

Long-term Complications of Lupus-Controlling Drugs

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Systemic lupus erythematosus is an autoimmune disease that affects many organs of the body and leads to a variety of clinical manifestations. Advances in the treatment of lupus have led to a reduction in morbidity and mortality. The types of medications used to treat lupus are non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, antimalarials, and immunosuppressors. Although proven to be beneficial in lupus, these drugs do have long-term side effects that patients need to be aware of.

Many patients with lupus are prescribed NSAIDs to reduce pain and inflammation. Examples of NSAIDs include ibuprofen (*Motrin*), rofecoxib (*Vioxx*), and diclofenac (*Voltaren*). The most common type of complication from use of NSAIDs involves the gastrointestinal tract. Patients can get erosions of the stomach wall, stomach ulcers, or bleeding from the gastrointestinal tract. Risk factors for developing these complications are age greater than sixty-five years old, a past history of peptic ulcerations, and the use of NSAIDs along with corticosteroids or blood thinners. Patients who have these risk factors may receive another medication to help protect their stomach, such as omeprazole (*Prilosec*), or the physician may use an NSAID that is less likely to irritate the stomach such as rofecoxib (*Vioxx*) or celecoxib (*Celebrex*). NSAIDs can also cause damage to kidneys by altering blood flow to the kidneys and should not be given to any patient with any evidence of kidney disease. Other side effects, which are less common, include anemia, low platelet and white blood cell count, rashes, worsening asthma, and headaches. NSAIDs also have many interactions with other medications; therefore patients need to inform their physicians that they are taking an NSAID whenever they are prescribed a new drug.

Frequently, lupus patients are prescribed corticosteroids, which are taken to reduce inflammation. Prednisone is the most common corticosteroid used. Prednisone causes changes in fat distribution and often changes a patient's appearance because of fat collecting in the face, trunk, and upper back. Prednisone can also cause new-onset diabetes or worsen existing diabetes and can worsen hypertension. Prednisone at doses greater than 7.5 mg each day causes accelerated bone loss, which can lead to osteoporosis and fractures of the spine and hip. For this reason, patients who are treated for a long period of time with prednisone are often given a bisphosphonate such as alendronate (*Fosamax*) or risedronate (*Actonel*) to prevent osteoporosis. Prednisone also predisposes patients to infections, causes cataract formation, makes skin thinner and more disposed to bruises, and in predisposed patients may induce depression or psychosis. Using the lowest dose necessary to obtain the desired effect can minimize many of these side effects.

Hydroxychloroquine (*Plaquenil*) is an antimalarial that is frequently used in lupus to help control joint and skin involvement. Side effects, which are generally mild, include rash, nausea, and vomiting. The most dangerous complication of hydroxychloroquine is vision loss. This complication is rare with the doses and preparations that are currently being used. It is recommended that patients taking hydroxychloroquine get an eye examination before starting the medication and then every six to twelve months. Stopping the medication can reverse damage to the eye if it is identified early. Patients taking hydroxychloroquine should contact their physician if they have any visual symptoms such as decreased night vision or loss of central or peripheral vision.

Cyclophosphamide (*Cytoxan*) is an immunosuppressive medication given to patients who have major organ damage due to lupus. This includes patients with kidney disease, central nervous system disease, or inflammation of the blood vessels (known as vasculitis). It can be given orally or as an intravenous infusion. There is a risk of infertility in both men and women who are prescribed cyclophosphamide. Women are also at risk for premature menopause. These risks are higher with increasing duration of therapy, larger doses of medication used, and older age. Infertility and amenorrhea are usually permanent. Some studies have shown a beneficial effect of certain hormonal therapies in preserving fertility in women who are taking cyclophosphamide.

Urologic side effects of cyclophosphamide include bleeding from the bladder wall and bladder cancer. This complication is less frequent when the medication is administered monthly by intravenous route. There is also an increased incidence of cancer after cyclophosphamide use, which may appear many years after the drug has been used. Cyclophosphamide also causes a decrease in the white blood cell count, which can predispose patients to infection. Many patients get nausea and vomiting with cyclophosphamide infusions but are usually given medication to help prevent this.

Other immunosuppressive drugs used in lupus include azathioprine (*Imuran*), methotrexate, and mycophenolate mofetil (*CellCept*). These medications have fewer side effects than cyclophosphamide but still require frequent monitoring for liver and hematologic toxicity.

The medications used to treat lupus are very beneficial to patients. However, they do have side effects that patients need to be aware of. Patients need to discuss these side effects with their physicians and let their physician know if anything about their health status changes. Many of the side effects can be prevented or treated with other medications and good patient-physician communication.

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