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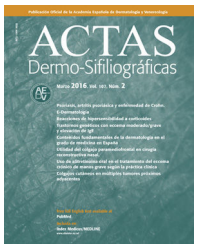

RESIDENT'S FORUM

Where Should We Position Antimalarial Drug Combinations in the Management of Refractory Cutaneous Lupus Erythematosus?☆

FR-¿Dónde posicionamos la combinación de antipalúdicos en el manejo del lupus eritematoso cutáneo refractario?

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Topical therapy with high-potency corticosteroids or calcineurin inhibitors combined with synthetic antimalarial drugs achieves satisfactory disease control in the majority of patients with cutaneous lupus erythematosus. However, the management of refractory cases is a real challenge in daily clinical practice. Very few case series and clinical trials have been published, and it was only with the development and validation of the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) in 2007 that it became possible to objectively assess the severity of the disease.[1]

The therapies most commonly used in refractory cases include particularly methotrexate, acitretin (with the highest level of evidence), mycophenolate mofetil, and dapsone. However, the combination of conventional antimalarial drugs (chloroquine [CQ] and hydroxychloroquine [HDQ]) with quinacrine (QN) is an option not always considered despite its good therapeutic results.

QN, which is seldom used as it has to be requested for use as a foreign medication, is effective both in monotherapy and in combination with other antimalarials. In 2010, González-Sixto et al.[2] presented a retrospective series of 8 cases with excellent results after using QN in combined therapies to treat different forms of cutaneous lupus erythematosus. CQ and HDQ have similar therapeutic and ocular toxicity profiles, and their combined use is not therefore recommended. However, a therapeutic advantage of QN is its absence of retinal toxicity. In contrast, its side effects do include a risk of severe and potentially fatal aplastic anemia. Periodic (3-monthly) complete blood counts must therefore be performed to detect this anemia in its hypocellular phase, which resolves on withdrawal of the drug; this phase is occasionally preceded by nonspecific lichenoid eruptions.

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A number of case series in the literature have described the combined use of synthetic antimalarial drugs, but the regimen typically used is the one proposed by McCune and González-Rivera[3] in 2001: HDQ (at a dose not higher than 6.5 mg/kg/d) combined, when necessary, with QN (100 mg/d). If no adequate therapeutic response is observed after 6 to 8 weeks of combined therapy, HDQ is substituted by CQ (at a dose below 3.5 mg/kg/d) while continuing with QN. Recently, in a review by Rodríguez-Caruncho and Bielsa,[4] we were reminded of the realities of this association; those authors drew attention to a series of unresolved issues, including whether there is a time limit for the use of this combination, whether drug holidays can be used, why the cardioprotective effect of QN has still not been studied in sufficient detail, possible additional risks of the combination, and whether QN can potentiate other side effects of HDQ.[5]

In view of these considerations and on the basis of our own experience, we believe that, in the management of cutaneous lupus erythematosus refractory to conventional treatments, it is necessary to reposition the combination of antimalarial drugs as a therapeutic option to be used prior to employing other immunosuppressive agents or systemic retinoids.

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