SITAGLIPTIN IMPROVES REGIONAL MYOCARDIAL FUNCTION DURING DOBUTAMINE STRESS IN TYPE 2 DIABETES MELLITUS AND CORONARY ARTERY DISEASE

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Background: Obstructive coronary artery disease (CAD) limits maximal myocardial perfusion and demand ischemia reduces regional myocardial contraction. Glucagon-like peptide-1 (GLP-1) may potentially protect the myocardium from ischemic dysfunction by reducing fatty acid oxidation. Sitagliptin is a DDP-4 inhibitor licensed for the treatment of Type 2 Diabetes Mellitus (T2DM) that reduces degradation of plasma GLP-1 (7-36). We investigated whether sitagliptin improved myocardial performance during dobutamine stress echocardiography (DSE) in patients with T2DM and CAD.

Methods: 12 patients (aged 69 ± 9 years, 9 men) with T2DM on oral hypoglycaemic therapy (OHT), obstructive CAD and preserved left ventricular (LV) systolic function were studied. Each subject underwent DSE on 2 separate occasions after an overnight fast; the first (control) whilst receiving standard OHT and the second after the addition of sitagliptin (100mg od) for 4 weeks. Tissue Doppler imaging was acquired in three apical views at rest, peak stress and 30 minutes recovery and regional LV wall motion assessed using a 12-segment model. Peak systolic tissue velocity (Vs), strain (S) and strain rate (SR) were calculated for each region from tissue Doppler velocity data averaged over three consecutive beats using an off-line workstation.

Results: Regional LV performance at rest was similar on both occasions. After sitagliptin, LV function at peak stress improved (data for 12 segments; Vs 10.8 ± 4.4 vs 9.9 ± 4.4cm/s, p<0.0001; S -15.7 ± 4.7 vs -14.8 ± 4.4%, p=0.03; SR -2.2 ± 0.5 vs -2.0 ± 0.5s-1, p<0.0001). The improvement was greater in those regions subtended by a coronary artery with >50% stenosis (Vs 9.4 ± 3.9 vs 8.3 ± 3.6cm/s, p<0.0001; S -15.2 ± 4.7 vs -14.1 ± 4.4%, p=0.03; SR -2.3 ± 0.5 vs -1.9 ± 0.5s-1, p<0.0001) than in regions supplied by a non-obstructed artery (Vs 12.0 ± 4.4 vs 11.2 ± 4.6cm/s, p=0.006; S -16.0 ± 4.6 vs -15.4 ± 9.3%, p=0.29; SR -2.2 ± 0.4 vs -2.1 ± 0.4s-1, p=0.04).

Conclusions: The DPP-4 inhibitor sitagliptin improved regional myocardial contractility during dobutamine stress in patients with T2DM and CAD, with greater benefit seen in ischemic versus non-ischemic segments.