Monitoring Drug Levels in Lupus

HCQ plays a central role in the management of SLE. It addresses both cutaneous and arthritis manifestations of the disease. It has been associated with improved survival, as well as an increased likelihood of complete response to interferon α-2b (IFN-α) in patients with SLE. HCQ has been linked to the prevention of seizures and thrombosis as well as a reduced risk of permanent organ damage. The excess risk of CVEs associated with HCQ use is a concern, particularly in patients with diabetes and renal disease. The half-life of HCQ is about 40 days. Although some plasma concentrations display considerable inter-individual variability, lower than expected blood concentrations strongly suggest nonadherence or partial adherence rather than intrinsic metabolic differences or a few missed doses.

Methods of Measuring HCQ Concentrations: As with many assays used in therapeutic drug monitoring, the test for HCQ blood levels is not commercially available and must be ordered from a reference laboratory. HCQ should be measured in whole blood rather than in plasma. The drug concentration in the cellular fraction of the blood, so that plasma levels are on average one-seventh of those in whole blood. Additionally, plasma concentrations display much greater within-patient variability than whole blood levels.

The half-life of HCQ at 2400 visits from 686 patients in the Hopkins Lupus Cohort was 347/452 days. Although some inter-individual differences in bioavailability have been observed, lower than expected blood concentrations strongly suggest nonadherence or partial adherence rather than intrinsic metabolic differences or a few missed doses.

Improving Treatment Adherence: We measured HCQ whole blood levels at each office visit in Hopkins Lupus Cohort participants receiving the drug. Individuals with a subtherapeutic concentration received an email notifying them of the finding and asking that they not miss any drug doses. The second HCQ blood level was discussed at the patient’s next visit. At the start of our study, 44% of patients (304/686) were deemed partially nonadherent based on low HCQ blood levels (<500 ng/mL). Roughly 29% of these (88/304) were completely nonadherent (HCQ blood levels <15 ng/mL) and measured counseling led to increased levels of adherence (Figure).

Supporting our choice of therapeutic HCQ blood level (≥500 ng/mL), we identified a significant trend for a decrease in disease activity (as measured by Systemic Lupus Erythematosus Disease Activity Index) as blood levels increased (P<0.004 for trend).

We work generally corroborates that of Costedoat-Chalumeau and colleagues, who reported a significant association of HCQ blood levels with risk of SLE exacerbation. This Paris-based group also found that patient self-reports of poor adherence were associated with very low HCQ blood levels (<129 mg/mL). Another study by these investigators indicated that subtherapeutic levels had a higher chance of spontaneous complete nonadherence increased after patients were enrolled in a study involving HCQ blood level monitoring, before any intervention began. These findings and our data suggest that patient awareness of blood level monitoring can encourage adherence.

Controversy About HCQ Dosing: HCQ dosing is a topic of discussion among ophthalmologists as well as rheumatologists because of the drug's rare association with retinopathy (1). HCQ has been linked to the prevention of seizures and thrombosis as well as a reduced risk of permanent organ damage. The excess risk of CVEs associated with HCQ use is a concern, particularly in patients with diabetes and renal disease.

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