GLP-1RA and DPP-4i and Heart Rate

email:Johnrgronaldgreat@gmail.com

There is growing evidence that GLP-1 receptor agonists may increase the heart rate (HR). however, some studies suggest no significant effects. On the other hand, most of this evidence relied on the positive chronotropic effect of these drugs on HR and suggested that this may be due to modulating the autonomic nervous system, leading to more sympathetic activity.

Oxidative stress thanks to radical overload may be a main upstream event in several pathologic conditions, including. Some proof indicated that GLP-1 receptor activation may improve aerophilic stress. This might be mediate via inhibition of radical generation by Cox a pair of and/or NADPH enzyme downregulation of the MAPK (mitogen-activated supermolecule kinase) pathway. Also, they'll shield against aerophilic injury in tube cells via inhibition of PKC-α (protein enzyme c-α) and NF-κb (nuclear issue letter of the alphabet b) signalling and activation of the Nrf2 nuclear issue and upregulation of protecting antioxidative enzymes like SOD (superoxide dismutase) and CAT (catalase).

However, there is only minimal direct evidence about the effects of GLP-1 on oxidative stress-induced HTN . Koren and coworkers demonstrated that sitagliptin ameliorated oxidative stress in vascular cells without remarkable effects on BP. Demonstrated that sitagliptin inhibits oxidative stress in vascular cells and improves arterial function of the kidneys and heart. Further evidence is still required to elucidate the exact role of GLP-1 induction in oxidative stress-dependent hypertension.Nitric oxide (NO) plays a significant role in vascular homeostasis and the normal physiologic function of the cardiovascular system.

demonstrated that GLP-1 receptor activation protects endothelial cells by upregulating NO synthesis. Ding and Zhang showed that the GLP-1 agonist induced NO mRNA expression and improved NO synthesis in endothelial cells of the umbilical vein. found that GLP-1 receptor activity is associated with endothelial NO synthesis and improvement in microvascular blood flow [81]. Moreover, Dong and colleagues reported that GLP-1 acutely stimulated eNOS phosphorylation. and NO production by a PKA-dependent pathway, leading to improved microvascular muscle blood flow.

We have similar evidence concerning DPP-4i and NO synthesis illustrated that DPP-4 inhibition with saxagliptin reduced BP by enhancing NO levels in hypertensive. one of the DPP-4is, improved vascular function and reduced BP by NO-dependent molecular mechanisms in rats. So we suggest that GLP-1 induction by either agonists or DPP-4i results in more NO synthesis leading to better vascular smooth muscle cell function and lower levels of BP.

Central nervous system (CNS) activity, especially the autonomic nervous system (ANS), has a prominent role in cardiovascular function and control of BP. Emerging evidence strongly suggests that GLP-1 receptor activation increases sympathetic activity and HR elevation leading to hypertension. GLP-1R expressed in many regions of CNS is involved in the lateral septum, the posterodorsal tegmental nucleus, the thalamus and hypothalamus, the subcortical organ, the area postrema, the interpeduncular nucleus, the nucleus of the solitary tract, and the inferior olive, and so, its activity makes potent inotropic effects leading to more HR and BP.

GLP-1 agonist of exendin-4 induced sympathetic activity and suppressed vagal nerves in human. GLP-1R stimulation by liraglutide induces sympathetic activity and increases HR and BP in patients with T2DM. DPP-4i, indicating that they intensify sympathetic activity in human. So it is strongly suggested that GLP-1R induction increases ANS activity and elevates BP.