Effect of Glucagon Like Peptide-1 Receptor Agonist (Liraglutide) and Melatonin on Gastric Ischemic Reperfusion Injury in Male Albino Rats.

Thesis
Submitted for partial fulfillment of doctorate degree in
Medical Physiology

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2017

Summary

Accumulating evidences documented that reactive oxygen species (ROS) play an important role in the ischemia/reperfusion (I-R) injury as they are released during the reperfusion period that further destroy the tissues.

Overweight is known to be a risk factor for ischaemia reperfusion (I-R) injury as it elicits oxidative stress since it causes excessive production of ROS.

Melatonin, a hormone secreted mostly by the pineal gland in the brain which maintains the body's circadian rhythm, was shown to have marked antioxidant properties and had a protective role against I-R injury in various organs including heart, liver, kidney, brain. Moreover, there is accumulating evidence of a weight-reducing effect of melatonin.

Glucagon-like peptide-1 (GLP-1) is produced naturally in the intestine and brain in both humans and rats. Previous studies have revealed profound insulinotrophic and antidiabetic effects of GLP-1, Available data reported a valuable effect of GLP-1R agonist on protection against I-R injury in multiple organs, but little data are available about its effect on gastric I-R injury. In addition, recent research reported weight-reducing effect of GLP-1 R agonist.

In view of this concept, the present work aimed to assess and compare the possible protective effect of glucagon like peptide-1 receptor agonist (Liraglutide) and Melatonin hormone on gastric ischemia-

reperfusion injury, body weight and the possible underlying mechanism in male albino rat.

This study was carried on sixty male albino rats, divided into six groups; standard chow diet fed control (n=10), high fat /sucrose diet fed control (n=10), melatonin treated standard chow diet fed rats (n=10), melatonin treated high fat/ sucrose diet fed (n=10), Liraglutide treated standard chow diet fed rats (n=10), Liraglutide treated high fat/ sucrose diet fed rats (n=10). They received treatments for four weeks then gastric I-R injury was induced in all rats by celiac artery occlusion and gastric tissue samples were investigated for percentage DNA fragmentation, myeloperoxidase, total oxidant status, total antioxidant capacity, oxidative stress index and histopathological examination.

It was found that gastric I-R injury of HFS fed rats significantly increased total oxidant status, oxidative stress index and myeloperoxidase in comparison to SCD, significantly decreased total antioxidant capacity. with insignificant change on % DNA fragmentation Melatonin pretreatment of gastric I-R injury reduced oxidative stress i.e. decreased Total oxidant status, increased Total antioxidant capacity, and decreased oxidative stress index, in addition, it decreased % DNA fragmentation and myeloperoxidase in both SCD and HFS fed rats. Similarly, Liraglutide pretreatment of gastric I-R injury reduced oxidative stress i.e. decreased Total oxidant status, increased Total antioxidant capacity, and decreased oxidative stress index, in addition, it decreased % DNA fragmentation and myeloperoxidase in both SCD and HFS fed rats.

High fat/sucrose feeding significantly increased body weight gain and BMI as compared to SCD-fed rats. Melatonin treatment in SCD-fed

rats insignificantly changed weight gain and BMI compared to SCD control rats, and, Melatonin treated HFS-fed rats significantly reduced weight gain compared to untreated HFS-fed rats. On the other hand. Liraglutide treatment in SCD-fed rats showed insignificant change in both weight gain compared to SCD control rats, While, its administration in HFS-fed rats, significantly decreased weight gain and BMI compared to untreated HFS-fed rats.

Conclusion: both Liraglutide and Melatonin are similarly effective in the treatment of gastric I-R injury through decreasing oxidative stress, decreasing apoptosis and decreasing cellular infiltration. In addition both drugs exert a weight reducing effect only with HFS feeding.