

PREVENTION OF LEG LENGTH DISCREPANCY IN YOUNG CHILDREN WITH PAUCIARTICULAR JUVENILE RHEUMATOID ARTHRITIS BY TREATMENT WITH INTRAARTICULAR STEROIDS

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Objective. To determine if intraarticular (IA) injection of triamcinolone hexacetonide (steroids) used early in the course of pauciarticular juvenile rheumatoid arthritis (pauci JRA) is associated with less leg length discrepancy (LLD) or thigh circumference discrepancy (TCD).

Methods. Children with pauci JRA who had asymmetric lower-extremity arthritis diagnosed before age 7 years in Seattle, Washington (WA; n = 16) and in Chapel Hill and Durham, North Carolina (NC; n = 14) were retrospectively identified. WA children were given IA steroids within 2 months of diagnosis; the injections were repeated if synovitis recurred in the same joint or in a different joint. These children were compared with NC children who were not treated with IA steroids. Thigh circumference was measured at 10 cm above the patella, and leg length was measured from the anterior superior iliac spine to the mid-medial malleolus, by a single observer. LLD and TCD are reported as the percentage of difference between leg measurements in each subject.

Results. The WA and NC subjects had comparable disease severity and duration of followup (in months). Twelve WA children had subsequent IA steroid injections (mean 3.25 injections per child over mean \pm SD 42 \pm 11 months). The WA subjects had significantly less LLD ($P = 0.005$, by Student's 2-sided t -test) and prescriptions for shoe lifts ($P = 0.002$, by Fisher's 2-sided exact test). There was not a significant differ-

ence in TCD between the 2 groups ($P = 0.139$, by Student's 2-sided t -test). Similar findings were obtained when the analysis was limited to children with monoarticular knee arthritis.

Conclusion. Early and continued use of IA steroids may be associated with less LLD in young children with pauci JRA. This may indicate decreased duration of synovitis.

The use of intraarticular (IA) steroids in children with pauciarticular juvenile rheumatoid arthritis (pauci JRA) is an accepted therapeutic option (1-7). In 1 survey of North American pediatric rheumatologists, the use of IA steroid injection was second only to nonsteroidal antiinflammatory drugs (NSAIDs) in the treatment of pauci JRA (8). In general, IA steroids have been found to be safe and to effect rapid resolution of the active symptoms and signs of inflammation. The optimal timing for IA steroids, however (at the onset of inflammation or after a period of failed therapy with oral NSAIDs), is unknown. In addition, no previous studies have determined whether the use of IA steroids is associated with long-term benefit (1).

The majority of children with pauci JRA do well and experience resolution of active synovitis regardless of whether they are treated with oral or intraarticular medication. The lasting sequelae of pauci JRA, besides ocular damage from uveitis, include leg length discrepancy (LLD) and thigh circumference discrepancy (TCD) (9,10). Accelerated linear growth of the involved leg is typical, since the knee and ankle are the most frequently involved joints and the arthritis is frequently asymmetric (11). Hyperemia to the juxtaposed growth plates is thought to be the mechanism for overgrowth in young children, although in adolescents, it may lead to early fusion of the growth plate and a shortened leg (9,10). The mechanism for TCD is unknown and may be due to

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Table 1. Joints initially and subsequently injected with intraarticular steroids in the Washington study group*

Patient	Initial joint(s) injected (no. of times)	Other joint(s) subsequently injected (no. of times)
1	Left knee (1)	None
2	Right knee (1), right elbow (1)	None
3	Right ankle (1), right elbow (1)	None
4	Right knee (1), left ankle (1), left elbow (1)	None
5	Right knee (3)	None
6	Right knee (1)	Left knee (1)
7	Left knee (4)	None
8	Right knee (4)	Left knee (2)
9	Left ankle (2), right ankle (1)	None
10	Left knee (3)	Right knee (3)
11	Right knee (1)	Right elbow (1), left knee (1)
12	Right knee (2)	None
13	Right knee (3), left knee (1), left ankle (1)	None
14	Right knee (2), an MTP (1)	None
15	Left knee (1), left ankle (2), a PIP (1)	None
16	Left knee (4)	None

* MTP = metatarsophalangeal; PIP = proximal interphalangeal.

disuse or decreased tone in the quadriceps muscle secondary to knee joint capsule distention (10). The degree of LLD or TCD in young children may therefore serve as a marker for the duration of synovitis.

In this study, we compared children who were and were not treated with early IA steroids in order to assess whether there were differences between LLD and TCD in the two groups.

PATIENTS AND METHODS

Patients. Children with pauci JRA as defined by the American College of Rheumatology (12) who were <7 years of age at diagnosis were retrospectively identified in 3 pediatric rheumatology centers, the University of Washington (WA), the University of North Carolina at Chapel Hill, and Duke University, Durham, North Carolina (the latter 2 centers designated NC). The medical records were reviewed for historical and treatment data; these data were confirmed by the accompanying parent during the study examination. All children had asymmetric arthritis of the knee or ankle and were diagnosed between January 1990 and March 1995. Children were excluded if they had other leg or foot conditions, including fractures. Approval of the institutional human subjects board was obtained in all 3 institutions.

All WA children were injected with IA steroids (20 mg of triamcinolone hexacetonide) within 2 months of diagnosis: 11 at diagnosis, 2 at 1 month, and 3 at 2 months following diagnosis. The 1- and 2-month delay in injecting 5 of the children occurred in order to meet the diagnostic criterion for pauci JRA that requires the arthritis to be present for 6 weeks. Since these children had few involved joints, we elected to treat them with IA steroids rather than with systemic oral medications. This included injecting knees, ankles, elbows, proximal interphalangeal joints, and metatarsophalangeal joints. All but

4 children received subsequent IA steroids (Table 1). The specific joints injected initially and subsequently are shown in Table 1.

There were 39 injection sessions (mean 2.4 injection sessions per child), for a total of 52 injections (mean 3.25 injections per child). The maximum number of joints injected in 1 session was 3. The maximum number of times any 1 joint was injected was 4. Only 3 of the NC children received a single IA injection in 1 knee late in the course of their illness (41 months, 54 months, and 56 months after onset).

Methods. All subjects were examined for LLD and TCD by 1 observer (DDS) in the summer of 1997. Thigh circumference was measured 10 cm above the patella until 3 consecutive measurements were the same. Leg length was measured from the anterior superior iliac spine to the mid-medial malleolus until 3 consecutive measurements were the same. Leg lengths were confirmed using 3 nonquantitative methods: checking the height of the knees while the child's pelvis was flat on the table and the medial malleoli were held together, checking the medial malleoli with the child's hips and knees flexed to 90° (13), and checking the height of the iliac crests with the child standing.

Routine hospital testing for antinuclear antibodies (ANA) was done at each center. All children were referred for ophthalmologic surveillance for uveitis, but this was done in the child's community for the most part and was not uniformly monitored. The presence of uveitis was ascertained by both the medical record and questioning during the study examination.

Statistical analysis. Statistical analyses included Fisher's 2-sided exact test and Student's 2-sided *t*-test, using SPSS 7.5 for Windows 95 (SPSS, Inc, Chicago, IL).

RESULTS

Thirty children with pauci JRA who were <7 years old were identified and available for study, 16 from

Table 2. Characteristics of children and their arthritis over the duration of the study*

	WA group (n = 16)	NC group (n = 14)	P
No. of girls	11	12	0.399
Mean \pm SD age at diagnosis	2.6 \pm 1.5	3.0 \pm 1.8	0.507
Mean \pm SD months of symptoms before diagnosis	2.4 \pm 1.7	2.4 \pm 1.2	0.922
No. with pain at diagnosis	11	12	0.399
No. with flexion contractures at diagnosis	11	5	0.141
No. with positive antinuclear antibody	14	6	0.019
No. with uveitis	4	4	1.0
Mean \pm SD months of followup	42 \pm 11	46 \pm 15	0.349
No. prescribed DMARD therapy	4	3	1.0
No. with physical therapy evaluation	7	8	0.715
No. with splints	5	6	0.707
No. with shoe lifts	0	7	0.002
No. of joints with arthritis over duration of study			
Knee	18	14	
Ankle	8	7	
Elbow	3	1	
Finger	2	10	
Toe	5	5	
Eventual no. of joints with arthritis			
One joint	5	5	
Two joints	6	4	
Three joints	4	2	
Four joints	0	2	
Seven joints	1	1	

* WA = Washington group, who received intraarticular steroids early in the disease which were repeated as needed. NC = North Carolina group, who did not receive intraarticular steroids early in the disease. DMARD = disease-modifying antirheumatic drug.

WA and 14 from NC. At diagnosis, the numbers of inflamed knees and ankles were 15 and 6, respectively, among the children in WA, and 12 and 4, respectively, among the children in NC. Comparison of the epidemiologic, diagnostic, and therapeutic variables for the WA and NC groups are shown in Table 2.

All children were Caucasian. The only significant difference in the 2 groups was fewer positive findings on ANA tests in the NC children. There was no difference in the joint disease with regard to location, eventual number of joints involved, need for physical therapy evaluation, need for splinting, and the requirement, in the judgment of the attending rheumatologist, for a disease-modifying antirheumatic drug.

There was a significant difference between the WA and NC groups regarding LLD (Table 3). No child in WA was found to have a measurable LLD, whereas 7 children in NC had LLD (range 0.5–3.5 cm, median 1.0 cm; $P = 0.002$, by Fisher's 2-sided exact test). The percentage difference in LLD was significant between the WA and NC group ($P = 0.005$, by Student's 2-sided t -test). No child in WA was prescribed a shoe lift, and 7 in NC were prescribed shoe lifts ($P = 0.002$, by Fisher's 2-sided exact test) (Table 2). Physical therapy evaluation, in addition to evalu-

ation by the rheumatologist, was similarly required for both groups (Table 2). The difference in TCD between the 2 groups was not significant, although there was a trend toward less discrepancy in the WA group (Table 3).

Table 3. Outcome of thigh and leg length measurements in patients who were injected with intraarticular steroids (WA) and those who were not (NC)*

	WA group (n = 16)	NC group (n = 14)	P
Leg length			
No. with unequal leg length	0	7†	0.002
Mean \pm SD % difference in leg length	0 \pm 0	1.0 \pm 1.4	0.005
Thigh circumference			
No. with unequal thigh circumference	10	13	0.085
Mean \pm SD % difference in circumference	1.7 \pm 1.8	2.7 \pm 1.8	0.139

* WA = Washington group, who received intraarticular steroids early in the disease which were repeated as needed. NC = North Carolina group, who did not receive intraarticular steroids early in the disease. † Of these 7 patients, 1 had 0.5 cm of leg length discrepancy, 5 had 1.0 cm, and 1 had 3.5 cm.

Since the epiphyses of the distal femur and proximal tibia account for 70% of the leg length, we analyzed the 14 children in WA and 10 children in NC who had asymmetric knee arthritis. Again, there were significant differences between the WA and NC groups in both the LLD (mean \pm SD $0.0 \pm 0.0\%$ difference in leg length in WA versus $1.2 \pm 1.5\%$ in NC; $P = 0.007$, by Student's 2-sided *t*-test) and in the use of shoe lifts (0 in WA versus 6 in NC; $P = 0.002$, by Fisher's 2-sided exact test), but not in the TCD ($1.9 \pm 1.8\%$ difference in thigh circumference in WA versus $2.9 \pm 2.1\%$ in NC; $P = 0.254$, by Student's 2-sided *t*-test).

DISCUSSION

The use of IA steroids to treat children with pauci JRA has been shown to quickly reduce the inflammation, and the effects may last for a prolonged time (up to 1 year) (2,3,5,7). IA steroids are associated with a reduction of pannus without deleterious effects on the cartilage (3,14). In one report, IA steroids used early in the treatment of pauci JRA did not influence the duration of remission, but LLD was not measured in that study (5). In the children injected by Padeh and Passwell later in the course of arthritis, there was a trend toward less LLD over time, with the mean discrepancy going from 1.5 cm to 0.8 cm over 2.5 years (7).

In the present study, we found a significant beneficial effect in children who were injected early and repeatedly as needed during the first several years of arthritis. This is consistent with the proposed mechanism for leg length overgrowth, that is, prolonged synovitis with concomitant local hyperemia (10). However, the ascertainment of LLD can be difficult (15), and radiographic measurements were not feasible because of the cost and the lack of clinical indications for radiographs; that is, most of these children did not have clinically significant LLD or enough LLD to be referred for possible surgical therapy (9). LLD was assessed by standard means, measuring from the anterior superior iliac spine to the medial malleolus, and was verified using 3 nonquantitative techniques. Each child was assessed by the same observer, who was not blinded to the location or treatment and who could have overestimated the degree of LLD. However, the records from the treating pediatric rheumatologists agreed with the presence of an LLD on all occasions. The physical therapy reports were also consistent. Findings of all of the above methods used to determine the presence of LLD agreed. The degree of LLD was similar to that in

other reports of pauci JRA patients who were not treated with IA steroids (10).

To enhance uniformity, we selected younger children with pauci JRA. Moreover, younger children have more leg growth potential and are therefore at increased risk of LLD. The 2 groups were statistically comparable with regard to age, race, sex, duration of arthritis, and degree of arthritis (although the WA group had slightly more flexion contractures at diagnosis). A significant number of children from the WA clinic have been reported as having painless JRA (16), so we were especially interested in the incidence of painless JRA in NC, since painless JRA may be present for a longer period of time before referral to a pediatric rheumatologist. Painlessness, too, proved to be similar between the NC and WA subjects in this study.

The only other difference observed was the relative infrequency of children in NC who had ANA. However, the numbers of children with uveitis, which is known to be associated with ANA, were equal in the WA and NC groups. The reason for this observation is unknown. It is possible that when a large number of variables is examined, there is the statistical risk that unimportant associations will be found. Another possibility is that children with spondylarthropathies were overrepresented in the NC group, but we have no corroborating evidence for this, such as the frequency of enthesitis or HLA-B27 test results (17).

Although the degree of LLD with inactive arthritis is probably not clinically significant nor a biomechanical problem (18), it does bespeak the duration of active synovitis. IA steroids, repeated as needed, seemed to adequately control the synovitis. This was not a prospective study and therefore the actual duration of synovitis was not ascertained, nor were the costs of IA steroids versus NSAIDs. The different treatment practices, such as frequency of monitoring laboratory studies on children using NSAIDs and frequency of clinic appointments, prevented determination of potential cost differences between our study groups. Other, intangible outcome variables such as need to administer oral medication multiple times a day, behavioral and other side effects of NSAIDs, distresses of injections, risk of anesthesia for injections, and the unwillingness of some children to wear shoe lifts was also not addressed due to the retrospective nature of this study, but these factors can be significant to many families.

The fact that thigh circumference was not different between the 2 groups is not entirely surprising since the mechanism for muscle atrophy is different than that for bony overgrowth (10). Use of IA steroids even

sooner in the course of illness may be necessary to avoid atrophy of the thigh muscles, perhaps with early physical therapy directed toward the thigh musculature after synovitis and flexion contractures have resolved. A larger number of children treated very early in the disease course with IA steroids would need to be studied to determine this.

IA steroids are not without possible side effects. The most commonly reported side effects are local skin atrophy, acute increase in pain, presumably due to irritation of the joint, and local calcifications (19,20). There is a transient suppression of the adrenocortical axis (21). Rarely, serious untoward effects can occur, including infection and anaphylaxis (22,23).

This study was limited to children with pauci JRA because the arthritis is usually asymmetric and involves the lower extremities. IA steroid therapy in polyarticular JRA was not investigated; however, these results may be applicable to children with more widespread arthritis involving the lower extremities. IA therapy may preclude the need for oral therapy in children with relatively limited arthritis.

In summary, the early and continued use of IA steroids in young children with pauci JRA involving the lower extremity may be associated with less LLD, presumably by decreasing the duration of synovitis.

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