CAN WE WITHDRAW LOW-DOSE PREDNISONE IN REMITTED PATIENTS?

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Maintenance of remission has become central in the management of systemic lupus erythematosus (SLE). However, an active disease-free state is generally maintained only when patients are on medication, which often leads to treatment-related complications. Therefore, once remission has been achieved, prolonged maintenance treatment inevitably requires a regimen of drug de-escalation. The recent EULAR recommendations for the treatment of SLE during chronic maintenance treatment advocate that glucocorticoids (GC) should be, when possible, withdrawn.\(^1\) However, in routine practice a significant proportion of treating physicians prefers to continue a low dose GC regimen, despite clinical remission, which is most likely due to the fear that withdrawal of low-dose GCs may lead to a severe flare, even after very long intervals of remission.\(^2\) In a recent prospective randomised controlled trial, we showed that, in SLE patients in remission and with stable treatment regimen for at least 1 year, withdrawal of 5 mg of prednisone was associated with a fourfold increase (i.e. 27%), in the risk of flare, as defined by the SFI or the BILAG index.\(^3\) Other SLE treatments remained unmodified during this study. In particular, at study entry 91% and 27% of the patients were also treated with hydroxychloroquine and an immunosuppressant, respectively. The 27% relapse rate observed in the withdrawal group in our study is in line with the ones recently reported in two recent cohorts.\(^4\) S Tani et al described the longitudinal study of a cohort of 91 SLE Italian patients who attempted stopping GC treatment.\(^4\) A total of 77 patients successfully stopped GC. For those patients who were successfully withdrawn from GC, 18 flares (23%) were recorded after a median follow-up period of about 2 years. As in our study, 72% of flares were mild. The time period since the last flare was the sole determinant predictor of disease flare identified. A recent observational study, performed by Goswami et al in India, reported that 21% of patients in remission underwent exacerbation of the disease after GC withdrawal with most of the flares occurring in the first year of follow-up.\(^5\) Therefore, until the availability of effective drugs with little or no toxicity, it is recommended to not abandon the option of using very low doses of GCs (i.e. ≤3 mg prednisone) given their potential benefits in SLE patients in remission, especially those at low cardiovascular risk.

Learning Objectives
- Define remission in SLE patients
- Discuss drug de-escalation in SLE patients in remission

REFERENCES

CAN WE WITHDRAW IMMUNOSUPPRESSANTS IN REMITTED PATIENTS?

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Remission has recently emerged as a potential target in the management of systemic lupus erythematosus (SLE), indeed remission is not uncommon and is associated with improved prognosis.\(^1\) \(^2\) Nevertheless, the best management of remitted patients, especially those in stable remission, remains elusive. In particular, whether immunosuppressive therapy (IST) may be
safely discontinued, without exposing remitted patients to a significant risk of flare, has not yet been clearly determined. Accordingly, available recommendations for the management of SLE underline the importance of progressive tapering of glucocorticoids (GCs) until withdrawal, but do not remark on the possibility of discontinuing IS in remitted patients. Moreover, the timing of IS discontinuation has not yet been established and in clinical practice it is quite common that remitted patients continue to receive the same treatment which led to remission, with the aim of preventing flares, for an indefinite period of time.

It has been recently reported that ISs were safely withdrawn after remission achievement in more than 75% of patients with SLE in a cohort of 319 patients treated with IS for different manifestations, including lupus nephritis (LN) (47%), arthritis (15.7%), haematological abnormalities (5.3%), skin rash (6.3%), neuropsychiatric SLE (1.9%), vasculitis (1.3%), serositis (0.6%), and multi-organ involvement (21.9%). The independent predictors of a safe discontinuation were hydroxychloroquine (HCQ) maintenance therapy after IS discontinuation and a longer duration of remission at IS discontinuation. Notably, being on HCQ and in remission for at least two consecutive years reduced the risk of flare by 81% and being on HCQ and in remission for at least three consecutive years by 86%. These findings are in keeping with recent recommendations, as antimalarials have been regarded as standard of care in all SLE patients unless contraindicated, including patients with LN, where antimalarials are proposed as an additional therapy. Interestingly, in this study maintenance therapy with 5 mg/day prednisolone equivalent alone did not protect against flares, as patients with low-dose maintenance therapy experienced a similar flare-rate compared to patients who discontinued all treatment at the time of IS withdrawal.

In LN, different studies found a variable flare rate after IS discontinuation due to achievement of stable remission, ranging from 15% to 38.7%. Antimalarial therapy and a longer duration of remission at IS discontinuation resulted predictive of flare-free remission in some but not all these studies. Notably, the protective role of HCQ therapeutic levels against LN flares has recently been reported. Indeed, among remitted patients, those with a subsequent renal flare during the follow-up had significantly lower HCQ levels compared with those in persistent remission. To date, different authors suggested a wide range of duration of IS maintenance therapy after remission achievement in LN, varying from 3 to 6.5 years.

Based on available data, we can conclude that IS may be withdrawn in selected SLE patients, based on the characteristics of the individual patient, including their maintenance therapy and the duration of remission, which requires a personalised approach. In this regard, long-term therapy with antimalarials should be recommended in all SLE patients. Continuous surveillance should be planned during treatment tapering and after withdrawal, to ensure any early signs or symptoms of disease relapse are detected.

Learning Objectives

• Explain why, although GCs should be de-escalated and withdrawn as early as possible in remitted patients, the timing of IS tapering until discontinuation in these patients is still an unresolved issue
• Describe the recent data suggesting that maintenance therapy with HCQ and a longer duration of remission at the time of IS withdrawal are protective against lupus flares
• Explain the importance of tight surveillance of lupus patients, during IS therapy tapering and after IS withdrawal in order to detect early signs or symptoms predictive of a disease relapse

REFERENCES


Workshop

15 MANAGEMENT OF REFRACTORY SKIN LUPUS

Management of refractory skin lesions in patients with lupus erythematosus involves combinations of local measures and systemic agents requiring adjustment to activity and development of the disease. The treatment options are fairly similar for the different cutaneous manifestations; however, no drugs have been licensed specifically for the treatment of skin lesions in this disease. Therefore, the aim of the European guideline was to achieve a broad consensus on treatment strategies for patients with cutaneous lupus erythematosus (CLE) by a European subcommittee, guided by the European Dermatology Forum (EDF) and supported by the European Academy of Dermatology and Venerology (EADV).

Standard treatment of CLE includes preventive measures such as smoking cessation and photoprotection. Ultraviolet (UV) A and B light is one of the most important risk factors for CLE, clearly documented by photoprovocation studies in large patient cohorts. In the past years, several trials have been performed to investigate the preventive effect of sunscreens in patients with UV-induced CLE. A randomised controlled trial demonstrated that the application of a broad-spectrum sunscreen with a high protection factor prevents UV-induced skin lesions under standardised conditions. First-line treatment options in CLE include topical corticosteroids or calcineurin inhibitors. Currently available topical calcineurin inhibitors (0.03% and 0.1% tacrolimus ointment, 1% pimecrolimus cream) have been licensed for the use in patients with atopic dermatitis. The major advantage of these agents is their better safety profile when compared to topical corticosteroids. A multicentre, randomised, double-blind, vehicle-controlled trial showed significant improvement for oedema and erythema of CLE lesions using 0.1% tacrolimus ointment compared to the vehicle.

In patients with disfiguring and widespread disease, systemic agents need to be applied. The first-line systemic treatment is antimalarials, such as hydroxychloroquine, chloroquine...