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REVIEW ARTICLE

DIABETIC NEPHROPATHY: NOVELTY ABOUT THE DIABETIC NEPHROPATHY TREATMENT IN CHILDREN

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ABSTRACT

The aim: To analyze and discuss the main aspects of the DN treatment in children.

Materials and methods: Basic and modern data about the new aspects of the DN treatment analyzed in current review paper.

Conclusions: DN is a major healthcare challenge and is a major cause of irreversible kidney damage. The DN course and progression leads to severe cardiovascular complications and early death. Treatment of DN is complicated clinical issue and requires individual and complex approach, including renoprotection, antihypertensive treatment. Nowadays, we are able to provide additional medications that can enhance the benefits of the renin-angiotensin-aldosterone (RAAS) blocking, Further search of neproprotective medicines for early DN correction in pediatric patients is still of high importance.

KEY WORDS: kidney damage, diabetic nephropathy, treatment, correction

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INTRODUCTION

T1DM increased by 4.8% year from 2002 to 2015, according to the Centers for Disease Control and Prevention, and it increased by 1.9% annually in children and adolescents under the age of 20 [1]. End-stage renal disease (ESRD) in adults is primarily brought on by DM worldwide. One in five persons with diabetes have diabetic nephropathy (DN). Incidence of DN in pediatric population has significantly increased in 2013 as compared to 2002 (1.16% to 3.44%) [1,2].

Diabetic nephropathy is a prominent side effect of both type 1 and type 2 diabetes. One in three adults who have diabetes also have diabetic nephropathy. The best ways to prevent or delay the formation of diabetic nephropathy include maintaining a healthy lifestyle, managing diabetes and high blood pressure, and exercising regularly [2]. From 2002 to 2015, the prevalence of type 1 diabetes (T1D) and the associated insulin-resistant phenotype increased annually in children and adolescents by 1.9% and 4.8%, respectively. Additionally, compared to adults, children and adolescents face a more aggressive clinical course of diabetes, which is defined by a muted response to current treatments as well as a faster loss of beta-cell activity, progression of insulin resistance, and development of end-organ issues. DN is becoming more common among kids and teenagers as a result [1-5].

Early detection and adequate treatment can halt or slow the progression of the disease while reducing the chance of complications. Kidney failure, also referred to as end-stage kidney disease, can result from DN. Kidney failure is a condition that can be fatal. The only treatments available at this time are dialysis or a kidney transplant. Positively, a number of pharmacological techniques are now available for the management of diabetes and have been shown to enhance cardiorenal outcomes. The goal of this review is to discuss and summarize the approaches available nowadays for DN treatment.

THE AIM

The aim of the paper was to analyze and discuss the main aspects of the DN treatment in children.

MATERIALS AND METHODS

Novel references reviewed. Basic and modern data about the aspects of the DN treatment analyzed in current paper.

REVIEW AND DISCUSSION

DIABETIC NEPHROPATHY. BASIC DATA

Hyperglycemia is a key disorder in diabetic nephropathy. It has many damaging effects including the following meta-

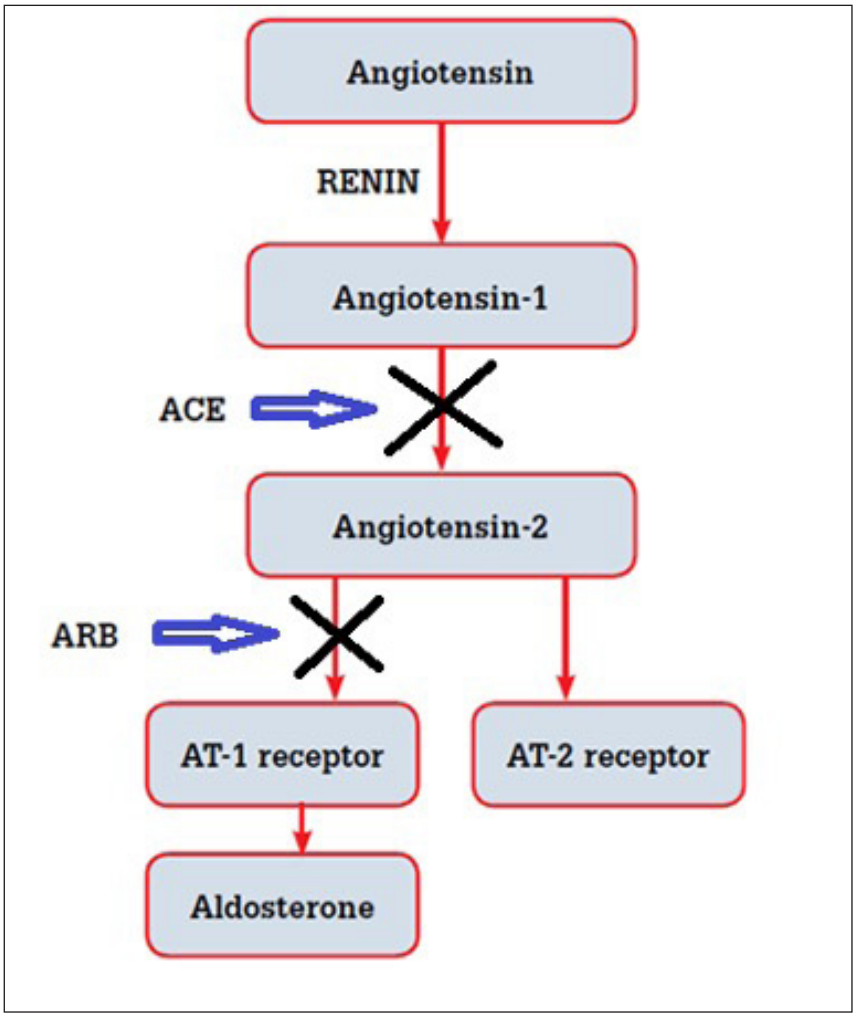

Fig. 1. Pathophysiological stages of DN

bolic changes, i.e. oxidative stress, activation of advanced glycation end products formation (AGE) etc. The latter disorders are dealing with inflammation. Development of inflammation associated with production of cytokines, growth factors, vasoactive substances (IL-6, MCP-1, transforming growth factor-beta, vascular endothelial growth factor. These events lead to fibrosis and vascular damages. Moreover, a podocytopathy has place under the hyperglycemic conditions. Beside these events intraglomerular hypertension and epithelial-mesenchymal cell transformation are activated. The outcome of these damages is fibrosis and chronic tubular disorders [3].

Stages of DN in patients with diabetes mellitus type:

- **stage 1** (hyperfiltration stage) - increased glomerular filtration rate (GFR) and capillary glomerular pressure possibly due to renal hypertrophy
- **stage 2** (silent stage) - usually normal GFR (dropped from stage 1) and no albuminuria, but with renal morphological changes, such as basement membrane thickening and mesangial expansion
- **stage 3** (microalbuminuria stage or stage of incipient nephropathy) - increased urinary albumin excretion rate (in range of 20-200 mcg/minute or 30-300 mg/day). Usually occurs 5-15 years after diagnosis of type 1 diabetes, but has been reported ≤ 2 years of diagnosis in younger patients. Persistent microalbuminuria (confirmed microalbuminuria at least twice at 3-6 months apart) is reported to be associated with widespread advanced glomerular structural changes. Microalbuminuria may be transient and reversible especially if short duration and in patients with glycated hemoglobin < 8%, systolic blood pressure < 115 mm Hg, and low cholesterol and triglyceride levels
- **stage 4** (macroalbuminuria stage) - urinary albumin excretion rate > 200 mcg/minute or > 300 mg/day
  - usually occurs 10-15 years after diagnosis of type 1 diabetes
  - reported association with arterial hypertension in two-thirds of patients
  - highly predictive of progression to renal failure if untreated
- **stage 5** (renal failure) - development of uremia and end-stage renal disease

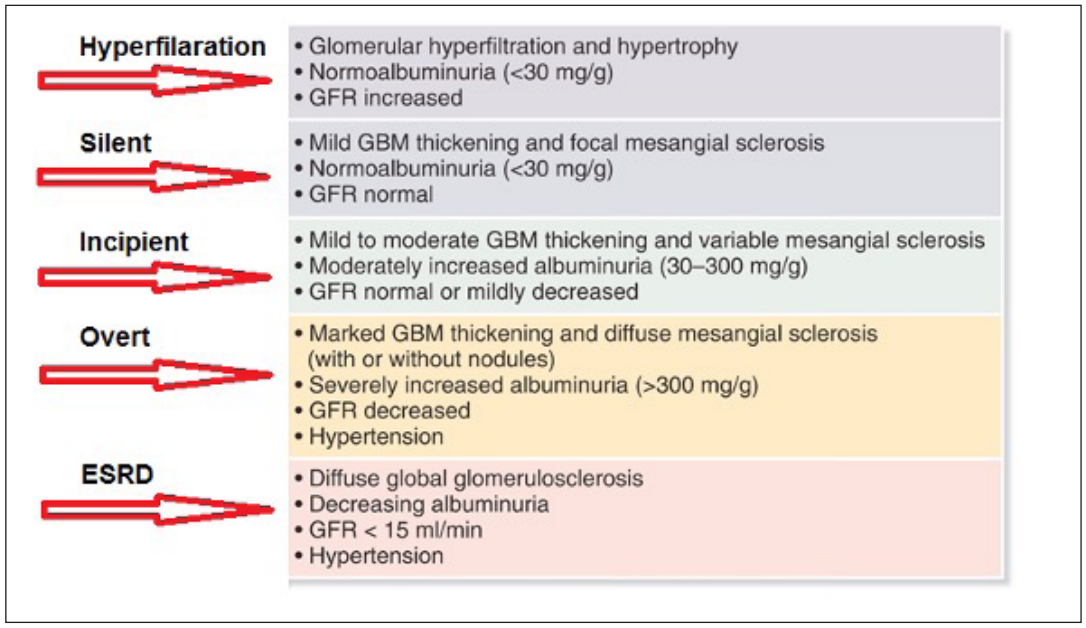

Fig. 2. Basic scheme of the renin–angiotensin–aldosterone system (RAAS) action and the mechanism of action of angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB).

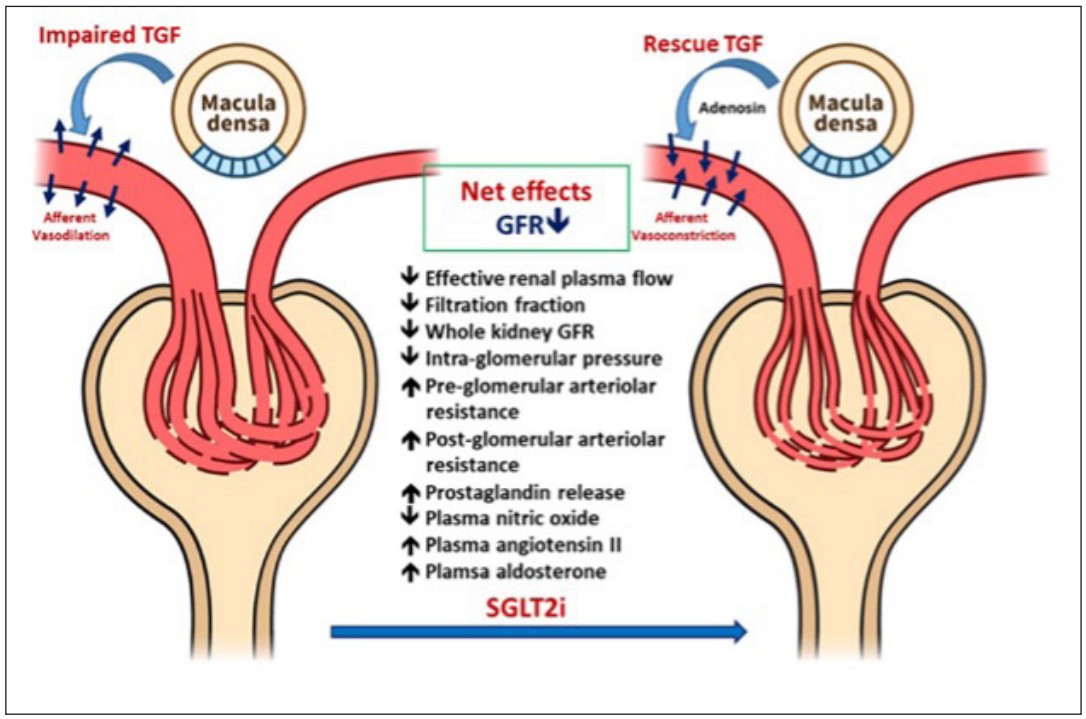

Fig. 3. Scheme of the topical action of SGLT2 inhibitors

oreported in up to 40% of patients
orequires dialysis or renal transplantation

Currently albuminuria categories which we use in practiceis following:

• A1 - albumin excretion rate (AER) < 30 mg/24 hours, albumin:creatinine ratio (ACR) < 30 mg/g (3 mg/mmol) (normal-to-mildly increased)

• A2 - AER 30-300 mg/24 hours, ACR 30-300 mg/g (3-30 mg/mmol) (moderately increased compared to young adult level)

• A3 - AER > 300 mg/24 hours, ACR > 300 mg/g (30 mg/mmol) (severely increased [including nephrotic syndrome]) [3-5].

Pathophysiological stages of DN described on Fig 1.

GFR and intraglomerular capillary pressure (PGc), glomerular hypertrophy, and microalbuminuria are the first steps in the progression of clinical diabetic nephropathy. Poor glycemic management and high systolic blood pressure make the condition worse by forcing the development of proteinuria, nodular glomerulosclerosis, tubulointerstitial damage, a decline in GFR, and ultimately ESRD (BP). It is generally agreed upon that the cumulative effects of a number of metabolic and hemodynamic factors lead to diabetic nephropathy. Kidney damages are brought on by the production of cytokines and growth factors as a result of

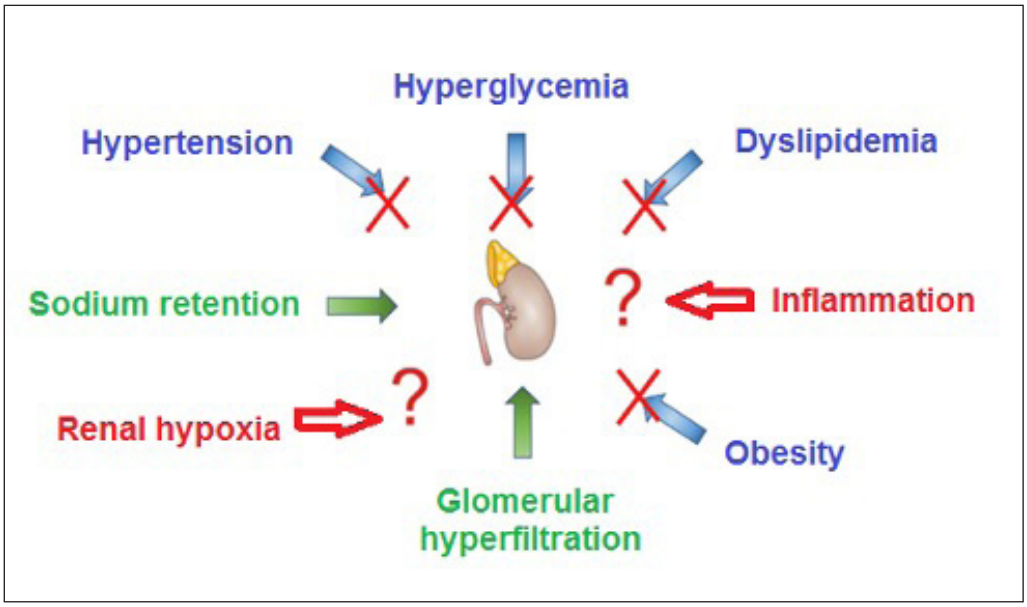

Fig. 4. Scheme illustrating mechanisms of GLP-1 agonists

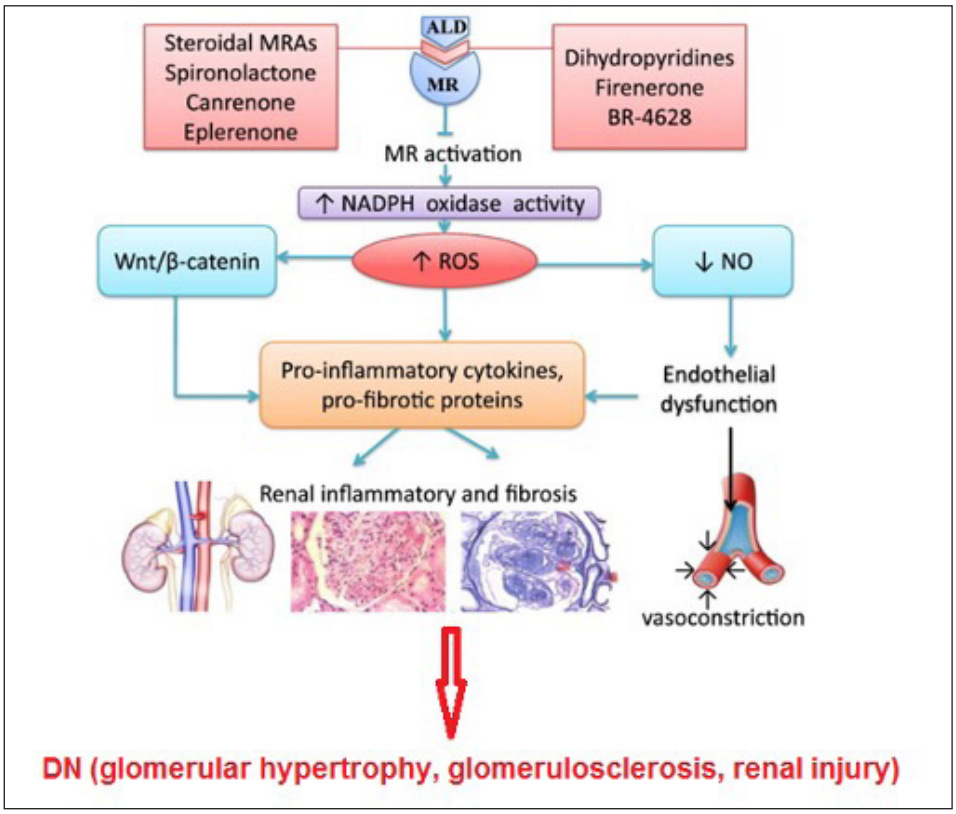

Fig 5. Mechanisms of MRAs nephroprotective effect

these common intracellular signaling pathways being activated [6].

CURRENT VIEW OF DIABETES NEPHROPATHY TREATMENT IN CHILDREN

DIETARY AND LIFESTYLE INTERVENTIONS

Increased physical activity promotion and dietary education, such as calorie counting, carbohydrate tracking, and eating foods with a low glycemic index, are all components of current treatment guidelines and are all associated with improved glycemic control. However, these strategies continue to be only marginally effective. When developing dietary recommendations for children, it's also important to consider the considerable prevalence of disordered eating behavior in young individuals with diabetes, which is connected to worse glycemic control and more detrimental consequences [7].

The American Diabetes Association (ADA) recommendations also recommend weight management, particularly for young T2D patients. However, com-

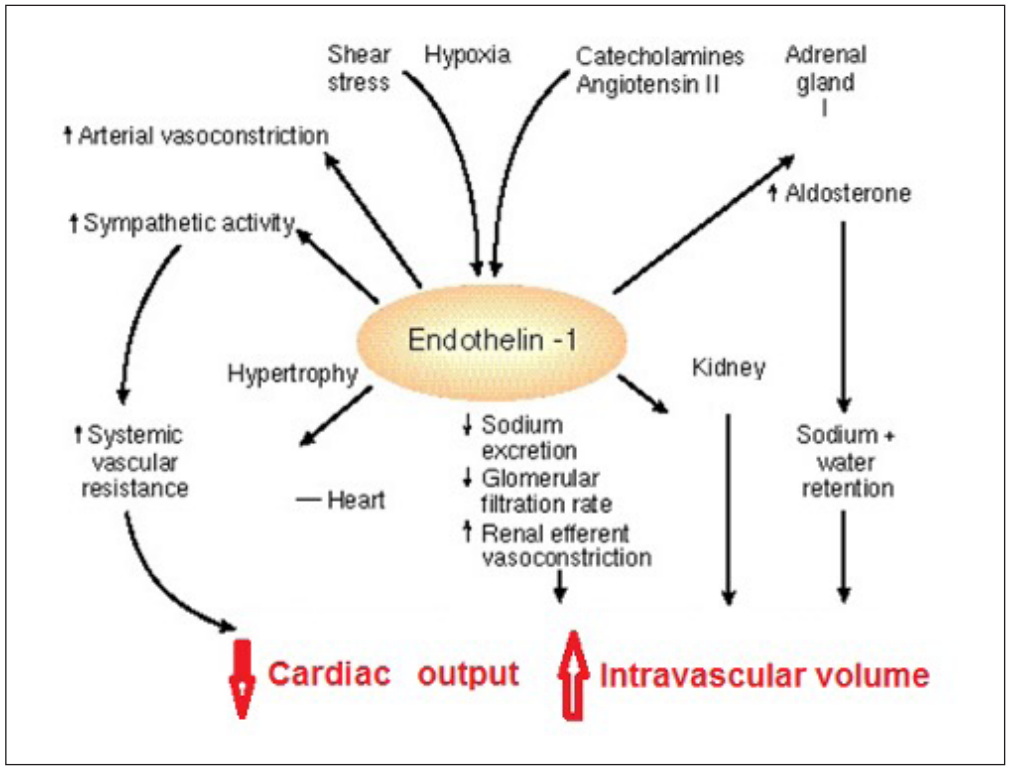

Fig. 6. Pathological effects of endothelins

prehensive lifestyle intervention programs with goals for food and exercise have not yet been successful in helping adolescents with T1D significantly enhance their glycemic control. In addition, decreasing weight and exercising are part of the treatment for diabetic nephropathy Gonzalez et al [7,8].

PHARMACOLOGICAL MANAGEMENT

RENIN ANGIOTENSIN ALDOSTERONE SYSTEM (RAAS) BLOCKADE (ACE-I AND ARB)

Kidney and heart disease have a strong association with the renin-angiotensin-aldosterone system. Angiotensin I is a vasoactive substance which is converted to angiotensin II. This is ongoing with angiotensin-converting enzyme (ACE). ACE has a plenty of effects, i.e., activation of inflammation, fibrosis [9]. Moreover, angiotensin II increases sympathetic activity, sodium and chloride absorption in tubuli and production of increases aldosterone. It is known that bradykinin metabolism is related to ACE activity too [9-13]. (Fig 2).

Patients with kidney and heart disorders have shown benefit from ACE inhibition and angiotensin blocking in the form of ACE inhibitors and angiotensin receptor blockers. As early as 1983, the effects of angiotensin on renal auto-regulation were documented. Numerous investigations conducted in the ensuing ten years shown a reduction in albuminuria [6] as well as reno-protective effects of RAAS blockage [13,14].

SGLT2 INHIBITORS

Nowadayd a new class of medication is widely used and called a sodium-glucose co-transporter-2 (SGLT-2). The key action of these medications is that they have capacity to inhibit the SGLT-2 proteins. The latter are located in cells renal proximal convoluted tubules of humans. Their key role is to prevent the absorbtion of filtered glucose from the tubular lumen. Currently, medical doctors allowed to use following medications: canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin. Each of those medications has an individual way of prescribtions (dose, regimen). They are high effective in type 2 diabetes mellitus (DM) treatment in addition to diet and adequate physical activity [15-17].

It is known that human proximal convoluted tubules have SGLT-2 proteins localized in their cells. The main role of the SGLT-2 proteins is to reabsorb the glucose from tubular filtrate. It is shown that SGLT-2 inhibitors lead to decreased reabsorption of glucose from tubular filtrate, increase excretion of glucose as a result.

Moreover, SGLT-2 causes the increased excretion of sodium form distal tubuli. In addition to inhibiting the renin-angiotensin-aldosterone system, this is also thought to control a number of physiological processes, including lowering renal intraglomerular pressure, enhancing tubuloglomerular feedback, decreasing sympathetic activity, and lowering preload and afterload in the heart.

Due to enhanced urine glucose excretion, SGLT2 inhibitors were first studied for their potential to help

patients with type II diabetic mellitus (T2DM) better control their blood sugar levels [18].

SGLT2 can reduce glomerular hyperfiltration. This is due to inhibition of SGLT2. In turn this leads to a natriuretic effect and realization of tubulo-glomerular feedback [18]. RAAS administration leads to decrease the glomerular pressure and as a result slows down the kidney damage. .

In addition to regulation of glomerular pressure SGLT2 inhibitors enhances glucose uptake in kidney and regulate extracellular matrix formation [19]. Moreover, SGLT2 inhibitors provide an antioxidant and anti-inflammatory activity and in turn decrease fibrosis, inflammation [20].

One more link says that SGLT2 inhibitors induce the low ketotic state. This is due to ketones synthesis and lowering their excretion. It is known that ketones can be oxidized which leads to oxidative stress in kidney and vessels.

Data show that cardiovascular and kidney effects of SGLT2 inhibitors are very effective in CKD prevention and in proteinuric states as well.

Dapagliflozin was authorized by the European Commission in March 2019 as an adjuvant treatment for type 1 diabetes. The use of SGLT2 inhibitors increases the incidence of DKA in people receiving insulin, according to prior studies. Dapagliflozin does not, however, appear to raise the risk of DKA in the near term, according to the current findings (24 weeks) [21].

GLP-1 AGONISTS

In response to meal consumption and an increase in plasma glucose, L-cells in the lower stomach produce the incretin hormone glucagon-like peptide-1. These incretin hormones promote the release of insulin from pancreatic ß islet cells, inhibit the release of glucagon, postpone the emptying of the stomach, and increase satiety. The lungs, stomach, and kidneys are only a few of the other organs that have GLP-1 receptors in addition to the pancreas [22,23].

Additionally, GLP-1 has been shown to have a variety of kidney-protective effects, including the ability to reduce albuminuria, glomerular hyperfiltration, glomerular hypertrophy, and mesangial matrix expansion in animal models. It has also been shown to reduce oxidative stress and inhibit albuminuria (Fig 4)., as well as an ability to ameliorate albuminuria, glomerular hyperfiltration, glomerular hypertrophy and mesangial matrix expansion in animal models [23,24].

MINERALOCORTICOID RECEPTOR ANTAGONISTS

The mechanisms of action of the mineralocorticoid receptor (MR) go beyond their antagonistic effects on the epithelial sodium channels (ENaC) in the collecting tubules. Numerous tissues, such as the vascular, cardiac, and colonic tissues, express MR. MRs contribute significantly to the adaptive response to damage in addition to fluid and ion transport [25]. Reactive oxygen species and inflammation have been demonstrated to rise with the activation of these receptors, and renal hypertrophy has been linked to the overexpression of this receptor.

The most commonly used mineralocorticoid receptor antagonists are spironolactone and eplerenone. Meta-analyses report data that steroidal MRAs are effective in lowering proteinuria rates in patients especially those treated with RAAS inhibitors. However, these drugs are still accurately used in patients with CKD, due to their side effects - hyperkalemia and effect on GFR [26,27].

Non-steroidal MRAs were first introduced, with finerenone being the most famous. They had great promise for perhaps improving cardiac and proteinuric conditions while having less of an impact on causing hyperkalemia. The tissue distribution of finerenone, the way it inactivates MR, and other pharmacologic characteristics are just a few of the characteristics that set it apart from steroidal MRAs [28].

Finerenone, which promises the similar advantages of steroidal MRAs with less side effects, is a welcome addition to our toolbox. Numerous ground-breaking studies showing the therapeutic potential of finerenone for DKD.

ENDOTHELIN ANTAGONISTS

Endothelin-1 (ET-1) is a 21 amino acid peptide and is the most potent vasoconstrictor in the human body. ET-1 is produced in almost all kidney cells. Most of the production of ET-1 in going in tubular cells, primarily principal cells of the inner medullary collecting duct [29].

There are substantial clinical evidence for increased plasma endothelin-1 (ET-1) levels in patients with diabetes mellitus, leading to endothelial dysfunction. The endothelin system consists of three isoforms - ET-1, ET-2, and ET-3. ET-1 is a potent vasoconstrictor peptide that plays a key role in controlling cell proliferation and regulating the accumulation of extracellular matrix and inflammatory cells. These events lead to fibrosis.

Endothelin receptors are expressed in the kidney [30], and diabetics have been shown to have an overexpression of these receptors. The renal endothelin system has been demonstrated to play a crucial role in normal renal function, and derangements of this system are involved in the onset and progression of DN [31].

It has been demonstrated that endothelin receptor antagonism enhances renal microcirculation and that it can decrease urine protein excretion [32].

Trials have been done to evaluate the benefits of endothelin antagonists in the treatment of DKD patients in light of this evidence of possible renal benefit.

CONCLUSIONS

DN is a major healthcare challenge, complicating the course of many people who live with diabetes, and is a major cause of ESRD. The DN course and progression leads to severe cardiovascular complications and early death. Prognosis of DN is quite different and depends on presense of kidney damage, i.e. albuminuria and hypertension. Treatment of DN is complicated clinical issue and requires individual and complex approach, including renoprotection, antihypertensive treatment. These may prevent early death. Literature data and reports from different research groups agreed on necessity of individual approach.

We were only able to prescribe patients with DN one treatment option for many years: RAAS inhibition with ACE-I and ARBs. These medications continue to be the key effectors in managements of DN patients. Nowadays, we are able to provide additional medications that can enhance the benefits of RAAS blocking.

SGLT2 inhibitors are revolutionizing nephrology thanks to their undeniable protective advantages that go beyond DN. According to the first KDIGO guidelines, GLP-1 agonists are now the preferred oral medications for treating diabetes in CKD patients. As we approach a medical therapy for DN that follows guidelines and includes an ACE-I or ARB, MRA, SGLT2 inhibitors, and maybe an SGLT3 inhibitor. These medications are very effective addition to our conventional treatment. The future of DN management may involve a more individualized strategy, where each patient can receive a treatment plan that is specific to their genetic and biomarker profile. Further search of neproprotective medicines for early DN correction in pediatric patients is still of high importance.

REFERENCES

1. American Diabetes Association. Standards of Care in Diabetes - 2023. Diabetes Care. 2023;46:1-291.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2020;98(4S):1-115.
3. A/L B Vasanth Rao VR, Tan SH, Candasamy M, Bhattamisra SK. Diabetic nephropathy: An update on pathogenesis and drug development. Diabetes Metab Syndr.2019; 13(1):754-762. doi: 10.1016/j.dsx.2018.11.054.
4. United States Renal Data System. USRDS 2018 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States; National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases: Bethesda, MD, USA. 2017. https://www.kidney.org.uk/chronic-kidney-disease?gclid=Cj0KCQjwiZqhBhCJARIsACHHEH9f79P6bnWbIzsepaiA6_nkQJy0FIqRDgAuGpqvjvMLE9uFLo_VdsaAlbTEALw_wcB [date access 13.03.2023].
5. International Diabetes Federation. IDF Diabetes Atlas; International Diabetes Federation: Brussels, Belgium. 2017. https://diabetesatlas.org/atlas/eighth-edition/ [date access 13.03.2023].
6. Sulaiman MK. Diabetic nephropathy: recent advances in pathophysiology and challenges in dietary management. Diabetol Metab Syndr. 2019;11:7. https://diabetesatlas.org/resources/?gclid=Cj0KCQjwiZqhBhCJARIsACHHEH9pxBfDHjSInNO8x12dvAxaxJYBu8ioH5d9XGMu34PrFy0nsN6kQsUaArnWEALw_wcB [date access 13.03.2023].
7. Onyenwenyi C, Ricardo AC. Impact of Lifestyle Modification on Diabetic Kidney Disease. Curr Diab Rep. 2010;15(9): 60. doi: 10.1007/s11892-015-0632-3.
8. The United States Renal Data System. Data source: National Health and Nutrition Examination Survey (NHANES). 2003–2006, 2007–2010, 2011–2014 and 2015–2018. 2020. https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/usrds [date access 13.03.2023].
9. Ames MK, Atkins CE, Pitt B. The renin-angiotensin-aldosterone system and its suppression. J. Vet. Intern. Med. 2019;33:363–382. doi: 10.1111/jvim.15454.
10. Montinaro V, Cicardi M. ACE inhibitor-mediated angioedema. Int. Immunopharmacol. 2020;78:106081. doi: 10.1016/j.intimp.2019.10608.
11. Brenner BM, Cooper ME, de Zeeuw D et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N. Engl. J. Med. 2001;345:861–869. doi: 10.1056/NEJMoa011161.
12. Lewis EJ, Hunsicker LG, Clarke WR et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N. Engl. J. Med. 2001; 345:851–860. doi: 10.1056/NEJMoa011303.
13. Yusuf S, Teo KK, Pogue J et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. N. Engl. J. Med. 2008;358:1547–1559. doi: 10.1056/NEJMoa0801317.
14. de Boer IH, Caramori ML, Chan JCN et al. Executive summary of the 2020 KDIGO Diabetes Management in CKD Guideline: Evidence-based advances in monitoring and treatment. Kidney Int. 2020;98:839–848. doi: 10.1016/j.kint.2020.06.024.
15. Sha S, Devineni D, Ghosh A et al. Canagliflozin, a novel inhibitor of sodium glucose co-transporter 2, dose dependently reduces calculated renal threshold for glucose excretion and increases urinary glucose excretion in healthy subjects. Diabetes Obes. Metab. 2011; 13:669–672. doi: 10.1111/j.1463-1326.2011.01406.x.

16. Devineni D, Morrow L, Hompesch M. Canagliflozin improves glycaemic control over 28 days in subjects with type 2 diabetes not optimally controlled on insulin. Diabetes Obes. Metab. 2012;14:539–545. doi: 10.1111/j.1463-1326.2012.01558.
17. Fioretto P, Zambon A, Rossato M et al. SGLT2 Inhibitors and the Diabetic Kidney. Diabetes Care. 2016;39:165–171. doi: 10.2337/dcS15-3006.
18. Xu B, Li S, Kang B et al. The current role of sodium-glucose cotransporter 2 inhibitors in type 2 diabetes mellitus management. Cardiovasc Diabetol. 2002;21:83. doi: 10.1186/s12933-022-01512-w.
19. Gilbert RE. Sodium-glucose linked transporter-2 inhibitors: Potential for renoprotection beyond blood glucose lowering? Kidney Int. 2014;86:693–700. doi: 10.1038/ki.2013.451.
20. Fonseca-Correa JI, Correa-Rotter R. Sodium-glucose cotransporter 2 inhibitors mechanisms of action: a review. Front Med. 2021;8:777861. doi: 10.3389/fmed.2021.777861.
21. Huang Y, Jiang Z, Wei Y. Efficacy and safety of the SGLT2 inhibitor dapagliflozin in type 1 diabetes: A meta-analysis of randomized controlled trials. Exp Ther Med. 2021;21(4):382. doi: 10.3892/etm.2021.9813.
22. Tanaka T, Higashijima Y, Wada T, Nangaku M. The potential for renoprotection with incretin-based drugs. Kidney Int. 2014; 86:701–711. doi: 10.1038/ki.2014.236.
23. Guyton J, Jeon M, Brooks A. Glucagon-like peptide 1 receptor agonists in type 1 diabetes mellitus. Am J Health Syst Pharm. 2019;76(21):1739-1748. doi: 10.1093/ajhp/zxz179.
24. Heinemann L, Nguyen KT, Nicole Y et al. Treating an Unconscious Patient With Diabetes Wearing a Device Attached to Their Body, Journal of Diabetes Science and Technology. 2002;16(3):583–586. doi: 10.1177/19322968221081888.
25. Kawanami D, Takashi Y, Muta Y et al. Mineralocorticoid Receptor Antagonists in Diabetic Kidney Disease. Front Pharmacol. 2021;12:754239. doi: 10.3389/fphar.2021.754239.
26. Dhaybi OA, Bakris GL. Non-steroidal Mineralocorticoid Antagonists: Prospects for Renoprotection in Diabetic Kidney Disease. Diabetes Obes. Metab. 2020;22 (1):69–76. doi: 10.1111/dom.13983.
27. Belden Z, Deiuliis JA, Dobre M, Rajagopalan S. The Role of the Mineralocorticoid Receptor in Inflammation: Focus on Kidney and Vasculature. Am. J. Nephrol. 2017;46:298–314. doi: 10.1159/000480652.
28. Alexandrou ME, Theodorakopoulou MP, Sarafidis PA. Role of Mineralocorticoid Receptor Antagonists in Diabetic Kidney Disease. Kidney Dial. 2022;2:163–182. doi:10.3390/kidneydial2020019.
29. Raina R, Chauvin A, Chakraborty R et al. The Role of Endothelin and Endothelin Antagonists in Chronic Kidney Disease. Kidney Dis. 2020;6:22–34. doi: 10.3390/kidneydial2020019.
30. Kittikulsuth W, Sullivan JC, Pollock DM. ET-1 actions in the kidney: evidence for sex differences. Br J Pharmacol. 2013;168(2):318–326. doi: 10.1111/j.1476-5381.2012.01922.x.
31. Kohan DE, Barton M. Endothelin and endothelin antagonists in chronic kidney disease. Kidney Int. 2014;86(5):896–904. doi: 10.1038/ki.2014.143.
32. Benigni A, Buelli S, Kohan DE. Endothelin-targeted new treatments for proteinuric and inflammatory glomerular diseases: focus on the added value to anti-renin-angiotensin system inhibition. Pediatr Nephrol. 2021;36(4):763–775. doi: 10.1007/s00467-020-04518-2.

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Conflict of interest:
The Authors declare no conflict of interest.

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A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article