Lupus
America's Least Known Major Disease

ANTIMALARIALS IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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ANTIMALARIALS & LUPUS

Antimalarials were originally used for the treatment of a parasitic infection called malaria. The first antimalarial used in the treatment of lupus was quinine, more than 100 years ago. Currently there are three different antimalarials, all in pill form, that are used for the treatment of lupus in North America:

- Hydroxychloroquine (Plaquenil)
- Chloroquine (Aralen)
- Quinacrine (Atabrine)

Hydroxychloroquine is, by far, the most prescribed antimalarial in the United States. It is thought to be the one with the least side effects.

HOW DO ANTIMALARIALS WORK IN LUPUS

Lupus is a disease of the defense system of our body, which is called the immune system. This system is overactive in patients with lupus, leading to tissue and organ damage. Another characteristic of lupus patients is that cells of their immune system produce molecules directed against other constituents of the body. These molecules are called auto-antibodies. This change in the immune system can lead to inflammation.

Antimalarials decrease the inflammation by affecting cells of the immune system in multiple ways. There is some laboratory evidence that they may influence the production of the damaging auto-antibodies.

Many patients with lupus are very sensitive to sunlight, which can cause disease flares. Antimalarials have been found to enter cells in the skin and protect the body from the damaging effects of sunlight. This might be particularly important for lupus skin disease.

Antimalarials may have other beneficial effects, like lowering cholesterol (LDL-cholesterol) and making the blood slightly thinner by affecting certain blood cells, called platelets.

USING ANTIMALARIALS

Lupus can affect multiple organs, including the brain, kidney, joints, skin and blood cells. Antimalarials have been used in lupus patients to control skin rashes and joint symptoms. Although they are not very useful in treating more severe complications such as kidney disease, they have been shown to be effective in treating the following conditions:

- Arthritis and joint pain.
- Skin rashes, including the severe forms of discoid lupus and subacute cutaneous lupus. Half the patients will have improvement of their skin problems with the use of Hydroxychloroquine (Plaquenil). Chloroquine (Aralen) and Quinacrine (Atabrine) are probably stronger but may cause more side effects. Occasionally, doctors use combinations of these drugs to treat resistant skin rashes.
- Inflammation of the lining around the heart (pericarditis) and the lungs (pleuritis).
- Fatigue and fevers.
- Maintenance therapy. Long term use of Hydroxychloroquine (Plaquenil) has been shown to prevent lupus flares.

CAUTIONS

Lupus patients tend to be on multiple medications to control their disease. Antimalarials have been safely used in combination with other medications such as steroids, blood thinners, non-steroidal anti-inflammatory medications and even chemotherapy drugs like Cyclophosphamide (Cytoxan), Azathioprine (Imuran) and Methotrexate. Patients on multiple medications should be closely monitored by a physician.

Traditionally, antimalarials have not been used in pregnant women, because of potential side effects that may affect the baby. Data from Europe and Canada do not show increased side effects in pregnant women who take Hydroxychloroquine (Plaquenil). Still, the fear of some adverse effects make many patients and doctors reluctant to use them during pregnancy. The best approach is to weigh the risks of

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the medications with the risks of a lupus flare in an individual patient. These decisions should be made in discussion between the patient and the physician.

Side Effects

Generally, antimalarials have few side effects and most patients tolerate them well. They are often thought to be the safest medications used in the treatment of rheumatic diseases. The most common side effects are in the skin, the stomach, the bowels and the brain. Eye complications are feared the most but are very rare.

- Skin rashes (most of them allergic) and changes in skin color can occur. Quinacrine (Atabrine) can cause a yellow discoloration of the skin that is reversible. Hair loss and dry skin happen infrequently.
- Gastrointestinal side effects are common, but most of the time mild. Patients can experience loss of appetite, nausea, upset stomach, bloating, stomach cramps and diarrhea. These drugs, however, do not cause ulcers or bleeding from the stomach.
- Headaches, dizziness, nervousness, irritability, muscle aches and weakness can trouble some patients. Severe neurologic side effects, such as seizures and confusion, are rare. If they happen, they should be reported to the physician immediately.
- Rarely have these drugs, especially Chloroquine (Aralen), been implicated in nerve, muscle, and heart muscle toxicity.

Most of the above side effects are mild and can go away with a decrease in the dose of the medication. Local creams for the skin rashes and antihistamines for upset stomach can help.

Antimalarials & Vision

Eye complications are still the most feared toxicity. They are generally very rare, but an ophthalmologist should monitor every patient who is taking these medications on a regular basis (every 6 -12 months). Antimalarials can cause:

- Inability to focus. Generally, this side effect is experienced early, within the first two weeks after the medication has been started. It is caused by dysfunction of the muscles that move the eyes. Very rarely, patients might experience double vision due to nerve dysfunction. These symptoms can go away without changing the dose of the medication.
- Chloroquine (Aralen) rarely, and even less commonly, Hydroxychloroquine (Plaquenil), can deposit on the frontal part of the eye, the area called the cornea. These deposits do not affect the vision and they go away when the drug is stopped. Use of hydroxychloroquine in smaller doses does not cause these deposits.
- Antimalarials can deposit on the retina, at the back of the eye. These deposits can affect the vision. Fortunately, there is an early stage that can be detected by an ophthalmologist. At this point, stopping the medication results in no further problems for the patient. If not attended to, this problem can cause serious visual problems, such as blurred vision, difficulty reading, flashing lights and blind spots.

Chloroquine (Aralen) is probably the most toxic medication for the eyes. Quinacrine (Atabrine) does not seem to cause eye problems. The most commonly used Hydroxychloroquine (Plaquenil) rarely can cause this complication, especially at doses less than 6.5 mg/kg body weight. For most patients, that means that taking 400 mg a day or less of Hydroxychloroquine (Plaquenil) will rarely cause serious visual problems. Currently, we recommend that patients see an ophthalmologist once a year. The eye exam should include an examination of the retina in the back of the eye.

Dosage

Hydroxychloroquine (Plaquenil) is the antimalarial used in most cases. Initially, it is started at a loading dose of 400 mg/kg a day (given as two 200 mg pills a day). Patients are kept at this dose for at least 6 months to a year. Most patients will then continue at the same dose, although there are patients who can be maintained on one 200 mg pill a day. Occasionally, the dose can be increased temporarily, usually for 2-3 months. This strategy is used to prevent or treat flares, such as worsening rashes in the summertime. This medicine must be taken regularly as ordered by your doctor in order for it to help you. It may take up to several weeks before any results are noticed and up to six months before the full benefit of these medications are felt.

Conclusion

Antimalarials are very safe medications that can control the joint pains and skin rashes caused by lupus and can help keep the disease in remission. The only serious side effect that needs to be considered is the eye problems they can cause. Every lupus patient taking these medications should have an eye exam by an ophthalmologist at least once a year.