

We asked the question:
*“For what symptoms do you prescribe
Plaquenil? What are the major risks and side
effects?”*

By: Dr. Stephanie Ensworth

This is a very important and “topical” question. At the recent International Lupus Meeting in New York in May 2004, with the biggest lupus researchers collected from all over the world, despite all of the presentations on the complicated details of what might be causing lupus, there was a lot of discussion and emphasis on the importance of treating persons with lupus with plaquenil!

“Plaquenil” is the manufacturer’s trade name for a medication called “hydroxychloroquine.” Whenever possible, we all should refer to medications by their “real” medication name and when writing articles such as this or research papers, the “real” medication name is always used; thus, in this article, I will refer to “Plaquenil” as “Hydroxychloroquine.” So that I don’t have to keep writing out this long medication name throughout this discussion, I will abbreviate “hydroxychloroquine” to what we, lupologists, abbreviate it to: “HCQ.”

HCQ is an extremely old medication, first used in 1630 to treat fevers. HCQ was one of many medications used worldwide for the treatment of malaria (although, HCQ has been used for so many decades to treat malaria, that most forms of malaria have now developed resistance to HCQ, so other medications now are used to treat malaria.) Nevertheless, HCQ is still referred to as an “anti-malarial” medication. Even in rheumatology, HCQ and its stronger “sister” medications, chloroquine and quinacrine, that are used to treat rheumatic disorders, including lupus, are all referred to by physicians and pharmacists as “anti-malarials.”

Older anti-malarial medications (other “sister” drugs of HCQ) were first stumbled upon and recognized to be effective in the treatment of lupus of the skin in 1894. Various anti-malarials have been used since then to treat many types of lupus of the skin. Chloroquine was actually patented in 1934. HCQ was first manufactured in the mid-1940s and was found to have less side effects than chloroquine or quinacrine. HCQ was released onto the market in 1955 after a lot of research revealed that HCQ was effective in the treatment of lupus and rheumatoid arthritis. Thus, HCQ and similar “sister” medications have been around for a very long time and have been safely taken for the treatment of lupus and rheumatoid arthritis by millions of people (plus the millions of people who took these medications for treatment of malaria). As these anti-malarial medications have been available for over a century and ingested by so many people, a lot is known about these medications. Over the many years, more and more beneficial effects of the anti-malarials, especially HCQ and even chloroquine, have been noted. Also noted have been the very few side effects, particularly with HCQ, and how well tolerated by patients this medication is. Thus, the risk versus benefit ratio of using anti-malarials in the treatment of rheumatic disorders, especially lupus, greatly favors the use of the medication and that is the

reason why most persons with lupus are taking an anti-malarial, most commonly, HCQ. When prescribing or recommending any type of treatment, physicians always look at the risk of the treatment versus its benefits. The treatment is only prescribed or recommended when the benefit exceeds the risk (potential side effects). In the case of HCQ, the potential benefits far exceed the rare potential risks.

HCQ is used for four different reasons in lupus patients:

1. To treat some active symptoms of lupus. HCQ is most effective in treating many different types of lupus skin disorders (acute cutaneous lupus including lupus butterfly facial rash, subacute cutaneous lupus and discoid lupus among others); and lupus arthritis. It is also helpful in the treatment of lupus pleuritis (inflammation around the linings of the lungs); lupus pericarditis (inflammation of the lining around the heart); and lupus fatigue. It has no role in the treatment of serious, vital organ involvement by lupus.
2. It can be used in lupus to help lower the prednisone dosage. This is called “a steroid sparing effect.” In other words, it can help treat lupus so that the prednisone dose can be lowered (prednisone has far more side effects than HCQ, thus, it is preferable to take HCQ and a lower dose of prednisone). Even though HCQ has no direct role in the treatment of serious, vital organ involving lupus, once the serious lupus flare is treated or under control, HCQ can help to lower the prednisone dose (along with the immunosuppressive therapy to treat serious lupus).
3. Help prevent lupus disease flare-ups and stabilize the disease. There are several studies on the stabilizing effects of HCQ and chloroquine on lupus and the decreased rate of flare in those patients who take these medications. HCQ is even used in lupus pregnancy to help prevent lupus flare in pregnancy; one study has found that those lupus patients who took HCQ in pregnancy had improved pregnancy outcomes compared to those lupus patients who did not take HCQ in pregnancy.
4. Amazingly, HCQ has many preventative actions. HCQ and chloroquine have “antithrombotic effects” (ie: help to prevent blood clots which lupus patients are more susceptible to than the normal population) by inhibiting the action of clotting cells, called platelets. HCQ has an aspirin-like effect on platelets but without the skin bruising caused by aspirin. It is important to note that HCQ is not as strong in inhibiting the action of platelets as aspirin. Often, HCQ and aspirin are used together to protect lupus patients from forming blood clots (thrombosis).

HCQ and chloroquine have mild blood pressure lowering effects and help in the treatment of mild hypertension (high blood pressure). They also help to decrease ventricular premature contractions (extra heart beats).

HCQ and chloroquine have cholesterol lowering properties and have been shown to decrease total serum (blood) cholesterol levels, LDL cholesterol levels (a very bad type of cholesterol) and triglyceride levels by up to 15 to 20%.

HCQ and chloroquine have blood glucose (sugar) lowering properties and thus help to prevent diabetes mellitus, particularly in lupus patients on prednisone. This effect can be so significant in some diabetic people that when starting a diabetic patient (who is receiving insulin or tablets

for treatment of diabetes), the HCQ has to be started carefully, at a low dose, with frequent monitoring of the blood glucose level, as there are reports of HCQ causing too much lowering of the blood glucose level (hypoglycemia). Of great benefit, HCQ and chloroquine do not cause the blood glucose level to drop in lupus patients who are not diabetic and have normal blood glucose levels (ie: these medications will not make a non-diabetic patient become hypoglycemic).

High blood pressure, higher cholesterol levels and precipitation of diabetes mellitus are all side effects of prednisone. Thus, not only is HCQ useful in lowering the prednisone dosage but it helps to protect against some of these prednisone side effects. It is felt that HCQ may help to prevent some acceleration of atherosclerosis (hardening of the arteries) that lupus patients are known to be at increased risk of developing.

Overall, Dr. Michelle Petri, of the famous Hopkins Lupus Cohort in Baltimore, Maryland, found that HCQ had “a favorable impact on the morbidity and mortality” in her lupus patients (ie: she found that her lupus patients who took HCQ had decreased damage to their bodies and a decreased death rate caused by lupus compared to her lupus patients who did not take HCQ). This is profound!

For a medication with so many diverse benefits in the treatment and protection of lupus patients, HCQ is one of the safest medications on the market! The safety of HCQ can be further assured when it is prescribed in the correct dosage of 5-6.5mg/kg lean body weight/day (I often find that patients have been prescribed too much HCQ for their body size, yet, even then, do not seem to have any side effects but I do recommend lowering the dose anyway). In terms of side effects, just like any medication, over the counter product, or naturopathic remedy, HCQ may cause allergic reactions, mainly skin rashes; and rarely, nausea, loss of appetite and weight loss (the latter of which most lupus patients are happy about rather than viewing weight loss as a side effect as we, physicians, do).

HCQ can rarely deposit in the retina (at the back of the eyeball), which can basically be made a “non-issue” if the patient is regularly reviewed by an ophthalmologist (eye specialist) every 12 to 18 months for colour vision and visual field testing. If any deposition of HCQ is noted in the retina of the eye, then, the HCQ is stopped and the deposits disappear. In approximately 5 to 10% of HCQ users, there will be some deposition of HCQ in the cornea (area covering the pupil and iris at the front part of the eye) but this usually causes no symptoms at all. If the ophthalmologist notices this deposition in the cornea, the patient is observed more closely and the HCQ dose might be reduced; it is rarely necessary to stop the HCQ for this side effect. Sometimes, when patients begin HCQ, transient visual blurring is noted; this usually always disappears and is not important. If the visual blurring persists (which is very rare), the patient should notify the rheumatologist or ophthalmologist for further assessment (the problem may or may not be due to the HCQ).

Some patients develop hyperpigmentation (darkening) of the skin, usually over the front part of the “shins” of the lower legs or loss of skin pigment (whitening). Gum pigmentation can also occur. These skin colouration changes are not at all serious and do not indicate “drug toxicity.” Most patients decide to continue HCQ. Occasionally, HCQ causes other types of annoying skin

changes such as dry or itchy skin or other skin rashes but rarely are these side effects bothersome enough that the patient decides to stop the HCQ.

The above discussed are the most common side effects of HCQ and ones which I inform patients about prior to commencing the medication. All of the discussed side effects are more common with chloroquine than with HCQ. There are a few very rare side effects. These side effects include: peripheral neuropathy (numbness and tingling in the hands and/or feet caused by some damage to the nerves which lupus patients suffer from much more commonly due to lupus itself than due to treatments); muscle weakness (extremely rare with HCQ and even rare with chloroquine and there are many other causes of muscle weakness in lupus patients that are more common than caused by the anti-malarials); and, extremely rarely (one case reported in a patient given massive doses of HCQ) is agranulocytosis (dangerously low white blood cell counts).

HCQ is a most helpful, yet safe, medication in the treatment of lupus. Its safety profile is well known because it is such an old medication, taken for decades by millions of people. Of all medications used to treat lupus, there is no other agent that has a lower risk versus benefit ratio. In one study, more than 90% of patients who were prescribed HCQ were still taking it one year later (for medication statistics, this is almost unbelievable; I have never heard of another regularly taken medication that has this amount of acceptance by the patients). HCQ is favored by patients and lupologists, both for its many beneficial effects (many of which the patients are not even aware of) and the lack of any side effects whatsoever in most patients.

Stephanie Ensworth, BSc(Pharm), MD, FRCP(C), FRCP(Rheum, Director, BC & Yukon Lupus Program, Mary Pack Arthritis Center Medical Advisor, BC Lupus Society. Clinical Assistant Professor, Division of Rheumatology, University of British Columbia.

This article was written for The Lupus Lighthouse, BC Lupus Society and is not to be reproduced or copied without permission of the author.