



Sociedad Española
de Reumatología -
Colegio Mexicano
de Reumatología

Reumatología Clínica

www.reumatologiaclinica.org



Special Article

Intra-articular Joint Injections in Juvenile Idiopathic Arthritis: State of the Art[☆]



Juan Carlos Nieto-González,* Indalecio Monteagudo

Servicio de Reumatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain

ARTICLE INFO

Article history:

Received 13 March 2018

Accepted 19 July 2018

Available online 15 February 2019

Keywords:

Juvenile idiopathic arthritis
Intra-articular joint injections
Ultrasound guidance

ABSTRACT

Objective: Intra-articular corticosteroid injections (IACI) are a fundamental part in the treatment of juvenile idiopathic arthritis. The current situation of IACI is reviewed in a population of children.

Methods: We conducted a narrative review of the literature related to IACI in children, with respect to the injection technique, use of local and general anaesthesia, ultrasound guidance of the procedure, indications, special joints and type of optimal corticosteroid.

Results: IACI are indicated in any subcategory of juvenile idiopathic arthritis, especially in oligoarticular juvenile idiopathic arthritis. The use of local anaesthetic is highly recommended, and in patients younger than 6 years or requiring multiple joint injections, conscious sedation can also be an option. Ultrasound guidance of injections is recommended in expert hands, but not in a generalised way. Triamcinolone hexacetonide is the corticosteroid of choice in large joints, whereas a more soluble corticosteroid is a better alternative in small or superficial joints (betamethasone or methylprednisolone) to avoid subcutaneous atrophy or hypopigmentation, the most frequent adverse effect of IACI.

Conclusions: IACI are performed heterogeneously and scientific evidence is limited in many cases.

© 2018 Elsevier España, S.L.U. and Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. All rights reserved.

Estado actual del tratamiento con infiltraciones intraarticulares en la artritis idiopática juvenil

RESUMEN

Objetivo: Las infiltraciones intraarticulares con corticoides (IAC) son parte fundamental en el tratamiento de la artritis idiopática juvenil. Se realiza una revisión sobre la situación actual de las IAC en población infantil.

Métodos: Revisión narrativa de la literatura de las IAC en población infantil, relacionada con la técnica de infiltración, el uso de anestesia local y general, la guía ecográfica, las indicaciones, las articulaciones especiales y el tipo de corticoide.

Resultados: Las IAC están indicadas en cualquier subcategoría de artritis idiopática juvenil y especialmente en la forma oligoarticular. El uso de anestésico local es recomendable, y en pacientes menores de 6 años o que requieran infiltración múltiple, también la sedación consciente. La infiltración guiada por ecografía es recomendable en manos expertas, pero no de forma generalizada. El hexacetónido de triamcinolona es el corticoide de elección en articulaciones grandes, mientras corticoides más solubles (betametasona o metilprednisolona) serían la alternativa ideal en articulaciones pequeñas o superficiales para evitar la atrofia subcutánea o la hipopigmentación, los efectos adversos más frecuentes.

Conclusiones: Las IAC se realizan de forma heterogénea y la evidencia científica es limitada.

© 2018 Elsevier España, S.L.U. y Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. Todos los derechos reservados.

Palabras clave:

Artritis idiopática juvenil
Infiltraciones intraarticulares
Guía ecográfica

[☆] Please cite this article as: Nieto-González JC, Monteagudo I. Estado actual del tratamiento con infiltraciones intraarticulares en la artritis idiopática juvenil. Reumatol Clin. 2019;15:69–72.

* Corresponding author.

E-mail address: juancarlos.nietog@gmail.com (J.C. Nieto-González).

Introduction

Juvenile idiopathic arthritis (JIA) encompasses all arthritis of unknown origin in individuals under the age of 16 years old which lasts for longer than 6 weeks.¹ In all of the sub-categories of JIA local treatment with the intra-articular infiltration of corticoids (IAC) is a part of normal therapeutic management.² Oligoarticular JIA is the type that affects 4 or fewer joints during the first 6 months of evolution of the disease, and it may sometimes be treated exclusively with IAC.² Although IAC is performed very frequently in the treatment of JIA, opinions vary widely regarding the use of general or local anaesthetics, the infiltration technique, ultrasound guiding of the procedure or the corticoid that should be used.^{3,4} The differing ages of the patients and the different locations mean that it would be complicated to standardise the IAC procedure in children. This narrative review of the literature summarises the different aspects of IAC procedures in the treatment of JIA.

Infiltration Technique

Although the infiltration technique has not been completely established, it is governed by the same recommendations that apply in adults, and these are summarised in [Table 1](#). The literature contains a great many single-centre studies which describe their experience in performing IAC,^{5–9} although there are no guides or recommendations about how to do so. IAC is a situation in which children feel stress and nervousness, so that it is positive to create a relaxed atmosphere before performing the procedure.³ IAC should be performed with exquisite asepsis and in as short a time as possible. It is important to use sterile gloves and clean the puncture area with a topical antiseptic. It is recommended that as much liquid as is possible be extracted from the joint before infiltrating the corticoid. The needle should be cleaned in physiological serum to prevent subcutaneous atrophy.¹⁰ As is the case in adults, it is also recommendable to rest the unsupported joint for from 24 to 48 h to prevent arthritis secondary to the introduced corticoid, even though this is very rare.¹⁰

Anaesthesia

It is recommendable to use a local anaesthetic in all IAC¹¹ procedures, with lidocaine that is either in an ointment (Emla[®]) or subcutaneous, chlorethyl in a spray or iontophoresis with lidocaine, depending on what is available. There is more evidence for the use of local anaesthetics or conscious sedation than is the case for other aspects of IAC.^{11–16} Uziel et al. compared the efficacy of a previous application of Emla[®] in reducing the pain reported by children with JIA during knee IAC.¹² This double-blind randomised clinical trial showed no significant differences between the patients who used Emla[®] and those who did not, although Emla[®] is in very widespread use as a local anaesthetic.¹¹ It is recommended that it be applied 60 min prior to the procedure using an occlusive dressing, giving rise to anaesthesia in the top 3–5 mm of the skin.¹¹ Nevertheless, in clinical practice it is sometimes hard to comply with the minimum

Table 1
General Recommendations for the Administration of Intra-articular Infiltrations in the Paediatric Population.

Recommendation
Infiltrate one or two joints per procedure
Reinfiltrate after at least 2–4 weeks, if necessary
Do not infiltrate the same joint more than 3–4 times per year
Painstaking asepsis during the procedure
Use a local topical or subcutaneous anaesthetic
Use general anaesthesia or conscious sedation when necessary
Rest the joint for 24–48 h after the procedure

time during which Emla[®] ointment should be applied. Lidocaine iontophoresis produces anaesthesia in somewhat more than the top 8 mm of the skin following a 20 min¹⁰ application. However, this technique is not available in the majority of hospitals. It is probable that restriction of the effect of Emla[®] to the superficial level of the skin is the reason for the lack of differences in pain during IAC found by Uziel et al. in their clinical trial.¹²

The use of local anaesthetics is widely accepted in paediatric rheumatology,¹³ and a combination of a topical local anaesthetic with subcutaneous lidocaine may be beneficial in certain patients.¹⁴ Weiss et al. undertook an observational study comparing the use of a local anaesthetic (Emla[®] or lidocaine iontophoresis) with subcutaneous lidocaine.¹⁴ They compared pain at 3 moments in the procedure: prior to the application of the local anaesthetic, after its application and just before the infiltration, and lastly after the IAC. They found no differences in reported pain between patients who had received subcutaneous lidocaine as well as a local anaesthetic and those who had only receive a local anaesthetic. The exception to this was post-IAC pain in girls, which was less when the methods of local anaesthesia were combined.¹⁴

Respecting general anaesthesia or conscious sedation, although some authors propose that this should be obligatory in all procedures,¹⁵ it is accepted more widely in specific situations.¹³ The situations in which it is recommended that some type of conscious sedation (nitrous oxide, propofol, midazolam or fentanyl¹¹) be used are: patients under the age of 6 years old, when there is a need to infiltrate 3 or more joints, or in complicated or small locations (the coxofemoral joint or subastragalus, for example).¹³ On the other hand, when parents and children were asked about their preference in the use of sedation, their opinions differed significantly.¹⁶ While the younger children preferred sedation, the parents preferred to avoid the risks this involves. Nevertheless, when the children are older or have had the disease for longer, a higher proportion of them prefer to avoid sedation.¹⁶

Ultrasound Scan Guidance

Ultrasound scan is an ideal imaging technique for evaluating the paediatric population, and it makes it possible to guide the needle during IAC.^{7–9} Ultrasound scan guidance in IAC has been proven to be more precise and effective in adults.¹⁷ However, in the paediatric population there is no enough scientific evidence to recommend the use of ultrasound scan guidance in all IAC procedures.^{7–9,18–22} There are many description of its use in different hospitals, but they do not compare the efficacy of procedures carried out with or without ultrasound scan guidance.^{20–22} In small or complicated joints such as the hip, due to its depth and the proximity to the vascular-nerve bundle, it is recommended that ultrasound scan guidance be used by an expert.¹⁸ The exception to this recommendation is at the level of the temporomandibular joint (TMJ).¹⁹ Resnick et al. compared the improvement in pain management and mouth opening between patients who had received IAC of the TMJ with and without ultrasound scan guidance. They found that the only difference between both groups was the time taken by the procedure, which lasted for 49 min longer in the group with ultrasound scan guidance.¹⁹

Indications

All patients with JIA are treatable using IAC or peritendinous AC as a single or complementary procedure.² The oligo-articular form may enter remission after one or several infiltrations. A recent systematic review found that IAC have a beneficial effect.²⁰

The use of systemic treatment with methotrexate in oligo-articular JIA is controversial, and it is not commenced in a routine

way, especially in patients with monoarthritis.²³ Recently the open, longitudinal and multicentre study by Ravelli et al. has shown that adding methotrexate to the treatment of patients with oligo-articular JIA after IAC of 2 or more joints may slightly increase the effect of infiltrations.²⁴ Nevertheless, the question of whether or not children with oligo-articular JIA benefit from starting treatment with methotrexate has yet to be answered.²⁴

Dysmetria is one of the most common complications that we may find in patients with JIA, especially those with the oligo-articular form and asymmetric synovitis. The hyperaemia that produces the inflammation leads to greater growth of the affected limb and this in turn causes a biomechanical problem that may give rise to complications in adult age. IAC prevent or reduces the severity of joint discrepancy.²⁵ A classic study of 1999 which compared patients with JIA monitored in a hospital where IAC was performed as part of knee synovitis treatment with patients in another hospital where IAC was not used, showed that joint discrepancy was significantly greater in the second group of patients.²⁵

Infiltration of Multiple Joints

Although there is no limit to the number of joints that may require infiltration, a systemic effect is inevitable when many joints are infiltrated.¹⁰ The efficacy of multiple infiltrations (3 or more joints per procedure) has been evaluated in descriptive single-centre studies.^{26,27} In 2013, Papadopoulou et al. published a retrospective observational study in which joint remission following multiple IAC was observed in one third of the patients included, with an average follow-up of 11 months, as opposed to the two thirds of patients who had a new joint relapse following the IAC in an average time of 6 months.²⁷ These results are not very favourable regarding the routine performance of multiple IAC.²⁷ On the other hand, the efficacy of multiple infiltrations has not been compared with the use of short cycles of systemic corticoids, and it could be asked whether both strategies have a similar level of efficacy, thereby preventing an invasive procedure such as multiple infiltrations.

These multiple procedures require general anaesthesia or at least conscious sedation, and they require a longer session duration, so they are not recommended as routine practice. In the authors' opinion the maximum recommendable number of IAC per session is 3 joints.

Temporomandibular Joints

TMJ are often affected by JIA and they must be examined in all patients, regardless of subcategory. IAC of the TMJ is a relative frequent procedure that improve pain and mouth opening.^{19,28–30} The improvement is greater in those patients with a shorter time of evolution of their arthritis.²⁹ In patients with morphological alterations and a longer time of evolution, hardly any functional improvement occurs and pain relief is temporary.³⁰ The most common adverse effect of IAC in this location is subcutaneous atrophy, as this is a superficial joint. It is recommended as a complementary treatment, and, as was pointed out above, although ultrasound guidance does not increase its efficacy, it does mean that a longer time is necessary for the procedure.¹⁹

Type of Corticoid

The type of corticoid to be administered depends on the size of the joint: **Table 2** shows the recommended dose and corticoid for each joint. It is here that the scientific evidence is the most solid, and where recommendations are the most widely accepted. IAC has longer-lasting efficacy when triamcinolone hexacetonide is

Table 2
Type of Corticoid and Recommended Dose for Each Joint.

	Type of corticoid	Dose
Large joints (shoulder, hip or knee)	Triamcinolone hexacetonide	1 mg/kg (maximum 40 mg) ^a
Medium-size joints (elbow, carpus and ankle)	Triamcinolone hexacetonide	0.75 mg/kg (maximum 30 mg) ^a
Small joints (metacarpus and finger joints)	Methylprednisolone	5–10 mg ^a
Special joints (subastragalus or tendon sheaths)	Methylprednisolone	20–40 mg ^a

^a The dose will depend on the age and size of each patient.

used rather than more soluble corticoids such as betametasone.³¹ The former also undergoes less systemic diffusion and it causes less alteration of cortisol and glucose levels.³² Respecting triamcinolone, hexacetonide has been shown to be more powerful than acetone in longitudinal studies as well as in retrospective ones.^{32–35} On the other hand, in spite of the fact that hexacetonide has been proven to have twice the anti-inflammatory effect than acetone, the use of a double dose of triamcinolone acetone does not give a greater benefit than the usual dose of triamcinolone hexacetonide.³³ The study by Zulian et al. included patients with JIA and symmetrical synovitis (the majority in the knees); one joint was infiltrated with the standard dose of hexacetonide and the other one received an infiltration of the double dose of acetone. A higher proportion of the joints infiltrated with hexacetonide went into remission, and they did so for a longer time.³³ Adverse effects, chiefly subcutaneous atrophy and hypopigmentation, are more frequent with depot corticoids, so that these are not recommended for small or superficial joints, where it is more suitable to use soluble corticoids (betamethasone or methylprednisolone).

Conclusions

IAC are very common procedures in the treatment of JIA, especially in the oligo-articular subcategory, together with systemic treatment or alone. It is highly recommendable to use local anaesthesia before or during the procedure, and to evaluate using conscious sedation in specific situations. Although ultrasound guidance is not recommended as a routine, it may be useful in expert hands to prevent complications in the procedure. In general, large joints benefit more from the administration of triamcinolone hexacetonide, while more soluble corticoids (betamethasone or methylprednisolone) are preferable for small or superficial joints.

Conflict of Interests

The authors have no conflict of interests to declare.

References

- Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Associations for Rheumatology. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol.* 2004;31:390–2.
- Beukelman T, Patkar NM, Saag KG, Tolleson-Rinehart S, Cron RQ, DeWitt EM, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res (Hoboken).* 2011;63:465–82.
- Scott C, Meiorin S, Filocamo G, Lanni S, Valle M, Martinoli C, et al. A reappraisal of intra-articular corticosteroid therapy in juvenile idiopathic arthritis. *Clin Exp Rheumatol.* 2010;28:774–81.
- Cleary AG, Murphy HD, Davidson JE. Intra-articular corticosteroid injections in juvenile idiopathic arthritis. *Arch Dis Child.* 2003;88:192–6.

5. Parra DA. Technical tips to perform safe and effective ultrasound guided steroid joint injections in children. *Pediatr Rheumatol Online J.* 2015;13:2.
6. Leow OM, Lim LK, Ooi PL, Shek LP, Ang EY, Son MB. Intra-articular glucocorticoid injections in patients with juvenile idiopathic arthritis in a Singapore hospital. *Singapore Med J.* 2014;55:248–52.
7. Young CM, Shiels WE 2nd, Coley BD, Hogan MJ, Murakami JW, Jones K, et al. Ultrasound-guided corticosteroid injection therapy for juvenile idiopathic arthritis: 12-year care experience. *Pediatr Radiol.* 2012;42:1481–9.
8. Young CM, Horst DM, Murakami JW, Shiels WE 2nd. Ultrasound-guided corticosteroid injection of the subtalar joint for treatment of juvenile idiopathic arthritis. *Pediatr Radiol.* 2015;45:1212–7.
9. Peters SE, Laxer RM, Connolly BL, Parra DA. Ultrasound-guided steroid tendon sheath injections in juvenile idiopathic arthritis: a 10-year single-center retrospective study. *Pediatr Rheumatol Online J.* 2017;15:22.
10. Courtney P, Doherty M. Joint aspiration and injection and synovial fluid analysis. *Best Pract Res Clin Rheumatol.* 2013;27:137–69.
11. Oren-Ziv A, Hoppenstein D, Shles A, Uziel Y. Sedation methods for intra-articular corticosteroid injections in juvenile idiopathic arthritis: a review. *Pediatr Rheumatol Online J.* 2015;13:28.
12. Uziel Y, Berkovitch M, Gazarian M, Koren G, Silverman ED, Schneider R, et al. Evaluation of eutectic lidocaine/prilocaine cream (EMLA) for steroid joint injection in children with juvenile rheumatoid arthritis: a double blind, randomized, placebo controlled trial. *J Rheumatol.* 2003;30:594–6.
13. Weiss JE, Uribe AG, Malleon PN, Kimura Y. Anesthesia for intra-articular corticosteroid injections in juvenile idiopathic arthritis: a survey of pediatric rheumatologists. *Pediatr Rheumatol Online J.* 2010;8:3.
14. Weiss JE, Haines KA, Chalom EC, Li SC, Walco GA, Nyirenda TL, et al. A randomized study of local anesthesia for pain control during intra-articular corticosteroid injection in children with arthritis. *Pediatr Rheumatol Online J.* 2015;13:36.
15. Pastore S, Gortani G, Taddio A, Barbi E. Procedural sedation for intra-articular corticosteroid injections in juvenile idiopathic arthritis (JIA) should be a standard of care. *Eur J Pediatr.* 2014;173:831.
16. Casado R, Lumbreras J, de Inocencio J, Remesal A, Merino R, García-Consuegra J. Sedation for intra-articular corticosteroid injections in juvenile idiopathic arthritis: the views of patients and their parents. *Eur J Pediatr.* 2013;172:1411–3.
17. Balint PV, Kane D, Hunter J, McInnes IB, Field M, Sturrock RD. Ultrasound guided versus conventional joint and soft tissue fluid aspiration in rheumatology practice: a pilot study. *J Rheumatol.* 2002;29:2209–13.
18. Habibi S, Ellis J, Strike H, Ramanan AV. Safety and efficacy of US-guided CS injection into temporomandibular joints in children with active JIA. *Rheumatology (Oxford).* 2012;51:874–7.
19. Resnick CM, Vakilian PM, Kaban LB, Peacock ZS. Is intra-articular steroid injection to the temporomandibular joint for juvenile idiopathic arthritis more effective and efficient when performed with image guidance? *J Oral Maxillofac Surg.* 2017;75:694–700.
20. Jennings H, Hennessy K, Hendry GJ. The clinical effectiveness of intra-articular corticosteroids for arthritis of the lower limb in juvenile idiopathic arthritis: a systematic review. *Pediatr Rheumatol Online J.* 2014;12:23.
21. Laurell L, Court-Payen M, Nielsen S, Zak M, Boesen M, Fasth A. Ultrasonography and color Doppler in juvenile idiopathic arthritis: diagnosis and follow-up of ultrasound-guided steroid injection in the ankle region. A descriptive interventional study. *Pediatr Rheumatol Online J.* 2011;9:4.
22. Laurell L, Court-Payen M, Nielsen S, Zak M, Fasth A. Ultrasonography and color Doppler in juvenile idiopathic arthritis: diagnosis and follow-up of ultrasound-guided steroid injection in the wrist region. A descriptive interventional study. *Pediatr Rheumatol Online J.* 2012;10:11.
23. Ringold S, Weiss PF, Beukelman T, DeWitt EM, Ilowite NT, Kimura Y, et al. American College of Rheumatology. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis Rheum.* 2013;65:2499–512.
24. Ravelli A, Davi S, Bracciolini G, Pistorio A, Consolaro A, van Dijkhuizen EHP, et al. Italian Pediatric Rheumatology Study Group. Intra-articular corticosteroids versus intra-articular corticosteroids plus methotrexate in oligoarticular juvenile idiopathic arthritis: a multicentre, prospective, randomised, open-label trial. *Lancet.* 2017;389:909–16.
25. Sherry DD, Stein LD, Reed AM, Schanberg LE, Kredich DW. Prevention of leg length discrepancy in young children with pauciarticular juvenile rheumatoid arthritis by treatment with intraarticular steroids. *Arthritis Rheum.* 1999;42:2330–4.
26. Lanni S, Bertamino M, Consolaro A, Pistorio A, Magni-Manzoni S, Galasso R, et al. Outcome and predicting factors of single and multiple intra-articular corticosteroid injections in children with juvenile idiopathic arthritis. *Rheumatology (Oxford).* 2011;50:1627–34.
27. Papadopoulou C, Kostik M, Gonzalez-Fernandez MI, Bohm M, Nieto-Gonzalez JC, Pistorio A, et al. Delineating the role of multiple intraarticular corticosteroid injections in the management of juvenile idiopathic arthritis in the biologic era. *Arthritis Care Res (Hoboken).* 2013;65:1112–20.
28. Stoll ML, Good J, Sharpe T, Beukelman T, Young D, Waite PD, et al. Intra-articular corticosteroid injections to the temporomandibular joints are safe and appear to be effective therapy in children with juvenile idiopathic arthritis. *J Oral Maxillofac Surg.* 2012;70:1802–7.
29. Stoustrup P, Kristensen KD, Verna C, Küsel A, Pedersen TK, Herlin T. Intra-articular steroid injection for temporomandibular joint arthritis in juvenile idiopathic arthritis: a systematic review on efficacy and safety. *Semin Arthritis Rheum.* 2013;43:63–70.
30. Stoustrup P, Kristensen KD, Küsel A, Pedersen TK, Herlin T. Temporomandibular joint steroid injections in patients with juvenile idiopathic arthritis: an observational pilot study on the long-term effect on signs and symptoms. *Pediatr Rheumatol Online J.* 2015;13:62.
31. Balogh Z, Ruzsonyi E. Triamcinolone hexacetonide versus betamethasone. A double-blind comparative study of the long-term effects of intra-articular steroids in patients with juvenile chronic arthritis. *Scand J Rheumatol Suppl.* 1987;67:80–2.
32. Zulian F, Martini G, Gobber D, Agosto C, Gigante C, Zacchello F. Comparison of intra-articular triamcinolone hexacetonide and triamcinolone acetonide in oligoarticular juvenile idiopathic arthritis. *Rheumatology (Oxford).* 2003;42:1254–9.
33. Zulian F, Martini G, Gobber D, Plebani M, Zacchello F, Manners P. Triamcinolone acetonide and hexacetonide intra-articular treatment of symmetrical joints in juvenile idiopathic arthritis: a double-blind trial. *Rheumatology (Oxford).* 2004;43:1288–91.
34. Eberhard BA, Sison MC, Gottlieb BS, Ilowite NT. Comparison of the intraarticular effectiveness of triamcinolone hexacetonide and triamcinolone acetonide in treatment of juvenile rheumatoid arthritis. *J Rheumatol.* 2004;31:2507–12.
35. Eberhard BA, Ilowite NT, Sison C. A dose schedule for intraarticular steroids in juvenile arthritis. *J Rheumatol.* 2012;39:374–6.