

Disease-Modifying Antirheumatic Drugs and Risk of Parkinson Disease

Nested Case-Control Study of People With Rheumatoid Arthritis

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Study Question

Is the use of disease-modifying antirheumatic drugs (DMARDs) associated with the risk of Parkinson disease (PD) in persons with rheumatoid arthritis?

What Is Known and What This Paper Adds

Previous studies have suggested that rheumatoid arthritis could be linked to risk of PD, but the direction of this association is controversial. The medications used to treat rheumatoid arthritis, especially DMARDs, could be the cause of the protective association, but there are few pharmacoepidemiologic studies on this topic. This study provides Class II evidence that in individuals with rheumatoid arthritis using DMARDs, only chloroquine/hydroxychloroquine was associated with a potentially decreased risk of developing PD (adjusted odds ratio [OR] 0.74, 95% confidence interval [CI] 0.56–0.97).

Methods

This case-control study was nested in the nationwide register-based Finnish Parkinson's Disease (FINPARK) study, which includes 22,189 community-dwelling Finns with clinically verified PD diagnosed during 1996 to 2015. This study included 315 PD cases with PD diagnosis from 1999 on and rheumatoid arthritis diagnosed >3 before PD diagnosis. Each PD case was matched with up to 7 controls (n = 1,571) by age, sex, duration of rheumatoid arthritis, and region. Exposure to different DMARDs was extracted from the Prescription Register since 1995, and only exposure that had occurred at least 3 years before the matching date was considered in the main analyses. DMARDs were categorized into sulfasalazine, methotrexate, chloroquine/hydroxychloroquine, immunosuppressants, and gold preparations. The associations between DMARD use (compared with nonuse) and PD were studied with conditional logistic regression adjusted for confounders.

Results and Study Limitations

The 3 most commonly used DMARDs in both cases and controls were sulfasalazine, methotrexate, and chloroquine/

Table Association Between DMARDs and PD

DMARD	Adjusted ^a odds ratio (95% confidence interval)
Sulfasalazine	1.01 (0.78–1.32)
Methotrexate	1.17 (0.90–1.52)
Chloroquine/hydroxychloroquine	0.74 (0.56–0.97)
Gold preparations	1.11 (0.83–1.47)
Immunosuppressants	1.06 (0.75–1.51)

Abbreviations: DMARD = disease-modifying antirheumatic drug; PD = Parkinson disease.

Drug use occurred before 3-year lag.

^a Asthma or chronic obstructive pulmonary disease, cancer history, cardiovascular diseases, diabetes, head injury, stroke, substance abuse.

hydroxychloroquine. Chloroquine/hydroxychloroquine use was associated with decreased risk of PD (adjusted OR 0.74, 95% CI 0.56–0.97, prevalence of exposure in PD cases and controls 37.5% and 44.8%, respectively). Other DMARD categories were not associated with risk of PD. On the basis of these results, DMARDs in general did not seem to modify the risk of PD among persons with rheumatoid arthritis. The mechanisms for the protective association of chloroquine/hydroxychloroquine with PD should be further investigated. Limitations of the study include lack of information on severity of rheumatoid arthritis and the relatively small sample size. On the other hand, restriction to people with rheumatoid arthritis decreased the risk of bias.

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