Antimalarials May Lower Risk for Cancer in Lupus

Diana Mahoney

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timalarials may confer some protection against cancer in lupus patients, according to the results of a prospective cohort study that linked treatment with antimalarials to improved cancer-free survival.

In a study of 215 patients with systemic lupus erythematosus (SLE) from an ongoing, prospective observational study, those who had been treated with antimalarials were significantly less likely to develop cancer over a median 10-year follow-up than those who had never been treated with the drugs, according to Dr. Guillermo Ruiz-Irastorza of the Hospital de Cruces in Barakaldo, Spain, and colleagues.

Previous studies have suggested that individuals with SLE are at increased risk for developing certain types of malignancies, although the causes for this increased susceptibility remain unknown. The possibility that antimalarial agents may have an anticarcinogenic effect might impact treatment decisions in this patient population, the authors wrote (Arthritis Rheum. 2007 Jan 4 [Epub doi:10.1002/art.206777]).

Antimalarials such as hydroxychloroquine (Plaquenil), chloroquine, and quinacrine are frequently used to treat the skin and systemic symptoms of mild to moderate lupus. Recent studies have demonstrated important long-term effects of the drugs in lupus patients, including a reduction in the accrual of disease-related damage and a reduction in long-term mortality, the authors wrote.

Antimalarials have also demonstrated potential antineoplastic properties in investigations looking at their use as adjuvant cancer therapy agents. Based on these collective findings, Dr. Ruiz-Irastorza and colleagues sought to determine the impact of antimalarials on cancer risk in lupus. Of the 235 patients included in the investigation, 156 had ever received antimalarial treatment and 79 had not. Only 2 of the patients in the antimalarial-treated group had developed a radiologically or histologically confirmed neoplasm during the study follow-up, compared with 11 of the 79 patients who had never been treated, the authors reported.

All of the patients in the study fulfilled the updated American College of Rheumatology criteria for the classification of SLE and were included in the cohort at the time of lupus diagnosis. Pediatric lupus patients (younger than 14 years) enrolled in the larger observational study were excluded from the current investigation.

As a per-study protocol, most of the patients in the cohort underwent clinical and immunologic assessment every 3 months. Patients with long-standing inactive disease required fewer visits, while those with active disease required more frequent visits.

The study criteria for antimalarial exposure included treatment with the drugs for any period of 6 months or longer. The median time on antimalarial drugs was 56 months.

To compare the frequencies of cancer in the patients ever treated with antimalarials and those who were never treated with the drugs, the investigators used a chi-square test and created Kaplan-Meier free-of-cancer survival curves. They also calculated proportional hazards model to adjust for variables that could potentially influence the development of neoplasms: age at diagnosis; year of diagnosis; gender; treatment with azathioprine, cyclophosphamide, and methotrexate; smoking history; and SDI at 6 months after lupus diagnosis. "Treatment variables were only counted if patients received the [antimalarial] drug pre- or to the time of diagnosis of cancer," the authors wrote.

The COX model showed that, compared with placebo, the patients who received antimalarials, the patients who received them were younger, more likely to have received methotrexate, and less likely to have severe organ damage at 6 months. In addition, patients diagnosed with lupus between 1996 and 2003 were more likely to receive antimalarials than those diagnosed prior to 1996.

With a total observation time of 2,620 patient-years, the incidence of cancer in the full cohort was 4.9/1,000 patient-years, according to the authors. The specific cumulative cancer-free survival rates for patients ever treated with antimalarials compared with the never-treated group was 0.98 vs. 0.73, respectively.

"The adjusted [hazards] rate of patients treated with antimalarials was 0.15," the authors wrote. The only additional variables that showed independent associations with cancer were age at diagnosis and male gender, Dr. Ruiz-Irastorza and colleagues reported.

The limitations of the current investigation included the fact that patients in the cohort who were ever treated with antimalarials were younger and had less severe organ damage at the time of diagnosis, although severity of damage was not associated with cancer in the analysis, the authors stressed. In addition, some patients in the antimalarial group spent some time at risk for malignancy before receiving the drug, although a "survival observation with a lower frequency of cancer is unlikely to be explained by this fact," they wrote.

Larger, more ethnically diverse cohorts (99% of the current cohort was white) are needed to confirm the benefit of antimalarials. The antimalarials exert some favorable action on malignancy before receiving the drugs, according to the authors. Such research could help "further define the potential role of antimalarials in cancer prevention," they concluded.