B-PO02-018 - Use Of Nicorandil Is Associated With Increased Risk Of Incident Atrial Fibrillation- A Population-based Nested Case-control Study And Molecular Studies To Explain The Association

View session detail

Author Block: Pang-Shuo Huang, MD; Chien-Chang Lee; Chia-Ying Chan; Kyle Rumery; Ke-Ying Su; Tze-Chun Hsu; Chia-Ti Tsai
Disclosure Block: P. Huang: Nothing relevant to disclose.

Background: Nicorandil is a potent vasodilator of coronary vessels through its effect on opening of ATP-sensitive potassium channel (KATP), and has been used as an antianginal agent. Activation of potassium channels play an important role in the mechanism of atrial fibrillation (AF) or atrial flutter (AFL). Accordingly, whether use of nicorandil might contribute to initiation and/or perpetuation of AF/AFL remained unknown.

Objective: To determine the relationship between use of nicorandil and risk of atrial fibrillation.

Methods: We performed a nested case-control study using a cohort of 1 million people assembled from the National Health Insurance Research Database (NHIRD) of Taiwan. The association between nicorandil use and risk of atrial fibrillation was estimated by logistic regression model. We also performed molecular and cellular studies to explain the association.

Results: A total of 715 individuals who experienced atrial fibrillation or atrial flutter were matched to 72,215 controls. To account for the potential unmeasured confounders, we identified nitrate users in the same cohort as an active comparator. After adjustment, new use of nicorandil was found to be associated with increased risk for atrial fibrillation or atrial flutter (odds ratio [OR], 2.34; 95% CI 1.07-5.13) compared to nitrate use. Activation of potassium channel shortens atrial action potential duration (APD), which subsequently perpetuates AF. Dysfunction of mutated sarcKATP channels in atrial cells may lead to electrical instability and atrial fibrillation. We found expression of KATP in human atrial tissues. Furthermore, nicorandil directly shortened APD and the QT interval of cultured induced pluripotent stem cell (iPSC) derived cardiomyocytes (iPSC-CMs).

Conclusion: Use of nicorandil, especially new use, was found to be associated with increased risk of AF or AFL. We also first showed the expression of KATP in human atria and use of nicorandil may promote or increase the risk of AF through activation of KATP and shortening of atrial APD.