Intra-articular steroids in radiologically confirmed tarsal and hip synovitis of juvenile idiopathic arthritis

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Abstract

Objective

To estimate the value of MRI or US imaging in the diagnosis of synovitis and the response to local steroid therapy in tarsal and hip synovitis.

Methods

32 patients with juvenile idiopathic arthritis (JIA), 19 of them with 22 tarsal and 13 of them with 20 hip synovitis, were followed up for 12 months after intra-articular corticosteroid treatment (IAST). MRI was taken from swollen ankles/feet to target the inflamed area before IAST. The synovitis in hip joints was assessed by both clinical and ultrasonographic examination.

Results

MRI showed that in the swollen tarsal area the inflammation was distributed widely in the joints and tendon sheaths. In 13/22 (59%) ankles/feet, synovitis was observed in multiple joint spaces. In 17/22 (77%) ankles/feet, tenosynovitis was present. In 32% of cases, the IAST induced clinical remission for up to 12 months. In hip synovitis, ultrasound supplemented clinical assessment. At 12 months after IAST, a successful treatment response was seen in 10/20 (50%) hips.

Conclusion

In unresponsive tarsal arthritis, the synovitic sites should be targeted by radiological imaging to improve the efficacy of corticosteroid injections. For pediatric rheumatologists, easy access to US is preferable to optimize the treatment of hip and tarsal synovitis in JIA.

Key words

Ankle, hip joint, juvenile idiopathic arthritis, intra-articular injections, magnetic resonance imaging, tarsal joints, ultrasound.

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Abbreviations:
DMARD: disease-modifying anti-rheumatic drug
IAST: intra-articular corticosteroid therapy
JIA: juvenile idiopathic arthritis
MP: methylprednisolone
MRI: magnetic resonance imaging
MTX: methotrexate
OXI: hydroxychloroquine
US: ultrasound
SZ: sulphasalazine
TH: triamcinolone hexacetonide

Introduction

Intra-articular corticosteroids are an established and effective treatment for juvenile idiopathic arthritis (JIA) (1-8), especially of the oligoarticular subtype. The efficacy of this treatment has been shown especially in knee arthritis (1, 2, 4, 5, 7, 9). A few studies have also evaluated the response of intra-articular corticosteroid therapy (IAST) in hip synovitis (3, 8, 10, 11).

In recent years, joint imaging techniques such as magnetic resonance imaging (MRI) and ultrasound (US) have improved the accuracy of the clinical diagnosis of arthritis and the evaluation of the treatment response in JIA patients (9-16). In these studies, US has been used to assess mainly hip or knee synovitis, whereas MRI has been used to evaluate other joints also.

Injecting a knee joint is technically straightforward, whereas it may be challenging to localize and target all the inflamed joint spaces in an inflamed ankle and foot. Although ankle joint arthritis may respond well to local steroid therapy (6,8,12), swollen and painful tarsal synovitis in JIA patients can sometimes be a diagnostic and therapeutic problem. Only a few studies (6, 8, 12) have evaluated the treatment response to IAST in tarsal synovitis, but none of them have reported on co-existent tenosynovitis in the ankle. In a previous study, tenosynovitis, especially in lower extremities, and tarsitis has been associated with juvenile onset ankylosing spondylitis (17).

This study was made to evaluate the response of hip and tarsal synovitis to local steroid therapy. The potential benefits of the use of US in hip synovitis, screened bedside by a pediatric rheumatologist, and MRI in the diagnosis of recalcitrant tarsal synovitis were assessed.

Patients and methods

Patients

This was a retrospective study of 19 consecutive patients with 22 swollen ankles/feet and 13 consecutive patients with synovitis in 20 hip joints. In this study, ankle, hindfoot and midfoot were defined as ankle/foot or tarsal region. All 32 patients enrolled in the study fulfilled the revised (Edmonton) criteria for the diagnosis of JIA (18). Patients were treated and followed up at the Department of Pediatric Rheumatology, the Hospital for Children and Adolescents, University of Helsinki. All the children had one or more actively inflamed joints at the time of local steroid injections. Of the 32 patients, 22 were on disease-modifying anti-rheumatic drugs (DMARDs) (Table I). 19 patients had one or two swollen ankles/feet. The swelling had persisted for at least 2 months, regardless of previous local and/or systemic medication. Enthesitis; tenderness at the insertion of a tendon, ligament, joint capsule or fascia to bone (18) was differentiated from tarsal synovitis/tenosynovitis clinically and by MRI. In 13 patients, synovitis of the hip joint(s) had persisted for at least 4 weeks. The diagnosis was confirmed by US examination.

Ultrasound

After clinical evaluation, all JIA patients suspected of having hip synovitis were routinely examined by US. The pediatric rheumatologist used a 10 MHz linear probe of the Acuson Aspen Advanced Unit. The distance between the collum of the femur and the capsule of the hip joint was measured (collum-capsule distance) and a distance of more than 6.0 mm with effusion (13, 15, 19) or a difference between the hip joints of more than 1.0 mm was considered indicative of hip synovitis (13).

Magnetic resonance imaging

All the ankles/feet with swelling and/or a limited range of motion and pain or tenderness were imaged by MR with gadolinium-enhancement. MR imaging was performed with a 1.5-T unit (Magneton Vision, Siemens). Images were obtained in sagittal and coronal plane and with some patients also in the axial plane with 512 x 512 matrix, 3-4 excitations and 3 mm section thickness. T2-weighted images with inversion recovery were taken and T1-weighted spin-echo 500-980/14 (time repetition msec/time echo msec) sequences with fat suppression were performed before and immediately after intravenous injection of 0.1 mmol/kg Gd-DTPA (Magnevist,

Table I. Characteristics of the 32 JIA (juvenile idiopathic arthritis) patients at the time of local steroid injection.

	Ankles/feet		Hip joints	
No. of patients	19		13	
Gender M / F	6 / 13		6 / 7	
Age, median (range) years	8.2	(2.8-17.4)	10.4	(2.3-16.9)
Onset of JIA, median (range) years	3.3	(1.0-12.8)	6.0	(1.8-14.5)
Disease duration, median (range) years	4.3	(0.5-8.1)	1.1	(0.5-10.9)
Type of JIA				
Persistent oligoarthritis (no.)	3	(16%)	2	(15%)
Extended oligoarthritis (no.)	7	(37%)	3	(23%)
Enthesitis related arthritis, no.	2	(10%)	1	(8%)
Seronegative polyarthritis (no.)	7	(37%)	7	(54%)
Seropositive polyarthritis (no.)	0		0	
HLA-B27 positive (no.)	5	(26%)	4	(31%)
ANApositive (no.)	4	(21%)	3	(23%)
Chronic uveitis (no.)	7	(37%)	5	(38%)
Medication (no.):				
MTX only	5	(26%)	5	(38%)
OXI only	4	(21%)	3	(23%)
SZ only	1	(5%)	0	
MTX and OXI	2	(11%)	1	(8%)
MTX and etanercept	1	(5%)	0	
No DMARDs	6	(32%)	4	(31%)
Low-dose oral prednisolone	5	(26%)	5	(38%)

HLA-B27: human leucocyte antigen B27; ANA: antinuclear antibody; MTX: methotrexate; OXI: hydroxychloroquine; SZ: sulphasalazine.

Schering) with the same planes and spacing. Images obtained before and after administration of contrast material were displayed with the same gray-scale level and window. The diagnosis of synovitis and/or tenosynovitis required the presence of effusion and thickening of the synovial tissue and increased uptake of gadolinium into the synovium. MR-images were analyzed by a radiologist.

Steroid injections

After radiological confirmation of the synovitis, in hips by US and in ankles/feet by MRI, all inflamed joints and tendon sheaths were treated with local steroid injections. Local steroids were injected during brief general anesthesia, with a few exceptions of local anesthesia for some adolescents with a single injection site. The intra-articular injection into the hip joints was given by the pediatric rheumatologist (VH or PL) with US guidance. After aspiration, triamcinolone hexacetonide (TH) was injected into the hip joint, the dose being 20-40 mg/joint, depending on the body weight, approximately 1 mg/kg. In swollen tarsal region, inflamed joints and tendon sheaths were treated with methylprednisolone (MP). The dose per site varied according to the size of the joint or the tendon sheath, the total number of injection sites and the size of the patient. MP dose in tibiotalar, talocalcanear and talonavicular joint was 15-40 mg, in calcaneo-cuboidal, cuneiform-navicular, cuneiform-cuboidal and tarsometatarsal joint 10-32 mg, in metatarsophalangeal joints 4-14 mg and in tendon sheaths 8-36 mg. The size of the injection needle was chosen according to the size of the joint. The largest needle, 0.7 x 40 mm (22G x 1.5") was used to inject tibiotalar joint and the smallest, 0.5 x 16 mm (25G x 5/8") to inject metatarsophalangeal joints. Whenever possible, aspiration of the synovial fluid was obtained.

Evaluation of outcome

All patients were included in the follow-up. Response to treatment was evaluated at 1, 3, 6, 9 and 12 months after the local steroid injections. In the ankles/feet the treatment response was evaluated by clinical examination. A successful treatment response was defined as reduction of swelling, absence of pain, absence of tenderness on motion and a normal range of motion. In cases of decreased but still remaining minor swelling with no other signs of synovitis, the treatment response was also interpreted as successful. In the hip joints the treatment response after IAST was evaluated by the pediatric rheumatologist both by clinical and US examination. The definition of a successful treatment response of the hip synovitis included a normal range of motion without pain and a US examination without joint effusion.

Statistical analysis

The effects of possible explanatory variables (CRP, SR, duration of JIA, age at baseline, height, weight, surface area) on the length of the successful treatment response were analyzed using simple and multiple linear regression. The effect of the type of JIA on treatment response was tested by ANOVA and paired t-test was used in case of dichotomous variables (gender, ANAAb, HLAB27, presence of uveitis). $P < 0.05$ was considered significant. The differences in baseline characteristics of the responders and nonresponders at 12 months were analyzed by the t-test with continuous variables and by the chi-square test with nominal variables.

Results

Synovitis and tenosynovitis in swollen tarsal region

Three of the 19 patients had bilateral synovitis in their tarsal region (Table II). Talonavicular with talocalcanear synovitis was found in 6/22 and tibiotalar with talocalcanear synovitis in 4/22 ankles/feet. In 3/22 ankles/feet, all these joints were inflamed. More than 1 affected joint was found in 13/22, more than 2 affected joints in 9/22 and more than 3 affected joints in 4/22 ankles/feet. Synovitis with tenosynovitis was observed in 17/22 ankles/feet. In one patient with polyarthritis, tenosynovitis

occurred without synovitis. Synovitis without tenosynovitis was found in 4 patients. The most common locations of tenosynovitis were the tendon sheaths of the tibialis posterior and hallucis longus muscles. Both of these tendon sheaths were inflamed in 10/22 ankles. Tenosynovitis was found in 4/5 of the HLA-B27 positive and in 12/14 of the HLA-B27 negative patients. Of the two patients with enthesitis related arthritis, the other had one tenosynovitis in the tarsal region, whereas the other had only a solitary tibiotalar synovitis.

Response to local steroid therapy in swollen tarsal region

In 22 ankles/feet of 19 patients, 0-6 joints (mean 2.1) and 0-5 tendon sheaths (mean 1.9) were injected at baseline. The duration of successful treatment response (Fig. 1) after the local steroid injections varied from 0.5 months to the end of the follow-up time, 12 months (mean 5.5 months, median 3.5 months). A positive clinical response was observed in 18/22 (82%) cases at 1 month, in 13 (59%) at 3 months, in 9 (41%) at 6 months and in 7 (32%) at 12 months. The patients' opinion on the treatment result was taken into consideration by assessing pain or tenderness on motion. At the end of the follow-up time, no difference was observed between the patients' subjective view and the clinical response assessed by the pediatrician.

There were slight differences in the baseline clinical characteristics between the responders and non-responders at 12 months (data not shown). However, none of these differences reached statistical significance. The drug therapy used varied considerably between patients. This led to small numbers on each drug/drug-combination. It was not possible to perform valid statistical comparisons between groups. No side effects such as subcutaneous tissue atrophy were observed in tarsal region of any patients during the follow-up time.

Response to local steroid therapy in hip synovitis

In all 20 hips there was an initial positive response at one month. The mean

Table II. The distribution of inflammation in joints and tendon sheaths examined by MRI in 22 swollen ankles/feet of 19 patients with JIA.

Joints	n	Tendon sheaths	n
Tibiotalar	12	Musculus tibialis posterior	13
Talocalcanear (subtalar)	10	Musculus flexor hallucis longus	13
Talonavicular	10	Musculus flexor digitorum longus	8
Calcaneo-cuboidal	6	Musculus peroneus longus	4
Cuneiform-navicular	2	Musculus peroneus brevis	2
Cuneiform-cuboidal	2	Musculus extensor hallucis	1
Tarsometatarsal	4		
Metatarsophalangeal	1		

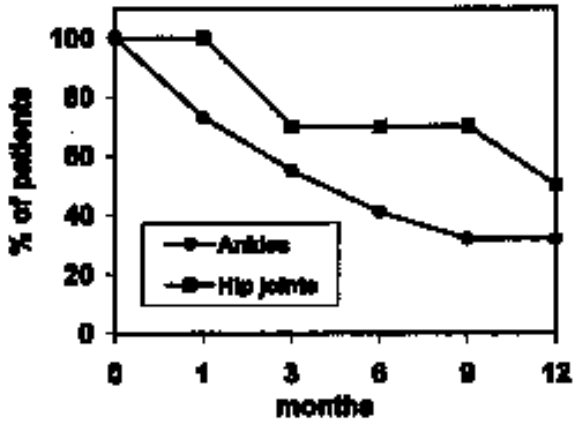

Fig. 1. The proportion of JIA patients (%) with a successful treatment response during a 12-month follow-up after local steroid injections of 22 ankle/foot or 20 hip synovitis.

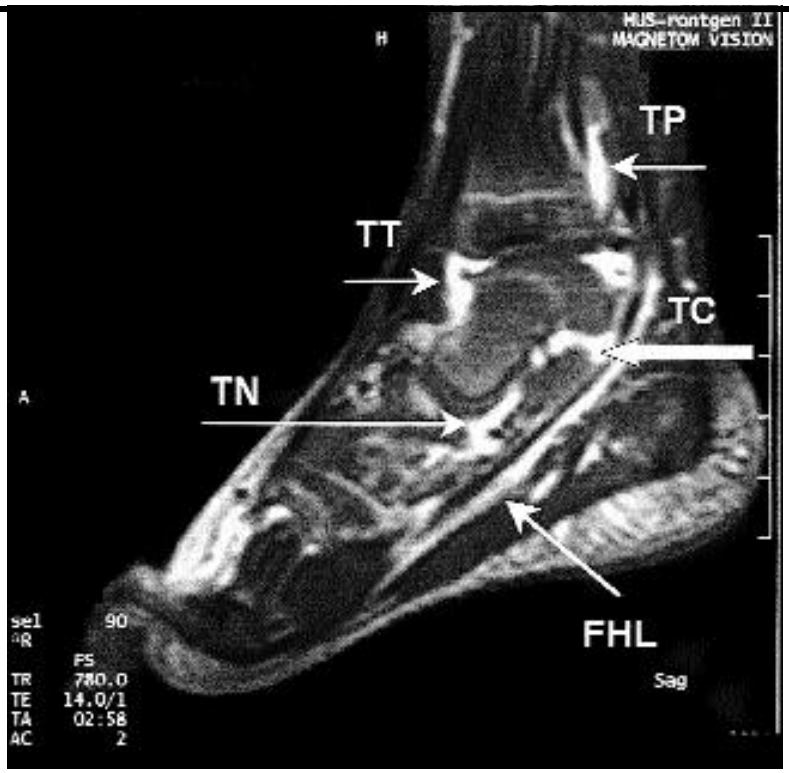

Fig. 2. Medial view of the left tarsal region of the 2.8-year-old girl with persistent oligoarthritis. Increased gadolinium uptake into inflamed synovium and tendon sheaths in a T1-weighted sagittal plane in tibiotalar (TT), talocalcanear (TC), talonavicular (TN) joints and sheaths of flexor hallucis longus (FHL) and flexor tibialis posterior (TP) tendon.

duration of efficacy was 8.3 months (median 11.5 months). In 14 (70%) hip joints both the clinical examination and ultrasound was normal at three months. In one hip the ultrasound finding was normal, but clinical examination revealed some pain on motion. Since our definition of a successful treatment response included both the absence of clinical signs and symptoms and no effusion in US, this hip joint was defined as active. During the remaining follow-up time, 14 hip joints (70%) at 6 months and 10 hip joints (50%) at 12 months did not show any signs of synovitis. The differences between the responders and non-responders at 12 months from baseline did not reach statistical significance (data not shown). No side effects due to IAST were observed during the follow-up time.

Discussion

This study shows the diversity of inflammation in swollen tarsal region and the value of MRI in assessing the localization and extent of synovitis. In the present series in patients with juvenile poly- or oligoarthritis, synovitis was found in multiple joint spaces in 59% of cases and tenosynovitis was present in 77% of cases. Our results suggest that a nonresponding tarsal synovitis in any patient with JIA, not just an HLA-B27 positive or enthesitis related arthritis patient, may in most cases be tarsitis: the inflammation is distributed widely in the joints and tendon sheaths. Clinical assessment of a swollen ankle/foot is a demanding task to be accomplished correctly without the aid of radiologic techniques.

The ultrasonographic bedside assessment of hip synovitis, done by the pediatric rheumatologist, is a safe and painless way of detecting synovial effusion in children. Measurement of the collum-capsule distance in hip joints can be used to monitor the response to IAST. As the technique itself is easy to learn, it is suggested that all pediatric rheumatologists should have easy access to a US unit. In hip synovitis, the median duration of efficacy after IAST in our study was 49 weeks, which seems to be in line with previous studies. In the extensive study of Breit *et al.* (8), the median duration of successful treatment responses in hip joints after IAST varied from 11 to over 48 weeks, depending on the JIA subtype. In the study of Neidel *et al.* (11), in 39/67 (58%) hip synovitis was absent for two years after a single IAST, and in 51/67 (76%) after repeated IASTs. In that study, US was also used in the diagnosis and follow-up of the hip synovitis and MRI was included in the final evaluation.

In injecting hip joints, TH was used because of its longer duration of efficacy, the large size of the joint and the possibility to guarantee intra-articular injection with US guidance. MP, a steroid with shorter duration of action (5), was injected into ankle and multiple tarsal joints, because of the higher risk of extra-capsular leakage and subcutaneous tissue atrophy (20) in small joint spaces. However, the different action spans of these two long-acting steroids, limit the comparison of the outcome of IAST between these joints. This difference also limits the comparison of our results of tarsal region injections to previous studies. TH was used to tibiotalar (6, 8, 9, 12), subtalar (8, 12), talonavicular (8), smaller tarsal and MTP, PIP and DIP joints (8), but the tendon sheaths were not injected in these studies. In ankles and some smaller joints, subcutaneous lipoatrophy was reported (8). Using MP, we did not have any of such adverse effects from IAST in the tarsal region of our patients.

In earlier studies, successful treatment response has been defined in various ways. This makes the comparison of the results complicated. The differences in the efficacy of IAST may reflect various characteristics of the patient series, e.g. JIA subtypes and differences in the use of DMARDs, the local corticosteroids (TH vs. MP), the duration of the follow-up and in the response criteria (improvement vs. full quiescence of inflammation). Internationally accepted Pavia's criteria (21) were not used in our study due to retrospective analysis, nor were they used in any of the referred studies either (6, 8,9, 12). In our series, in cases of ankle/foot swelling the response to IAST seemed not to be as good as in previous studies. The mean duration of efficacy was 22 weeks (median 15 weeks) and the favorable response lasted up to 12 months in only 32% of the cases. Our study group consisted only of ankles/feet that were unresponsive to previous local steroids. Furthermore, while in our study we aimed at complete recovery, not only at the improvement of the inflamed joints and tendon sheaths, Breit *et al*. (8) defined positive response as a 50% reduction of the signs of synovitis compared to the situation before IAST (8). In that study, the median duration of a successful treatment response after IAST into ankles varied from 30 to 72 weeks, depending on the JIA subtype (8). In the study of Remedios *et al.* (12), the overall mean duration of efficacy was 38 weeks after a guided (fluoroscopy-enhanced) IAST and 14 weeks after an unguided IAST. MRI taken before IAST in 13 ankles was found to be more sensitive than clinical examination for detecting synovitis, especially in subtalar synovitis (12). However, an excellent response (full recovery) was seen only in 22% and 33% of the patients, respectively (12). In another study long-lasting results to IAST with complete resolution of signs of synovitis were reported, but the duration of the response was not subdivided into individual joints (6).

Ablind injection of some of these sites of tarsal region cannot always be guaranteed to reach the proper site, even in experienced hands. Direct US guidance (8,12) might enable the use of TH even in smaller joints of tarsal area and improve the efficacy of IASTs. In our relatively small patient series, explanation for inadequate treatment response was sought among other variables also from the medication, but the use of DMARDs seemed to reflect more the overall disease activity than the response to a solitary IAST.

This is a non-controlled clinical follow-up study with all the shortcomings that a setting of this kind brings with it. Bearing this in mind, we still dare to make the following suggestions: if repeated injections are needed in ankle/foot arthritis, synovitic sites should be

localized by radiologic imaging, preferably MRI, to improve the targeting and efficacy of the subsequent corticosteroid injections. Secondly, for pediatric rheumatologists an easy access to US is preferable to optimize the treatment of hip and tarsal synovitis in JIA.

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