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Original article

Intra-articular injection in patients with juvenile idiopathic arthritis: factors associated with a good response

Ana Luiza Garcia Cunha[a,*], *Vanessa Bugni Miotto e Silva*[a,b], *Fabiane Mitie Osaku*[a], *Luísa Brasil Niemxeski*[b], *Rita Nely Vilar Furtado*[c], *Jamil Natour*[c], *Maria Teresa de Sande e Lemos Ramos Ascensão Terreri*[a,b]

[a] *Universidade Federal de São Paulo (UNIFESP), Departamento de Pediatria, Disciplina de Alergia, Imunologia Clínica e Reumatologia, São Paulo, SP, Brazil*

[b] *Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil*

[c] *Universidade Federal de São Paulo (UNIFESP), Departamento de Medicina, Disciplina de Reumatologia, São Paulo, SP, Brazil*

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ABSTRACT

Introduction: Intra-articular injection of corticosteroids (IIC) for treatment of patients with juvenile idiopathic arthritis (JIA) is increasingly used in Pediatric Rheumatology.
Objectives: To describe the clinical course of patients undergoing IIC in our Pediatric Rheumatology Unit.
Methods: Retrospective study of patients with JIA undergoing IIC from January 2008 to December 2012, with a minimum follow-up of six months after the injection. Good response to IIC was set as the presence of inactivity on the infiltrated joint by at least six months.
Results: Eighty-eight patients underwent a total of 165 IICs. Of these, 75% were girls and 35.2% had persistent oligoarticular JIA. The mean age at diagnosis was 6.8 years, and when IIC was carried out, 12.2 years. Regarding patients, younger age at diagnosis ($p = 0.037$) and the occurrence of uveitis in the course of the disease ($p = 0.015$) were associated with good response to IIC. From 165 IICs, 63% had a good response and joints remained inactive for a median of 18.1 months. The type of joint injection ($p = 0.001$), lesser values stated in the overall visual analog scale by the physician ($p = 0.015$) and by parents/patient ($p = 0.01$) have been associated with a good response to IIC. Nine adverse events (5.4%) were observed.
Conclusion: In our study, more than half of the joints showed a good response to IIC. Younger patients at diagnosis and uveitis during the course of the disease had good response to IIC. Knees, wrists and elbows were the joints that best responded to IIC. IIC proved to be a safe procedure.

* *Corresponding author.*
E-mail: analuiza.cunha@gmail.com (A.L.G. Cunha).

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Infiltração intra-articular em pacientes com artrite idiopática juvenil: fatores associados à boa resposta

Palavras-chave:
Infiltração intra-articular
Artrite idiopática juvenil
Hexacetonido de triancinolona
Tratamento e uveíte

RESUMO

Introdução: A infiltração intra-articular de corticosteroides (IIC) para tratamento de pacientes com artrite idiopática juvenil (AIJ) é cada vez mais usada em reumatologia pediátrica.
Objetivos: Descrever a evolução clínica dos pacientes submetidos à IIC em nosso setor de reumatologia pediátrica.
Métodos: Estudo retrospectivo de pacientes com AIJ submetidos à IIC de janeiro/2008 a dezembro/2012, com seguimento mínimo de seis meses após a infiltração. Boa resposta à IIC foi definida como inatividade na articulação infiltrada por, no mínimo, seis meses.
Resultados: Foram submetidos a 88 pacientes a 165 IICs. Desses, 75% eram meninas e 35,2% apresentavam AIJ oligoarticular persistente. A média de idade ao diagnóstico foi de 6,8 anos e à IIC de 12,2 anos. Em relação aos pacientes, a menor idade ao diagnóstico ($p = 0,037$) e a ocorrência de uveíte no curso da doença ($p = 0,015$) foram associados à boa resposta à IIC. Das 165 IICs, 63% apresentaram boa resposta e as articulações permaneceram inativas por um tempo médio de 18,1 meses. O tipo de articulação infiltrada ($p = 0,001$), menores valores na escala visual analógica global do médico ($p = 0,015$) e dos pais/paciente ($p = 0,01$) foram associados a uma boa resposta à IIC. Nove efeitos adversos (5,4%) foram observados.
Conclusão: Em nosso estudo, mais da metade das articulações mostrou boa resposta à IIC. Os pacientes com menor idade ao diagnóstico e uveíte durante o curso da doença tiveram boa resposta à IIC. Os joelhos, punhos e cotovelos foram as articulações que mais bem responderam à IIC. A IIC mostrou ser um procedimento seguro.

Introduction

Juvenile idiopathic arthritis (JIA) is a chronic rheumatic disease most common in childhood, being a significant cause of disability and reduced quality of life.[1]

The goal of JIA treatment is to control inflammation and prevent a premature loss of cartilage and joint function. JIA can be treated with a combination of non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs (DMARDs), biologic drugs, systemic corticosteroids, intra-articular injections of corticosteroids (IIC) and physiotherapy.[1–4]

IIC is often used to treat JIA.[5,6] Currently this procedure is in use not only in patients with the oligoarticular subtype (i.e. those with a poor response to NSAIDs and as a first-line therapy), but also in those suffering a lengthy or complicated arthritis (accompanied by joint contractures and growth disorders), or even in those cases where one is awaiting by the therapeutic effect of DMARDs.[2,7–10]

Although the long-term efficacy and the potential effect on activity and progression of JIA still need more studies, IIC can promote significant pain relief, functional joint improvement, and an increased likelihood of deformity correction and of adaptation of bone growth. In addition, IIC is considered as a safe and effective method to treat affected joints.[1,11–16] Furthermore, this procedure allows an early rehabilitation and a reduction – or even discontinuation – of systemic medications.[16,17]

Most of our knowledge on joint injection comes from studies in adults, with few reports in children. This study describes the clinical outcome of patients undergoing IIC in a Pediatric Rheumatology Unit at UNIFESP over a period of five years, and also evaluates factors associated with a good response to this therapy.

Patients and methods

This is a retrospective study of medical records of patients with JIA, who were followed at the Pediatric Rheumatology unit of UNIFESP and submitted to IIC in the period from January 1, 2008 to December 31, 2012. Their inclusion criterion was a minimum 6-month follow-up after the joint injection. Patients with IICs procedures performed in other units were excluded.

Demographic and clinical data of each patient were assessed, and a preliminary classification and evolution of JIA was carried out according to the criteria of the International League of Associations for Rheumatology (ILAR)[18]: the presence of uveitis in the course of disease, the presence of autoantibodies (antinuclear antibody – ANA – considered as positive for children with titles $\geq$1:160, and rheumatoid factor – RF) and of human leukocyte antigen (HLA) B27.

For each intra-articular injection, we assessed the dose of medication used into each joint and the patient's body weight, a clinical classification of the severity of joint effusion (mild, moderate or severe) at the time of injection, and whether the physician used ultrasound (US) to guide the injection. We also evaluated the patient's age, number of active and restricted joints, systemic medications used, the Childhood Health Assessment Questionnaire (CHAQ) score, a global

visual analog scale (VAS, 0–10) value assigned by the physician and by parents/patient, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) at the time of injection. Adverse events were recorded after each injection.

IICs were performed by a single pediatric rheumatologist trained according to protocols specific for each type of joint.[19] Injections were performed under local anesthesia with 2% lidocaine without vasoconstrictor. The only medication used was triamcinolone hexacetonide in doses of 1–2 mg/kg for large joints, 0.5–1 mg/kg for medium joints, and 4–10 mg for small joints, with a maximum dose of 100 mg. The patients were asked to rest their joint after the procedure for a period of 48 h.

We considered a joint as inactive in the absence of arthritis checked by clinical examination and/or US. The patient was considered as with a good response to IIC when all injected joints remained inactive for at least six months (complete response) or when some of injected joints remained inactive for at least six months (partial response). Poor response was defined as when all infiltrated joints remained active or exhibited reactivation within a period under six months after IIC. The answer to IIC in each joint was ranked as "good response" (the infiltrated joint remained inactive for at least six months) and "poor response" (the infiltrated joint did not answer, or its reactivation occurred in less than six months).

Demographic and clinical characteristics were described in absolute and relative frequencies, means ± standard deviation, and minimum and maximum values, according to the nature of the variables. To compare the distributions of continuous variables between two groups, Student's *t* test or Mann–Whitney test was used, taking into account the data normality. Categorical variables between groups were compared using the Chi-squared test or Fisher's exact test. The statistical significance was set at 5%.

This study was approved by the Research Ethics Committee of the Universidade Federal de São Paulo (Opinion Number: 326 891).

Results

From January 2008 to December 2012, 88 patients with JIA were subjected to a total of 165 IICs, with a mean of 1.87 (range, 1–6) injections per patient. The mean length of follow-up was 7.1 (0.8–17.1) years.

Sixty-two patients (70.4%) had a good response to IIC, 39 (44.3%) patients achieved a complete response, 23 (26.1%) were benefited with a partial response to IIC, and 26 patients (29.5%) exhibited a poor response to all IICs to which they were subjected. For the sake of our statistical analysis, subtypes of JIA were grouped according to the course of the disease in: oligoarticular – 37.5% (persistent oligoarticular JIA, enthesitis-related arthritis [ERA], and psoriatic JIA [patients with a maximum of 4 affected joints]), polyarticular – 58% (polyarticular RF-positive JIA, polyarticular RF-negative JIA, and extended oligoarticular JIA) and systemic – 4.5%. Regarding our evaluation per patient, a good response to IIC was associated with younger age at diagnosis of JIA ($p = 0.037$) and also for those patients with uveitis occurring at any time in the course of the disease ($p = 0.015$). Of 21 patients with uveitis, 13 were ANA positive. Eleven patients were investigated for the presence of HLA-B27 and all of them were negative. Table 1 lists demographic and clinical data for the group of patients.

Regarding the 165 joints injected, 104 (63%) showed good response to IIC, which was associated with lower VAS values assigned by the physician ($p = 0.015$) and by parents/patient ($p = 0.010$). The lowest values of VAS were associated with a better general condition of the patient with good response to IIC, and with less pain and inflammatory activity. Furthermore, the type of joint submitted to injection ($p = 0.001$), also was associated with a good response to IIC; knees, wrists, and elbows were those joints showing better response to IIC. Table 2 lists data relating to intra-articular injections.

Generally, US-guided injections in this small sample of 16 patients with longer disease duration and previous injections showed poor response to IICs ($p = 0.02$); this fact is associated with higher values of CHAQ ($p = 0.03$), higher number of injections with poor response ($p = 0.01$) and a shorter time to relapse ($p = 0.02$) compared to patients submitted to blindly performed procedures. Data related to US-guided injections are shown in Table 3.

The joints that responded favorably to IIC remained inactive for a mean of 18.1 ± 13.2 months. On the other hand, in those joints with poor response, there was recurrence after a mean period of 2.6 ± 2.1 months.

Of the 165 injections carried out, 43 (26.1%) were applied in 17 patients whose joints were infiltrated in more than one occasion (14 knees, 3 ankles, and 2 hips), with a mean of 2.26 (range, 2–3) IICs per joint. Among these joints, 24 (55.8%) had a good response to IIC, with a mean time of 12.3 months of joint inactivity after the procedure.

Taking into account the total number of IICs performed, nine (5.4%) adverse effects occurred in nine patients: five cases of periarticular hypotrophy and four cases of hypochromia at the site of injection.

Discussion

In this study, we observed a good response to IIC in more than half of patients, especially those younger-aged at the diagnosis of JIA, and patients presenting uveitis during the course of the disease. Additionally, the type of injected joint (knees, wrists, and elbows) and low values of VAS assigned by the physician and by the parents/patient were associated with a good response to IIC. The use of US to guide the procedures was associated with worse responses to IIC.

Of the total number of IICs performed out, more than half presented inactivity of arthritis for more than 6 months, with a mean duration of about one and a half years. The inactivity rates after the injection varies depending on the study: around 56.1–82% after six months, 42–80% after 1 year, and 30–63% after 2 years.[5,10,12–14,20–22] The literature reveals a wide variation among studies with respect to mean response duration time in patients with JIA, ranging from 6 to 23.5 months.[7,23–25]

Among the potential factors associated with a good response to IIC described in the literature, we found absence of ANA,[11,23] presence of HLA-B27,[23] absence of atrophy in the local of injection,[23] concomitant use of MTX,[7,10,23] oligoarticular subtype of JIA,[7,10,20] and use of sedation.[23] In this study,

Table 1 – Demographic and clinical data of patients who underwent joint injections.

Variables	Total of patients ($n=88$)	Good response to IIC ($n=62$)	Poor response to IIC ($n=26$)	p-Value
Demographic data				
Female gender	66	48 (72.7%)	18 (27.3%)	0.42[a]
Time elapsed between the first symptoms and diagnosis (months)	10.5 (±16.5)	11.7 (±18.9)	7.8 (±7.8)	0.73[b]
Age at diagnosis of JIA (years)	6.8 (±4.0)	6.2 (±3.7)	8.3 (±4.4)	0.037[b]
Mean follow-up to the last visit (years)	7.1 (±4.0)	7.5 (±3.9)	6.1 (4.1)	0.08[b]
ANA, positive	37	30 (81%)	7 (19%)	0.126[a]
RF, positive	9	8 (88.9%)	1 (11.1%)	0.271[c]
Uveitis associated with JIA	12	12 (100%)	0	0.015[c]
JIA subtype				0.076[a]
Systemic	4	1 (25%)	3 (75%)	
Oligoarticular, persistent	31	22 (70.9%)	9 (29.1%)	
Oligoarticular, extended	17	14 (82.3%)	3 (17.7%)	
Polyarticular, RF positive	9	8 (88.9%)	1 (11.1%)	
Polyarticular, RF negative	25	17 (68%)	8 (32%)	
Psoriatic	1	0	1 (100%)	
ARE	1	0	1 (100%)	
Clustered subtype of JIA				0.08[a]
Oligoarticular	33	22 (66.7%)	11 (33.3%)	
Polyarticular	51	39 (76.4%)	12 (23.6%)	
Systemic	4	1 (25%)	3 (75%)	

IIC, intra-articular injection of corticosteroids; ANA, antinuclear antibody; RF, rheumatoid factor; JIA, juvenile idiopathic arthritis; ARE, arthritis related to enthesitis.

[a] Chi-squared test.
[b] Mann–Whitney test.
[c] Fisher's exact test.

presence of ANA, use of DMARDs, and JIA subtype were not associated with a better or worse response to IIC. Among our patients, none was HLA B-27-positive and in none of them IIC was performed under sedation, which prevented the assessment of these factors.

The literature also describes as indicators of worse response: absence of ANA (contrary to the studies cited above),[7,10] increases in CRP and ESR,[7,10,22] systemic and polyarticular JIA subtypes,[7,10,20,25] and elbow infiltration.[10] In our study we found a good response to elbow injection. Despite the small number of patients with systemic JIA in this study, and taking into account that no statistical significance was found, we also noted worse responses to IIC in patients with systemic JIA, showing that the procedure in this disease subtype should be evaluated individually.

No association was observed between the occurrence of uveitis and a better response to IIC in the study conducted by Marti et al.,[23] contrary to our study, where the occurrence of uveitis was associated with a better response to IIC.

Compared to VAS values assigned by the physician and by parents/patient, these parameters were not associated with response to IIC in the study by Ravelli et al.[22] On the other hand, the study by Moretti et al.[26] showed that a lower VAS value assigned by the physician was a good predictor of response to IIC in patients with the oligoarticular subtype. In our study, higher procedure values of VAS, both assigned by the physician and the patient, were associated with a worse response to IIC.

Studies suggest that the best time for the completion of an IIC procedure is as early as possible in the course of the disease – and this is a factor of good response to IIC.[11,16] In our study, we found that younger-aged patients at diagnosis showed a good response to IIC. This may be related to the most common subtype in this age group, which is the oligoarticular subtype; but also demonstrates that, by being younger, these patients could be in an earlier stage of the disease, which is in line with literature findings.

One may obtain a long-lasting answer to IIC when using hexacetonide triamcinolone *versus* acetonide triamcinolone.[5,21,23,27,28] Thus, we chose to use hexacetonide triamcinolone in all of our injections.

There is evidence in favor of a better response to IIC when the procedure is guided by an imaging technology (ultrasound or MRI), especially in the wrist, ankle and hip.[3,29,30] Contrary to this, we found a poor response to US-guided IIC injection. This finding may be due to the fact that, in our study, guided injections were performed on joints that had already showed a poor response to blindly-conducted IIC, and is likely that this played a role in our results. Prospective studies in joints never subjected to injection should be conducted, in order to better assess the utility of US to guide IIC in children.

The completion of multiple injections into the same joint proved to be a successful alternative therapy, taking into account that in our study, more than half of patients undergoing this procedure have been benefited. In our routine, we wait for at least 1 month to repeat the infiltration in the same joint.

Table 2 – Demographic and clinical data related to joints subjected to injection.

Variables	Total of patients (*n* = 165)	Good response to IIC (*n* = 104)	Poor response to IIC (*n* = 61)	*p*-Value
Descriptor				
Time from diagnosis to IIC (years)	5.3 (±3.8)	5.6 (±3.8)	4.9 (±3.8)	0.25[a]
Age at IIC (years)	12.2 (±4.3)	12.1 (±4.5)	12.5 (±4.1)	0.53[a]
CHAQ (*n* = 28), mean (range)	0.41 (0–2.25)	0.30 (0–2.25)	0. 67 (0–1.75)	0.53[a]
VAS parents/patient (*n* = 80), median (range)	0 (0–9)	0 (0–9)	3 (0–8)	0.015[a]
VAS physician (*n* = 60), median (range)	1 (0–8)	0 (0–7)	4 (1–8)	0.010[a]
CRP (*n* = 124) ± SD	10.2 (±18.5)	10.5 (±21.6)	9.6 (±11.9)	0.22[a]
ESR (*n* = 129) ± SD	25.8 (±24.5)	27.2 (±26.7)	23.2 (±20.3)	0.41[a]
Active joints ± SD	3.1 (±4.3)	2.6 (±3.0)	4.1 (±5.8)	0.09[a]
Restricted joints ± SD	3.2 (±6.1)	3.0 (±5.6)	3.5 (±6.9)	0.77[a]
Injected joint				0.001[b]
Knees	100	71 (71%)	29 (29%)	
Ankles	30	11 (36.7%)	19 (63.3%)	
Wrists	15	10 (66.7%)	5 (33.3%)	
Elbows	9	9 (100%)	0	
Shoulders	3	1 (33.3%)	2 (66.7%)	
Hips	6	2 (33.3%)	4 (66.7%)	
Proximal interphalangeal joints	2	0	2 (100%)	
Joint effusion degree (*n* = 156)				0.49[b]
Mild	55	33 (60%)	22 (40%)	
Moderate	84	56 (66.7%)	28 (33.3%)	
Severe	17	9 (52.9%)	8 (47.1%)	
Guided by ultrasound	16	6 (37.5%)	10 (62.5%)	0.02[b]
Drugs in use at the time of IIC				0.32[b]
None or NSAIDs	55	39 (71%)	16 (29%)	
DMARDs	80	48 (60%)	32 (40%)	
Biologicals	30	17 (56.7%)	13 (43.3%)	
Use of oral corticosteroids	21	12 (57.1%)	9 (42.9%)	0.55[b]

IIC, intra-articular injection corticosteroids; SD, standard deviation; CHAQ, Childhood Health Assessment Questionnaire; VAS, visual analog scale; CRP, C-reactive protein, ESR, erythrocyte sedimentation rate; NSAIDs, nonsteroidal anti-inflammatory drugs; DMARDs, disease-modifying antirheumatic drugs.

[a] Mann–Whitney test.

[b] Chi-squared test.

Table 3 – Comparison between injection guided *versus* not guided by ultrasound (US).

Variables	US-guided infiltrations (*n* = 16)	Infiltrations unguided by US (*n* = 149)	*p*-Value
Descriptor			
Time from diagnosis to IIC (years)	5.9 (±3.4)	5.2 (±3.7)	0.63[a]
Age at IIC (years)	12.1 (±5.2)	12.2 (±4.2)	0.94[a]
CHAQ (*n* = 28), mean (range)	1.6 (1–2.25)	0.3 (0–1.75)	0.03[a]
VAS parents/patient (*n* = 80), median (range)	5 (1–6)	0 (0–9)	0.42[a]
VAS physician (*n* = 60), median (range)	1 (1–4)	3 (0–8)	0.46[a]
CRP (*n* = 124) ± SD	11 (±17.5)	10 (±18.6)	0.89[a]
ESR (*n* = 129) ± SD	25.3 (±18.4)	25.8 (±25.2)	0.73[a]
Active joints ± SD	4.5 (±6.7)	2.9 (±3.9)	0.55[a]
Restricted joints ± SD	6.7 (±12.8)	2.8 (±4.8)	0.30[a]
Number of injections with poor response	1.4 (±0.8)	0.8 (±0.8)	0.01[a]
Relapse time (months)	6.5 (±7.2)	13 (±13.2)	0.01[a]
Joint effusion degree (*n* = 156)			0.29[b]
Mild	7	48	
Moderate	8	76	
Severe	0	17	

IIC, intra-articular injection of corticosteroids; SD, standard deviation; CHAQ, Childhood Health Assessment Questionnaire; VAS, visual analog scale; CRP, C-reactive protein, ESR, erythrocyte sedimentation rate.

[a] Mann–Whitney test.

[b] Chi-squared test.

The most common adverse events are: local subcutaneous tissue atrophy at the IIC site,[5,7,10,21–23,25,29] local skin hypopigmentation,[25,29] acute onset of pain (joint irritation by crystals of the drug),[27] local calcification,[25] adverse effects related to general/local anesthesia,[23] and possible systemic effects of corticosteroids (facial flushing, increased appetite, mood swings).[23,25,29] Post-injection infection is a rare event in adults,[27] and there are no published reports of pediatric cases. In our study, we observed a low rate of adverse events, none of which was characterized as a severe event.

Our study showed that IIC is an effective and sustained therapeutic modality; more than half of our patients presented a good response to the procedure. Furthermore, ICC is a safe method with a low rate of adverse events. To the best of our knowledge, this is the first study in children and adolescents with JIA in our population, that sought to assess the factors associated with IIC response. However, this study has some limitations, such as its retrospective design, which affected data collection. And we also did not include data from injections applied to these patients in other units, which occurred in a few cases. More prospective studies are needed to better define the profile of patients with JIA who may benefit from IIC procedures.

Our study also showed that a younger age at the diagnosis of JIA, occurrence of uveitis in the course of the disease, as well as knee, wrist and elbow injection and lower VAS values both from the physician and patient were factors associated with a better response to IIC. IIC is an effective therapeutic modality presenting a sustained response. Furthermore, it is also a safe procedure that can contribute to improving the quality of life of patients with JIA.

Conflict of interests

The authors declare no conflict of interests.

REFERENCES

1. Petty RE, Cassidy JT. Chronic arthritis in childhood. In: Cassidy JT, Petty RE, editors. Textbook of pediatric rheumatology. Philadelphia: WB Saunders; 2011. p. 211–34.
2. Beukelman T, Patkar NM, Saag KG, Tolleson-Rinehart S, Cron RQ, DeWitt EM, et al. 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.
3. Kan JH, Graham TB. Combined pre-injection wrist and ankle MRI protocol and steroid joint injections in juvenile idiopathic arthritis. Pediatr Radiol. 2011;41:1326–32.
4. Hashkes PJ, Laxer RM. Medical treatment of juvenile idiopathic arthritis. JAMA. 2005;294:1671–84.
5. 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. Rheumatol. 2003;42:1254–9.
6. Beukelman T, Guevara JP, Albert DA, Sherry DD, Burnham JM. Usage of intra-articular corticosteroid injections for the treatment of juvenile idiopathic arthritis: a survey of pediatric rheumatologists in the United States and Canada. Clin Exp Rheumatol. 2008;26:700–3.
7. Papadopoulou C, Kostik M, Gonzalez-Fernandez MI, Bohm M, Nieto-Gonzalez JC, Pistorio A, et al. Delineating the role of multiple intra-articular corticosteroid injections in the management of juvenile idiopathic arthritis in the biologic era. Arthritis Care Res (Hoboken). 2013;65:1112–20.
8. Ruth NM, Passo MH. Juvenile idiopathic arthritis: management and therapeutic options. Ther Adv Musculoskelet Dis. 2012;4:99–110.
9. Ravelli A, Lattanzi B, Consolaro A, Martini A. Glucocorticoids in paediatric rheumatology. Clin Exp Rheumatol. 2011;29 Suppl 68:S148–52.
10. 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.
11. Lepore L, Del Santo M, Malorgio C, Presani G, Perticarari S, Prodan M, et al. Treatment of juvenile idiopathic arthritis with intra-articular triamcinolone hexacetonide: evaluation of clinical effectiveness correlated with circulating ANA and T gamma/delta + and B CD5+ lymphocyte populations of synovial fluid. Clin Exp Rheumatol. 2002;20:719–22.
12. Ünsal E, Makay B. Intra-articular triamcinolone in juvenile idiopathic arthritis. Indian Pediatr. 2008;45:995–7.
13. Breit W, Frosch M, Meyer U, Heinecke A, Ganser G. A subgroup-specific evaluation of the efficacy of intraarticular triamcinolone hexacetonide in juvenile chronic arthritis. J Rheumatol. 2000;27:2696–702.
14. Padeh S, Passwell JH. Intraarticular corticosteroid injection in the management of children with chronic arthritis. Arthritis Rheum. 1998;41:1210–4.
15. Wallace C. Intra-articular steroid injections in JIA. Reumatología. 2002;18:111–4.
16. Broström E, Hagelberg S, Haglund-Akerlind Y. Effect of joint injections in children with juvenile idiopathic arthritis: evaluation by 3D-gait analysis. Acta Pediatr. 2004;93:906–10.
17. Weitoft T, Rönnblom L. Randomised controlled study of post injection immobilization after intra-articular glucocorticoid treatment for wrist synovitis. Ann Rheum Dis. 2003;62:1013–5.
18. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Association for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31:390–2.
19. Furtado R, Natour J. Infiltrações no aparelho locomotor: técnicas para realização com e sem o auxílio de imagem. 1ª ed. Porto Alegre: Artmed; 2011.
20. Neidel J, Boehnke M, Küster RM. The efficacy and safety of intraarticular corticosteroid therapy for coxitis in juvenile rheumatoid arthritis. Arthritis Rheum. 2002;46:1620–8.
21. 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. Rheumatol. 2004;43:1288–91.
22. Ravelli A, Manzoni SM, Viola S, Pistorio A, Ruperto N, Martini A. Factors affecting the efficacy of intraarticular corticosteroid injection of knees in juvenile idiopathic arthritis. J Rheumatol. 2001;28:2100–2.
23. Marti P, Molinari L, Bolt IB, Seger R, Saurenmann RK. Factors influencing the efficacy of intra-articular steroid injections in patients with juvenile idiopathic arthritis. Eur J Pediatr. 2008;167:425–30.
24. Brown GT, Wright FV, Lang BA, Birdi N, Oen K, Stephens D, et al. Clinical responsiveness of self-report functional assessment measures for children with juvenile idiopathic arthritis undergoing intraarticular corticosteroid injections. Arthritis Rheum. 2005;53:897–904.

25. Bloom BJ, Alario AJ, Miller LC. Intra-articular corticosteroid therapy for juvenile idiopathic arthritis: report of an experiential cohort and literature review. Rheumatol Int. 2011;31:749–56.
26. Moretti C, Viola S, Pistorio A, Magni-Manzoni S, Ruperto N, Martini A, et al. Relative responsiveness of condition specific and generic health status measures in juvenile idiopathic arthritis. Ann Rheum Dis. 2005;64:257–61.
27. Cleary AG, Murphy HD, Davidson JE. Intra-articular corticosteroid injections in juvenile idiopathic arthritis. Arch Dis Child. 2003;88:192–6.
28. 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.
29. Young CM, Shiels WE, 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.
30. Tynjälä P, Honkanen V, Lahdenne P. Intra-articular steroids in radiologically confirmed tarsal and hip synovitis of juvenile idiopathic arthritis. Clin Exp Rheumatol. 2004;22:643–8.