Rheumatology International (2019) 39:723–727
https://doi.org/10.1007/s00296-019-04266-z

Rheumatology
INTERNATIONAL

PHARMACOVIGILANCE

Use of systemic glucocorticoids in patients with psoriatic arthritis by Argentinian and other Latin-American rheumatologists

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Received: 28 January 2019 / Accepted: 26 February 2019 / Published online: 4 March 2019

Abstract

To analyse the administration of systemic glucocorticoids (SGC) to patients with Psoriatic arthritis (PsA). Online, anonymous, multiple-choice, closed-ended survey on SGC use in PsA, dose, duration of therapy, and the reason for administration. One hundred and twenty rheumatologists from Argentina (ARG) and 75 from other countries in Latin-America (LAT) completed the survey. Only 6% of the respondents indicated that they did not prescribe SGC, and 65% claimed that they administered them to less than 10% of their patients. Among those physicians who used SGC, 71% prescribed between 5 and 10 mg/day of prednisone, and only 5% over 10 mg/day. Seventy-three percent of the respondents administered SGC for less than 3 months, and 93% associated them with DMARDs, Biological Therapy (BT), or DMARDs plus BT. Clinical indications for SGC were (more than one option was possible): peripheral arthritis (79%), dactylitis (23%), enthesitis (20%), cutaneous involvement (11%), and axial involvement (8%). Thirty-four percent of ARG physicians versus 21% of LAT used SGC in over 10% of their patients (p 0.07) while 76.5% of ARG versus 59% of LAT administered doses higher than 5 mg/day of prednisone (p 0.01). SGC were indicated by most of the rheumatologists surveyed, but only to a reduced number of patients with PsA, at low doses, for short periods of time, associated with DMARDs/BT, and with the aim of treating peripheral joint manifestations. Argentinian physicians tended to prescribe SGC to more patients and at slightly higher doses.

Keywords Psoriatic arthritis · Spondyloarthritis · Glucocorticoids

Introduction

Psoriatic arthritis (PsA) is part of the family of the spondyloarthritis, and can be defined as an *"inflammatory arthropathy associated with psoriasis and usually negative for rheumatoid factor"* [1]. It is sustained by up to 42% of the patients with psoriasis, and it is characterised by enthesitis, dactylitis, synovitis, and spondylitis. The cutaneous disease typically precedes the joint disease in 7–12 years in 75% of the patients [2, 3].

Systemic glucocorticoids (SGC) are usually prescribed to complement disease-modifying antirheumatic drugs (DMARDs) in inflammatory arthritis treatment. For example, although administration of SGC is not advised as monotherapy in Rheumatoid Arthritis (RA), it is agreed that low doses can be included as bridge therapy during 3 months in conjunction with DMARDs [4].

In 1968, Baker and Ryan published an analysis of 104 patients with generalised pustular psoriasis in which at least one-third of the cases had been prompted by abrupt withdrawal from SGC [5]. Since then, textbooks have not recommended or have even forbidden the use of SGC for psoriasis treatment even though there is no hard evidence that they can cause that adverse event when they are used at low doses along with biological therapies (BT) or at disease onset with slow-acting drugs such as methotrexate [6].

During the 2000s, different randomised clinical trials carried out to prove the efficacy of anti-TNF in PsA allowed the inclusion of patients who were being administered stable doses of SGC (up to 10 mg/day of prednisone) between 2 and 4 weeks prior to the trial, and around 10% were on SGC when the trial started [7–9]. This scenario has continued to

This study was presented as a poster in the 20th Pan-American League of Associations of Rheumatology Congress, that took place in Buenos Aires, Argentina in April 2018. (https://journals.lww.com/jclinrheum/toc/2018/04001).

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prevail during the current decade when new anti-TNF and non-anti-TNF BTs have been developed [10–13].

A study published in 2005 evaluated a cohort of 1306 Italian patients with PsA treated in 37 centres and showed that 41.2% had been administered SGC at some point in their lives and that 61.7% of them were receiving SGC at the time of the study, the medication was well-tolerated (92.2%), and efficacy rates were high (95.0%) [14].

A study published in 2006 analysed a comprehensive national database of the *German Collaborative Arthritis Centres* and indicated that out of 1863 patients with PsA treated in Germany, 26.6% used low doses of SGC (up to 7.5 mg/day of prednisone) and 3.2% used higher doses [15]. Furthermore, in an analysis performed by Agustin et al assessing a vast database of patients with psoriasis in Germany, it was observed that SGC were the most frequently prescribed drugs in 2007; these data did not change if patients with PsA were excluded from the analysis. It is noteworthy that at the time, SGC were not recommended by the German Society of Dermatology guidelines, and that most of the physicians who prescribed SGC were general practitioners and internists [16].

A study published in 2014 by Al-Dabagh et al examined a database of the medications prescribed in the United States between 1989 and 2010, and pointed out that SGC were among the most frequently administered drugs for psoriasis, and that no significant changes regarding prescription were observed for the duration of their research [17].

Although the EULAR 2015 recommendations for the management of PsA accept local injections of glucocorticoids, it is asserted that SGC should be used with caution and at the lowest possible effective dose. In any case, it is acknowledged that to date, there is no shred of evidence to warrant fears for psoriasis reactivation due to the administration of SGC in a rheumatologic context [18].

The GRAPPA guidelines for PsA conditionally recommend the use of SGC at the lowest possible effective dose (usually lower than 7.5 mg/day of prednisone) and for short periods of time to treat peripheral arthritis in order to minimise the adverse events, among which psoriasis flares after withdrawal of treatment are highlighted [19].

Since in Latin-America, to our best knowledge, there are no data published as to the use of SGC in PsA, the implementation of the current study was deemed appropriate. The objectives were to analyse how often rheumatologists prescribe SGC to patients with PsA, doses, duration of administration, and most frequent indications, and to determine whether there were differences in the administration of SGC between Argentinian and other Latin-American physicians.

Materials and method

Seven hundred and seventy Argentinian (ARG) and 1948 from other Latin-American countries (LAT) rheumatologists were contacted via email to take part in an anonymous survey consisting of 10 multiple-choice, closed-ended questions they could answer over the Internet.

These emails unambiguously explained to the professionals that they were invited to participate in a research study so as to assess the use of SGC in PsA in their daily clinical practice in terms of frequency, duration of administration, and doses. It was made clear that the survey would be evaluated through an Internet platform, and data would be stored in an anonymous database. Two different direct links to the survey were made available to Argentinian and Latin-American physicians, respectively, at the end of the email. Only data about prescribing patterns of SGC in daily practice were recorded.

Professionals were not asked personal information: Argentinian rheumatologists were not asked in what city they practised medicine, and Latin-American professionals were not asked country of residence.

Professionals from the following countries were summoned: Brazil, Colombia, Costa Rica, Ecuador, Mexico, Panama and Venezuela.

All of them were requested to state whether they worked in either a public or a private facility, and the number of patients with PsA they assessed per week and average time of evolution of their psoriasis.

They also had to specify the frequency with which they prescribed SGC to patients with PsA, doses, duration of therapy, and reasons for administration. Finally, they were enquired whether, in their opinion, the use of SGC was associated with an increase of flares of cutaneous psoriasis, and if they attributed the development of cutaneous flares to a specific precipitating factor (several options were provided).

Statistical analyses

Descriptive statistics were used for the general analysis. Nominal variables were compared by means of the chi-square test. A p value < 0.05 was considered statistically significant. Windows Excel and EPI Info Version 3.5.4. were employed for the statistical analysis.

Results

A total of 195 rheumatologists filled in the survey, 120 from Argentina and 75 from other Latin-American countries. Eighty-nine (46%) worked in public hospitals while 106

(54%) worked in either private practices or hospitals that treated patients with private health insurance or social security. One hundred and forty-two (73%) of the respondents examined as many as 5 patients with PsA per week, and 53 (27%) over 5 patients with PsA per week. Sixty-one (31%) respondents of the respondents stated that on average, their patients had psoriasis of less than 5 years of evolution, 114 (59%) between 5 and 10 years, and 20 (10%) over 10 years.

When they were asked about SGC, 12 (6%) mentioned that none of their patients were administered these drugs, 126 (65%) maintained that less than 10% used them, 44 (22.5%) indicated between 10 and 50%, 8 (4%) answered between 50 and 75%, and 5 (2.5%) over 75% or more.

Among those who prescribed SGC, 45 (25%) used doses lower than 5 mg/day of prednisone, 129 (70%) between 5 and 10 mg/day, and 9 (5%) over 10 mg/day. In general, SGC were used for short periods of time: 52 (28%) of the respondents administered them for less than 1 month, 76 (42%) between 1 and 3 months, 30 (16%) between 3 and 6 months, 21 (11%) for over 6 months, and 6 (3%) did not answer.

Among those who prescribed SGC, 13 (7%) administered them either as monotherapy or associated with NSAIDs, 123 (67%) along with DMARDs, 36 (20%) with DMARDs plus a BT, and 11 (6%) with a BT.

Clinical indications for SGC administration were (more than one option was possible): peripheral arthritis in 154 (79%), dactylitis in 44 (23%), enthesitis in 39 (20%), cutaneous involvement in 22 (11%), and axial involvement in 15 (8%) (See Fig. 1).

When they were asked whether the administration of SGC was associated with a higher frequency of cutaneous flares, 86 (44%) answered affirmatively. When they were enquired if they attributed the development of cutaneous flares to a specific precipitating factor (several options were provided), 113 (58%) answered the cause was discontinuation of DMARDs/BT, 82 (42%) ascribed them to intrinsic features of psoriasis that do not depend on the administration of SGC, 82 (42%) attached them to tapering or discontinuation of SGC, and 47 (24%) considered that the reason was patients do not undergo control tests in due time.

There were no significant differences between physicians who worked in public hospitals and those who did not.

Forty-one (34%) of ARG versus 16 (21%) of LAT physicians claimed that they used SGC in over 10% of their patients (χ^2, $p = 0.07$). (See Fig. 2).

Ninety-two (76.5%) of ARG versus 44 (59%) of LAT rheumatologists administered SGC at doses higher than 5 mg/day of prednisone (χ^2, $p = 0.01$). (See Fig. 3).

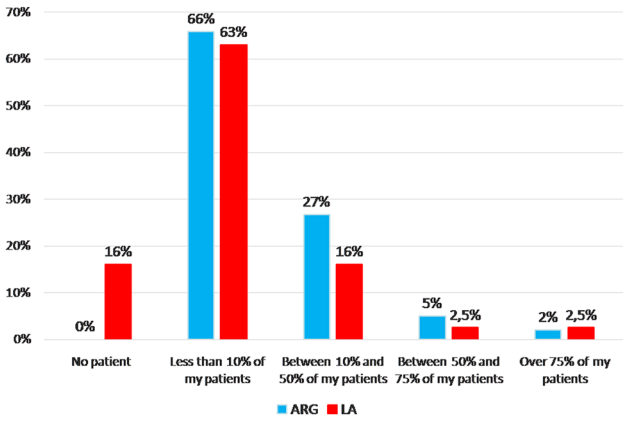

Fig. 2 Usa of SGC in patients with PsA (%) by Argentinian and other Latin-American rhenumatologists

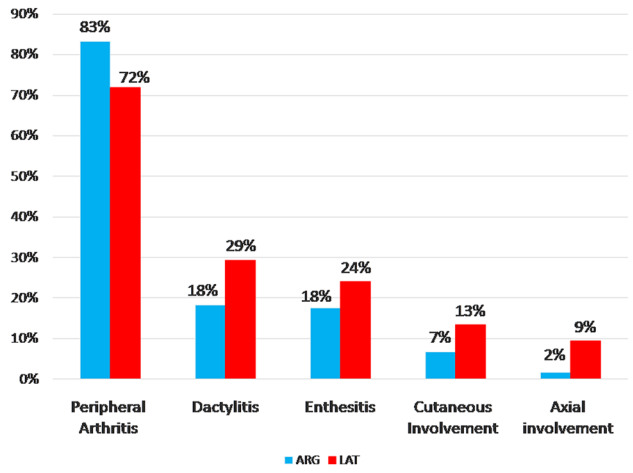

Fig. 1 Argentinian and other Latin-American rheumatologists's reasons for prescribing SGC

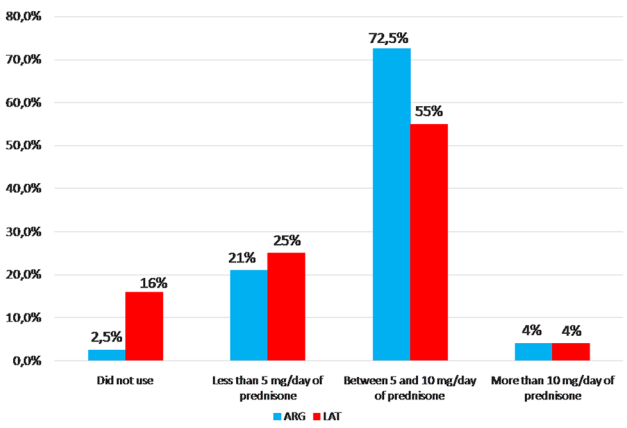

Fig. 3 Daily dose of SGC prescribed by Argentinian and other Latin-American physicians

Discussion

PsA and RA share a number of characteristics: they are both chronic inflammatory joint diseases that decrease the quality of life, bring about disability, and are related to high morbimortality. Besides, anti-inflammatory drugs, methotrexate, leflunomide, and Anti-TNF are part of their treatment.

However, although there is an undeniable overlap between these disorders, there are also relevant differences that must be addressed in terms of epidemiology, clinical practice, physiopathology, and assessment and treatment of patients. Therefore, not every agent employed in RA can be empirically administered in PsA [20].

After several approaches were used and discarded, SGC seem to have found their place in the treatment of RA. Though there is currently a vast arsenal of biological and non-biological medications to control joint involvement in RA, the use of SGC is accepted when flares turn out to be tricky to handle [4].

Fortunately, there are new and different treatment options for psoriasis that have proven effective to manage disease compromise, and more resources are expected to be available in the near future. Nonetheless, the fact that some medications attain fast and sustained remission in cutaneous psoriasis does not imply that they exhibit the same efficacy when it comes to joint involvement.

As above-mentioned, the administration of SGC in PsA was advised against for a long time. Nevertheless, according to some authors, SGC may be helpful in patients with PsA owing to their fast anti-inflammatory effect, and it is feasible to minimise the risks their use entail when they are administered along with DMARDs or BT during short periods of time [6, 21]. Since SGC are readily-available, low-cost drugs, they appear to have been commonly prescribed in the clinical practice [14–16] which does not mean that their use was correct in every case.

For example, SGC administration may be advantageous, at the lowest possible dose and for short periods of time, in a patient with PsA who experiences a polyarticular flare, when access to BTs is not possible promptly.

Most physicians included in this survey have acknowledged they prescribe SGC, but only to a reduced number of patients, and at a similar dose and a slightly higher proportion than the ones in the clinical studies aforementioned [7, 13].

This study has the following limitations: it is a survey, not an audit. Hence, it is possible that respondents do not convey what they actually do in their daily clinical practice, but their opinions and academic knowledge [21].

The use of SGC in PsA remains controversial and lacks scientific evidence about its efficacy and safety to guide clinical practice. Although this survey does not advance scientific evidence as it only explores the prescribing pattern of the participating rheumatologists, it provides valuable insight into the clinical practice of Latin-American rheumatologists when it comes to PsA treatment.

The survey comprised 10 questions, which on the one hand, favoured participation, but on the other hand, hindered the acquisition of complementary information relevant to other more exhaustive analyses. Sixteen percent of Argentinian rheumatologists participated in the survey, but other Latin-Americans' involvement was much lower. Therefore, the conclusions of this study should not be deemed representative of the course of action of most of the physicians in the region. Moreover, since personal data have not been collected, conclusions of this study should not be considered based on the opinion of preeminent researchers or thought-leaders in PsA and psoriasis of the region. Yet, 73% of the respondents examined as many as 5 patients with PsA per week and 27% over 5 patients with PsA per week.

Only rheumatologists were consulted in this survey. Thus, it is not representative of the opinions of dermatologists, clinicians, and general practitioners.

Even so, a significant number of professionals who responded willingly and anonymously was included. In addition, this study was carried out over a decade after the audits above-mentioned [14–17]. Nowadays, there are different BTs readily available, and treatment guidelines have been published by international scientific associations [18, 19] that neither proscribe nor limit treatment options for patients with PsA and constitute unavoidable reading material for every rheumatologist that assesses patients with PsA on a regular basis.

In summary, SGC were indicated by most of the rheumatologists surveyed, but only to a reduced number of patients with PsA, at low doses, for short periods of time, associated with DMARDs/BT, and with the aim of treating peripheral joint manifestations. Argentinian physicians tended to prescribe SGC to more patients and at slightly higher doses.

Acknowledgements The authors wish to thank Professor Ana Insausti for her cooperation in the translation of this research paper.

Author contributions Both, CA and VC took part in the conception and design of the study; VC and GS took part in the data management and analysis. All the authors write the article and approved the final manuscript.

Funding This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval In view of the fact that this paper is an anonymous, online survey not levelled atpatients but at physicians, with the purpose of deriving opinions as to theirprescribing pattern of glucocorticoids in patients with psoriatic arthritis,authorisation from the Bioethics Committee was not requested

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