The use of benzodiazepine receptor agonists and the risk of pneumonia: a nationwide population-based, nested case-control study

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Objective: The relationship between the use of benzodiazepine receptor agonists (BZRAs) and the risk of pneumonia remains inconclusive. This study aimed to explore the association between the use of BZRAs and pneumonia occurrence in a general population. The comparative risk of pneumonia across different BZRAs was also investigated.

Methods: This population-based, nested case-control study used Taiwan's National Health Insurance Research Database between 2002 and 2012. We only included new users who did not have any BZRAs prescription record in the preceding two years and identified 12,002 patients with hospitalization for pneumonia (ICD-9 codes: 480-486) and 12,002 disease risk score matched controls. A logistic regression model was used to determine the odds ratio of BZRAs use. The exposure date, dose-response relationship, and classes of BZRAs were also comprehensively assessed.

Results: Current BZRAs exposure was associated with pneumonia occurrence (adjusted OR [aOR]:1.88; 95% CI: 1.78-1.99).Benzodiazepine hypnotics (aOR: 2.49; 95% CI: 2.23-2.79) had higher risk of pneumonia than benzodiazepine anxiolytics (aOR: 1.54; 95% CI: 1.45-1.63) and non-benzodiazepine hypnotics (aOR: 1.63; 95% CI: 1.48-1.79). The pneumonia risk was increased with short-acting agents, higher defined daily dose, and number of anxiolytics/hypnotics used. Among individual BZRAs examined, midazolam had a higher risk (aOR: 5.77; 95% CI: 4.31-7.73) of pneumonia occurrence than others.

Conclusion: This study suggests that current BZRAs use may increase the risk of pneumonia. In addition, oral form midazolam had a higher risk of pneumonia occurrence. These findings have implications for clinical practice and further studies are required to evaluate the safety of BZRAs in the context of respiratory infection.

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