

Disease-Modifying Anti-Rheumatic Drug (DMARD) Exposures and Serious Infections in Older Ontarians with Rheumatoid Arthritis (RA): A Nested Case-Control Study

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Objective: To assess the association between exposure to DMARDs and risk of a serious infection in patients with RA.

Methods: Our cohort was assembled using physician billing, pharmacy, and hospitalization data for Ontarians aged ≥ 65 years. Our primary outcome, assessed over 1998-2007, was an infection requiring hospitalization. Cases were matched to controls, and based on the date of hospitalization (index date); current drug exposures were defined using prescription duration, plus a 50% grace period. Past exposures (within the preceding year) were similarly defined. Multivariate logistic regression analyses assessed independent exposure effects, adjusting for demographics, co-morbidity, and markers of RA severity/activity.

Results: Comparing the drug exposures of cases (N=4,376) and controls (N=9,783), the crude odds ratios (OR) for infection with current and past anti-TNF biologics exposure were 3.4 (95% confidence interval: 1.7-6.8) and 6.0 (2.5-14.8), respectively. The respective adjusted ORs were 3.2 (0.4-26.8) and 2.8 (0.2-43.8). For methotrexate, the crude ORs for current and past exposure were 1.3 (1.2-1.5) and 1.5 (1.3-1.8), respectively. The respective adjusted ORs were 1.0 (0.8-1.3) and 1.0 (0.7-1.4). For cyclophosphamide, the crude ORs for current and past exposure were 3.2 (1.1-9.5) and 7.8 (2.1-28.6), respectively. The respective ORs were 1.2 (0.1-10.4) and 1.7 (0.2-13.3). The most precise effect estimate was for current systemic corticosteroids: OR 1.5 (1.2-1.8).

Conclusions: Corticosteroids are an important independent risk factor for serious infection in patients with RA. Crude ORs suggested increased infection risk with other agents; but adjusted estimates were imprecise, possibly related to infrequent exposure to these drugs.

N=250