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Intra-articular injections of triamcinolone hexacetonide in rheumatoid arthritis: short and long-term improvement predictors

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ABSTRACT

Objectives: Identify good response predictors to intra-articular injection (IAI) with triamcinolone hexacetonide (TH).
Methods: This study was carried out in rheumatoid arthritis (RA) patients (American College of Rheumatology criteria) submitted to IAI (mono, pauci or polyarticular injection).
Assessment: a "blinded" observer prospectively evaluated joints at one week (T1), four weeks (T4), twelve weeks (T12) and 24 weeks (T24) after IAI. Outcome measurements included Visual Analogue Scale (0-10 cm) at rest, in movement and for swollen joints. Clinical, demographic and variables related to injection at baseline were analyzed according to IAI response.
Results: We studied 289 patients with RA (635 joints) with a mean age of 48.7 years (±10.68), 48.5% of them Caucasians, VAS for global pain = 6.52 (±1.73). Under univariate analysis, the variables relating the best responses following IAI (improvement > 70%) were: "elbow and metacarpophalangeal (MCP) IAI, and functional class II". Under multivariate analysis, "males" and "non-whites" were the predictors with the best response to IAI at T4, while "elbow and MCP IAI", "polyarticular injection", "use of methotrexate" and "higher total dose of TH" obtained the best response at T24.
Conclusion: Several predictors of good response to IAI in patients with RA were identified. The best-response predictors for TH IAI of long term were "inject elbow and MCP IAI" and "perform polyarticular injection".

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Infiltrações intra-articulares de triancinolona hexacetonida na artrite reumatóide: preditores de melhora a curto e longo prazo

Palavras-chave:
Infiltração
Triancinolona hexacetonida
Artrite reumatoide
Prognósticos

RESUMO

Objetivos: Identificar fatores preditores de resposta à infiltração intra-articular (IIA) com hexacetonide de triancinolona (HT).
Métodos: Este estudo foi realizado em pacientes com artrite reumatoide (AR) (segundo critérios do *American College of Rheumatology*) submetidos à IIA (infiltração mono, pauci ou poliarticular).
Avaliação: Um observador "cego" avaliou prospectivamente as articulações uma semana (T1), quatro semanas (T4), 12 semanas (T12) e 24 semanas (T24) após IIA. As medidas de desfecho foram Escala Visual Analógica (0-10 cm) em repouso, em movimento e para articulações edemaciadas. As variáveis clínicas e demográficas e aquelas relacionadas à infiltração no início do estudo foram analisadas de acordo com a resposta à IIA.
Resultados: Foram estudados 289 pacientes com AR (635 articulações) com média de idade de 48,7 (± 10,68) anos; 48,5% eram caucasianos, EVA para dor global = 6,52 (± 1,73). Na análise univariada, as variáveis relativas às melhores respostas seguida à IIA (melhora >70%) foram: "IIA no cotovelo e metacarpofalangeanas (MCF)" e "classe funcional II". Na análise multivariada, "homens" e "não brancos" foram os preditores com melhor resposta à IIA em T4, enquanto "IIA no cotovelo e MCF", "infiltração poliarticular", "uso de metotrexato" e "dose total maior de HT" obtiveram a melhor resposta em T24.
Conclusão: Foram identificados diversos fatores preditores de boa resposta à IIA em pacientes com AR. Os preditores de melhor resposta para IIA de HT em longo prazo foram "realizar IIA no cotovelo e MCF" e "realizar infiltração poliarticular".

Introduction

Although intra-articular injection of corticosteroids (IAIC) has been a commonly used procedure among rheumatologists for over half a century,[1] few studies have been conducted to demonstrate its benefits in accordance to scientific methodology.

Rheumatoid arthritis (RA) is the rheumatic condition that most severely affects the joints. *Pannus*, the hypertrophic and hyperplasic synovial membrane formed, is an aggressive tissue that damages articular and periarticular structures, whether through the release of metaloproteinases or its mechanical invasion of the surrounding joint space.[2–4]

Even though RA treatment has evolved in recent decades with the advent of immunobiological therapy allied with disease-modifying antirheumatic drugs (DMARDs),[5] patients with mono or oligoarticular synovitis may persist. In these cases, IAIC can be a useful therapeutic tool.

It is known that triamcinolone hexacetonide (TH) is the drug of choice for intra-articular treatment of RA, given its synovial atrophying properties and slow absorption from the injection site.[6–13] On the other hand, if injected outside of the joint, it can cause serious adverse local effects.[14]

Though some concepts concerning IAIC have been established, few studies have been conducted to evaluate response predictors in adult RA patients.[15] In addition, to the best of our knowledge, none of them evaluated TH IAIC response predictors in patients with established RA.

The aim of this study was to identify variables (clinical, demographic and related to injection) that serve as the best predictors of response to TH IAIC over short term (4 weeks) and long term (24 weeks) in patients with established RA.

Materials and methods

A prospective non-controlled study was conducted on a cohort of patients with established RA receiving treatment at the Interventional Rheumatology Unit at Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil.

Patients were classified according to American College of Rheumatology – ACR[16] criteria, and had been referred for IAIC (mono, pauci or polyarticular).

Inclusion criteria were: age between 18 and 65; functional class II or III;[17] stable DMARD for the last 3 months; stable oral corticosteroid for the last month; indication for IAIC injection (persistent synovitis with swelling and articular pain) and must have signed the informed consent form.

Exclusion criteria were: IAIC in any joint within the last 6 months; any symptoms of systemic or articular infection; any form of clotting disturbance; diagnosis of diabetes *mellitus* or systemic arterial hypertension; known allergy to contrasts or radioisotopes, and suspicion of pregnancy.

Most of the joints injections were not guided. Fluoroscopy and ultrasound were used for guided injections, as needed. Image-guided IAIC was recommended in cases of difficult blind access or where the use of radioisotopes was recommended.

Intervention

Patients received IAIC in one or more of the following joints: shoulder (glenohumeral), elbow, wrist, metacarpophalangeal (MCP), knee and ankle. The procedure was carried only at the baseline by the same rheumatologist, with over ten years of experience in interventional rheumatology (RNV Furtado). The IAIC was mono, pauci (up to three infiltrations at once) or polyarticular (4 to 8 simultaneous IAIC), depending on the number of joints indicating pain and swelling.

The only corticosteroid used was triamcinolone hexacetonide (20 mg/mL). Depending on the size of the joint space, dose of corticosteroid was considered low (1), medium (2) and high (3). The dose of TH used for each joint studied were: shoulder, 80 mg (3); elbow, 40 mg (2) or 60 mg (3); wrist, 30 mg (2) or 40 mg (3); metacarpophalangeal, 10 mg (2) or 20 mg (3); knee, 40 mg (1), 60 mg (2) or 80 mg (3); and ankle, 40 mg (2) or 60 mg (3).

Patients received the IAIC procedure in dorsal decumbency after the injection site had been cleansed with topical povidine. Only sterile needles and syringes were used. Xylocaine chloride 2% without vasoconstrictor was used for anesthetic purpose. TH was only administered once the needle had been corrected positioned inside the joint space.

In patients submitted to knee IAIC with radioisotopes, all the safety norms for radioactive material handling were followed. The dose applied was 5 mCi Yttrium-90 plus 40 mg of TH, or 15 mCi Samarium-153 hydroxyapatite plus 40 mg of TH, depending on availability. These drugs were used only in cases of refractory synovitis only in the knee.

All patients were warned to rest for a period of 48 hours after injection, only allowed to move around to meet their physiological needs. An orthotic immobilizer was used in case of IAI with radioisotopes.

Assessment

"Blinded" examination at T0 (baseline), T1, T4, T12, and T24 weeks post-injection were performed. Outcome measures included: visual analogue scale (0-10 cm) for joint pain at rest (VASr); visual analogue scale (0-10 cm) for joint pain in movement (VASmv) and visual analogue scale for swollen joints (VASs).

IAIC response was assessed in relation to the injected joint (rather than the patient as a whole) and was measured as percentage (%) of improvement on the VASr, VASmv and VASs scales for each joint at times T1, T4, T12 and T24. Improvement between 50% and 70% was considered *moderate*, and over 70% was considered *significant*. The association between improvement percentages for VASr, VASmv and VASs was made in isolation (50%-70% and >70%) and concomitantly (improvement >50% in all three VAS at once) and multiple baseline variables were factored in.

Baseline variables considered under this analysis were: demographic (gender, age and skin color – white or non-white); related to disease (duration, functional class II or III, presence of rheumatoid factor, DMARDS in use, use of oral corticosteroid and presence of extra-articular disease) and related to injection (joint injected, previous IAI, number of joints injected, TH dose, total TH dose per patient, image guided IAI and use of radioisotope or contrast agent).

Statistical analysis

The continuous variables were described in mean and standard deviation (SD), and the categorical variables in frequencies and percentages.

Comparison between continuous and categorical baseline variables was made using Kruskal-Wallis univariate analysis, while comparison between categorical baseline variables was performed using chi-square or Fisher's exact tests.

Only those joints showing improvement percentages higher than 50% concomitantly for all three VAS (VASr, VASmv and VASs) were subjected to multivariate logistic regression analysis, with the chance of improvement measured in Odds Ratio (OR) (IC 95%).

Significant p value was set at 5%.

Ethics

Written informed consent was obtained from all subjects, and the Ethics Committee of the university approved the study.

Table 1 – Demographic, related to disease and related to injection data of the baseline sample.

Variables	
Age in years, mean (±SD)	47.6 (±10.81)
Disease duration in years, mean (±SD)	11.2 (±8.23)
Women:men ratio	9:1
Global pain, VAS mean (±SD)	6.52 (±1.73)
White skin color n (%)	308 (48.5)
Functional class II N (%)/III n (%)	368 (58.0)/267 (42.0)
Using methotrexate n (%)	469 (73.9)
Using leflunomide n (%)	103 (1.2)
Using chloroquine n (%)	164 (25.8)
Using immunobiological drugs n (%)	1 (0.2)
Using oral corticosteroid n (%)	467 (73.5)
Rheumatoid factor positivity n (%)	411 (64.7)
Extra-articular disease n (%)	71 (11.2)
Previous IAIC n (%)	300 (47.2)
Polyarticular injection n (%)	312 (49.1)
Image-guided IAIC n (%)	90 (14.2)
Radioisotopes in IAIC n (%)	30 (4.7)
Number of joints injected:	
Shoulder n (%)	35 (5.5%)
Elbow n (%)	48 (7.6%)
Wrist n (%)	160 (25.2%)
MCP n (%)	142 (22.4%)
Knee n (%)	152 (23.9%)
Ankle n (%)	98 (15.4%)
Patientes and joints evaluated from T0 to:	
T4	289/635 joints
T12	185/403 joints
T24	35/313 joints

n (%), frequency (percentage); SD, standard deviation; IAIC, intra-articular injection with corticosteroid; MCP, metacarpophalangeal joints; VAS, Visual Analogue Scale.

^{153}SmPHYP was provided by Instituto de Pesquisas Energéticas e Nucleares do Brasil (IPEN). ^{90}Y was imported by IPEN from Cis Bio Schering International (France). All procedures that used radioisotopes were performed under biosafety rules at the Nuclear Medicine Sector.

Results

We studied 289 patients with RA with a mean age of 47.6 years (SD ± 10.81) and mean disease duration of 11.2 years (SD ± 8.23), 48.5% white and women-to-men ratio of 9:1, VAS for global pain 6.52 (±1.73). Monoarticular injection occurred in 175 patients (60.55%); pauciarticular injection in 68 patients (23.53%), and polyarticular injection in 46 patients (15.92%). Six hundred and thirty-five (635) joints were injected and prospectively studied through T4; 403 through T12, and 313 through T24. Table 1 presents the demographic data and data related to disease and related to injection for the sample patients.

Baseline variables that did not correlate statistically with VAS improvement at any of the assessment times were: image-guided IAIC, use of radioisotopes and use of contrast in IAIC.

Univariate analysis (Kruskal-Wallis) between VAS improvements and baseline variables revealed various IAIC response predictors.

In terms of moderate improvement (50-70%) on post-IAIC, the statistically associated baseline variables were ($p < 0.05$): ***VASmv***, at T4 – lower use of NSAIDs at baseline; at T24 – knee IAIC; ***VASr***, at T4 – higher dose of MTX; at T12 – knee IAIC, higher total TH dose per patient; at T24 – wrist IAIC, longer disease duration, higher use of NSAIDs at baseline; ***VASs***, at T12-knee IAIC, medium dose of TH per IAIC, male gender (Table 2).

The best outcome predictors for significant improvement post-IAIC (> 70%) were ($p < 0.05$): ***VASmv***, at T4 – elbow and knee IAIC, longer disease duration; at T12 – MCP IAIC, higher dose of TH per IAIC, polyarticular injection, higher total dose of TH per patient, lower mean age, functional class II, use of chloroquine, no use of leflunomide; no previous IAIC; at T24 – MCP IAIC, higher TH dose per IAIC, higher total TH dose per patient, polyarticular injection, lower mean age, non-white skin color, functional class II, more extra-articular disease, no use of leflunomide; ***VASr***, at T4 – wrist and knee IAIC, higher TH dose per IAIC, use of methotrexate; at T12 – MCP IAIC, higher TH dose per IAIC, higher TH dose per patient, non-white skin color, functional class II, no use of leflunomide; at T24 – MCP

Table 2 – Association between improvement of 50%-70% and > 70% on VASmv, VASr and VASs assessments after IAIC and the presence of baseline predictors.

	VASmv Improvement (%)				VASr Improvement (%)				VASs Improvement (%)			
	T4		T24		T4		T24		T4		T24	
Baseline predictors	50-70	>70	50-70	>70	50-70	>70	50-70	>70	50-70	>70	50-70	>70
IAIC in elbow	-	+	-	-	-	-	-	-	-	+	-	+
IAIC in wrist	-	-	-	-	-	+	+	-	-	-	-	-
IAIC in MCP	-	-	-	+	-	-	-	+	-	+	-	+
IAIC in knee	-	+	+	-	-	+	-	-	-	-	-	+
Size of TH dose per IAIC (1/2/3)	-	-	-	+ (3)	-	+ (3)	-	+ (3)	-	+ (3)	-	+ (3)
Polyarticular injection	-	-	-	+	-	-	-	+	-	+	-	+
Total TH dose per patient (H/L)	-	-	-	+ (H)	-	-	-	+ (H)	-	+ (H)	-	+ (H)
Age (H/L)	-	-	-	+ (L)	-	-	-	-	-	-	-	-
Gender (fem/male)	-	-	-	-	-	-	-	-	-	-	-	-
Skin color (W/NW)	-	-	-	+ (NW)	-	-	-	+ (NW)	-	-	-	-
Functional class (2/ 3)	-	-	-	+ (2)	-	-	-	+ (2)	-	-	-	+ (2)
Extra-articular disease (Y/N)	-	-	-	+ (Y)	-	-	-	-	-	-	-	-
Disease duration (H/L)	-	+ (H)	-	-	-	-	+ (L)	-	-	-	-	-
Use of chloroquine (Y/N)	-	-	-	-	-	-	-	-	-	-	-	-
MTX (H/L dosage)	-	-	-	-	+ (H)	+ (H)	-	-	-	-	-	-
Use of LFU (Y/N)	-	-	-	+ (Y)	-	-	-	+ (S)	-	+ (N)	-	+ (N)
Total number of DMARDS (H/L)	-	-	-	-	-	-	-	-	-	+ (H)	-	-
Previous IAIC (Y/N)	-	-	-	-	-	-	-	-	-	-	-	-
Use of NSAIDS (Y/N)	+ (N)	-	-	-	-	-	-	-	-	+ (Y)	-	-
Dose of OC (H/L)	-	-	-	-	-	-	+ (H)	+ (L)	-	-	-	-

IAIC, Intra-articular injection with corticosteroid; VASmv, Visual Analogue Scale for Pain in movement; VASr, Visual Analogue Scale for pain at rest; VASs, Visual Analogue Scale for swollen joints; TH, triamcinolone hexacetonide; MCP, metacarpophalangeal joint; Size of TH dose 1- low, 2-medium, 3-high; RF: rheumatoid factor; MTX, methotrexate; LFU, leflunomide; DMARD, disease-modifying anti-rheumatic drug; H, higher; L, lower; Y, yes; N, no; W, White; NW, Non-white; Fem, female; OC, oral corticosteroid; Statistical test, Kruskal Wallis. +, $p < 0.05$; -, $p > 0.05$.

Table 3 – Association between > 50% concomitant improvement on VASmv, VASr and VASs post-IAIC and the presence of variables at baseline.

Variables	T4		T24	
	OR	P	OR	p
Joint type (compared to the knee)				
1. Elbow	NS	NS	4.4	0.008
2. Wrist	0.59	0.03	NS	NS
3. MCP	0.46	0.002	2.75	< 0.001
4. Shoulder	NS	NS	NS	NS
5. Ankle	0.55	0.03	NS	NS
Poly-injection (yes/no)	0.26	< 0.001	2.37	0.02
Sex (male/female)	2.19	0.008	NS	NS
Skin color (non-white/white)	2.47	< 0.001	0.55	0.04
Rheumatoid factor (yes/no)	NS	NS	0.34	< 0.001
Functional class (3/2)	NS	NS	0.42	0.003
Chloroquine (yes/no)	0.61	0.03	0.52	0.03
MTX (yes/no)	NS	NS	1.90	0.013
Use of oral corticosteroid	NS	NS	0.95	0.02
Total Dose of TH	0.99	< 0.001	1.00	0.02

IAIC, Intra-articular injection with corticosteroid; VASmv, Visual Analogue Scale for pain in movement; VASr, Visual Analogue Scale for pain at rest; VASs, Visual Analogue Scale for swollen joints; OR, odds ratio; TH, triamcinolone hexacetonide; MTX, methotrexate; MCP, metacarpophalangeal joint; NS, no statistical significancy (p > 0.05); Statistical test, multivariate logistic regression.

IAIC, higher TH dose per IAIC, polyarticular injection, higher total dose of TH per patient, non-white skin color, functional class 2, no use of leflunomide, less use of oral corticosteroid; **VASs**, at T4 – elbow and MCP IAIC, higher TH dose per IAIC, polyarticular injection, higher total TH dose per patient, no use of leflunomide, lower number of DMARDS, NSAID use; at T12 – MCP IAIC, polyarticular injection, higher total TH dose per patient, no previous injection, lower dose of oral corticosteroids; at T24 – elbow, MCP and knee IAIC, higher TH dose per IAIC, polyarticular injection, higher total dose of TH per patient, functional class II, no use of leflunomide (Table 2).

Multivariate logistic regression also showed that some of the variables presented at baseline were considered IAIC response predictors (Table 3).

In the short term (T4), the only variables that were predictors of **best** IAIC response were: "male gender" and "non-white skin color". On the other hand, "wrist, MCP and ankle IAIC", "do polyarticular injection", "be using chloroquine" and "higher total dose of TH per patient" were the predictors for the **worst** IAIC response in the short term.

In the long term (T24), various baseline variables were predictors of the **best** IAIC response, the most important of which was "do elbow IAIC" (with a 4.4 times higher chance of success), followed by "do MCP IAIC", "do polyarticular injection", "be using MTX" and "higher total dose of TH" per patient (Table 3). The baseline variables associated with the **worst** long-term IAIC response were: "non-white skin color", "rheumatoid factor positivity", "functional class III", and "be using chloroquine and oral corticosteroid". Multivariate logistic regression did not show any medium-term (T12) improvement predictor.

Only mild and transitory local adverse effects were observed. Post-IAIC inflammatory flare was observed in 37.82% of the patients (related by the patients but not observed by the blinded observer at T1). Skin atrophy, skin hypochromic and articular instability were observed in 1.9%, 15.3% and 2.0% of the patients, respectively.

Discussion

This was a prospective, non-controlled study conducted on a cohort of patients with established RA receiving TH IAIC injection, a description of a great experience of our group. Though known as the most effective corticosteroid for intra-articular use,[6–8,10–12] we are unaware of other similar studies in which TH was used as an IAIC drug.

Our group has already published few studies in which RA patients were submitted to TH IAIC injection. Monoarticular and polyarticular IAIC effectiveness was considered superior to systemic use of corticosteroids;[10,11] ankle was considered the joint with lowest accuracy for blinded IAIC;[6] the use of ultrasound to guide TH injection did not increase its effectiveness in wrists joint,[12] and the use of radioisotopes (Yttrium-90 and Samarium-153-particulate hydroxyapatite) did not improved TH IAIC effectiveness when compared to injection of TH IAIC alone.[7,8]

Uncommon TH doses, as 20 mg for MCP joint or 80 mg for knee joint, were used in our study. The ideal TH doses for IAIC have not been already established, but the most commonly used dosages are 40 mg of TH for large joints and 10-20 mg for small to medium-sized joints.[6,11,14,18,19] Some authors, however, have used optimized doses of TH somewhat similar to ours,[6,11,14] without the occurrence of any significant adverse effects.

In our study, the use of radioisotopes was not related to any articular improvement at any of the evaluation time's post-IAIC. Increased IAIC effectiveness when associated with the use of the Yttrium-90 and Samarium-153 Hydroxyapatite has been questioned by previous studies.[7,8,20,21]

Univariate analysis found that baseline variables as "higher TH doses applied via IAIC and per patient", "polyarticular injection" and "be using leflunomide" were associated with the worst IAIC responses. Perhaps a more aggressive TH dose administered via IAIC and a greater number of joints injected are associated with higher post-IAIC articular flare and, therefore, with a clearer perception of short-term aggravation.

On the other hand, the variables "do MCP" and "do elbow" IAIC, "functional class II" and "higher doses of TH per joint and per patient" were repeatedly associated with best IAIC responses, especially over the long term. Some of these variables have already been shown to be best response predictors for IAIC using TH, most notably "do elbows" and "do MCP" IAIC.[6,11] However, "functional class III", "higher oral dose of corticosteroid" and "higher dose of TH per patient" had not been identified as good IAIC response predictors over the long term. Higher dose of TH correctly introduced into the joint space might prove to be more effective than a lower dose, though this conclusion needs to be confirmed with prospective studies.

Other studies that evaluate IAIC response predictors[15,22–25] have been already published, but few of them used TH as the chosen corticosteroid.[22,24]

In the study conducted by Green *et al.*,[15] fifty-one patients, with less than or equal to five joints with synovitis, were treated with methylprednisolone IAIC. Predictors of response were studied being the primary endpoint a complete response at 12 weeks. Twenty-nine patients (57%) had a complete response at 2 weeks. The best predictor of response at 12 and 26 weeks was the complete response at 2 weeks.[15] The present study used TH rather than methylprednisolone; it evaluated a higher number of patients and did not study the relationship between IAIC responses obtained at the first assessment time and those obtained during subsequent evaluation times.

Eder *et al.*[25] evaluated IAIC responses in two hundred and twenty patients with psoriatic arthritis submitted to 245 IAIC. Clinical factors associated with good response included duration of psoriasis [Odds Ratio (OR) 1.03] and the use of MTX or anti-TNF agents at the time of injection (OR 2.68). Injection into large joints (OR 4.58), elevated sedimentation rate (OR 15.0) and MIF polymorphism (OR 3.2) were factors associated with relapse, whereas absence of clinical and/or radiographic damage (OR 0.23) and duration of disease (OR 0.92) reduced risk of relapse.[25] Similarly to our study, Eder *et al.*[25] also studied a greater number of patients and found that the use of MTX was a predictive factor of IAIC response. However, the diseases studied were different, which make it difficult to compare both sets of results.

Hetland *et al.*[23] evaluated betamethasone IAIC response in 160 patients with early RA. One thousand three hundred and seventy-three joints (ankles, elbows, knees, MCP, metatarsophalangeal, proximal interphalangeal (PIP), shoulders, wrists) were injected (once or repeated injections) during 2 years. All joint areas had good 2-year joint injection survival, longest for PIP joints: 73.7%. A higher MRI synovitis score of MCP joints and anti-CCP-negativity were associated with poorer joint injection survival, whereas IgM-RF and C-reactive protein were not. Like our study, IAIC injection of small hand joint was a good IAIC-response predictor. However, the presence of positive rheumatoid factor was associated with worse IAIC responses at T24 and repeated injections in the same joint space were not performed. The time of onset of RA and the drug injected were important differences between the studies.

According to our multivariate logistic regression analysis, an association with best IAIC response was observed in only seven baseline variables. "Being male" and "non-white skin color" was associated with best IAIC responses over the short term. However, the stronger associations with best IAIC response over the long term (24 weeks) were observed for the variables "do elbow and MCP IAIC", "do polyarticular injection", "be using methotrexate" and "higher total dose of TH per patient". As initially shown by univariate analysis, "do elbow" and "do MCP" IAIC remained the baseline variables predictive of best IAIC response. The benefit of polyarticular injection, which implies the use of a higher total dose of corticosteroid per patient, was proven by previous controlled studies using methylprednisolone and TH.[11,26] As already suggested by Eder *et al.*,[25] "be taking methotrexate", given its disease-modifying action on synovitis, favor a positive IAIC response in comparison to when this drug is not in use in psoriatic arthritis patients.

In the present study "do MCP IAIC", "do polyarticular injection" and "higher total dose of TH per patient" were both worst and best-response predictors over the short and long term, respectively. This suggests that post-IAIC articular flare may be cause of the worst responses in the short term.

The worst long-term response predictors – "having a positive rheumatoid factor and functional class III" and "be using oral corticosteroid at the time of IAIC" – suggest a worse IAIC response in patients suffering from a more serious condition. However, "be using chloroquine" is associated with worse IAIC response over both the short and long term. Perhaps the mechanism of action of chloroquine interferes with intra-articular-administered TH, a microcrystalline corticosteroid. But this association has never been studied, and a specific prospective study is needed to clarify this doubt.

One of the limitations of this study is that anticitruline antibodies were not measured in our sample patients. As only 0.2% of the patients studied were receiving immunobiological therapy, predictive variables for best IAIC response identified in this study cannot be extrapolated for those patients receiving this therapy.

Finally, this is the first study to identify, in RA patients, baseline predictors for worst and best responses to IAIC with TH, the most atrophying corticosteroid for intra-articular use. Defining predictive factors for IAIC response may prove to be extremely helpful in obtaining more adequate recommendations for IAIC, and, therefore, better therapeutic management for RA patients.

Conflicts of interest

The authors declare no conflicts of interest.

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