

# Antimalarial Drug for RA Also Cuts Diabetes Risk

*Hydroxychloroquine use may improve insulin secretion and sensitivity in the general population.*

BY MARY ANN MOON  
Contributing Writer

Patients who take hydroxychloroquine for their rheumatoid arthritis symptoms also show a dose-dependent reduction in their risk for developing diabetes, results of a large study suggest.

Diabetes risk decreased by as much as 77% in patients who took the antimalarial drug hydroxychloroquine for more than 4 years, “a finding that is comparable or superior to that of other drugs studied in clinical trials: rosiglitazone, combination hormone therapy, estrogen [only], metformin, acarbose, and ramipril,” the study researchers reported.

This is the first evidence that has ever been reported suggesting that hydroxy-

chloroquine reduces the risk of diabetes in RA patients, wrote Dr. Mary Chester M. Wasko, of the University of Pittsburgh, and her associates.

Antimalarials are known to cause hypoglycemia and are thought to improve insulin secretion and peripheral insulin sensitivity. They “have been explored as an adjunct to insulin and oral hypoglycemic agents for poorly controlled type 2 diabetes,” Dr. Wasko and her associates said.

The investigators studied the possible link between use of hydroxychloroquine and diabetes risk in an established RA cohort with more than 20 years of follow-up.

The 4,905 subjects in this longitudinal observational study were treated at seven RA practice sites across North America from 1976 through 2004. A total of 1,808

reported use of hydroxychloroquine at some time during the study, most of them for an average of 3 years.

Diabetes developed in 70% of the subjects who had never taken the antimalarial drug, compared with only 48% of those who had ever taken it.

Diabetes incidence rates were 8.9 per 1,000 patient-years of observation among those who had never before taken hydroxychloroquine, compared with 5.2 per 1,000 patient-years for those who had taken the drug.

In addition, “the relative risk of developing diabetes progressively declined with increasing time taking hydroxychloroquine,” the investigators said (JAMA 2007;298:187-93).

Patients who did develop diabetes after taking the antimalarial were less likely than were those who hadn’t taken it to need oral hypoglycemic medication.

“Hydroxychloroquine use may modify the clinical manifestations of hyperglycemia, or it may attenuate hyper-

glycemia and reduce the need for medications once this diagnosis is established,” Dr. Wasko and her associates commented.

Although antimalarials do not address RA signs and symptoms as well as other current treatment options, their toxicity profile is better, so they are used for mild to moderate disease and in combination therapy.

Unlike the traditional RA medications, antimalarials are well tolerated, do not require routine laboratory monitoring for toxicity, confer no increased risk of infection or malignancy, and carry “minimal” risk for adversely affecting internal organs when dosing is tailored to body weight, the researchers said.

Even though this study involved only RA patients, the results also may apply to people who do not have RA, because hydroxychloroquine may prove beneficial in preventing diabetes in high-risk members of the general population, the researchers added. ■

**Diabetes developed in 70% of the subjects who had never before taken the antimalarial drug, compared with 48% of subjects who had taken it.**

## Alternative Interventions Promoted for Osteoarthritis

BY DAMIAN McNAMARA  
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BIRMINGHAM, ENGLAND — Structural modification that could be achieved through mechanical, behavioral, and nutritional therapies may be a worthwhile goal in osteoarthritis treatment and a way to focus on therapy that involves more than just symptom relief, according to a presentation at the annual meeting of the British Society for Rheumatology.

A multitude of nonpharmacologic options for osteoarthritis can be pursued prior to drug treatment, Dr. Paul Dieppe said. For example, small studies support the theory that mechanically shifting the load off an affected lower-extremity joint modifies structure and alleviates symptoms of osteoarthritis.

Osteotomy, shoe wedging, and knee braces, as well as weight loss in the obese, are other options.

“If we kept thin, ate sensibly, maintained good muscle strength, avoided injuring our joints, and wore sensible shoes . . . there might not be as much osteoarthritis,” said Dr. Dieppe, professor of rheumatology and dean of the faculty of medicine, University of Bristol (England).

Dr. Dieppe says he is unhappy with the fact that people borrow the term “disease-modifying treatment” from the rheumatoid arthritis field and apply it to osteoarthritis.

“We go on pretending that osteoarthritis is related to rheumatoid arthritis, and just a bit different. What might disease-modifying treatment mean in osteoarthritis? We are talking about structure modification,” he said. ■

Structural changes can be achieved with Ilizarov frames—more commonly used by orthopedists to correct limb length discrepancies. The frames pull and increase the space between joints.

“Strangely, most of the data [so far have come] from the ankle joint,” Dr. Dieppe said. “The trials are small in numbers, but suggest very positive outcomes with recovery of the joint space in many cases, as well as symptom relief.”

Success with these frames provides proof of the concept that if the joint is unloaded, there is structure and symptom modification.

**Structural changes can be achieved with Ilizarov frames, which are more commonly used by orthopedists to correct limb length discrepancies.**

“It looks gruesome, but clearly, it can work,” Dr. Dieppe said.

Investigators should assess crepe shoes, shoe wedging, and other less invasive interventions, he added.

Osteoarthritis of the knee begins when a kinematic change occurs and shifts the load of the joint to a region unaccustomed to the new loading, according to a review article (Curr. Opin. Rheumatol. 2006;18:514-8). The authors state that the progression of osteoarthritis thereby is associated with the degree of this increased load during ambulation.

In terms of nutritional modification, trials are underway to assess any roles for vitamin C or vitamin D to slow the pathogenesis or progression of osteoarthritis, Dr. Dieppe said. Altering the course of osteoarthritis with certain dietary supplements does not work, he said, adding, “That chondroitin or glucosamine causes structural changes is a silly idea.”

“The relationship between symptom change and structural change requires further study,” he concluded. ■

**Connect them to a therapy designed to enhance not interfere with their bisphosphonate.**