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Medication Exposures and Serious Infections in a Populationbased Cohort of Older Individuals with Rheumatoid Arthritis (RA)

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Purpose: To assess drug exposures and risk of hospitalization for infections, using a case-control sample nested within an RA cohort.

Methods: Cohort was assembled using Ontario billing and hospitalization data (1992-2007) for persons aged>65.Cohort entry criteria were an RA diagnosis based on ≥2 billing diagnoses,≥60 days apart but within 5 years. Cohort members were further required to have ≥1 prescription for a glucocorticoid, DMARD, or biologic. Our primary outcome, assessed over 1998-2007, was a 1sttime infection, based on 'most responsible' hospital discharge diagnoses. Cases were matched(age,sex, year of cohort entry) to RA controls using risk-set sampling. Based on index date (date of infection for each case-control set), current drug exposures were defined using estimated duration of each prescription, plus a 50% grace period.Past exposures(in the 365 days prior to index date), were similarly defined. Multivariate logistic regression assessed independent effects of exposures, adjusting for demographics (age, sex, income, rurality index), comorbidity, and markers of RA severity/activity (rheumatology visits, history of joint replacement, extraarticular features, and NSAIDs).

Results:Cohort members experienced 4376 first-time infections requiring hospitalization. Comparing drug exposures of the cases to controls (N=9783), the crude odds ratio, OR (for all infections requiring hospitalizations) with current anti-TNF exposure was 3.4 (95% CI1.7,6.8) and for past exposure, 6.0 (2.5,14.8). Respective adjusted ORs were 3.2 (0.4,26.8) and 2.8(0.2,43.8). For methotrexate, the crude OR for current exposure was 1.3(1.2,1.5) and for past exposure 1.5(1.3,1.8). Respective adjusted ORs were 1.0(0.8,1.3) and 1.0(0.7,1.4). For cyclophosphamide, crude OR for current exposure was 3.2(1.1,9.5) and for past exposure, 7.8(2.1,28.6). Respective adjusted ORs were 1.2(0.1,10.4) and 1.7(0.2,13.3).The most precise estimate of an independent effect was for current systemic corticosteroid exposure(adjusted OR 1.5, 1.2,1.8).

Conclusions:Our results emphasize corticosteroids as an important independent risk factor for serious infection in RA. Crude ORs suggested increased risk of infection with several other agents;however our adjusted estimates were imprecise, likely related to relatively infrequent exposure to specific agen