中文題目：Tramadol 增加類風溼性關節炎病患死亡率與嚴重心臟不良事件的風險—以全國人口為對象的世代研究

英文題目：Tramadol Use Increases Mortality and Risk of Major Adverse Cardiovascular Events in Rheumatoid Arthritis Patients—a Population-Based Cohort Study

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Background: As a weak opioid agonist, tramadol has been commonly utilized in pain management, especially in patients with chronic pain conditions. Clinically, previous study indicated that opioid use was of high rate in patients with rheumatoid arthritis, and tramadol was one of the most utilized opioid agonists (71.1%).[1] An English cohort reported higher mortality in tramadol users with osteoarthritis. However, risk of cardiovascular death in tramadol user was not statistically significant.[2] Though the adverse effect in cardiovascular system has been discussed in previous literatures, evidences related to the risk of major adverse cardiovascular events (MACE) in tramadol users with rheumatoid arthritis is currently lacking.

Materials and Methods: We designed a population-based retrospective cohort study to evaluate the influence of tramadol to subsequent MACE risk and mortality in RA patients. In this study, we utilized datasets from the Longitudinal Health Insurance Database (LHID), a subset of National Health Insurance Research Database (NHIRD) in Taiwan. LHID included one million randomly chosen beneficiaries and provided information regarding outpatient visits, hospitalizations, and medications.

Patients diagnosed with RA (ICD-9-CM: 714) from 2000 to 2012 were included. Index date was set as the first prescription of tramadol. We excluded patients with previous MACE (including ischemic heart disease, congestive heart failure, acute ischemic stroke and intracranial hemorrhage), major depression, cancer and those with previous related drug use (tramadol, Panadol and NSAIDs) before index date. Ultimately, 440 tramadol users with RA were included as study group, serving as the tramadol-using cohort. After 1:2 matching of age, sex and year of RA diagnosis, 880 matched tramadol non-users with RA were matched and served as the comparison cohort. Utilizing Cox proportional regression model, we evaluated the adjust hazard ratio (aHR) of developing future MACE in the tramadol user group, comparing with non-users. Kaplan–Meier methods and log-rank test was also performed to

compare the difference in the cumulative incidence between the two cohorts. Each cohort was tracked 144 months with Kaplan-Meier curves.

Results: The result of this study suggested that comparing with non-tramadol users, RA patients using tramadol was of higher risk developing subsequent MACE and the overall mortality was significantly higher. The incidence rate of death events in the tramadol cohort was 16.06 per 10,000 person-months, whereas in the non-tramadol cohort, the incidence rate was 5.50 per 10,000 person-months. The aHR of death event for tramadol-using RA patients was 3.936-fold higher than non-users (95% C.I., 1.864 to 8.314). After the adjustment of potential confounders such as age and sex, the adjust hazard ratio of tramadol user group developing MACE was 1.715 (95% C.I., 1.082 to 2.718), indicating a significantly higher risk. The incidence rate of MACE for non-tramadol cohort and tramadol cohort were 19.26 and 30.12 per 10,000 person-months, respectively.

Conclusion: As a conclusion, we report that tramadol usage could increase a 70%-higher risk of developing MACE and have a 3.936-fold mortality in RA patients. Clinicians should be aware of the association in management of RA patients.

References

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