ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

DIABETIC RETINOPATHY (LITERATURE REVIEW)

Yuldasheva M. Nodirakhon MD

RSSPMC Endocrinology named after

Acad.Y.KH.Turakulov,

The head of the Department of

Retinal and Optic Nerve Pathology,

Doctor of Medical Sciences.

Fazliddinova Sh. Mekhribonu MD

Tashkent Pediatric Medical Institute

Annotation. The article provides a review of the literature on the topic of diabetic retinopathy. In this regard, reliable literature is used and current information is highlighted.

Key words: diabetic retinopathy, type 2 diabetes mellitus, dynamics, symptoms.

Abstract. Retinal damage is one of the specific complications of diabetes mellitus, which is the main cause of blindness in this category of patients. Currently, there are 5 million blind people and 180 million with low vision in the world. Presumably, by 2030, the number of blind people will increase by 27%, and people with low vision by 45% (WHO, 2002). Diabetic retinopathy (DR) was first described more than 100 years ago by Mac Kenzi in 1879, however, today this complication of diabetes mellitus is a major problem for health care.

Despite the widespread introduction of new effective drugs and instrumental methods for diagnosis and treatment, DR still remains the main cause of vision loss. Different figures are given for the prevalence of DR in type 1 and type 2 diabetes in different countries. In patients with undiagnosed type 2 diabetes, signs of DR are detected at the time of diagnosis in 7-30% of patients. Moreover, proliferative DR is not a big problem for them, in contrast to type 1 diabetes, while diabetic maculopathy becomes the main cause of visual acuity deterioration. Among the factors causing DR progression are the degree of compensation of carbohydrate metabolism, duration of diabetes, age, arterial hypertension, nephropathy, pregnancy, and smoking. DR is characterized by the presence of specific vascular anomalies andRetinal damage is one of the specific complications of diabetes mellitus, which is the main cause of blindness in this category of patients. Currently, there are 5 million blind people and 180 million with reduced vision in the world. Presumably, by 2030, the number of blind people will increase by 27%, and people with reduced vision by 45% (WHO, 2002). Diabetic retinopathy (DR) was first described over 100 years ago by Mac Kenzi in 1879, however, this complication of diabetes mellitus still represents a major health problem today. Despite the widespread introduction of new effective drugs and instrumental methods for diagnosis and treatment, DR remains the main cause of vision loss. Different figures are

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

given for the prevalence of DR in diabetes mellitus types 1 and 2 in different countries. In patients with undiagnosed DM 2, signs of DR are detected at the time of diagnosis of the disease in 7-30% of patients. Moreover, proliferative DR is not a big problem for them, in contrast to DM 1, while diabetic maculopathy becomes the main cause of visual acuity deterioration. Among the factors causing DR progression, the degree of compensation of carbohydrate metabolism, duration of diabetes, age, arterial hypertension, nephropathy, pregnancy, and smoking are distinguished. DR is characterized by the presence of specific anomalies of the vessels and tissues of the retina. It is characterized by a change in the caliber and tortuosity of the retinal vessels, the appearance of microaneurysms, hemorrhages, edema, hard and soft exudates, newly formed vessels, glial proliferation, and vitreoretinal traction. The study of the morphological picture of DR revealed thickening of the basement membrane, loss of capillary pericytes, and as a result, the development of capillary acellularity, which leads to the fact that the microcapillaries are represented by tubes consisting of the basement membrane. Oxygen perfusion through the wall of the latter deteriorates and retinal ischemia and hypoxia develop. All this leads to the development of neovascularization, the newly formed vessels, in turn, are functionally defective and become a new source of hemorrhages. According to the authors, the retina may be especially sensitive to damage, since it has the highest rate of glucose and oxygen utilization per unit weight than any other tissue, and has a high activity of the glycolytic and anaerobic pathological pathway of glucose metabolism.

It is an undeniable fact that chronic hyperglycemia plays the main role in the development of DR. There are data obtained as a result of multicenter studies performed in diabetes mellitus, confirming the primary importance of normoglycemia. Maintaining the state of normoglycemia in patients with type 1 diabetes confirmed a significant reduction in the risk of progression of microvascular complications.

The results of the international study – Diabetes Control and Complication Trial showed that maintaining satisfactory glycemic control in a group of people without vascular complications contributed to a decrease in the risk of developing: diabetic retinopathy – by 76%, diabetic neuropathy – by 60%, microalbuminuria – by 30%, albuminuria – by 54%. A multicenter study conducted in patients with type 2 diabetes in the UK and its results were presented in 1998. Normoglycemia reduces the risk of complications of diabetes by 12%, myocardial infarction by 16%, microvascular complications by 25%. BP control reduces all complications by 24%, strokes by 44%, heart failure by 56%, microvascular complications by 37%, mortality by 32%.

The age of patients with type 1 diabetes can be considered as a risk factor. It is well known that DR is extremely rare in childhood. However, with the onset of puberty, microvascular complications, including diabetic retinopathy, rapidly progress. This is due to the fact that during this period, there is a powerful hormonal restructuring, accompanied by the production of a large number of counter-insular factors - pituitary tropic hormones, sex steroids, growth factors. The decompensation of diabetes that develops during this period can be explained by a rapid increase in body weight and, as a result, an increase in the need for insulin. The puberty period is the most threatening in terms of DR progression. The participation of hypertension as a major risk factor in the development and progression of DR has been proven. The results of the Wiscongin Epidemiological Study of Diabetic Retinopathy (WESDR) showed that an increase in diastolic pressure by every 10 mm

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

Hg. increases the risk of progression of proliferative DR by 50%. There is data on the relationship between systemic hypertension and the frequency of development of exudates, hemorrhages, and other severe retinal damage. The presence of dyslipidemia also adversely affects the course of DR. Clinical data on a close relationship between the level of cholesterol and the presence of hard exudates in the retina have been published. Thus, an increase in the cholesterol level by 50 mg% in elderly patients with type 1 diabetes caused an increase in the frequency of hard exudates in the retina by 50% (WESDR). In these groups of ETDRS (barby Treatment of Diabetic Retinopathy Study), a close relationship was shown between elevated levels of cholesterol, low-density lipoproteins (LDL) and triacylglycerides (TG) with the frequency of detection of hard exudates in the retina.

The relationship between smoking and retinopathy progression is unclear. Smoking probably causes hypoxia and cerebral vasospasm, which affects DR progression. The WESDR study (1998) found a relationship between different HLA antigens and DR, a relationship with glycated hemoglobin levels, hypertension, diabetes duration, and increasing proteinuria. Proliferative retinopathy was found to develop 5.4 times more frequently compared to the group without HLA haplotypes DR3 and DR4. At the same time, observation of a cohort of patients with HLA DR4 did not reveal any progression of DR compared to the group without these antigens. This process is probably controlled to a greater extent by other risk factors. The biochemical processes that lead to morphological changes in the retina have been studied quite well. The trigger is chronic hyperglycemia, which leads to activation of aldose reductase activity, increased non-enzymatic glycation of proteins, changes in myo-inositol phosphatidimenositol mechanism, increased activity of protein kinase C, decreased heparin sulfate proteoglycan, increased glucose autoxidation, changes in the activity and levels of vasoactive substances such as endothelin, prostanoids, nitric oxide, histamine, etc. One of the mechanisms of the pathological process may be thickening of the capillary basement membrane, which in turn, hypothetically leads to closure of the retinal capillaries. However, this hypothesis was not confirmed, since the use of aldose reductase inhibitors in patients with type 1 diabetes did not prevent the progression of DR with their help.

The relationship between non-enzymatic and/or enzymatic glycation of proteins and the progression of diabetic retinopathy has been proven. According to the authors, diabetic retinopathy develops as a consequence of retinal ischemia. Vascular damage, consisting of thickening of the basement membrane, loss of pericytes, focal proliferation of endothelial cells, obliteration of capillaries, the appearance of microvascular shunts - this entire complex of lesions is diagnosed as diabetic microangiopathy. In addition to damage to the vessel wall, there is a change in blood viscosity and properties of formed elements of the blood. Hyperglycemia, which is a consequence of insulin deficiency, causes an increase in the release of growth hormone. An increase in the level of growth hormone in conditions of hypoinsulinemia changes the synthesis of proteins by hepatocytes, which leads to dysproteinemia; increased fibrinogen and α2-globulin levels enhance erythrocyte aggregation, hyperglycemia worsens prostocyclin production by endothelial cells; increased erythrocyte and platelet aggregation causes hemodynamic disturbances in the microcirculation system; impaired blood flow in the microcirculation system leads to hypoxia and retinal ischemia; hypoxia and retinal ischemia cause excessive production of vasoproliferative growth factor, which stimulates the growth of new vessels around the optic nerve head and in other areas of the retina. Vasoproliferative factors are peptides with

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

pronounced mitogenic properties. Similar properties are attributed to fibroblast growth factors - FGF, vascular endothelial factor - VEGF, insulin-like growth factor - IGF and others.

Thus, chronic hyperglycemia, being the initiating factor in the development of diabetic retinopathy, causes a number of biochemical disorders. This is followed by functional changes in the retina: slowing of blood flow and oxygen saturation, disruption of retinal electrophysiology, increased capillary permeability.

All this leads to morphological changes in the retinal vessels: loss of pericytes, thickening of the basement membrane, development of capillary acellularity, desolation of capillaries, formation of microaneurysms and hemorrhages, proliferation of the endothelium, neovascularization.

Classification of diabetic retinopathy

Currently, most countries use the classification proposed by Kohner E. et al. There are three stages: Stage I – non-proliferative DR (there are microaneurysms, hemorrhages, edema, exudates; the indicated pathophysiological changes are not sharply expressed and are isolated); Stage II – preproliferative DR (characterized by the presence of venous anomalies, a large amount of exudates, multiple large retinal hemorrhages); Stage III – proliferative DR (there are massive hemorrhages in the retina, vitreous body, neovascularization of the optic nerve head and/or peripheral areas of the retina, fibrous tissue in the area of preretinal hemorrhages, vitreoretinal tractions and retinal detachment). Newly formed vessels of the iris (rubeosis) are often the cause of secondary glaucoma. It should be noted that in the early stages of diabetic retinopathy, there are no changes in visual acuity, and therefore patients do not seek help. In this regard, the importance of screening for diabetic retinopathy increases.

Treatment of diabetic retinopathy consists primarily in reducing risk factors and includes control of hyperglycemia, hypertension, hyperlipidemia, detection and treatment of retinal damage itself. At present, the issue of the need to maintain a high degree of compensation of carbohydrate metabolism in all patients with diabetes has been clearly resolved. The appearance of fresh hemorrhages in the retina after hypoglycemia has been established. For this reason, it is necessary to select adequate hypoglycemic therapy, gradually achieving a decrease in glycated hemoglobin (HbA1c) by about 1% per month.

A number of drugs were used for drug treatment of DR: anabolic steroids, drugs that prevent platelet aggregation (aspirin, dipyridamole, ticlopidine), aldose reductase inhibitors, clofibrate, pravastatin, aminoguanidine, ACE inhibitors, hormonal antagonists of growth hormone (octreotide, somatostatin), protein kinase C inhibitors. The latter drugs reduce the production of various growth factors that play a decisive role in the development of neovascularization. A promising direction in conducting research on the effective treatment and prevention of diabetic retinopathy, especially in the early stages of its development, are herbal preparations, the advantage of which is determined by low toxicity, "softness" and a wide range of pharmacological effects. Complex herbal therapy as a means of additional treatment in combination with synthetic drugs can find application in the initial stages of the disease, at the stage of anti-relapse and rehabilitation therapy.

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

Conclusion

It is necessary to conduct the first examination by an ophthalmologist 1.5-2 years after the onset of the disease in patients with type 1 diabetes and together with the diagnosis in patients with type 2 diabetes. In childhood, the first examinations should begin at the age of 10 (from the beginning of puberty).

If the disease is progressing favorably, these examinations should be repeated once a year, if pathology is detected - once every 3-6 months. In the presence of additional risk factors (pregnancy, nephropathy, arterial hypertension), the question of the frequency of examinations is decided individually. If complaints of a sudden decrease in visual acuity appear, it is necessary to urgently refer the patient to an ophthalmologist.

Thus, a promising direction in the treatment of diabetic retinopathy remains the education of patients and doctors, achieving the highest possible level of glucose and blood pressure control throughout the life of a patient with diabetes, providing patients with the most modern hypoglycemic drugs, including herbal preparations, self-monitoring tools, mandatory and timely screening and monitoring of patients, and the development of new effective drugs and treatment methods.

References

1. BrennerB. et al. Renaal Study Investigators: effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy // N. Engl. J. Med. – 2001. –Vol. 345. – P. 861–869.

2. Castello I.B. Hyperlipidemia: a risk factor for chronic allograft dysfunction // Kidney mt. –2002.–Vol. 61 (suppl. 80). – P. 1923–1928.

3. Coresh J., ActorB.C., GreenT. Etal. Prevalence chronic kidney disease and decreased kidney function in the abult US population: third national health and nutrilion examination survey // Am. J. Kidney Dis. – 2003. – N 41. – P. 1–12.

4. Decochez K., Truyen I., AuweraB.V. et al. (Belgian diabetes Relgian) Combined positivity for HLA DQ2(DQ8 and 1A-2 antibodies defines population and high risk of developing type 1 diabetes // Diabetologia. – 2005. – Vol. 48, N 4. – P. 687–690.

5. Forhan J.M., Balkan B. et al. Is microalbuminuria an integrated risk marker for cardiovascular disease and insulin anct in both men and women? // J. Cardiovasc. risk. – 2001. – Vol. 8. – P. 1007–1009.

6. Go A.S., Chertov G.M., Fan D. et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization // N. Engl. J. Med. – 2004. – Vol. 351 (suppl 13). – P. 1296–1304.

7. Halteren A.G.S., Kardol M.J., Mulder A. Homing of human autoreactive T-cells into pancreatic tissue of NOD-SCID mice // Diabetologia. – 2005. – Vol. 48, Suppl. 1. – P. 75–82.

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

8. Han D., Hamilton R.T., Lam P.J. et al. Lipoic acid: energy production antioxidant activity and health effects. – N.Y.: CRC Press, 2008. – P. 293–315.

9. Januzewsky A.S., Alderson N.L., Metz T.O.et al. Role of Lipides in chemical modification of proteins and development of complications in diabetes // Biochem. Soc. Trans. – 2003. – Vol. 31, N 6. – P. 1413–1416.

10. Sjoilie A.K., Klein R., Porta M. et al. Direct Programme Study Group, Effect of Candesartan on progressin and regression retinopathy in type 2 diabetes (DIRECT-Protect2); a randomised placebocontrolled trial // Lancet. – 2008. – Vol. 372. – P. 1385–1393.

11. Verma S., Fedak P.W.M., Eeisel R.D. Fundamentals of reperfusion injury for the clinical cardiologist // Circulation. – 2002. – Vol. 105. – P. 2332–2336.

12. Yamasaki M., Kawabe A., Nishimoto t al. Dihidroalpha-lipoic acid has more patent cytotoxicity than alpha-lipoic acid // In Vitro Cell. Dev. Biol. Amm. – 2009. – Vol. 45, N 5–6. – P. 275–280.