Glucocorticoid use and abuse in SLE
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Abstract
Glucocorticoids (GCs) are potent anti-inflammatory and immunosuppressive agents. They act by two different mechanisms: the genomic and the non-genomic pathways. The genomic pathway is considered responsible for many adverse effects of GCs, most of them are time and dose dependent. Observational studies support a relationship between GCs and damage in SLE. GCs have been associated with the development of osteoporosis, osteonecrosis, cataracts, hyperglycaemia, coronary heart disease and cognitive impairment, among others. Although no clinical trial has compared high vs low doses of GCs, some studies have shown the efficacy of medium doses in severe forms of SLE. The dose below which treatment can be considered safe has not been defined, but daily doses <7.5 mg of prednisone seem to minimize adverse effects. Combination therapy with HCQ and the judicious use of immunosuppressive drugs help to keep prednisone therapy within those limits.

Key words: prednisone, methylprednisolone, anti-malarials, HCQ, osteoporosis, osteonecrosis, damage, mortality, prognosis, SLE.

Introduction
GCs are potent anti-inflammatory and immunosuppressive agents. They are widely used in clinical practice to treat systemic autoimmune diseases, and also a number of diverse conditions, such as asthma, skin diseases, allergic reactions and other systemic diseases. The utility of cortisone for the treatment of RA was proved by Hench et al. [1], who was awarded the Nobel Prize for Medicine in 1950. Following Hench et al.’s initial discovery, new CSs have been developed. These new drugs have lower mineralocorticoid and higher GC activity, showing a higher anti-inflammatory potency. Despite their important clinical efficacy, GCs produce several adverse reactions, most are time and dose dependent, limiting their clinical usefulness. These adverse effects are particularly relevant in chronic diseases that require long treatment periods. A clear example is SLE and other autoimmune diseases.

In this article, we aim to critically review the relation between the dose of GCs, mainly prednisone and prednisolone, and their efficacy and unwanted side effects, based on the pharmacological basis of GC actions and specifically focusing on SLE. We will try to defend the idea that a sensible use of lower doses of prednisone is not associated with less clinical efficacy, while substantially reducing corticoid-related damage.

Pharmacology of GCs
GCs exert their anti-inflammatory and immunosuppressive effects by reducing the expression of cytokines and adhesion molecules, inhibiting leucocyte traffic and access to inflammation site and interfering with leucocyte, fibroblast and endothelial cell function. Almost all primary and secondary immune cells are target for their effects. GCs reduce the number of circulating monocytes and macrophages by decreasing their myelopoiesis and release from the bone marrow. Besides, they reduce the expression of MHC and Fc receptors as well as the synthesis of pro-inflammatory cytokines, such as IL-2, IL-6, TNF-α and PGs. GCs also have an effect on T-cells, lowering the production and action of IL-2 and diminishing the overall number of circulating T-cells. In addition, GCs act on endothelial cells by decreasing vascular permeability, adhesion molecule expression and production of IL-1 and PGs. Furthermore, GCs affect granulocyte function by increasing the number of circulating neutrophils and reducing the amount of eosinophils and basophils. Lastly, GCs also have an impact on fibroblast function by lowering their proliferation and production of fibronectin and PGs [2].
Mechanisms of action of GCs: the genomic and non-genomic pathways

Steroids are highly lipophilic molecules that easily diffuse through cellular membranes, reaching the cytosol and interacting with intracellular structures [3]. The anti-inflammatory and immunosuppressive actions of GCs are exerted by two different mechanisms. In the genomic pathway, GCs modulate the expression of proteins via their interaction with the cytosolic GC receptor (GR) [4]. On the other side, there is a newly described and faster mechanism, known as the non-genomic pathway [5].

The genomic way is triggered by the union of GC with GR, which is a member of the steroid hormone receptor family, a super-family of ligand-inducible transcription factors. After reaching the cytosol, GCs are available to bind with high affinity to the cytosolic GR that became activated. This fact leads to translocation of the GC–GR complex into the cellular nucleus, where it binds to specific DNA binding sites, the GRE [6].

The interaction between the GC–GR complex and GRE determines modulation of gene expression either positively (transactivation) or negatively (transrepression). Transrepression induced by the GC–GR complex inhibits many pro-inflammatory molecules and it has become one of the most important explanations for the immunosuppressive and anti-inflammatory effects of GC [7, 8]. In contrast, transactivation is responsible for transcription of enzymes linked to gluconeogenesis and other adverse reactions like osteoporosis, skin atrophy, growth retardation and Cushingoid habit; therefore, it is thought to be responsible for most adverse effects of GCs [2].

The process by which the GCs activate the genomic pathway and then modulate the protein expression takes at least 30–60 min. However, the overall immunosuppressive and anti-inflammatory effects will take hours or days before they are evident [9, 10].

GCs can also act by non-genomic mechanisms, which explain some of the rapid immunosuppressive and anti-inflammatory effects [11]. It is well known that high and very high systemic methylprednisolone doses may quickly improve many processes such as anaphylactic reactions or systemic autoimmune disease flares. Thus there is a way by which GCs can act faster than by the classical genomic way, offering additional therapeutic benefits.

The non-genomic pathway works in a different way. First, GCs can interact with the cytosolic GR in a GR-dependent but transcriptional-independent mechanism [11]. This phenomenon may be explained because the GR complex, after binding to GC, is able to interact not only with DNA via the classic genomic mechanism, but also with intracellular proteins, leading to a rapid inhibition of inflammatory mediators such as arachidonic acid. Secondly, GCs may produce their effects by interacting with biological membranes, particularly cellular and mitochondrial membranes. By this mechanism, GCs can reduce ATP that is essential for immune cells to maintain their functions. Thirdly, GC may interact with a membrane-bound GR [5].

Dose–effect relationship of GCs

As noted above, the anti-inflammatory potency is related to the GC effects of each molecule. Table 1 compares the mineralocorticoid activities and the relative anti-inflammatory potencies by genomic and non-genomic pathways of some of the most used GCs [12, 13].

It has been suggested that equivalent GC doses should be calculated using prednisone as the comparator of the group and regarding the different potencies showed in Table 1. In the clinical setting, GC doses can be clustered using the following scheme: low doses are ≤7.5 mg of prednisone-equivalent doses; medium doses are between 7.5 and 30 mg; high doses >30 mg and up to 100 mg prednisone-equivalent per day; very high doses >100 mg prednisone-equivalent per day; finally, when doses are >250 mg of prednisone-equivalent per day for few days, usually no more than 5 days, it is termed as pulse therapy [14].

Of note, the capacity to recruit both genomic and non-genomic pathways is different for the different compounds. Besides, genomic effects are related with the degree of cytosolic receptor saturation even though there is no such exact linear relationship between them. At doses up to 30 mg/day of prednisone or equivalent, the cytosolic GR is saturated at ~50%. GR saturation reaches 100% above that dose. In other words, between 30 and 100 mg/day of prednisone-equivalent, the genomic way is fully operating. In contrast, the non-genomic pathway is

<table>
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<tr>
<th>GC</th>
<th>Anti-inflammatory potency by genomic way</th>
<th>Anti-inflammatory potency by non-genomic way</th>
<th>Mineralocorticoid activity</th>
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<tbody>
<tr>
<td>Cortisol/hydrocortisone</td>
<td>1</td>
<td>Low</td>
<td>2</td>
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<tr>
<td>Prednisone/prednisolone</td>
<td>4</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Methylprednisolone</td>
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<td>Dexamethasone</td>
<td>20–30</td>
<td>20</td>
<td>0</td>
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<tr>
<td>Betamethasone</td>
<td>20–30</td>
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Table 1 Relative potency of some GCs by the two different ways and its mineralocorticoid activity [12–14]
operating at clinically relevant levels at doses >100 mg/day of prednisone-equivalent [14, 15].

**GC side effects**

It is well known that GCs produce a wide spectrum of adverse effects at many organ levels. These effects are mainly related to their genomic mechanism of action, and are dose and time dependent.

In a historic cohort study of patients with RA in low-dose, long-term therapy with prednisone, the authors showed that daily prednisone doses between 10 and 15 mg/day strongly correlated with the development of adverse effects such as fractures, serious infections and cataracts [odds ratio (OR) = 32.3, 95% CI 4.6, 220] [16].

In the musculoskeletal system, GCs can cause osteoporosis, osteonecrosis and myopathy. Osteoporosis is one of the most common adverse effects of chronic use of GCs, even at low doses [17]. GCs inhibit osteoblastic function, leading to decreased bone formation, loss of BMD and consequently to an increased risk of fracture. Bone loss starts at the beginning of GC treatment and maximizes at 6 months, which decreases after the therapy is stopped. It affects mainly bone with high trabecular content, like vertebrae [18]. A meta-analysis by van Staa et al. [19] found a strong correlation between cumulative doses and loss of BMD as well as between daily doses and risk of fracture. The authors conclude that prednisone doses >5 mg/day or equivalent increase the risk of fracture during the treatment period [19]. Osteonecrosis is another severe side effect of GCs. It has been suggested that it is more related with high prednisone doses than with cumulative doses [20]. It is worth mentioning that there is a paradoxical action of GCs in RA bone damage. GCs at low doses used for short periods have been shown to reduce periarticular osteoporosis and radiographic disease progression, whereas when used for long periods and/or at higher doses GCs are highly damaging for bone [21, 22].

Endocrine and metabolic adverse effects of GCs are important aspects to take into account. GCs increase the risk of hyperglycaemia in a dose- and time-dependent manner in diabetic as well as non-diabetic patients [23]. It has been suggested that hyperglycaemia may appear at doses as low as 2.5 mg/day of prednisone-equivalent [24]. The capacity of GCs to induce redistribution of body fat is well known, and it occurs even at low doses. Cushing syndrome is dose and time dependent. It can become evident from the first month of treatment and at doses as low as 5 mg prednisone-equivalent per day. GCs at high doses also lower the levels of oestrogens and testosterone. However, the occurrence of infertility or decreased libido has not been proved [17].

GCs have been suggested as an independent risk factor for cardiovascular diseases. Wei et al. [25], using a record linkage database, compared 68,781 GC users to 82,202 non-users, most of them with IBD or chronic obstructive pulmonary disease. They found that doses >7.5 mg/day significantly increased the risk for myocardial infarction and cerebrovascular events. Of note, the association between GC use and cardiovascular events remained after adjustment for traditional cardiovascular risk factors [25]. A recent systematic review showed a poor association between cardiovascular risk and long-term prednisone-equivalent doses up to 10 mg/day. The authors found an increase in insulin resistance but no effects on the lipid profile or blood pressure. However, they found a trend of increasing risk of major cardiovascular events with exposure to such doses. This trend persisted even after adjustment on RA severity, activity or comorbidities [26].

Another remarkable adverse effect is related to the potential of GCs to increase susceptibility to major infections, a well-known cause of morbidity and mortality in many inflammatory diseases. This effect may increase with dose and duration of treatment, although it is not clear if there is a threshold below which GC therapy is safe. A population-based cohort of 609 RA patients found that GCs were strong predictors of infection in both the univariate and multivariate analyses [27]. A nested case–control study of 16,207 RA patients from Quebec showed that GC therapy increases the risk of non-serious infections in patients >65 years of age in a dose–response manner. Patients treated with doses <5 mg/day of prednisone-equivalent had a relative risk of 1.1 (95% CI 0.99, 1.22) compared with those treated with doses >20 mg/day, which had a relative risk of 1.85 (95% CI 1.68, 2.05) [28].

Another chapter to consider is the dermatological impact of GCs. The dermatological manifestations include cutaneous atrophy, striae, purpura, easy bruisability, impaired wound healing, acne and hair defects. Although there are no accurate data regarding dose and time of occurrence for these cutaneous adverse effects, it has been suggested that long periods of treatment with medium to high doses of GCs are needed for them to appear [17]. Ophthalmological adverse effects can be very disabling. They include cataracts and an increased risk of glaucoma, which may lead to visual field loss and even blindness. The presence of previous glaucoma and a family history of glaucoma are recognized risk factors for ocular hypertension associated with the use of GCs [29]. It has been suggested that open angle glaucoma is more common in patients exposed to doses >7.5 mg/day prednisone-equivalent for >1 year. Cataracts were found more frequently in RA patients treated with a mean of 6 mg/day of prednisone-equivalent for a mean of 6 years compared with RA patients not treated with prednisone [16]. It is important to highlight that although intraocular pressure may return to normal after stopping the GC treatment, cataracts may be irreversible [17].

Finally, GCs may produce many psychological and behavioural disorders, including disturbances of mood, cognition, sleep as well as psychosis. The most common adverse effects of short-term GC treatment are euphoria and hypomania, whereas long-term therapy may induce depressive symptoms [30]. Such disturbances are related to dose and may occur immediately after the initiation of treatment and even after discontinuation of treatment. The
Boston Collaborative Drug Surveillance Program found that the incidence of psychiatric manifestations was 1.3% in patients receiving 40 mg/day prednisone-equivalent or less and 18.4% in patients receiving doses >80 mg/day [31].

Table 2 shows some of the most important adverse effects and their time and dose relationship.

**GCs in SLE**

**GCs and damage in lupus**

Irreversible organ damage is an important predictor of morbidity and mortality in SLE [32]. Whereas lupus itself can be a cause of damage in several organ systems, such as the kidney and the CNS, drugs used to treat lupus can also induce chronic organ dysfunction. In particular, GCs may be potentially associated with several domains within the SLICC/ACR Damage Index (SDI): osteoporosis, osteonecrosis, cataracts, diabetes and cardiovascular disease, among others. A number of observational studies support this relation of GCs with global damage in SLE.

Gladman et al. [33] reported on the course of a subgroup of 73 patients within the prospective Toronto Lupus Cohort. All these patients formed an inception group, with a follow-up of at least 15 years. Damage was recorded yearly using the SDI, and classified as definitely associated with GCs (ocular and musculoskeletal entries), possibly related with GCs (cardiovascular, peripheral vascular disease, neuropsychiatric and diabetes) and independent of GCs (renal, pulmonary, gastrointestinal and skin, SDI entries, premature gonadal failure and malignancy). Overall, 87.7% of patients received GCs, at a mean maximum dose of 37.7 mg/day. Seventy per cent of patients received anti-malarials at some point, and 50% were treated with immunosuppressive drugs. The mean SDI increased over time from a mean of 0.33 at the first 6 months to 1.99 at 15 years. Within the first year of follow-up, 42% of damage was considered independent of GCs (mainly gastrointestinal and skin SDI entries), 42% possibly related with GCs (mainly cardiovascular and neuropsychiatric) and the remaining 16% definitely secondary to GCs (ocular and musculoskeletal entries). By the 15th year of follow-up, only 20% of new accrued damage was independent of GCs, whereas 31% was possibly related with CSs and 49% definitely associated with CSs [33]. A similar distribution of new SDI entries was found at 5 and 10 years of follow-up. Overall, musculoskeletal damage was the most frequent in all ethnic subsets.

A second study from the Hopkins Lupus Cohort analysed the influence of steroid treatment on the accrual of first damage in 539 patients using Cox proportional hazard models [20]. Four different CS exposure variables were used: the cumulative GC dose (total number of milligrams of prednisone plus pulse methylprednisolone, expressed as prednisone-equivalents); the cumulative prednisone dose; the high-dose prednisone therapy (every period of at least two months taking 5 60 mg/day of prednisone); and the number of i.v. pulse methylprednisolone doses (1000—3000 mg each). Eighty-five per cent of the cohort had ever taken prednisone. Of them, 21% ever received high-dose prednisone therapy. Damage was observed in 60% of patients during the follow-up. The cumulative GC dose was associated with an increased risk for osteoporotic fractures, avascular necrosis, cataracts, diabetes mellitus, coronary artery disease, pulmonary fibrosis and cognitive impairment/psychosis, with adjusted risk ratios ranging between 1.5 and 2. On further refining of the analysis, the cumulative prednisone dose was found to increase the risk for osteoporotic fractures, cataracts and coronary artery disease (with adjusted risk ratios ranging between 1.7 and 2.5 for each equivalent of 10 mg/day of prednisone during 10 years). Likewise, treatment with high-dose prednisone increased the risk of avascular osteonecrosis and stroke by 20%. On the other hand, no such complications were associated with pulse methylprednisolone, which were only related with the occurrence of cognitive impairment/psychosis.

A third study was conducted by the same group [34]. In this case, 525 patients diagnosed with SLE within the 6 months prior to enrollment into the Hopkins Lupus Cohort were included in the analysis. The primary outcome variable was the accrual of first damage, as measured by the

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<th><strong>Table 2</strong> Adverse effects of GCs—time and dose relationship</th>
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<td><strong>Adverse effect</strong></td>
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<td>Increased risk of infections [27, 28, 56]</td>
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*aExpressed as prednisone-equivalent daily doses.*
SDI. The main independent variable was the cumulative prednisone dose, categorized in five levels: 0 mg/month, >0–180 mg/month, >180–360 mg/month, >360–540 mg/month and >540 mg/month. For the analysis, a time-varying Cox model was fitted with the inclusion of several potential confounders, including lupus disease activity measured as the mean SLEDAI score. One hundred and forty-one patients suffered damage during the follow-up. The risk of damage increased with the cumulative prednisone dose. However, the risk did not substantially increase with cumulative doses <180 mg/month (equivalent to 6 mg/day). Thus this study points to a cut-off value of between 5 and 7.5 mg/day for prednisone, above which the risk of damage begins to increase. Interestingly, this study reproduces the results found in non-SLE patients as well as the pharmacological limit proposed by the authors suggest the possibility that CSs may actually be a marker of lupus activity rather than a real risk factor for vascular disease.

This point has been raised by other authors. In the case–control study by Roman et al. [47], lupus patients with carotid plaque by US study actually had a lower average daily dose of prednisone during the past 5 years (although a non-significant longer period of exposure) [47]. The cumulative dose of prednisone was not higher in lupus patients with atherosclerotic vascular disease in a study from the Toronto Lupus Cohort [48].

Two recent studies may shed light on this controversy. A retrospective analysis of the Montreal Lupus Cohort showed that both the cumulative prednisone dose received within the previous year and the mean SLEDAI increased the levels of cardiovascular risk factors (lipids, systolic blood pressure, BMI and blood glucose levels) as well as the estimated 2-year coronary heart disease risk (by 15 and 5%, respectively) [49]. Of note, the effect of both was independent of each other, but the effect of GCs was higher in patients with higher disease activity. On the other hand, both GC dose and SLEDAI were closely associated, as expected. A study in a paediatric SLE cohort analysed the predictors for carotid intima–media thickness in 221 patients with a mean age of 15 years [50]. The effects of baseline prednisone were studied. The authors found that doses <0.15 mg/kg/day and >0.4 mg/kg/day increased carotid intima–media thickness, whereas in-between doses decreased it.

In summary, it is very difficult to disclose the effect of GCs on cardiovascular disease in lupus, and, particularly, to split such effect from that of lupus-associated inflammation. However, it seems that the possible beneficial effect of prednisone in decreasing lupus activity is overshadowed by the adverse influence of GCs on traditional cardiovascular risk factors. The dose and duration of treatment that mark the cut-off point for an increased cardiovascular risk are not well established.

**Other GC-related complications**

Osteonecrosis, a major complication in patients with SLE, has been related with CS therapy. More precisely, studies
have consistently found a strong relation with early high doses of prednisone over a reduced period of time [51–54]. One study also reported an association between high-dose pulses of methylprednisolone (1000 mg/day) and avascular necrosis [55].

The risk factors for major infections have recently been addressed in a nested case-control study within the Lupus-Cruces cohort. Prednisone dose was found to be an independent predictor of serious infections, with a median dose of 7.5 mg/day in patients with major infections vs 2.5 mg/day in those without. In the logistic regression model, the odds of suffering a major infection increased by 12% with each milligram/day of prednisone [56].

Insulin resistance was also found to be more prevalent in patients receiving CS, in a dose-dependent manner. A recent cross-sectional study from Spain found that it was almost 6-fold higher in patients taking >7.5 mg/day of prednisone (median 10 mg/day) compared with those treated with lower doses [57].

**GC dose and efficacy in lupus**

In terms of efficacy, no clinical trial has actually compared the effects of higher vs lower doses of prednisone in lupus. Thus the usual dose of 1 mg/kg/day recommended for severe manifestations of lupus is essentially empirical. On the other hand, recent randomly assigned controlled trials on LN might offer us an indirect clue of the efficacy of different doses of prednisone in the prototypical severe manifestation of SLE. The Euro-Lupus Nephritis Trial compared low- vs high-dose CYC for the induction therapy of proliferative LN [58]. In both groups, the initial dose of prednisone was 0.5 mg/kg/day, preceded by three i.v. pulses of methylprednisolone. Treatment failure, the main end-point, happened in 16 and 20% of patients, respectively. Illei et al. [59] conducted a clinical trial comparing i.v. methylprednisolone, i.v. CYC or both as induction treatment of proliferative LN. Prednisone was given at an initial dose of 0.5 mg/kg/day in all three groups. Response rates were 33, 63 and 81%, respectively. In a small randomly assigned clinical trial sponsored by the EULAR, comparing continuous vs pulse CYC therapy in patients with proliferative LN, no differences in the outcome were found between both arms [60]. Interestingly, patients in the continuous therapy group received prednisone at an initial dose of 0.85 mg/kg/day, whereas those in the pulse therapy group were initially treated with 0.3 mg/kg/day. Treatment responses in recent clinical trials comparing CYC and MMF combined with oral prednisone at initial doses of 1 mg/kg/day ranged from 30 to 90% [61–64]. It is important to note that different remission criteria as well as diverse immunosuppressive regimes were used across the studies, in fact that hampers comparisons. Anyhow, the resulting response rates do not seem different between those studies using high initial doses of 1 mg/kg/day of prednisone and those combining pulse methylprednisolone with lower doses between 0.3 and 0.5 mg/kg/day, whether CYC or MMF were used. On the other hand, the mean daily dose of prednisone received during the first 6 months with each therapeutic scheme differed substantially, with all patients treated with high starting doses receiving mean doses well above 20 mg/day (Table 3).

A recent observational study from the Lupus-Cruces cohort has addressed the efficacy of induction therapy of LN with starting doses of prednisone not higher than 30 mg/day combined with HCQ and immunosuppressive drugs (pulse CYC, MMF of AZA, depending on the histological subclass) and pulse methylprednisolone in proliferative forms [65]. This scheme resulted in a 90% long-term partial or complete response rate, resulting in a mean daily prednisone dose of 10 mg during the first 6 months of therapy. In addition, CS-related side effects, including Cushingoid habit, were not seen.

Recently, Pepper et al. [66] reported on the favourable outcome of a cohort of 18 patients with biopsy-proven Class II/IV/V LN treated with an induction regime consisting of rituximab, either alone or combined with i.v. methylprednisolone, followed by maintenance therapy with MMF. Overall, 78% of patients achieved a complete or partial remission and 67% had a sustained response at 1 year. Prednisone was used at induction at a median dose of 10 mg/day, with progressive reduction that allowed prednisone discontinuation in one-third of patients at 2 years, with no patients requiring >10 mg/day [66]. A new off-prednisone regime based on rituximab and i.v. methylprednisolone followed by MMF and HCQ as maintenance therapy is currently being evaluated by the same group [67]. Whether induction therapy with rituximab is indicated in all patients with proliferative LN is a logical criticism of this therapeutic scheme.

With regard to pulse methylprednisolone, recent retrospective and prospective studies report similar efficacy of 500 mg/day during three consecutive days vs 1000 mg/day for three to five consecutive days in treating severe lupus flares [68, 69]. The lower-dose group suffered a significant lower number of serious infections.

**Summary**

GCs are among the most potent immunosuppressive and anti-inflammatory drugs. Their efficacy in treating SLE is beyond doubt. However, GC-related side effects are many and serious. Indeed, prednisone use has been consistently shown to increase irreversible damage in lupus patients, a major predictor of morbidity and mortality.

Recent data have shown that many side effects are dose related, and closely linked with the degree of activation of the genomic pathway. In general, serious toxicity starts at doses of 7.5 mg/day, the limit between low and medium pharmacological doses. Moreover, the need for high doses of 1 mg/kg/day in severe lupus activity is now being questioned, since significantly lower doses may be equally effective. Finally, pulse methylprednisolone, 500 mg/day during three consecutive days, is a potent therapy for severe acute lupus flares with few associated side effects.

Every effort should be made to avoid GC side effects. It should be borne in mind that GCs are not the therapy of lupus, but part of the treatment of lupus manifestations.
Concomitant use of anti-malarials [70] and immunosuppressive drugs [71] may help keep daily doses of prednisone <7.5 mg/day, or even to withdraw it. GC-induced osteoporosis should be prevented following available guidelines [72]. Osteonecrosis may be reduced by avoiding high prednisone doses during the early phases of disease. In general, using GCs in a more restrictive way should help prevent major complications in patients with SLE.

**Rheumatology key messages**

1. GCs are effective in treating inflammatory manifestations of lupus.
2. Oral prednisone therapy is a cause of important time- and dose-dependent toxicity in patients with lupus.
3. Using lower doses of GCs in SLE would prevent major side effects without reducing their efficacy.

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**Disclosure statement**

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Glucocorticoids and SLE


