SCIENTIFIC RESEARCH GROUP:

Parchami Ghazaee Sepideh
PhD in biological sciences, assistant,
assistant of the Department of Pharmacology and Pharmacotherapy
Kyiv Medical University, Ukraine

Marchenko-Tolsta Kateryna
MD, Senior lecturer,
Senior lecturer of the department of pharmacology and Pharmacotherapy
Kyiv Medical University, Ukraine

Sereda Petro
Doctor of medical sciences, Professor,
Head of the department of pharmacology and Pharmacotherapy
Kyiv Medical University, Ukraine

Lane Sandra
1st year student of medicine,
Department of Clinical and Biomedical Sciences
University of Exeter, United Kingdom

RENOPROTECTIVE PROPERTIES OF NOVEL ANTI-DIABETIC AGENTS

Chronic Kidney Disease (CKD) is the steady loss of renal function over time. CKD can also constitute abnormalities in the kidney structure. Kidney damage is measured using albuminuria, structural abnormalities, electrolytes and other abnormalities, prior kidney transplant or a projected glomerular filtration rate (eGFR) <60 mL/min/1.73 m [1]. Even though CKD has no known cure, its advancement can be slowed down by regulating the risk factors like high blood glucose levels, high blood pressure and dyslipidemia [2]. According to Mohamed et al. [3] diabetes accounts for almost 44% of all new CKD cases; this means that approximately 1 in 3 patients with diabetes also have kidney disease. For this reason, this investigation was chosen to analyze the agents that can regulate blood glucose levels while having renoprotective effects that have been shown to be enormously beneficial in this patient group.

Recent trials have identified novel antidiabetic agents like sodium-glucose cotransporter 2 (SGLT-2) inhibitors, glucagon-like peptide 1 (GLP-1) agonists and dipeptidyl peptidase 4 (DPP-4) inhibitors as agents that also have Renoprotective properties. SGLT-2 inhibitors are proteins that are expressed in the renal proximal intricate tubes that perform their physiological functions by reducing the reabsorption of filtered glucose, promoting the excretion of urinary glucose and decreasing the renal threshold for glucose. There are four SGLT-2 inhibitors that are approved by the Food Drug Administration (FDA) for use in adults: canagliflozin, empagliflozin, dapagliflozin and ertugliflozin. By inhibiting the reabsorption of SGLT-2-dependent sodium and glucose, these inhibitors increase the distal tubular sodium weight. This inhibits the renin-angiotensin-aldosterone system while also regulating some physiological functions such as reducing renal intraglomerular pressure and downregulating sympathetic activity [4].

DPP-4 inhibitors, on the other hand, are antihyperglycemic drugs used to manage type 2 diabetes. DPP-4 inhibitors approved by the FDA are linagliptin, sitagliptin, alogliptin and saxagliptin. DPP-4 is a pervasive enzyme that acts on incretin hormones such as GLP-1 and GIP. The presence of these hormones in the kidneys indicates that the incretin system has a role to play

in the regulation of kidney functions since these hormones maintain glucose homeostasis by increasing the secretion of insulin and decreasing the secretion of glucagon. GLP-1 is secreted by enteroendocrine L cells in the small intestine to lower blood glucose by stimulating the secretion of insulin and reducing the secretion of glucagon while GIP is secreted in the stomach and neuroendocrine K-cells of the small intestines. These hormones have half-lives of approximately 2 minutes and 7 minutes respectively and are released almost immediately after food intake. DPP-4 destroys these hormones immediately because of their short half-life. By inhibiting the DPP-4 enzyme, the inhibitors increase GLP-1 and GIP levels, thereby increasing the secretion of beta-cell insulin in the pancreas and reducing hyperglycemia [3,5].

The glucagon-like peptide 1 (GLP-1) agonists are drugs that imitate the actions of a hormone called glucagon-like peptide 1 (Greco et al., 2019). When the blood sugar levels start to rise after eating, the drugs stimulate the production of more insulin which helps to lower the sugar levels. GLP-1 has also been shown to possess other renoprotective elements such as inducing glomerular hyperfiltration, increasing the filtered electrolyte load after eating, modulating lipid and energy metabolism and improving the renal hemodynamic function [6].

In conclusion, SGLT-2 inhibitors have demonstrated advantages in CKD patients regardless of diabetes status, opening up interesting possibilities for the use of these medicines in individuals at risk for or with advanced kidney disease without Type 2 diabetes mellitus.

References:

1. Andrassy KM. Comments on 'KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. 2013 Sep; 84(3): 622–23. [doi: 10.1038/ki.2013.243] [PMID: 23989362]
2. Leite KM, Long AM, Ostroff ML, Borges L, Braden G. A review of the renoprotective effects of novel Antidiabetic Agents. J Pharm Pract. 2021 Feb; 34(1): 141–8. [doi: 10.1177/089719002090234] [PMID: 32067559]
3. Mohamed RH, Sedky AA, Hamam GG, Elkhateb L, Kamar SA, Adel S, et al. Sitagliptin's renoprotective effect in a diabetic nephropathy model in rats: The potential role of PI3K/AKT pathway. Fundam Clin Pharmacol. 2022 Apr;36(2):324-37. [doi: 10.1111/fcp.12736] [PMID: 34735026]
4. Krishnan A, Shankar M, Lerma EV, Wiegley N, GlomCon Editorial Team. Kidney Med. 2023 Feb;5(4):100608. [doi: 10.1016/j.xkme.2023.100608] [PMID: 36915368]
5. Gallwitz B. Clinical Use of DPP-4 Inhibitors. Front Endocrinol (Lausanne). 2019 Jun;10: 389. [doi: 10.3389/fendo.2019.00389] [PMID: 31275246]
6. Greco EV, Russo G, Giandalia A, Viazzi F, Pontremoli R, De Cosmo S. GLP-1 Receptor Agonists and Kidney Protection. Medicina (Kaunas). 2019 May;55(6): 233. [doi: 10.3390/medicina55060233] [PMID: 31159279]