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• 計畫英文名稱	Effect of 3-Hydroxy-3-Methyl-Glutaryl-Coenzyme a (HMG-CoA) Reductase Inhibitor, Statins on the Electrophysiological Characteristics and Arrhythmogneic Activity of Pulmonary Vein and Atrial Cardiomyocytes
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• 中文摘要	心房顫動乃是臨床上常見之心律不整，且會造成心臟功能不良以及腦中風，雖然許多抗心律不整藥物已經被用於治療與預防心房顫動，然大多具有相當之副作用而無法長期使用。最近研究顯示 HMG-GA 還原酵素阻礙素 statins，乃是廣泛用於治療高血脂症之藥物，被發現可減少心房顫動之產生，然而其電生理機轉以及預防心房顫動的原因仍不清楚，再則，是否不同的 statins 會有不同的效果也未明瞭。肺靜脈已知是引發心房顫動之病灶所在，過去的研究已知肺靜脈含心肌細胞且有其特有之電生理特性可引發心律不整活性，長時間心房電刺激，以及使用發炎物質都會增加肺靜脈心肌細胞引發心律不整活性，反之，一氧化氮則被發現可用抑制肺靜脈心肌心律不整之作用，由於 statins 已知會增加一氧化氮之生理活性以及明顯之抗發炎作用，這些結果顯示，statins 或可藉者抑制肺靜脈心肌之心律不整活性而達到其抑制心房顫動的效果，因此本研究旨在探討 statins 對肺靜脈之心律不整活性之作用。方法：傳統電極記錄記錄肺靜脈之動作電位，以及收縮力在接受 Simastatin 0.1、1μM 後之變化，以及在 1μM 之 Simastatin 下，使用 L-NAME100μM 後的變化。結果：Simastatin 在 1μM 的濃度下可以於 1 小時後抑制肺靜脈心肌細胞之自動性從 1.7±0.1Hz 到 1.5±0.1Hz，並在 2 小時後到達平穩的抑制狀態約 1.4±0.1Hz。這個動作可以被 100μM 的 L-NAME 所抑制而回復肺靜脈之節律。再則 1μM Simastatin 可以稍微延長肺靜脈心肌之動作電位從 88±7ms 到 93±7ms。結論：本實驗顯示 Simastatin 可以抑制肺靜脈引發心律不整活性，且此機轉與一氧化碳之產生有關。這些結果可能是造成 Statin 減少心房顫動的機轉。

- 英文摘要

Atrial fibrillation is the most common cardiac arrhythmia seen in clinical practice and induce cardiac dysfunction and stroke. Although several antiarrhythmic drugs have been used in treating and preventing atrial fibrillation, drugs with little adverse effects effectively to prevent atrial fibrillation. Recent studies have shown that use of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitor, statins reduce the occurrences of atrial fibrillation clinically. However, knowledge about the electrophysiological effects of statins on cardiomyocytes and the mechanisms of anti- fibrillation were limited and it is not clear whether different statins may have different cardiac effects. Pulmonary veins (PVs) were known to be important sources of ectopic beats with the initiation of paroxysmal atrial fibrillation. Our previous have found that PVs have cardiomyocytes with distinct electrophysiological characteristics and arrhythmogenic activities. Long-term rapid atrial pacing and inflammatory cytokine increased PV arrhythmogneic activity. In contrast, nitric oxide was found to decrease PV arrhythmogenic activity with the reduction of atrial fibrillation. Because statins increases nitric oxide bioavailability and has anti-infllammation effects, it is possible that the statins may inhibit atrial fibrillation through the decrease of PV arrhythmogenic activity. Therefore, the purposes of the present study are to investigate the effects of statins on the arrhythmogenic activity of PV cardiomyocytes. Methods: Conventional microelectrodes were used to record the action potential (AP) and contractility in isolated rabbit PV tissue specimens before and after the administration of simvastatin (0.1, 1 .mu.M). L-NAME (100 .mu.M)was administrated in the presence of simvastatin (1 .mu.M). Results: Simvastatin (1 .mu.M, but not 0.1 .mu.M) decrease the PV firing rates from 1.7+-0.1 to 1.5+-0.1 Hz at one hour and achieve steady state firing rates of 1.4+-0.1 Hz at 2 hour. This effect is reversed after the administration of L-NAME (100 .mu.M, inhibitor of nitric oxide production). Moreover, simvastatin (1 .mu.M) mildly prolonged the action potential duration from 88+-7 ms to 93+-7 ms (n=5). Conclusion We demonstrated the simvastatin may decrease the PV arrhythmogenesis through the production of nitric oxide. These results may underlie the anti-arrhythmic potential of statin and result in the decrease of atrial fibrillation.