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Effect of soluble receptor for advanced glycation end products (sRAGE) in the blood for the development of cardiovascular complications - vascular type 2 diabetes

Wpływ poziomu rozpuszczalnego receptora dla końcowych produktów zaawansowanej glikacji (sRAGE) we krwi na rozwój powikłań sercowo – naczyniowych w cukrzycy typu 2

Mateusz Czerwiński[1], Izabela Mirlak[1], Kamil Radajewski[1], Natalia Ciesielska[1], Walery Zukow[2], Remigiusz Sokołowski[1]

[1]Department and Clinic of Geriatrics, Nicolaus Copernicus University Collegium Medicum, Bydgoszcz, Poland
[2]Department Physical Culture, Health and Tourism, Kazimierz Wielki University, Bydgoszcz, Poland

Keywords: Type 2 diabetes, cardio - vascular advanced glycation end products (AGEs), a soluble receptor for advanced glycation end products (sRAGE).

Słowa kluczowe: Cukrzyca typu 2, powikłania sercowo – naczyniowe, końcowe produkty zaawansowanej glikacji (AGE), rozpuszczalny receptor dla końcowych produktów zaawansowanej glikacji (sRAGE).

Abstract

Introduction. Today, type 2 diabetes as a problem of almost unimaginable scale requires increased vigilance doctors aim accurate diagnosis and the detection and treatment of late complications of the disease. This disease threatens people primarily in connection with its late complications of micro-and macrovascular and neuropathy, significantly impairing the quality of life of many patients. To effectively treat it alone is not enough control of hyperglycemia, the main symptom of diabetes. In connection with the development of our knowledge about this disease is increasing need for new predictive markers that would allow better detection, treatment and control of diabetes. One of them is soluble receptor for advanced glycation end products (sRAGE) which was able to significantly increase diabetic hyperglycemia. The determination of this factor may become in the future, the key to take control over the epidemic of the XXI century, which is type 2 diabetes
Purpose. Effect of soluble receptor for advanced glycation end products (sRAGE) in plasma for the development of cardiovascular complications - vascular type 2 diabetes
Materials and methods. Using the key words searched international bibliographic databases: *Embase, Medline, ScienceDirect, Web of Sciences*. We analyzed clinical trials, published in English in international journals.
Results. SRAGE acts as a trap for capturing AGE and transports them from the plasma and then to the liver spleen, where they are degraded.He is a very important function to protect the system against the toxic influence of AGEs-RAGE complex. This limits the reaction cascade thus induced by binding of AGEs with their cellular receptor RAGE. In addition, sRAGE may be a useful

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biomarker for indicating the individual differences in susceptibility to diabetes type 2 diabetic retinopathy.

Conclusions. In studies to date indicate that sRAGE a vital protective role against the toxic influence of AGEs-RAGE complex. However, we still need for further research on the potential marker and associated signaling mechanisms, because they can contribute to a better control of diabetes and to improve the prognosis and therapeutic effects.

Streszczenie

Wstęp. Współcześnie, cukrzyca typu 2 jako problem o wręcz niewyobrażalnej skali wymaga od lekarzy wzmożonej czujności celem dokładnej diagnostyki oraz wykrywania i leczenia późnych powikłań tej choroby. Choroba ta zagraża ludziom przede wszystkim w związku z jej późnymi powikłaniami mikro i makronaczyniowymi oraz neuropatią, znacznie pogarszając jakość życia wielu pacjentów. Aby skutecznie ją leczyć nie wystarczy sama kontrola hiperglikemii, głównego objawu cukrzycy. W związku z rozwijaniem naszej wiedzy na temat tej choroby rośnie potrzeba poszukiwania nowych markerów predykcyjnych, które umożliwiałyby lepsze wykrywanie, leczenie i kontrolę cukrzycy. Jednym z nich jest rozpuszczalny receptor dla końcowych produktów zaawansowanej glikacji (sRAGE), którego poziom istotnie wzrasta w stanie hiperglikemii cukrzycowej. Oznaczanie tego czynnika może stać się w przyszłości kluczem do zapanowania nad epidemią XXI wieku jaką jest cukrzyca typu 2.

Cel. Wpływ poziomu rozpuszczalnego receptora dla końcowych produktów zaawansowanej glikacji (sRAGE) w osoczu na rozwój powikłań sercowo – naczyniowych w cukrzycy typu 2.

Materiały i metody. Posługując się słowami kluczowymi przeszukano zagraniczne bazy bibliograficzne: *Embase, Medline, ScienceDirect, Web of Science.* Przeanalizowano badania kliniczne, opublikowane w języku angielskim w międzynarodowych czasopismach.

Wyniki. sRAGE działa jako pułapka dla AGE i wychwytując je z osocza transportuje następnie do śledziony oraz wątroby, gdzie są degradowane. Pełni to bardzo ważną funkcję chroniącą ustrój przed toksycznym wpływem kompleksów RAGE-AGE. Ogranicza to w ten sposób kaskadę reakcji wywoływaną przez wiązanie się AGE z jej komórkowym receptorem RAGE. Ponadto sRAGE może być użytecznym biomarkerem wskazującym na indywidualne różnice w podatności chorych na cukrzycę typu 2 na rozwój retinopatii cukrzycowej.

Wnioski. Z przeprowadzonych dotychczas badań wynika, że sRAGE pełni znaczącą rolę ochronną przed toksycznym wpływem kompleksów RAGE-AGE. Jakkolwiek, wciąż potrzeba dalszych badań nad tym potencjalnym markerem i związanymi z nim mechanizmami sygnałowymi, ponieważ mogą się one przyczynić do lepszej kontroli cukrzycy oraz poprawy rokowania i efektów terapeutycznych.

Introduction

Diabetes, especially the type 2, is now a huge problem in even scale, both in Poland and in the world. Currently, it is one of the most serious and common health problems with which every physician meets every day in professional practice. In 2012, diabetes suffered more than 371 million of the world population, but almost half of the patients with diabetes were undiagnosed, and died at her 4.8 million people. 10% of the adult population in Poland diabetes. It is more than 3

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million people. Another 5 million are patients with glucose intolerance, and the 2,011 years diabetes was the cause of over 29,000 deaths. This disease is both one of the most important risk factors for cardio - vascular, but it is considered a risk equivalent, synonymous with the presence of symptomatic cardiovascular disease - vascular. Patients with type 2 diabetes have even 2-4 times higher risk of developing peripheral vascular disease, stroke, or coronary heart disease than the healthy population. This disease causes a greater hospital mortality and post-hospital patients after myocardial infarction, a higher risk of complications associated with myocardial infarction and the risk of retinopathy, nephropathy, and neuropathy. The primary cause of high morbidity and mortality in patients with diabetes are cardio - vascular diseases. Therefore, the search for new markers of cardiovascular risk in diabetic vascular serves ever better understanding of the disease, its control and treatment. [1]

Purpose.

Effect of soluble receptor for advanced glycation end products (sRAGE) in plasma for the development of cardiovascular complications - vascular type 2 diabetes

Materials and methods.

Using key words: *Type 2 diabetes, cardio - vascular advanced glycation end products (AGEs), a soluble receptor for advanced glycation end products (sRAGE)* Foreign searched bibliographic databases: *Embase, Medline, Science Direct, Web of Science.* We analyzed clinical trials, published in English in international journals.

Results and Discussion.

Receptors advanced glycation end products.

Glycation is a reaction involving non-enzymatic modification of proteins primarily by simple sugars such as glucose and fructose, as well as by the carbonyl compounds. In this complex process consisting of a number of transformations called the Maillard reaction, which results in the so-called first. early glycation products. In the next stages of this process is related to oxidative stress and carbonyl stress. Finally, in the final stage by condensation and crosslinking products resulting in the formation highly crosslinked irreversible advanced glycation end products (AGE) with a large number of crosslinks of variable molecular weight. Under conditions of full AGE homeostasis are decomposed in the lysosomes of cells, and the degradation products are transported into the circulation and excreted in the urine. Some role in the removal of AGEs from the blood through the liver fully Kupffer cells and the endothelium. Glycation occurs both inside and extracellularly and under physiological conditions is a continuous process extending throughout life, leading to aging. In this way are mainly modified proteins such as collagen, lens crystallin or serum albumin. As mentioned earlier, AGEs are proteins having a large amount of highly crosslinked. This makes these proteins become more rigid, they lose their function, are more resistant to degradation and therefore removed from the body more difficult. The accumulation of such proteins results in stiffening of the walls of blood vessels and tissues. Therefore, the phenomenon of glycation is associated with the development of age-related diseases. By using antibodies specific for certain AGE shown that advanced glycation end products build up in the skin, lungs, kidneys, intestines, heart and blood vessels, and in the spinal cord, not only in the elderly, but also in patients with diabetes. Chronic hyperglycemia because it stimulates the glycation process which is important in the earlier accumulation of AGEs in the circulation, tissues and organs. This correlates significantly with the development of late complications of diabetes, and the

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pathophysiological changes in the disease are additionally stimulated by oxidative stress accompanying the process of glycation. AGE bind to receptors on the surface of various cells so that intracellular processes. Best known group of these receptors are known. RAGE receptors. They are located on the surface of macrophages, hepatocytes, endothelial cells and vascular smooth muscle, mesangial cells, or nerve cells. These receptors are cell surface protein of the immunoglobulin superfamily. RAGE receptor expression on the cell surface can be induced due to their severe increase in the activation by ligands for RAGE, or AGE. This happens precisely in patients with diabetes. This feedback stimulation leads to permanent damage of cells and tissues. This receptor has many different structural forms. One of the detected in the circulation is secreted form thereof, or soluble RAGE (sRAGE) which is formed by proteolysis of RAGE. In addition, sRAGE has its own unique form called endogenous secreted sRAGE (esRAGE).

The role of sRAGE is to capture AGE and transporting them to the liver and spleen, where they are degraded. It is a very important function to protect against the toxic influence of AGEs-RAGE complex. SRAGE levels in the state of hyperglycemia and hypercholesterolemia is much lower than in healthy subjects, and statins raise its level. Moreover, in patients without diabetes sRAGE concentration grows with AGE and it is closely related to the BMI. The increase in the concentration of serum sRAGE is also influenced by factors such as gender and alcohol consumption.

Good knowledge of RAGE-ligand interactions and associated signaling mechanisms may be important in the therapeutic aspect. [2]

Diabetic retinopathy

Diabetic retinopathy is one of the most common ocular complications of type 2 diabetes and is responsible for the majority of new cases of blindness in adults between 20 and 74 years of age with diabetes. Among the risk factors for diabetic retinopathy, the most important of them is the duration of diabetes. The *Wisconsin Epidemiologic* study *of Diabetic Retinopathy Study* (WSEDR) demonstrated that younger patients with diabetes after 3 years of diabetes retinopathy percentage was 8% after 5 years of 25% after 10 years of 60% and 80% after 15 years. Furthermore, the incidence of new cases of retinopathy increases with the duration of the disease. In younger patients, patients with diabetes 4-year incidence of retinopathy increased from 0% in the five years to almost 30% after 13-14 years of diabetes. In the study shown WESDR prevalence of retinopathy, where 3.6% of patients with type 1 diabetes and in 1.6% of patients with type 2 diabetes is defined as the blind. Diabetic retinopathy was the cause of this condition in 86% of cases of type 1 diabetes and one third of cases of type 2 diabetes [3]

Changes in the vessels of the retina in diabetes are gradual progression. Beginning are benign, no proliferation, which increase vascular permeability, which act so called. non-proliferative retinopathy (NPDR), in the course of which there is a gradual closing of blood vessels light. The next step is to move in the proliferative retinopathy (PDR), in which there is a proliferation of new blood vessels of the retina. During the development of retinopathy may develop macular edema, and thickening of the retina, which causes an increase in vascular permeability, and exudative changes. At each stage of retinopathy may be a faster progression in the results of other factors such as pregnancy, puberty, poor glycemic control or cataract surgery.

The cause of vision loss in the case of this complication is the proliferation of new blood vessels in the retina tissue and contraction leads to distortion of the retina and retinal detachment. The result of this is often to irreversible vision loss. In the case of newly formed vessels can lead to vitreous hemorrhage and hemorrhage before retina.

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Now, using the latest methods of treatment can in many patients with diabetes effectively prevent or delay the development of diabetic retinopathy, and blindness. This mainly concerns the proper glycemic control and blood pressure. Moreover, implementation of timely laser treatment can prevent vision loss in many patients with advanced diabetic retinopathy or macular changes.

In the DCCT *(Diabetes Control and Complications Trial)* investigated the effect of glycemic control on the progression of diabetic retinopathy. Intensive diabetes treatment (insulin administered three or more times per day or continuous subcutaneous insulin infusion) resulted in a reduction in the risk of retinopathy 0 76% (95% CI 62-85) in the primary prevention (patients with no identified retinopathy at baseline) and reduced the risk of progression of retinopathy by 54% (CI 39-66) in the secondary prevention (patients diagnosed with non-proliferative retinopathy degree from the minimum to moderate).

Glycemic control in order to prevent the development and progression of retinopathy was also demonstrated in the study of *United Kingdom Prospective Diabetes Study* (UKPDS), in which the overall incidence of microvascular complications decreased by 25% in patients with type 2 diabetes treated intensively. The decrease in HbA1c of 1% was associated with a 35 percent reduction in risk of microvascular complications. This study also examined the effect on blood pressure control, the development of complications such as diabetic retinopathy. In patients with intensive antihypertensive treatment were observed 34 percent reduction in progression of retinopathy and a 47-percent reduction in the risk of visual impairment in lowering the pressure of 10/5 mmHg.

The DRS *(Diabetic Retinopathy Study)* demonstrated that photocoagulation treatment significantly reduced the rate of loss of vision, wherein the beneficial effect was most pronounced among patients with multiple risk factors for retinopathy. On the other hand, in patients with high risk features of this effect was much smaller. Due to the fact that signs of retinopathy are scarce or not present at all, must be continuously and systematically monitored patients at risk of developing. [3]

Hyperglycemia is a known pathogenetic factor of diabetic complications. It causes increased production of free radicals by autooxidation of glucose, the imbalance between oxidizing and reducing agents, the interaction of AGEs with their receptors, oxidative phosphorylation, the action of enzymes such as lipoxygenase, cytochrome P450 and nitric oxide synthase. Excessive production of reactive oxygen species leads to loss of both enzymatic and non-enzymatic antioxidants such as which inevitably leads to damage to the cells.

In the hyperglycemic state of nonenzymatic glycation occurs which results in the formation of advanced glycation end products (AGE). One well-known of this group of compounds is pentosidine. AGE formation is accompanied by intense oxidation. There is evidence that the process of AGE-binding soluble form of the receptor (sRAGE) is involved in the formation of microvascular complications of diabetes. sRAGE is the RAGE isoform lacking the transmembrane domain, which acts as an inhibitor of vascular injury mediated by AGE-RAGE complexes. However, sRAGE relationship with other biomarkers of oxidative glycation such as pentosidine and advanced glycation products (AOPP) and the formation of diabetic retinopathy is still unclear.

In their study, Zhi Xiang et al have demonstrated that the ratio of the level of pentosidine sRAGE may be a potential risk factor in the development of retinopathy in Type 2 diabetes Namely Patients with type 2 diabetic retinopathy and retinopathy had significantly higher levels of pentosidine, sRAGE, AOPP and lower plasma levels of antioxidant enzymes compared to the control group. Index sRAGE / pentosidine in patients with diabetic retinopathy was significantly lower than in patients without retinopathy. Patients with proliferative retinopathy had significantly

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higher levels of pentosidine, sRAGE, AOPP and index sRAGE / pentosidine levels than patients with non-proliferative retinopathy. In this study the risk factors of diabetic retinopathy was found high levels of HbA1c, long-lasting diabetes type 2 and a low rate of sRAGE / pentosidine. The results showed that the rate of sRAGE / pentosidine could be considered as a risk factor in the development of diabetic retinopathy in type 2 diabetes because the ratio positively correlates with the severity of retinopathy. [4]

Predictive factors of diabetic complications remain a major role in the prevention of these complications and controlling. Kerkeni et al. in their study of the Tunisian population demonstrated that the level of AGEs and pentosidine sRAGE in plasma are associated with diabetic retinopathy. The duration of diabetes and the level of pentosidine were independently associated with the severity of diabetic retinopathy. [5]

Test results Al-Mesallama et al indicate that the sRAGE is an endogenous factor that protects against the onset of accelerated diabetic retinopathy. sRAGE protection factor is a potential as acting as a trap for capturing and AGE them from the plasma, thereby reduces the cascade reaction caused by binding of AGEs with their cellular receptor RAGE. The results of the study showed that plasma levels of sRAGE was significantly lower in patients with both nonproliferative and proliferative diabetic retinopathy in patients compared to healthy controls and patients without retinopathy. There was no significant difference between sRAGE in plasma levels in healthy control subjects and diabetic patients without retinopathy. The study shows that sRAGE, limiting interactions AGE RAGE receptor on the cell surface can protect blood vessels from the toxic effects of AGE. In addition, the results indicate that sRAGE may be a useful biomarker for indicating the individual differences in susceptibility to diabetes type 2 diabetic retinopathy.

In addition, in the aforementioned study plasma levels of the compound sought soluble form of VCAM-1 (sVCAM-1), nitrogen oxide, and sRAGE severity of diabetic retinopathy. [6]

Atherosclerosis

Atherosclerosis is a progressive inflammatory disease characterized by endothelial dysfunction, accumulation of lipids and fibrous elements in the arterial wall. [7] Hyperglycemia is a risk factor of atherosclerosis. Consequently, it has become extremely important to know various kinds of metabolic pathways and reactions that are involved in the formation of atherosclerotic plaques in the state of hyperglycemia. One of the most important research objectives in this regard have become interactions between AGE and RAGE receptor, which exists both as a transmembrane receptor and as a circulating form (sRAGE).

Diabetic vasculopathy significant factor is endothelial function disorder, and its key role in the inflammatory cytokine plays a dysfunction of TNF - α (tumor necrosis factor-α), which among others. Oxidative stress is responsible for. On the other hand, hyperglycemia contributes to the formation of AGE (advanced glycation end products). AGE and its receptor (RAGE) stimulate the production of peroxide which aggravate oxidative stress and interfere with the bioavailability of nitric oxide (NO). In patients with diabetes, AGEs accumulate in the blood and arteries faster than normal. [8] On the surface of endothelial cells which is multiligand receptor RAGE, which is generally at a low level at the time of homeostasis and increases during stress or trauma. [12] Diabetic rats treated aminoguanidine (substances that prevent the formation of AGEs) showed improvement in the nerves and the blood supply to a gradual improvement of signal transmission by nerves. [9] This suggests that blocking the formation of AGEs can be used in treatment of diabetic neuropathy. It is believed that the arrangement of AGE / RAGE contribute to endothelial dysfunction, both directly and by regulating the expression of TNF-α in Type 2 diabetes [17]

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Advanced glycation end products (AGEs) and their receptors are strongly involved in the development of diabetic complications. Receptors stimulated by AGEs (rages) induce inflammation and contribute to disease progression. [11] In this study, it was found decreased levels of sRAGE in patients with hypertension and ischemic heart disease without diabetes compared to healthy subjects. [10] In other studies, the low level of sRAGE was significantly associated with the risk of diabetes, coronary heart disease and increased mortality, but did not correlate with ischemic stroke. They showed that low levels of sRAGE was a determinant of the risk and mortality in patients with chronic diseases, and correlated with inflammation. [11] RAGE plays a role in the pathogenesis of myocardial infarction by the activation of RAGE-dependent cells, causing oxidative stress and inflammatory, proliferative responses leading to vascular dysfunction. [12]

There is a strong correlation between the level of sRAGE and acute coronary incidents, which confirms the clinical relevance of these biomarkers as indicators of inflammation. SRAGE in plasma concentration is inversely correlated with total triglyceride level and cholesterol. Moreover, the level does not differ sRAGE in patients with acute coronary syndrome disaggregated coronary quantity. Lower levels of sRAGE concentration occurs in patients with acute coronary syndrome patients than instable angina. [9] The axis-AGE RAGE may be involved in plaque rupture and erosion of the endothelium, which constitutes the two main causes of coronary thrombosis. Low levels can trigger an increased sRAGE AGEs-RAGE interaction at the cell surface, resulting in increased production of cytokines [14], and reactive oxygen species [15]. Over-expression of matrix metalloproteinases, which are activated by reactive oxygen Foma weakens the atheromatous plaque and causes it to break. [16] In addition, the interaction between HMGB1 and RAGE can activate inflammatory pathways. [17]

Diabetic nephropathy

Diabetic nephropathy (NC) occurs in 30% of people with type 1 diabetes and 25-40% of people with type 2 diabetes. NC is the most common cause of end-stage renal disease (ESRD) in the west, which represents more than 50% of new cases of kidney failure. Patients who have type 2 diabetes coexists and V degree of chronic kidney disease have a poor prognosis because of the high risk of cardiovascular events [18]. Poor diabetes control and prolonged hyperglycemia induced tissue damage in the kidney which is closely associated with the excessive accumulation of advanced glycation end products of proteins (AGEs), activation of aldose reductase and increased activity of the renin-angiotensin-aldosterone system (RAAS) and subsequent increase in glomerular filtration rate (GFR) . [20] Advanced glycation end products of some of the main proteins include molecular structures such as CML (carboxymethyllysine) and pentane (pentosidine), whose accumulation in the tissue affects the structure and function of matrix proteins [19]. Accumulation of AGEs in the kidneys and other tissues in diabetic patients has been associated with the development of diabetic nephropathy and other microvascular diseases in the course. [22]

That two basic mechanisms of tissue damage by AGE: 1) change in the cell matrix structure of nonenzymatic glycation of proteins to form protein binding and 2) the modulation of cell function by interacting with specific receptors on the cell surface. The best known receptor is RAGE receptor [23]. The binding of AGE RAGE receptor pathway activates cellular mechanisms associated with the production of transforming growth factor (TGF), vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF), whose concentration is elevated in diabetic nephropathy, it is believed that the reason for this is also for the development of other complications of diabetes. [24, 25]. There is also increased production of cytokines which are mediators of inflammation, including the above-mentioned cause damage to podocytes, mesangial cell proliferation, and changes in the glomerular basement membrane, which initially manifested by

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proteinuria (by increasing the permeability of the basement membrane). Prolonged action of inflammatory mediators will result in glazing of glomerular and interstitial fibrosis which is a consequence of the development of renal failure.

The receptor for advanced glycation end products (RAGE) has been associated with a complication of diabetes which are microangiopathy. There are several arguments suggesting that the soluble isoform of RAGE (sRAGE) may protect against damage to the blood vessels from the damaging effects of AGE. A study was conducted wherein the measured levels of sRAGE and CML (which characterizes glycation end products of proteins associated with diabetic microangiopathy) in serum of patients with diabetes mellitus with or without microvascular complications. SRAGE levels in the blood were similar in both trials, the control in patients with diabetes without microvascular complications. In patients with complications sRAGE average level in the blood was significantly reduced (1068 ± 231pg/mL) compared to patients without diabetes complications ($p = 0.028$). CML protein plasma concentrations increased in all patients with diabetes, but to a greater extent in patients who had microvascular complications. Low levels of sRAGE concentration and high concentration of protein CML patients who develop complications of diabetes as microangipoathia confirms the hypothesis that the level of concentration of sRAGE protects the vessel ahead of glycation of proteins. [26] Because little is known about the regulation of endogenous levels of sRAGE, also attempted to determine whether serum levels of sRAGE affects circulating AGEs and the severity of nephropathy in patients with type 2 diabetes SRAGE levels were measured in diabetic patients with proteinuria, microalbuminuria and normoalbuminuria. The study showed that the highest levels of sRAGE was in patients with proteinuria, which also correlates with the severity of diabetic nephropathy. [27]

In another study attempted to demonstrate the relationship between sRAGE, renal function and genetic variation in the gene Ager diabetic patients. The study was conducted diabetes type 1, 2 or LADA with normoalbuminuria (patients without nephropathy) or diabetic nephropathy. The level of sRAGE (as assessed by ELISA) was significantly higher in patients with diabetic nephropathy in patients with non normoalbuminuria ($p = 0.007$) and positively correlated with age, levels of urea, creatinine and albuminuria amount and the concentration of protein glycation end products (measured by the spectrophotometer) . However negatively correlated with GFR (all $p < 0.05$). Size glomerular filtration rate was the only independent variable associated with sRAGE ($p = 0.047$). In conclusion the study, GFR is a major determinant of sRAGE concentration and a gradual increase in sRAGE in patients with progressive renal impairment and is associated with serum AGEs. [21]

In a study in mice in which diabetes was induced by streptozotocine, which is characterized by defects in the AT2 receptor. Next, the effect of the protective evaluated blockade of advanced glycation end products (RAGE) by modulating the AT2 receptor on the progression of diabetic renal disease. It has been shown that in mice in which diabetes and defect occur RAGE, albuminuria is smaller. Are also minimized: hyperfiltration and severity of glomerular sclerosis. The study authors conclude that RAGE is a modulator of expression receptorówAT2. It seems, therefore, that the integration of RAGE-AT2 plays an important role in the progression of diabetic nephropathy. [23] Also, several recent studies have demonstrated that angiotensin receptor antagonists ((ARB) and ACE inhibitors lower blood AGE RAGE and change the operation [28]. These effects suggest that these drugs may provide protection of the kidney by inhibiting the expression of VEGF and TGF that are responsible for epithelial damage and fibrosis, which are characteristic of diabetic nephropathy. [18]

Results

Czerwiński Mateusz, Mirlak Izabela, Radajewski Kamil, Ciesielska Natalia, Zukow Walery, Sokołowski Remigiusz. Effect of soluble receptor for advanced glycation end products (sRAGE) in the blood for the development of cardiovascular complications - vascular type 2 diabetes = Wpływ poziomu rozpuszczalnego receptora dla końcowych produktów zaawansowanej glikacji (sRAGE) we krwi na rozwój powikłań sercowo – naczyniowych w cukrzycy typu 2. Journal of Health Sciences. 2014;04(06):011-020. ISSN 1429-9623 / 2300-665X.

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In studies to date indicate that sRAGE a vital protective role against the toxic influence of AGEs-RAGE complex. Its level in diabetes is significantly lower than in healthy populations which contribute to the further spread of inflammation, oxidative stress, endothelial damage, and finally diabetic complications. However, we still need for further research on the potential marker and associated signaling mechanisms, because they can contribute to a better control of diabetes and to improve the prognosis and therapeutic effects.

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