Glucagon-like peptide-1 and related agents: Novel anti-arrhythmic agents during myocardial ischemia and reperfusion

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Myocardial ischemia and reperfusion lead to derangements in cellular electrical stability and the generation of ventricular arrhythmias. Most of myocardial ischemia-induced ventricular arrhythmias and reperfusion-induced ventricular arrhythmias are malignant ventricular arrhythmias and are susceptible to life-threatening [1]. Thus, preventing ischemia-induced ventricular arrhythmias and reperfusion-induced ventricular arrhythmias is critical for reducing the morbidity for acute myocardial infarction patients.

Glucagon-like peptide-1 (GLP-1), a gut incretin hormone secreted from L cells in the intestine in response to food intake, has currently been considered as an attractive agent for the management of type-2 diabetes mellitus and could reduce the risk of cardiovascular events for type-2 diabetes mellitus patients [2]. The GLP-1 receptor agonist-exendin-4, a 39 amino acid peptide, has been shown to activate GLP-1 receptors to increase intracellular cAMP in pancreatic acinar cells and has no effect on VIP receptors, functioning identically to GLP-1. Similarly, GLP-1 analogue-exenatide also could function identically to GLP-1. There is emerging evidence that GLP-1, GLP-1 receptor agonists, GLP-1 analogues and inhibitors of GLP-1 degradation could provide beneficial effects for cardiovascular diseases in both experimental models and patients [3–8].

Previous studies showed that GLP-1 and inhibitors of GLP-1 degradation for prolonging GLP-1 effect could reduce myocardial ischemia and reperfusion injury (including reduce infarct size) and improve cardiac function, and at last improve cardiovascular outcomes [3–6]. Similarly, Sonne et al. [7] found that GLP-1 receptor agonists-exendin-4 could reduce myocardial ischemia and reperfusion injury. Timmers et al. [8] demonstrated that GLP-1 analogue-exenatide could also reduce infarct size and improve cardiac function by inhibiting myocardial apoptosis and oxidative stress induced by myocardial ischemia and reperfusion. In addition, recent studies further showed that GLP-1 related agents could provide an anti-arrhythmic effect during myocardial ischemia and reperfusion. Dipeptidyl peptidase-4 inhibitor is a new anti-diabetic drug for type-2 diabetes mellitus patients by postponing the degradation of GLP-1. Recently study found that dipeptidyl peptidase-4 inhibitor could provide an anti-arrhythmic effect during myocardial ischemia and reperfusion besides reducing infarct size [9,10]. Chinda et al. [10] showed that dipeptidyl peptidase-4 inhibitor, a drug for inhibiting the degradation of GLP-1 to prolong the effect of GLP-1 during myocardial ischemia and reperfusion, could attenuate the shortening of the effective refractory period, decrease the number of ventricular premature beats and increase the ventricular fibrillation threshold. These results indirectly suggest that GLP-1 may be helpful in decreasing reperfusion-induced ventricular arrhythmias by maintaining electrical stability.

Recently, Zhang et al. [11] further found that exendin-4, a GLP-1 receptor agonist, could also attenuate the genesis of ventricular arrhythmias including decreasing the duration of ventricular arrhythmias, the number of ventricular arrhythmias episodes and the severity of ventricular arrhythmias during myocardial ischemia without affecting hemodynamics. Yamamoto et al. [12] showed that GLP-1 receptor stimulation by exendin-4 could increase blood pressure and heart rate in a dose dependent manner. However, the affection was maintained for a short time and the increased blood pressure and heart rate returned to basal levels within 40-50 minutes. In this study, they injected exendin-4 1 h before ischemia, eliminating the effect of exendin-4 on the hemodynamics during myocardial ischemia period. These further indicated that...
GLP-1 receptor agonists or related agents may provide an anti-arrhythmic effect during myocardial ischemia.

In conclusion, GLP-1, GLP-1 receptor agonists, GLP-1 analogues and inhibitors of GLP-1 degradation not only could reduce infarct size and improve cardiac function during myocardial ischemia and reperfusion, but also may maintain electrical stability and provide an anti-arrhythmic effect, including ischemia-induced ventricular arrhythmias and reperfusion-induced ventricular arrhythmias. These results suggest that GLP-1 and related agents may become novel potential anti-arrhythmic agents for myocardial ischemia and reperfusion.

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References

A retrospective observational study to model the progression curve of aortic stenosis

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Aortic stenosis is the most common cardiac valve disorder in the developed world and its incidence is increasing especially as the population is ageing [1]. It is a progressive disease but one which has an effective treatment in the form of surgical or percutaneous aortic valve replacement. The surveillance of patients is critically important to avoid them presenting with late stage disease when surgical mortality [2] is higher and by which time they have been exposed to the risk of sudden cardiac death [3].

The majority of the literature points to a linear progression of the disease with a rate of worsening of approximately 0.1 cm² per year or increase in maximal aortic jet velocity of 0.36 m/s per year [4]. A limitation of the current literature is that the end point of aortic valve replacement is not reached in all subjects, meaning the full progression curve has not been defined. To further understand the nature of aortic stenosis progression, we retrospectively evaluated the preceding results of a cohort of patients undergoing aortic valve intervention for the primary indication of aortic stenosis who had been in systematic valve monitoring prior to intervention.

Patients from Eastbourne District General hospital who had been referred for aortic valve intervention for aortic stenosis as the primary indication were identified from the hospital’s valve clinic database. They were cross-referenced for completeness with the database. They were cross-referenced for completeness with the following criteria:

Table 1

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</table>

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