Letters to the Editors

Discontinuation rates and timing of antimalarial drugs in primary Sjögren's syndrome

Sirs,

The antimalarial drugs (AM) chloroquine (CQ) and hydroxychloroquine (HCQ) have been employed for the treatment of many systemic autoimmune diseases for the last half century (1). Recently emerging data showing their multiple beneficial effects, support long-term usage of AM in patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and other connective tissue disorders (CTDs) (2-11).

Despite their unquestionable benefits, a number of observational studies have reported a not irrelevant discontinuation rate of AM in SLE and RA (12, 13). This trend reflects the general poor compliance to long term treatments and the insufficient surveillance for iatrogenic and disease-related comorbidities among patients affected by chronic rheumatic diseases (14). Recently, Jover *et al*. (15) analysed the use and causes of discontinuation of CQ and HCQ in a cohort of 778 rheumatologic patients, mostly represented by patients affected by RA and SLE. The authors found that the IR of global discontinuation was 204 (95% CI 186–224) and that 52% of the treatments stopped were due to adverse events mainly related to non-ophthalmologic reasons. These findings are in line with the general belief that in clinical practice AM discontinuation rates are somehow higher than those previously reported and that a more individualized team-based monitoring system will decrease the number of unnecessary AM discontinuations (12, 16). Herewith, we would like to highlight that AM discontinuation is quite common also in primary Sjögren's syndrome (pSS) as well as in SLE and RA patients. Primary SS is a complex autoimmune disease characterised by a progressive hypofunction of the salivary and lachrymal glands, frequently associated with a variety of extraglandular manifestations, including malignant lymphoproliferative disorders (17, 18). The disease is challenging to early diagnose and to evaluate, and no specific treatments are known to be effective (19). Nonetheless, AM are among the most commonly employed drugs for pSS in clinical practice. (2) Similarly to Jover *et al*. (15) we assessed the reasons for and timing of discontinuation of HCQ in our cohort of 495 patients (diagnosis of pSS made according to AECG criteria). Reasons for drug discontinuation were assessed by medical record review from inception to May 2012. Out of the 495 pSS patients, 202 (5 M: 197 F; age at diagnosis 50.4±14.5 years; mean follow-up = 41.4± 44.4 months) had received HCQ. The incidence rate of global discontinuation in our cohort was 6.34 per 1,000 patient-year (95% IC 4.8–8.2) with 53/202 (26%) of the patients discontinuating HCQ at least once over the follow-up. Reasons for discontinuation were: lack of efficacy in 5/53 (11%), adverse events in 19/53 (35.8%), non-compliance in 22/53 (41%) and miscellaneous causes such as surgery/comorbidities and concomitant medications in 7/53 (13%). In line with Jover *et al*. we found that adverse events discontinuations were mostly related to non-ophthalmologic reasons: skin rashes (11/19; 58%) and gastrointestinal symptoms (6/19; 27%) accounting for most causes of HCQ discontinuation. Non-retinal eye problem were detected in 2/19 patients (7.7%). We did not find any case of AM-related definitive retinal toxicity, this difference may be due to the fact that while in the Spanish study two thirds of the patients received CQ, our patients were mainly treated with HCQ. When timing of HCQ withdrawal was separately considered we found that discontinuation due to adverse events occurred after 4.4±5.9 months of treatment. Discontinuation due to lack of efficacy and to non-compliance were documented significantly later over the follow-up: after a mean period of 16.8±18.2 months (p=0.01) and 40.6±33.5 months (p<0.0001) respectively. We concluded that, despite generally well tolerated, HCQ discontinuation is relatively quite common also in pSS. Discontinuation is not a consequence of ocular toxicity but it is mainly related to cutaneous and gastrointestinal adverse events. The discontinuation curve is characterized by a bimodal distribution: an "early" peak due to non-ophthalmologic adverse events and a "late" peak related to lack of efficacy and patients' non-compliance.

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