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Gabapentinoids and Risk for Severe Exacerbation in Chronic Obstructive Pulmonary Disease

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Gabapentinoids, namely gabapentin and pregabalin, are anticonvulsant drugs used to treat epilepsy and neuropathic pain. Although the approved indications for gabapentinoids are limited and vary worldwide, prescriptions have surged across North America and Europe as physicians are reportedly using them as safer alternatives to opioids.

The prescription uptick is of concern because gabapentinoids are not effective in many off-label indications yet they expose patients to potentially serious adverse effects. North American and European health agencies recently warned of severe breathing problems associated with gabapentinoids, particularly for patients with respiratory risk factors, including COPD. Yet, despite the risks and warnings, no population-based studies have been done among patients with COPD on the potential respiratory adverse effects of gabapentinoids.

In this study, we assessed whether gabapentinoid use was associated with severe exacerbation (hospitalization) among patients with COPD with an approved or off-label indication for gabapentinoids (epilepsy, neuropathic pain, or other chronic pain) using a time-conditional propensity score (TCPS)–matched, new-user design.

We used patient data from the three computerized health care databases of Quebec, which included information on medical services and prescription medications for all residents covered by the Public Prescription Drug Insurance Plan. Within a base cohort of patients with COPD between 1994 and 2015, patients initiating gabapentinoid therapy with an indication (epilepsy, neuropathic pain, or other chronic pain) were matched 1:1 with nonusers on COPD duration, indication for gabapentinoids, age, sex, calendar year, and TCPS.

The results showed that gabapentinoid use is associated with increased risk of severe COPD exacerbation both overall (HR, 1.39; 95% CI, 1.29-1.50) and across the 3 indications of epilepsy (HR, 1.58; 95% CI, 1.08-2.30), neuropathic pain (HR, 1.35; 95% CI, 1.24-1.48), and other chronic pain (HR, 1.49; 95% CI, 1.27-1.73). The peak increase in severe exacerbation risk occurred approximately 6 months after continuous gabapentinoid use.

Our study has limitations, one being that we identified patients with COPD using relevant medications instead of International Classification of Diseases (ICD) codes. Therefore, we may have misclassified patients with asthma as patients with COPD since they could be prescribed the same medications. However, patients with asthma were likely excluded during cohort selection with those previously hospitalized for asthma or taking medications for asthma. Also, residual confounding must be considered, including the lack of smoking history.

In conclusion, in patients with COPD, gabapentinoid use was associated with increased risk for severe exacerbation. Our study supports the warnings from regulatory agencies and highlights the importance of considering this potential risk when prescribing gabapentin and pregabalin to patients with COPD.

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