中文題目: Sitagliptin 在心肌梗塞老鼠身上藉由調節活性氧分子及間質腺苷酸來減弱心臟交感神經活性

英文題目: Sitagliptin attenuates sympathetic innervation via modulating reactive oxygen species and interstitial adenosine in infarcted rat hearts

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前言: We investigated whether sitagliptin, a Dipeptidyl peptidase-4 (DPP-4) inhibitor, attenuates arrhythmias through inhibiting nerve growth factor (NGF) expression in postinfarcted normoglycemic rats, focusing on adenosine and reactive oxygen species production. DPP-4 bound adenosine deaminase has been shown to catalyse extracellular adenosine to inosine. DPP-4 inhibitors increased adenosine levels by inhibiting the complex formation.

材料及方法: Normoglycemic male Wistar rats were subjected to coronary ligation and then randomized to either saline or sitagliptin in *in vivo* and *ex vivo* studies.

結果: Post-infarction was associated with increased oxidative stress, as measured by myocardial superoxide, nitrotyrosine, and dihydroethidium fluorescent staining. Measurement of myocardial norepinephrine levels revealed a significant elevation in vehicle-treated infarcted rats compared with sham. Compared with vehicle, infarcted rats treated with sitagliptin significantly increased interstitial adenosine levels and attenuated oxidative stress. Sympathetic hyperinnervation was blunted after administering sitagliptin, as assessed by immunofluorescent analysis and western blotting and real-time quantitative RT–PCR of NGF. Arrhythmic scores in the sitagliptin-treated infarcted rats were significantly lower than those in vehicle. *Ex vivo* studies showed a similar effect of erythro-9-(2-hydroxy-3-nonyl)adenine (an adenosine deaminase inhibitor) to sitagliptin on attenuated levels of superoxide and NGF. Furthermore, the beneficial effects of sitagliptin on superoxide anion production and NGF levels can be reversed by 8-cyclopentyl-1,3-dipropulxanthine (adenosine A_1 receptor antagonist) and exogenous hypoxanthine.

結論: Sitagliptin protects ventricular arrhythmias by attenuating sympathetic innervation via adenosine A_1 receptor and xanthine oxidase-dependent pathways, which converge through the attenuated formation of superoxide in the non-diabetic infarcted rats.