provided this first followup was within 0.25 years (13 wks) of injection. All charts were reviewed for any mention of complications from the injections, including the development of hypopigmentation or subcutaneous atrophy at any time.

The primary analysis was performed using only one injection per patient. In patients who underwent multiple subtalar injections, the initial injection was used in the primary analysis. In patients who underwent initial bilateral subtalar injections, the right subtalar joint was arbitrarily chosen for the primary analysis. For the purpose of comparison of efficacy, outcome data were also collected on corticosteroid injections of the knee performed concurrently with the initial subtalar injections, again arbitrarily selecting the right-sided joint in cases of bilateral injection. All subtalar injections performed during the study period were evaluated in the secondary analysis. Statistical analyses were performed with JMP IN version 5.1 software (SAS Institute, Cary, NC, USA) using t test, least squares linear regression, Fisher's exact test, Pearson correlation coefficient, and one-way ANOVA, where appropriate.

RESULTS

Patient demographics. Thirty-eight JIA patients underwent 55 subtalar injections during the study period. Their demographic characteristics are displayed (Table 1). There was a strong female predominance, as to be expected for most subtypes of JIA. The mean age at diagnosis of JIA was 5.4 years old. Patients with all JIA subtypes were represented.

DMARD use was common in this patient sample. A few patients developed subtalar arthritis while receiving DMARD therapy: 2 patients taking methotrexate (MTX), one taking a tumor necrosis factor- α (TNF- α) inhibitor, and one taking

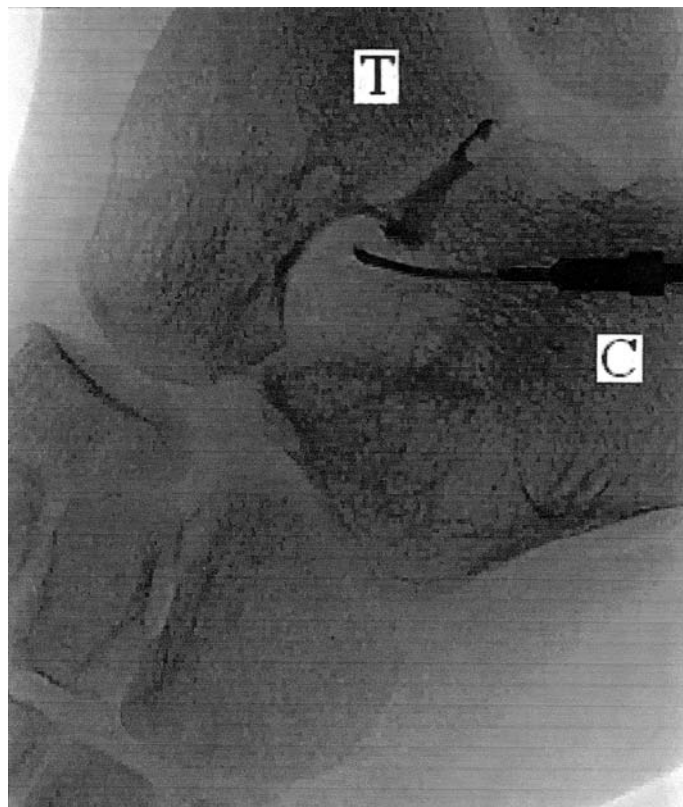


Figure 1. Intraarticular injection of subtalar joint under fluoroscopic guidance. Contrast is seen flowing into the posterior subtalar (talocalcaneal) joint. (T = talus, C = calcaneus)

Table 1. Demographics of the study patients.

| | |
|---|------------------|
| No. females/males | 33/5 |
| Age at diagnosis of JIA, yrs | |
| Median (range) | 4.4 (1.2–13.6) |
| Mean (\pm SD) | 5.4 (\pm 3.5) |
| Frequency of JIA subtypes (%) | |
| Oligoarthritis, persistent | 11/38 (29) |
| Oligoarthritis, extended | 5/38 (13) |
| Polyarthritis (RF-positive) | 2/38 (5) |
| Polyarthritis (RF-negative) | 12/38 (32) |
| Systemic arthritis | 2/38 (5) |
| Enthesitis related arthritis | 4/38 (11) |
| Psoriatic arthritis | 1/38 (3) |
| Undifferentiated arthritis | 1/38 (3) |
| Laboratory test results (%) | |
| ANA-positive | 23/37 (62) |
| RF-positive | 3/26 |
| HLA-B27-positive | 2/18 |
| Age at diagnosis of subtalar arthritis, yrs | |
| Median (range) | 5.0 (1.2–13.6) |
| Mean (\pm SD) | 5.9 (\pm 3.5) |
| DMARD use at time of subtalar injection (%) | |
| Methotrexate (subcutaneous) | 14/38 (37) |
| TNF- α inhibitor | 3/38 (8) |

JIA: Juvenile Idiopathic Arthritis, SD: standard deviation, RF: rheumatoid factor, ANA: antinuclear antibody, DMARD: disease modifying antirheumatic drug.

both MTX and a TNF- α inhibitor. At the time of the initial intraarticular subtalar injection, 11 patients were receiving MTX alone and 3 patients were receiving both MTX and a TNF- α inhibitor. During the course of followup, a TNF- α inhibitor was added to MTX for one patient, and an additional patient began taking MTX.

Thirty-one patients (82%) had subtalar arthritis at the time of their initial diagnosis with JIA. Most patients underwent subtalar injection(s) shortly after the arthritis was recognized; the median elapsed time from arthritis to injection was 0.1 years (range 0–7.6 yrs). However, 8 patients (21%) underwent initial injection one year or more after the recognition of subtalar arthritis.

Thirty-two patients (84%) had tibiotalar ankle arthritis concomitantly with subtalar arthritis. Unguided corticosteroid injection of the tibiotalar joint was performed concurrently in 21 patients (55%) and previously in 8 patients (21%).

Twenty-five patients (66%) underwent a single subtalar injection. Four (11%) underwent initial bilateral injection of their subtalar joints. Three (8%) had subsequent injection of the contralateral subtalar, and 7 (18%) had at least one reinjection of a subtalar joint.

Primary analysis (initial 38 subtalar injections). Triamcinolone hexacetonide was used in 13 of the initial injections and triamcinolone acetonide was used in 24. (For one injection, the medication and dose were not clearly documented.) Thirty-one of 37 patients (84%) received a 1 ml injection with the remaining patients receiving a smaller, freely injected volume ranging from 0.5 to 0.8 ml.

Improvement was noted at the first followup visit in 34 (89%) of the initial 38 injections. First followup came at a median of 6 weeks (range 1–30) after injection. Of those improved, the mean duration of improvement was 1.2 years (SD \pm 0.9) and the median was 1.1 years (range 0.2–3.3) (Figure 2). Twenty-one subtalar joints (55%) remained improved at the last documented followup visit. If this last observation is carried forward to the end of the study period, the duration of improvement is increased to a mean of 1.6 years (SD \pm 1.0), with a median of 1.3 years (range 0.2–4.2).

In univariate analysis, duration of improvement was not associated with any of the variables evaluated, including: type of corticosteroid injected, dose of corticosteroid injected (ml/kg of patient weight), elapsed time from the appearance of arthritis to injection, concurrent use of MTX or TNF- α inhibitor therapy, presence of concomitant tibiotalar ankle arthritis, previous or concurrent tibiotalar injection, patient age, or JIA subtype (Table 2).

Thirty-two patients (84%) had their initial followup within 13 weeks (0.25 yrs) of injection and thus satisfied the eligibility criteria for resolution of arthritis (see Materials and Methods). Fourteen (44%) of these patients had resolution of subtalar arthritis following injection. Of the 8 patients in whom more than one year had elapsed between the initial recognition of subtalar arthritis and subsequent intraarticular injection, only one (13%) achieved resolution of arthritis. By contrast, when injections were performed less than one year following the recognition of subtalar arthritis, 13 of 24 patients (54%) had resolution ($p = 0.05$, Fisher's exact). However, all 8 of the patients with delayed injection (100%) showed improvement following injection, even though the arthritis did not completely resolve.

Ten patients underwent corticosteroid injections of the knee at the same time as the initial subtalar injections, with comparable results. All 10 knee injections resulted in improvement of arthritis, compared to 9 of the subtalar injections. Using the last observation carried forward, the subtalar injections in these patients resulted in improvement for a mean duration of 1.4 years (SD \pm 1.0), with a median of 1.2 years (range 0–2.9). The duration of improvement for the knee injections in these patients was essentially the same ($p = 0.83$, paired t test), with a mean duration of 1.3 years (SD \pm 0.8) and median of 0.9 years (range 0.5–3.0).

Secondary analysis (all 55 subtalar injections). Improvement at first followup visit occurred following 50 (91%) of all 55 subtalar injections. Of those joints improved, the mean duration of improvement was 1.3 years (SD \pm 0.9) and the median was 1.1 years (range 0.1–3.3). Thirty-four joints (68%) remained improved at the last visit. Using this last observation carried forward, the duration of improvement is increased to a mean of 1.6 years (SD \pm 1.0), with a median of 1.3 years (range 0.2–4.2).

Seven patients had their subtalar joints reinjected (2 patients more than once). There were 10 reinjections in total;

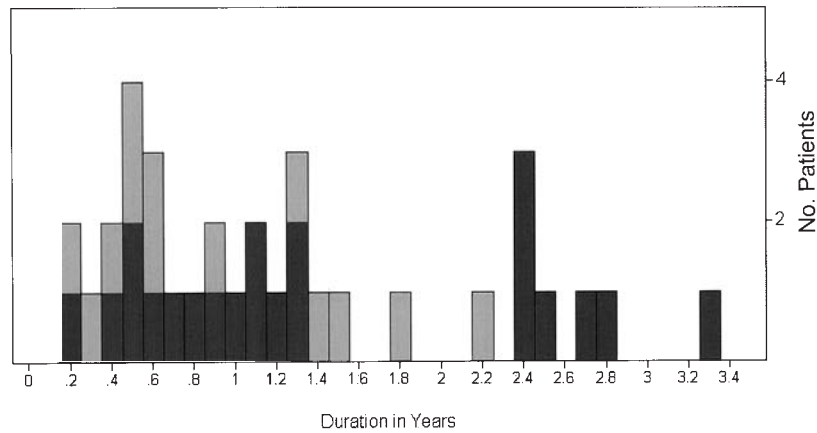


Figure 2. Duration of documented improvement. The darker bars represent patients with sustained improvement at their last documented followup.

Table 2. Testing of variables for association with duration of improvement.

| Variable | p | Test |
|---|------|-------------------|
| Corticosteroid injected (triamcinolone acetonide vs hexacetonide) | 0.97 | t test |
| Corticosteroid dose (ml steroid/kg patient weight) | 0.91 | Linear regression |
| Elapsed time from recognition of arthritis to injection | 0.11 | Linear regression |
| Methotrexate use | 0.38 | t test |
| Use of TNF- α inhibitor | 0.93 | t test |
| Concomitant tibiotalar ankle arthritis | 0.22 | t test |
| Previous tibiotalar injection | 0.60 | t test |
| Concurrent tibiotalar injection | 0.16 | t test |
| Patient age at injection | 0.44 | Linear regression |
| Patient diagnosis (JIA subtype) | 0.75 | One-way ANOVA |

3 were performed following inadequate clinical response and 7 were performed for recurrence of arthritis. All 10 (100%) of these reinjections resulted in improvement for a mean of 1.2 years (SD \pm 1.0), with a median of 0.85 years (range 0.1–3.1).

Complications. Subcutaneous atrophy and hypopigmentation were common complications and are considered together for the purposes of analysis. During the study period, 20 patients (53%) developed subcutaneous atrophy or hypopigmentation at the site of injection. In all cases, the lesions were superficial and of only cosmetic significance. There were no other noted complications of the intraarticular injections. Among the 25 patients who had only a single injection during the study period, 12 (48%) developed subcutaneous atrophy or hypopigmentation. Comparatively, 8 of 13 patients (62%) who underwent more than one injection developed subcutaneous atrophy or hypopigmentation. However, this higher complication rate did not reach statistical significance ($p = 0.51$, Fisher's exact).

An attempt was made to identify variables associated with an increased risk of atrophy or hypopigmentation. To simplify this analysis, only the 30 subtalar joints from the primary analysis that were not reinjected were considered. Of these, 12 (40%) were complicated by subcutaneous atrophy or hypopigmentation. Variables analyzed for a possible association are shown in Table 3.

Subtalar joints injected with a larger volume of corticosteroid per kg of patient body weight were associated with higher rates of this complication (Figure 3). The patients who developed subcutaneous atrophy or hypopigmentation had received a mean of 0.056 ml of triamcinolone per kg of body weight (SD \pm 0.017), while those without this complication had received only a mean of 0.038 ml/kg (SD \pm 0.021). Similarly, no patient who received less than 0.03 ml/kg of triamcinolone (equivalent to 0.6 mg/kg of hexacetonide) developed this complication, and all patients who received greater than 0.08 ml/kg of triamcinolone (equivalent to 1.6 mg/kg of hexacetonide) later developed subcutaneous atrophy or hypopigmentation.

An increased risk of subcutaneous atrophy or hypopigmentation was also associated with younger patient age at the time of injection. However, because the majority of patients were injected with 1 ml, patient age at the time of injection and the injected corticosteroid volume per kg of patient body weight were highly negatively correlated (Pearson correlation coefficient = -0.81), making the distinction between these 2 risk factors difficult.

There was also a trend toward a higher complication rate in the patients who underwent intraarticular injection at the beginning of the study period. Of the first 7 intraarticular

Table 3. Testing of variables for association with increased rate of hypopigmentation or subcutaneous atrophy.

| Variable | p | Test |
|---|------|----------------|
| Corticosteroid injected (triamcinolone acetone vs hexacetonide) | 0.42 | Fisher's exact |
| Corticosteroid dose (ml steroid/kg patient weight) | 0.02 | t test |
| Patient age at injection | 0.01 | t test |
| Shorter duration of improvement of arthritis | 0.56 | t test |
| Lack of resolution of arthritis | 0.04 | Fisher's exact |

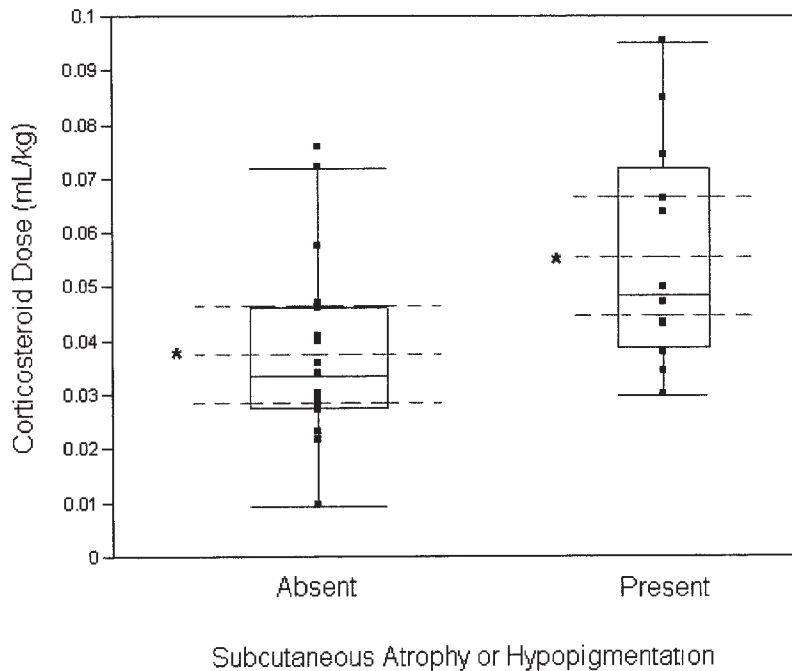


Figure 3. Association of the dose of intraarticular corticosteroid with subcutaneous atrophy or hypopigmentation. Plots represent the medians, 25–75 percentiles, and most extreme non-outlier values. Broken lines represent the means (asterisk) and 95% CI.

injections performed, 5 (71%) resulted in subcutaneous atrophy or hypopigmentation. By comparison, 7 of the following 23 injections (30%) had this complication ($p = 0.08$, Fisher's exact).

Resolution of subtalar arthritis following intraarticular injection was associated with a decreased incidence of atrophy or hypopigmentation. Only 2 of 13 patients (15%) in whom the arthritis resolved developed this complication, compared to 7 of 12 patients (58%) in whom the arthritis did not resolve.

DISCUSSION

Subtalar arthritis in JIA is common. Magnetic resonance imaging (MRI) examination of swollen ankles in patients with JIA has revealed subtalar arthritis in 45–77%^{1,2}. Our study identified 38 patients with JIA over a 5 year period with subtalar arthritis diagnosed by decreased foot inversion or eversion. The true number of patients with subtalar arthritis during this time period is likely higher given that not all patients may

have been referred for injection. Additionally, not all subtalar arthritis may be easily appreciated on examination¹³. Remedios, *et al* found physical examination to be poorly correlated with MRI. In children with JIA and swollen ankles, clinical findings of possible or definite subtalar arthritis were 80% sensitive compared to MRI, and the absence of clinical findings had a negative predictive value of only 50%¹.

The presence of subtalar arthritis should be considered in any patient with JIA. Subtalar arthritis was detected in all JIA subtypes. It was present in many patients with oligoarticular disease and regardless of rheumatoid factor or HLA-B27 status. It occurred frequently with concomitant tibiotalar ankle arthritis, but also occasionally in its absence. Tibiotalar injections often do not treat subtalar arthritis as shown by the 8 patients in this study with prior ankle injections and the observations of others¹⁴. This suggests that the subtalar joint should be injected independently of the tibiotalar joint whenever inversion or eversion of the foot is compromised.

Approximately 90% of all subtalar corticosteroid injec-

tions resulted in improvement, and more than one-half remained improved for at least one year. This efficacy is similar, if not superior, to previously published data on the efficacy of 147 ankle injections in JIA⁸ and comparable to the results of other publications of intraarticular injections in JIA in general¹⁵. Additionally, subtalar injections were as efficacious as concurrent injections of the knee in this patient sample.

The efficacy of subtalar injections in this study was very likely improved by utilizing fluoroscopic guidance. Unguided injection of the subtalar can be technically challenging and was not attempted during or prior to the study period. A previous small study of ankle injections showed increased 6 month improvement rates from 1 of 9 (11%) to 6 of 9 (67%) with the use of fluoroscopic guidance¹. Ultrasound and computerized tomography have also been proven useful as a means of guiding intraarticular injections, but they are not likely to substantially increase the high rate of improvement demonstrated in this study using fluoroscopic guidance.

The outcome data suggest that corticosteroid injection of an inflamed joint is efficacious under most circumstances. Subtalar joints that were not injected for more than one year following the onset of arthritis all showed some improvement following injection. Additionally, subtalar joints that were re-injected resulted in outcomes comparable to all other injections.

Although there was a high rate of sustained improvement, the rate of complete resolution of arthritis at early first followup was only 44%, which is lower than reports for other joints⁹. Similar to studies of the temporomandibular joint⁷, this outcome suggests an inherent difficulty in effectively treating synovitis of the subtalar joint, particularly since many of these children were already being treated with MTX, and some with TNF- α inhibitors, at the time of injection (Table 1). Additionally, the low rate of resolution may be related to the complex mechanics of foot inversion and eversion, which may also involve elements of the talonavicular, anterior talocalcaneal, and calcaneocuboid joints. Synovitis of these other articulations has been demonstrated by MRI in some patients with ankle arthritis^{2,13}. The subtalar injections performed in this study were aimed at the posterior talocalcaneal joint, which is the primary determinant of foot inversion and eversion. However, MRI examination to identify areas of synovitis was not performed routinely prior to subtalar injection during the study period.

The complications of subcutaneous atrophy and hypopigmentation were frequent. The complication rate of 48% for patients who underwent only one injection is significantly higher than reports of 3–16% for ankle injections^{8,16}. However, published complication rates specific to subtalar injections are lacking, aside from a single report of no occurrences in 6 patients¹. The use of triamcinolone hexacetonide did not result in a higher rate of hypopigmentation or subcutaneous atrophy than that of triamcinolone acetonide, despite the fact that it has a longer duration of efficacy^{12,17}.

A higher volume of injected corticosteroid per kilogram of

patient weight was associated with an increased complication rate. This may be the result of a local overdose of corticosteroid or an overfilling of a given joint space, leading to corticosteroid tracking up the path of the needle after its removal¹⁶. The association of younger age with an increased complication rate likely reflects the influence of smaller joint spaces and resultant overfilling. Therefore, the complication rate would likely be decreased by adjusting the corticosteroid dose roughly based on patient weight as follows: 1 ml (20 mg) of triamcinolone hexacetonide for patients over 25 kg and 0.5 ml (10 mg) of triamcinolone hexacetonide for patients less than 25 kg. This has been adopted as the standard in our practice.

The decreasing complication rate over the course of the study supports the notion of a learning-curve effect. The additional step of flushing the needle tract may have contributed to this improvement, though incomplete documentation did not allow for formal analysis. Accuracy of needle placement may have also been a factor. The association of younger age with an increased complication rate may reflect difficulties with accurate needle placement into relatively smaller joint spaces. Additionally, subtalar joints in which the injections resulted in resolution of arthritis were less likely to develop complications. These injections may have had more accurate needle placement than those that did not result in resolution of arthritis.

This study was limited by its retrospective chart review design, subjective diagnostic and outcome measures, and lack of treatment controls. Foot eversion and inversion were qualitatively and subjectively recorded in the patient charts and no quantitative goniometry was performed. In the proper clinical context, decreased foot inversion and eversion was attributed to subtalar arthritis, and confirmatory studies, such as MRI, were not performed. Individual patients were examined by their same treating physician before and after the injection, but no attempts were made to determine interrater or intrarater reliability. As this was a retrospective study, the examining physician was not blinded to the injection procedure. Patients with subtalar arthritis who did not undergo injection could not be easily identified within this clinic sample for comparison.

Nevertheless, intraarticular injections of long-acting corticosteroids appear to effectively treat subtalar arthritis in children with JIA. Subtalar arthritis affects all subtypes of JIA and can occur even during therapy with MTX and TNF- α inhibitors or in the absence of tibiotalar ankle arthritis. Although cosmetic complications can occur with injections, adjusting the dose of corticosteroids based on the patient's body weight will likely lower the incidence of these side effects. We propose the use of fluoroscopically guided intraarticular corticosteroid injections of subtalar joints in children with JIA who have evidence of subtalar arthritis by MRI or clinical examination.

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