343

Effect of Hydroxychloroquine on Influenza Prevention

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Abstract. The aim of this study was to assess whether long-term administration of hydroxychloroquine (HCQ) is protective from influenza in patients with rheumatoid arthritis and systemic lupus erythematosus. Using a propensity score-matched design, patients who were prescribed HCQ for more than 10 months were matched with patients of the same gender, age group, and Charlson Comorbidity Index score who did not receive HCQ. A logistic regression model was used to estimate the association between the HCQ exposure and influenza after adjusting for covariates. We found no evidence that long-term HCQ exposure can provide a protective effect against influenza during an influenza season.

Keywords. Hydroxychloroquine, influenza, MarketScan, case-control design

1. Introduction

Even though many studies have identified that hydroxychloroquine (HCQ) has effective antiviral properties in-vitro or in animal models [1], there are no systematic studies to assess its effect on influenza viral infection. Therefore, the aim of this study was to assess whether the administration of HCQ is protective from influenza.

2. Method

In this retrospective observational study, records between Jan 1, 2017, and Feb 28, 2019, were extracted from the IBM MaketScan Database. Adult patients with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) who did not receive flu shots were included in the study. HCQ exposure group comprised patients who have received the HCQ prescription for at least 10 months per year. Patients without any HCQ prescriptions comprised the non-HCQ exposure group. The outcome was defined as patients' in-hospital or outpatient diagnosis of influenza or influenza-related conditions during the 2018-2019 influenza season. The independent variables included age, gender, and Charlson comorbidity index (CCI) score, which were all collected based on patients' initial medical records.

The propensity-score matching with the nonparametric nearest neighbor method [2] was used to generate the matched groups at a ratio of 1:1. A logistic regression model was used to estimate odds ratios (ORs) for the association between long-term HCQ use

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and influenza incidence. All probabilities were 2-sided, and a p-value of < 0.05 was considered as statistically significant.

3. Results

A total of 6,339 RA or SLE adult patients with long-term administration of HCQ and 6,339 propensity-score matched individuals were analyzed in the study. The incidence of influenza during the 2018-2019 influenza season was similar between both cohort groups (HCQ:50.8% vs. Non-HCQ:49.2%). However, there were significant differences in influenza incidence rates by age, gender, and CCI score. In the logistic regression analysis, the probability of people having influenza among patients with long-term HCQ was similar to the non-HCQ groups (HCQ vs. non-HCQ, OR=1.04, 95% CI: [0.80-1.35]; P=0.79). Males were 36% less likely to have influenza than female (male vs. female, OR=0.64, 95%CI: [0.41-1.00]; p=0.05). We found that HCQ does not provide a significant protective effect against influenza for RA or SLE patients despite long-term HCQ administration (>10 months/year).

4. Discussion

Our study has several limitations. We only included outpatient or in-hospital influenza diagnoses in the MarketScan Database, thus possible influenza-related records could have been missed. Besides, asymptomatic cases were considered free of influenza and may not have been documented in a medical record. Previous studies demonstrated that HCQ as a long-term prophylactic therapy may increase the risk of side effects [3]. Advanced machine learning approaches may be more instrumental for identifying latent disease clusters in large patient cohorts [4].

5. Conclusions

Based on our study results, the long-term administration of HCQ as a prophylactic drug against influenza is not warranted.

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