ORIGINAL ARTICLE

Role of Intra-Articular Corticosteroid Injection in Children with Juvenile Idiopathic Arthritis

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Pak Pediatr J 2024; **48(3):** 211-17

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Received 11th July 2024;
Accepted for publication
27th July 2024

ABSTRACT

Objective: To determine the role of intra-articular corticosteroid injection (IACI) in inducing remission of synovitis in children with Juvenile idiopathic arthritis (JIA).

Study Design: Quasi-experimental study

Place and Duration of Study: Pediatric Medicine/Rheumatology Department at The University of Child Health Sciences Lahore from July 2021 to July 2022.

Material and Methods: All patients, regardless of gender, who met the JIA criteria set forth by the International League of Associations for Rheumatology were enrolled and given IACI (single or multiple). Data from pre- and post-IACI (after 6 months) were recorded, including synovitis symptoms and signs, erythrocyte sedimentation rate (ESR), and patients' and doctors' visual analogue pain scale (VAS). SPSS version 23 was used for the statistical analysis. The post-IACI response for quantitative variables was ascertained using a paired sample t-test. A significant P-value was defined as ≤ 0.05.

Results: A total of 45 joints from 27 individuals were injected. There were 16/27 (60%) males and a 1.5:1 M:F ratio. At IACIs, the average age was 9.1 ± 3.5 years. Knee joint was the most common joint implicated in 33/45 (73.3%). Movement restriction was one of the indications of a synovitis flare, along with warmth, edema, and pain in 21 joints (46.7%). Post-IACI, 34 joints (76%) had established remission. Regarding joint synovitis (p=0.005), ESR (p=0.005), VAS physicians (p=0.006), and VAS parents/patient (p=0.009), there was a statistically significant improvement after IACI.

Conclusion: IACI is a type of local therapy used to treat JIA patients by reversing joint synovitis and improving ESR and VAS (patient/ parent, and physician).

Key Words: *Juvenile Idiopathic Arthritis, JIA, Synovitis, flare, Intra-articular steroids, IACI, ESR, VAS*

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a diverse group of illnesses that share the clinical presentation of arthritis and is the most common rheumatic disease in children. The global prevalence of JIA varies between 0.8 to 22.6 per 100,000 infants annually. The International League of Associations for Rheumatology (ILAR) suggested

a classification system for JIA that includes all kinds of chronic juvenile arthritis. There are seven subcategories: systemic arthritis, oligo-arthritis, polyarthritis-rheumatoid factor (RF) positive, polyarthritis-rheumatoid factor (RF) negative, psoriatic arthritis, enthesitis-related arthritis, and undifferentiated arthritis.[1]

Diagnosis of JIA is almost always clinical and laboratory investigations are used for confirmation and to rule out other possible causes of childhood arthritis. JIA may cause severe morbidity in terms of joint abnormalities such as leg-length disparity, joint contractures, or vision loss from chronic uveitis if proper and early aggressive treatment is not received.[1,2]

The main goals of medical management are to support normal growth and nutrition while also reducing inflammation and causing remission before irreversible joint injury and impairment arise. Additionally, children with this disease have a better quality of life when their mental and physical well-being is preserved.[3-5] As the disease course is characterized by relapses, treatment is aimed not only to induce remission but also to prevent relapse with the minimum side effects of medications, although sustained remission without medication is yet to be achieved.[6] JIA can be treated with combinations of non-steroidal anti-inflammatory drugs (NSAIDS), disease modifying anti-rheumatic drugs (DMARDs), biological drugs, corticosteroids either topical, systemic or intra articular and physiotherapy.[1,3] Newer treatment options including TNF-alpha blockers, Interleukin-6 blockers are increasingly used to treat children with JIA and prevent deformities and improve quality of life.[6]

IACI is frequently used in children with JIA and are thought to be a safe and efficient way to treat the pain, edema, and restricted joint motion associated with active synovitis. IACI is frequently utilized as a first line of treatment for patients with oligoarticular JIA and as supplemental therapy for individuals with other subtypes of JIA, such as polyarticular JIA, when synovitis is limited to one or a few joints, and systemic onset JIA.[3,7,8] Following their initial IACI, some patients get a long-lasting remission and do not go on to develop chronic illness.[9] Furthermore, compared to oral or intravenous corticosteroids, IACI is linked to far lower systemic toxicity.[8] It also helps to relieve joint contractures, reduce leg-length disparity, stop oral steroid use, and thus prevent steroid adverse effects. All these benefits go beyond just relieving active synovitis.[8,10] Ultrasound in patients with JIA is useful to detect synovitis, as well as declaration of remission. It is ideal to guide needle during IACI, specifically small joints and complicated joints like hip joint. When a patient needs repeated joint injections or is younger than six years old, the use of local anaesthetic drugs is strongly advised. Midazolam sedation is a further option.[11] IACI is most frequently linked to local side effects such infection, hypopigmentation, local skin atrophy, intra- or periarticular calcification, and avascular necrosis of the epiphyseal bone.[11-13]

As JIA is a less common as compare to infectious diseases in South East Asia, so less research work available related to this disease and regarding IACI in patients with JIA. This study is planned with the aim to determine the role of IACI in inducing remission of synovitis in children with JIA. The study results would benefit JIA patients not only with oligoarticular subtype but in children with polyarticular subtype. This will also create an evidence for use of IACI as an alternative to the use of systemic steroids making these children free of pain and limp, and overcoming the issues of compliance associated with systemic steroids and their side effects. Given the fact that no such study has been conducted nationally, peculiarity of the genetic makeup of Pakistani children and context specific treatment pathways, this study will generate evidence of strengthening knowledge base for management of JIA patients.

MATERIAL AND METHODS

Between July 2021 and July 2022, this quasi-experimental study was carried out at the University of Child Health Sciences & The Children's Hospital Lahore at the Department of Pediatric Medicine/Rheumatology. Every patient, regardless of gender, who met the ILAR criteria for JIA and having signs and symptoms (S/S) of synovitis in one or more joints were enrolled in the study. Informed consent from enrolled patients or parents of patients were taken after a detailed description of the procedure and its adverse events. Demographic data including gender and age at the time of enrollment, duration of disease

at presentation, sub-types of JIA as per ILAR classification and type of joint injected, laboratory parameters including erythrocyte sedimentation rate (ESR), rheumatoid factor (RF) and anti-nuclear antibody (ANA) and other medications used by patients were recorded. Visual analogue scale (VAS) for pain was utilized to assess the patient's status of pain in joints (VAS 0-10 cm score). S/S of synovitis included swelling/effusion of joint, or two of those symptoms: elevated body temperature, tenderness or pain during motion, and limited range of motion.

Triamcinolone acetonide (TA) was used as IACI (single or multiple) in this study. IACI was given according to the age, type of joint and weight of patient mixed with lignocaine injection. Typically, 1 mg/kg (maximum dose of 40 mg) was applied to the knees, and 0.5 mg/kg (maximum dose of 20 mg) was applied to the ankles, elbows, and wrists. A maximum dose of 10 mg was administered (0.3 mg/kg) in the wrist, midtarsal, and subtalar joints. The clinical decision of IACI was taken by pediatric rheumatologist after detailed evaluation. Before performing the procedure, efforts will be made to counsel the patient to decrease the stress of the procedure. Same rheumatologist injected into the joints to decrease the bias. An ultrasound scan was done to guide the needle for ankle, wrist and PIP joints. It was used in the knee joint when a small amount of effusion was suspected. Topical local anaesthetic with subcutaneous lidocaine 1% will be used to decrease the procedural pain in all children except for proximal interphalangeal (PIP) joints. Intravenous midazolam (0.3 -0.5 mg/kg) will be given to patients under the age of 6 years in addition to local anaesthetic agents. After aseptic measures and local anaesthesia, 5 ml / 10ml needle (1 ml for PIP joint) was inserted into the joint cavity. Synovial fluid was aspirated and joint was injected with TA and sterile dressing was done. Rest the joint was advised for 48h after the procedure. Pre-and post-IACIs (after 6 months of IACI) data including S/S of synovitis, erythrocyte sedimentation rate (ESR), visual analogue pain scale (VAS) of physicians and patients were noted. Remission of synovitis was documented when there was absence of signs and symptoms of synovitis that include no swelling/effusion of joint or improvement in range of motion, no tenderness or pain on motion and decreased heat.

With SPSS v.23, statistical analysis was carried out. For the quantitative data, including age, length of disease at presentation, and ESR, a mean with standard deviation was computed. For qualitative factors such as gender, the kind of joint injected, the frequency of arthritic subtypes, and the remission of synovitis (pain, swelling, limited movement, and elevated temperature), percentages were computed. The response in post-IACI was ascertained using a paired sample t-test. A P-value of less than 0.05 was deemed significant.

RESULTS

Out of 30 patients enrolled, 27 were completed the study in whom 45 joints injected with IACIs. (fig1). There were 60% males (16/27) with M:F = 1.5:1 and the commonest age group was between 6-10 years. (fig 2). Mean age at time of IACIs was 9.1±3.5 years and mean duration of disease at presentation was 2.53 ± 1.53 SD. The commonest sub-type of JIA was oligo-arthritis (both persistence and extended) in 40.7%. Almost all patients were on oral medications including NSAIDS, DMARDs and/or oral steroids. (Table 1).

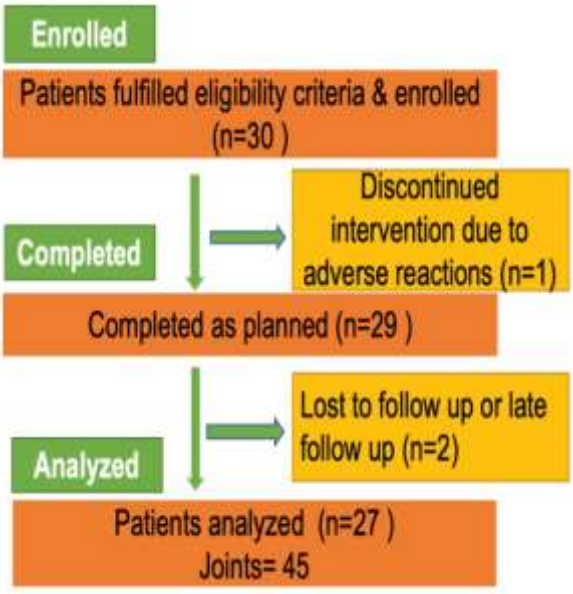

Fig 1: Flow chart of patients enrolled

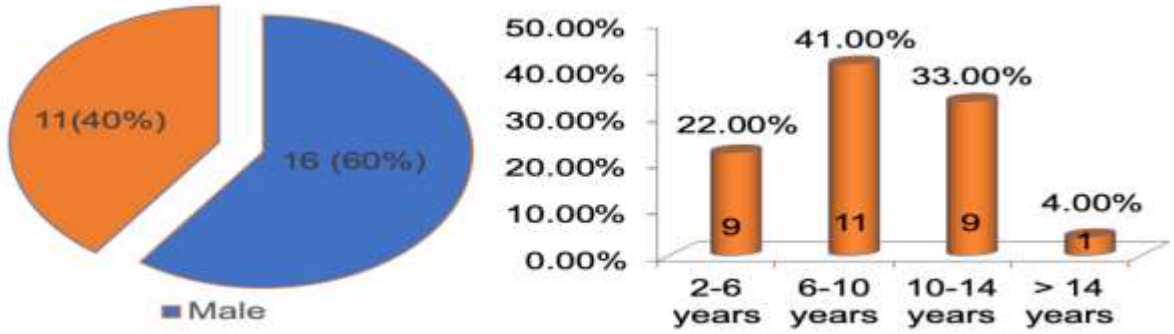

Fig 2: Gender & age distribution of JIA patients (n=27)

The knee joint was the most often injected (73.3%) of the 45 joints. (fig 3). Movement restriction is one of the symptoms of synovitis, along with swelling, warmth and pain in 21 joints (46.7%) while limitation of movement with pain and swelling in 16 joints (35.6%), limitation of movement and pain in 8 joints (17.8%). Remission at 3 months after IACI was noted in 34 joints (76%).

TABLE 1: Characteristics of JIA patients (n=27)

	No.	Percentage
JIA sub –types		
Systemic onset Disease	4	14.8
Oligoarthrit persistence	8	29.6
Oligoarthrits extended	3	11.1
Polyarticular RF negative	9	33.3
Polyarticular RF positive	2	7.4
Enthesitis-related arthritis	1	3.7
Rheumatoid Factor positive	2	7.4
Antinuclear antibodies positive	7	30.0
NSAIDS alone	3	11.0
NSAIDS+ oral steroid	6	22.0
NSAIDS + DMARD's	10	37.0
NSAIDS+ DMARD's+ oral steroid	8	30.0

There was no significant relationship of the gender, subtype of JIA, RF, ANA with remission of synovitis. Children >10 years of age who underwent IACIs achieved remission (p=0.001). (Table 2). Joint synovitis (p=0.005), as shown in fig 4. ESR (p=0.005), VAS physicians (p=0.006), and VAS parents/patient (p=0.009) all showed statistically significant improvements following IACI. (Table 3).

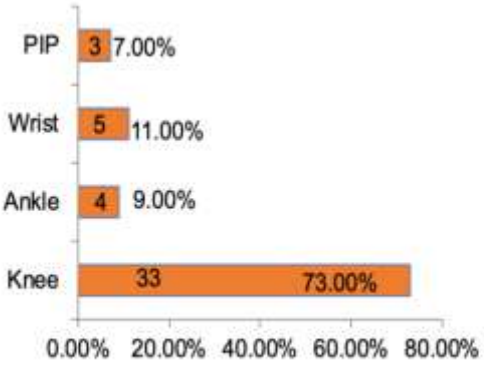

Fig 3: Types of Joint injected IACI (n=45)

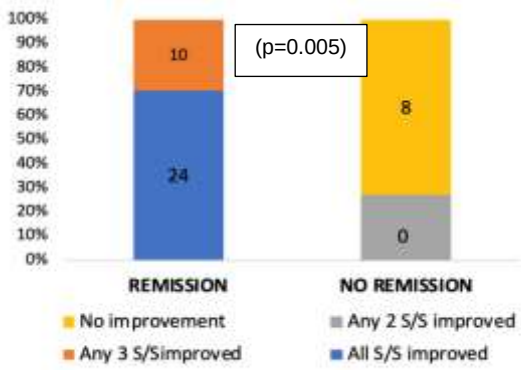

Fig 4: Sign / symptoms of Synovitis-Outcome (P value= 0.005)

TABLE 2: Comparison of various parameters in remission & no remission group (n=27)

	Remission (%)	No Remission (%)	Total (%)	p-value
Gender				
Male	10(62.5)	6(37.5)	16(100.0)	
Female	9 (81.8)	2(18.2)	11(100.0)	0.28
Age in groups				
2-6 years	0 (0.0)	6 (100.0)	6 (100.0)	
6-10 years	9 (81.8)	2 (18.2)	11 (100.0)	**0.001**[a]
10-14 years	9 100.0)	0 (0.0)	9 (100.0)	
>14 years	1 (100.0)	0 (0.0)	1 (100.0)	
JIA subtype				
Oligoarthritis persistence	4 (50.0)	4 (50.0)	10 (100.0)	
Oligoarthritis extended	3 (100.0)	0 (0.0)	3 (100.0)	
Polyarticular RF+	1 (50.0)	1 (50.0)	2 (100.0)	0.712[a]
Polyarticular RF-	6 (66.7)	3 (33.3)	10 (100.0)	
Systemic onset JIA	3 (75.0)	1 (25.0)	4 (100.0)	
Enthesitis-related arthritis	1 (100.0)	0 (0.0)	1 (100.0)	
Rheumatoid factor				
RF positive	1 (50.0)	1 (50.0)	2 (100.0)	
RF negative	17 (68.0)	8 (32.0)	25(100.0)	0.603[b]
ANA				
ANA positive	7 (87.5)	1 (12.5)	7 (100.0)	
ANA negative	12 (63.2)	7 36.8)	19 (100.0)	0.364[a]

[a]Chi square test, [b]Fisher's exact test

TABLE 3: Comparison of pre & post IACI treatment (n=45)

Variable	Pre-IACI (Mean ± SD)	Post-IACI Mean ± SD)	Confidence interval (CI)		p-value
			Lower	Upper	
ESR	39.8 ± 21.8	29.1 ± 19.5	5.22	16.15	0.005
VAS Patient/Parent	8.29 ± 1.21	3.36 ± 2.7	4.18	5.68	0.009
VAS Physician	7.60 ± 1.54	2.62 ±2.57	4.25	5.70	0.006

In terms of side effects of IACIs, one patient was excluded from study due to development of hemorrhage in joint while giving injection. Out of 45 IACI, 8 joints (17.8%) had skin hypopigmentation, 2 (4.4%) had sub-cutaneous atrophy on follow up.

DISCUSSION

A set of recommendations issued by American College of rheumatology (ACR), designed meant to help medical professionals choose the JIA treatment that is both safe and effective.[14] IACI is frequently used as the first line of treatment for people with oligoarticular JIA. They are also utilized as an adjuvant treatment for patients with other subtypes of JIA to quickly decrease inflammation until systemic drugs take its action.[7] Response rates at six months range from 53.4% to 100%, indicating the effectiveness of TA.[7,15]

The patients in this study had a mean age of 9.1± 3.5 years and a male to female ratio of 1.5:1. In contrast to Western literature that indicates a female prevalence in JIA,[1] multiple research carried out in Pakistan and India to ascertain the spectrum of JIA revealed that the number of male and female cases was nearly equal.[2,16-18] Numerous studies from various South-East Asian studies have revealed late age at presentation.[16,17] In another study from Karachi, Gowa et al., 55% of the participants were female and 85% had ages ranging from 6 to 10.[19] These studies are all conducted in the same geographic area and are hospital-based. When demographics of JIA patients who underwent IACI, similar results were found with Male dominance male-female ratio of 1.5:1, as conducted by Leow et al. at Singapore.[20] Unsal et al. did a study by enrolling

Turkish children with an average age of 7.3 ± 3.7 years and male to female ratio of 1:1.5.[21]

The commonest sub-type of JIA was oligo-arthritis (both persistence and extended) in 40.7%, which is consistent with studies conducted by Angela et al, Rubin et al and Cunha et al, at their centers.[8,12,22] Some studies like Harhay et al, at Oishei Children's Hospital, Buffalo enrolled only those patients having oligoarticular JIA.[7] Knee joint was the commonest joint in many international studies[3,7,12] similar to our study. The reason being more patients of oligo-arthritis JIA were enrolled. Remission in synovitis after IACI was seen in 3/4 of the patients which is similar to many studies conducted in various parts of world.[3,12] According to an international study, IACI showed to be an efficient treatment with a mean time of relapse as 10.47 ± 0.42 months.[23] In another study, total of 165 intra-articular injections were performed on 88 patients; 63% of them showed favorable results, and their joints remained immobile for a median of 18.1 months.[22] Leow et al, observed a very high frequency of remission (80.95%) 2 months after injection, which lasted for more than 6 months.[20] Similarly, in another trial, 109 children with juvenile idiopathic oligo-arthritis were followed up for a total of 4.3 years after receiving their first intra-articular corticosteroid injection. The results revealed that over 40% of the children who had oligoarticular JIA and required IACI did not develop a chronic illness.[9]

The present study is first of its kind in local population and has established the role of IACI in Pakistani children with JIA. The frequency of remission at 6 months was 76% which is comparable to that already published in literature. In the light of this evidence, it can be advocated that in future practice, JIA children presenting with synovitis should be treated with intra-articular steroid injection. This will also minimize the risks associated with systemic steroids.

Limitation: The present study was small sample size. To validate our results, larger prospective studies evaluating response of the IACI and response factors, such as the dosage of the medicine, should be considered. Furthermore, long term side effects of IACI particularly damage to the growth plates, should be considered in future research.

CONCLUSION

IACI is an effective local therapy in inducing remission of joint synovitis in three-fourth of the injected joints. Moreover, there is significant improvement in ESR and VAS (patient / parent and physician), more effective in patients older than 10 years of age. Follow up study is needed to evaluate the effectiveness of steroids in decreasing/stopping the systemic steroids, thus avoiding its toxic side effects.

Conflict of interest: Nil

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