

Risk of flare higher with hydroxychloroquine reduction or discontinuation



Decisions to maintain, reduce or stop SLE treatment may affect specific subgroups differently.

INTRODUCTION

Systemic lupus erythematosus (often called Lupus or SLE) is an autoimmune disease. It often starts in women between the ages of 15 and 45, but it can occur at any age, and 10% of patients are male. SLE symptoms can vary. People with SLE sometimes have visible symptoms like swollen joints and a ‘butterfly’ rash on their cheeks. But SLE may also affect a person’s inner organs, such as their kidneys, lining of the lung or heart. It can also have an impact on blood cells, affecting the numbers of white cells, red cells, and/or clotting cells. SLE is caused by overactive immune cells and the production of *autoantibodies*. An antibody is a protein that the immune system makes to attack foreign substances in the body, such as viruses or bacteria. In autoimmune diseases, the body makes antibodies that attack its own tissues. These are called autoantibodies.

There is no single treatment for SLE, but many drugs are available to calm down the inflammation caused by the overactive immune system. The aim is to reduce the damage caused by inflammation.

Hydroxychloroquine is a drug used to treat SLE. People with SLE often take this medicine for the rest of their life. Many people ask if they can lower or stop their hydroxychloroquine, and doctors have tried to identify when it would be safe to stop or reduce the dose, and in which groups of people.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to help answer questions around tapering or stopping hydroxychloroquine in a way that would allow individuals to make the right decision for them, which is called personalised treatment. They set out to determine whether reducing or stopping the drug was linked to an increased risk of SLE flares. They also wanted to know whether certain factors could be used to predict which people would be more likely to suffer from a flare once hydroxychloroquine was reduced or stopped.

WHO WAS STUDIED?

The study looked at 1,460 people with SLE who were taking hydroxychloroquine. These people were followed by research doctors at 33 sites in Europe, Asia, and North America.

HOW WAS THE STUDY CONDUCTED?

This was a prospective observational study. These people were not randomised to receive any particular drug, but simply observed and their data recorded. The study used data from the SLE International Collaborating Clinics (SLICC) cohort – a database collecting information about people with SLE. Information was collected from 1999 to 2019, with data recorded at time of diagnosis and then once a year after that.

The researchers used this information to study people with SLE who had reduced or stopped (discontinued) their hydroxychloroquine. They compared SLE flare rates between this group and a second group of people who continued their hydroxychloroquine dose.

WHAT WERE THE MAIN FINDINGS OF THE REVIEW?

The main finding was that continuing hydroxychloroquine was associated with a lower flare risk than reducing or stopping hydroxychloroquine, even in people with low or no disease activity.

There were some differences depending on people’s individual factors. For example, among people who stopped hydroxychloroquine, those with a low level of education had an increased flare risk. People taking prednisone (a steroid medicine) or other immunosuppressors were also at higher risk of flare.

Over the course of the study, most people (over three quarters) experienced a flare, emphasising the need for better approaches to SLE treatment.

ARE THESE FINDINGS NEW?

Decades ago, a study suggested that maintaining hydroxychloroquine dose might greatly reduce SLE flares. However, it was hard to know if these findings specifically applied to people in whom doctors would want to reduce treatment – for example, people in remission or with very low disease activity. Clinical experience suggests that hydroxychloroquine reduction or withdrawal may be safer in some stable patients, but it was hard to be sure of the absolute and relative risks in each situation.

The results of this new study mean that if a patient were to ask, “if someone decreases hydroxychloroquine, what are the chances of flaring sooner than if they stay on the same dose?” the physician could reply: “according to this research, on average, after decreasing hydroxychloroquine there is about a 55% probability that a flare will occur sooner than for a patient staying on the same dose, but after stopping hydroxychloroquine, there is over 60% probability of flaring sooner than a given patient continuing on hydroxychloroquine.” We also now know that decisions to maintain, reduce, or stop hydroxychloroquine may affect specific groups of people differently, including those on prednisone or with low levels of education.

WHAT ARE THE LIMITATIONS OF THE STUDY?

One limitation in this study was that the definition of flare used cannot clearly separate mild from moderate or severe flares. It was also not possible to evaluate hydroxychloroquine blood levels (which are not part of usual care at most centres in the SLICC cohort), or self-reported adherence. Nevertheless, in adjusting for sex, age, race/ethnicity, education and multiple medications, the authors accounted for factors that are themselves strong predictors of adherence.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

These results can be used in discussions with patients to help them understand the potential implications of lowering or stopping hydroxychloroquine and support them in making decisions about their treatment. The results can also be used to develop electronic tools that could help with decision-making.

The authors will also be running some more studies to confirm whether considering baseline hydroxychloroquine levels (not just the prescribed dose) predicts flares after reducing or stopping the drug. They also hope to study the preferences of patients when it comes to balancing the risks and benefits of this drug.

WHAT DOES THIS MEAN FOR ME?

If you are taking hydroxychloroquine for SLE, you may be more likely to have a flare if you reduce or stop your treatment.

If you have any concerns about your disease or its treatment, you should speak to your doctor.

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