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Medi Quest BRS Hospital

A monthly News letter from BRS Hospital

NEWER THERAPUETIC AGENTS FOR DIABETIC NEPHROPATHY

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INTRODUCTION

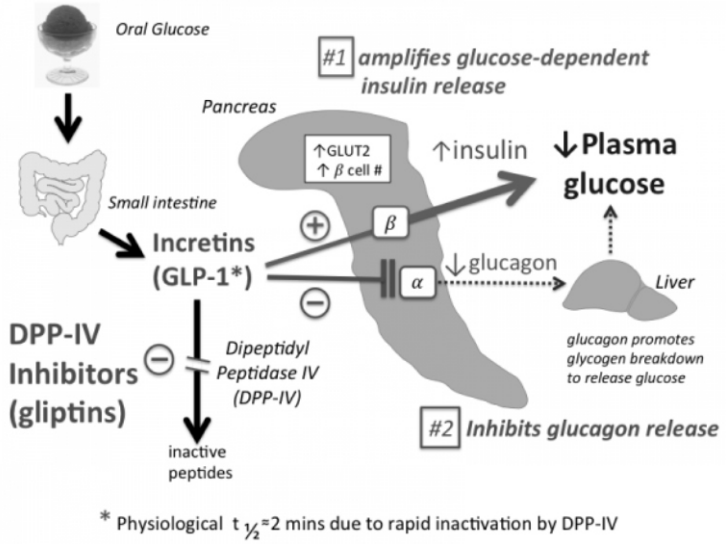
The prevalence of Diabetes Mellitus has been increasing markedly over time. From 2005 to 2015 Diabetes has become the 7th leading cause of death from the 11th position. The situation in Tamilnadu also shows a high prevalence of Type 2 DM. In ICMR-INDAB study published in Lancet 2017 done in 15 states and few Union Territories Chandigarh had the highest prevalence of DM. Tamilnadu had the second highest prevalence of 10.4 per cent. Nearly one in every 10 had DM-2 in our state.

This situation calls for urgent measures to prevent DM-2 and also to prevent complications arising from DM-2. Upto 35% of patients of with DM develop nephropathy over a period of 25 yrs and is associated with high mortality. The important preventive measures for DM Nephropathy include ACE Inhibitors / Angiotensin receptor blockers, Tight glycemic control (HbA1C of 7%), Tight BP control (< 130/80 mm Hg), control of hyperlipidemia, smoking cessation and mangement of obesity .

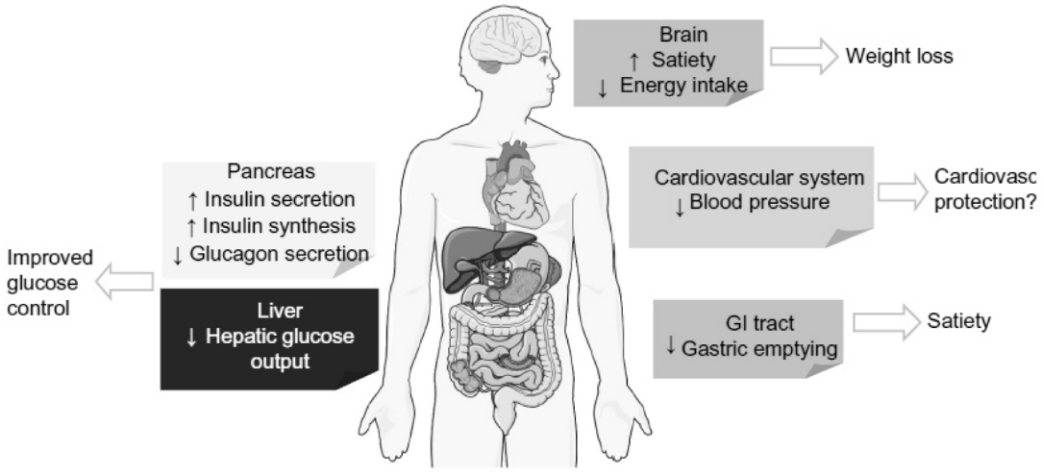
NEWER THERAPUETIC AGENTS :

Several new drugs have come into vogue in the recent past which have shown promise in preventing cardiac and renal complications arising from DM-2.

1. GLP - 1 (Glucagon like peptides) ANALOGUES :



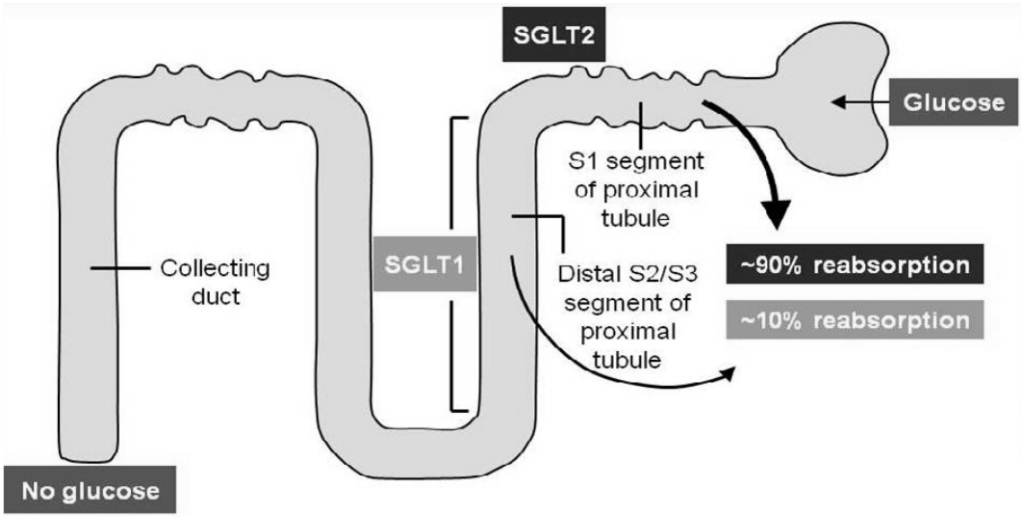
The intestines releases incretins in response to food in the stomach. These hormones increase insulin production from the pancreatic beta cells, suppress Glucagon production thereby suppressing hepatic gluconeogenesis, increase satiety thereby decreasing appetite. GLP-1 analogues have a longer half-life compared to natural incretins enabling therapeutic potential.



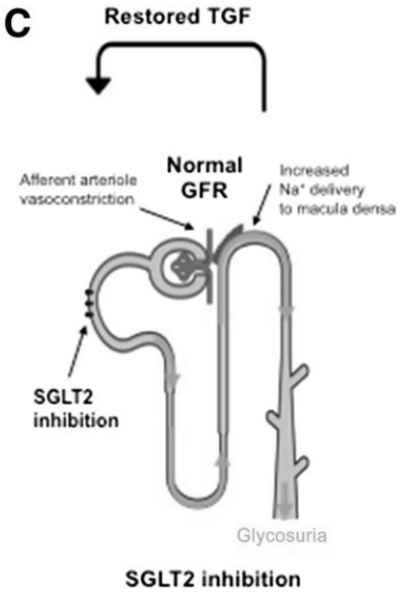
Liraglutide is a GLP-1 analogue given once daily as a subcutaneous injection and Dulaglutide is a once weekly subcutaneous injectable drug which have shown promise in preventing progression of DM Nephropathy. This effect has been found to be independent of glycemic control or use of ACEI/ARB. These drugs have also shown a significant weight loss likely due to increased satiety contributing to beneficial effects. The progression of microalbuminuria and fall in GFR have been found to be much lower with these drugs compared to standard care with insulin. Their main side effects are higher incidence of acute gall stone disease and raised pancreatic enzymes. There is also higher incidence of medullary thyroid carcinomas in animals - though this is not reported in humans.

2. SGLT 2 - INHIBITORS :

These drugs inhibit proximal tubular reabsorption of glucose along with sodium via SGLT-2 receptors. They cause glycosuria and natriuresis as a result. They are weak hypoglycemic agents by themselves causing a HbA1c reduction by about 0.5 to 1%. There are four SGLT 2 inhibitors in use - Empaglifozin, Canaglifozin, Dapaglifozin and Ertuglifozin.



These drugs have shown renoprotective and cardioprotective effects in several trials . The proposed mechanisms for beneficial results are multifactorial. The enchanced distal tubular delivery of sodium leads to restored tubuloglomerular feed back - leading to afferent arteriolar vasoconstiction - and decreased intraglomerular pressures. This is proposed to have renoprotective effects. The other possible effects are related to osmotic diuresis, slightly lowered BP, decreased afterload and preload on heart due to diuresis, enhanced utilisation of ketone bodies by heart and kidneys and marginal weight loss.



SGLT2 inhibition

There are clinical situations to watch out for with these medications. There is higher incidence of Genital infections and urosepsis due to glycosuria. Marginally higher incidence of PVD or amputations are reported - usually at metatarsal level. Marginally higher incidence of fractures or osteoporosis is also noted. These drugs should be avoided in DKA prone and those with concurrent diuretic use .

3. 3RD GENERATION ALDOSTERONE ANTAGONISTS :

The first and second generation steroidal alosterone antagonists - spironolactone and eplerenone have been found to decrease proteinuria and cardioprotective properties. But their main drawback is higher chance for hyperkalemia especially when used in addition with ACEI /ARB which most of these patients require. Finrenone is a novel nonsteroidal 3rd generation aldosterone blocker which has shown low risk of hyperkalemia when used in addition to ACEI/ARB.

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