10.
BÖLÜM

ENDOKRİNOLOG GÖZÜ İLE TİP 2 DİYABET VE RETİNOPATİYE YAKLAŞIM

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1. GİRİŞ

Tip 2 diyabet (DM) genetik, çevresel, immünolojik mekanizmalar temelinde insülin sekresyonunda ve/veya insülin etkisinde defekt gelişmesi sonucu oluşan multipl organ ve sistemleri etkileyen kronik bir hastalıktır. Oluşan hiperglisseminin multisistemik toksik etkisi sonucu retinopati, nefropati, nöropati ve vasküler komplikasyonlar gibi mikrovasküler komplikasyonlara neden olmaktadır. Komplikasyonlar özellikle glukozun insülinden bağımsız bir şekilde hücre içine girdiği kalp, sinir sistemi, göz ve mikrovasküler dokularda daha sık gözlenmektedir. Obezite ile birlikte tüm dünyada pandemi haline gelmiş kardiyometabolik hastalıktır. Diyabetik bireylerde glisemik değişkenliğe bağlı refraksiyon kusurları, nöropatiye bağlı diplopi, yaşa bağlı katarak erken prezentasyonu ve hızlı progresyonu gibi diğer göz problemleri daha sık olmakla beraber diyabetik retinopati (DR); diyabetik bireylerdeki görme kaybının en önemli nedenidir. Retinopati gibi mikrovasküler komplikasyonlu diyabetik bireyler kardiyovasküler hastalık açısından çok yüksek riskli (10 yıllık KV ölüm riski >%10) kabul edilmektedir.

2. EPİDEMİYOLOJİ

Uluslararası Diyabet Federasyonu (IDF) verilerine göre diyabetin dünyada 462 milyon kişiyi etkilediğini ve bu pandeminin devam etmesi durumunda rakamın 2035 yılında 592 milyona ulaşabileceği tahmin edilmektedir. Tüm diyabetlilerin %80-90'ını Tip 2 diyabet oluşturmaktadır. DR'nin yıllık insidansı % 2,2 ile % 12,7

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KAYNAKLAR

1. C. Sabanayagam, R. Banu, M. L. Chee et al., "Incidence and progression of diabetic retinopathy: a systematic review," The Lancet Diabetes and Endocrinology. 2019; 7(2):140– 149.
2. M. Oubaha, K. Miloudi, A. Dejda et al., "Senescence-associated secretory phenotype contributes to pathological angiogenesis in retinopathy," Science Translational Medicine. 2016;8 (362):144.
3. Q. Y. Yi, G. Deng, N. Chen et al., "Metformin inhibits development of diabetic retinopathy through inducing alternative splicing of VEGF-A," American Journal of Translational Research. 2016;8(9): 3947–3954,.
4. J. Han, Y. Li, X. Liu et al., "Metformin suppresses retinal angiogenesis and inflammation in vitro and in vivo," PLoS One. 2018;13(3) article e0193031.
5. K. Hosono, H. Endo, H. Takahashi et al., "Metformin suppresses colorectal aberrant crypt foci in a short-term clinical trial," Cancer Prevention Research, 2010;3(9): 1077–1083.
6. Silva PS, Cavallerano JD, Sun JK, Aiello LM, Aiello LP. Effect of systemic medications on onset and progression of diabetic retinopathy. Nat Rev Endocrinol. 2010;6:494–508
7. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016;375:1834–44.
8. Goncalves A, Leal E, Paiva A, Teixeira Lemos E, Teixeira F, Ribeiro CF, et al. Protective effects of the dipeptidyl peptidase IV inhibitor sitagliptin in the blood-retinal barrier in a type 2 diabetes animal model. Diabetes Obes Metab. 2012;14:454–63.
9. Goncalves A, Marques C, Leal E, Ribeiro CF, Reis F, Ambrosio AF, et al. Dipeptidyl peptidase-IV inhibition prevents blood- retinal barrier breakdown, inflammation and neuronal cell death in the retina of type 1 diabetic rats. Biochem Biophys Acta.2014;1842:1454–63.
10. Maeda S, Yamagishi S, Matsui T, Nakashima S, Ojima A, Maeda S, et al. Beneficial effects of vildagliptin on retinal injury in obese type 2 diabetic rats. Ophthalmic Res. 2013;50:221–6.
11. Chung YR, Park SW, Kim JW, Kim JH, Lee L. Protective effects of dipeptidyl peptidase-4 inhibitors on progression of diabetic retinopathy in patients with type 2 diabetes. Retina. 2016;36:2357–63.
12. Bailey CJ, Gross JL, Pieters A, Bastien A, List JF. Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial. Lancet. 2010;375:2223–33.
13. Y. Zheng, M. He, and N. Congdon, "The worldwide epidemic of diabetic retinopathy," Indian Journal of Ophthalmology. 2012;60(5): 428–431.
14. M. Wakisaka and T. Nagao, "Sodium glucose cotransporter 2 in mesangial cells and retinal pericytes and its implications for diabetic nephropathy and retinopathy," Glycobiology.2017;27(8): 691–695.
15. Takakura S, Toyoshi T, Hayashizaki Y, Takasu T. Effect of ipragliflozin, an SGLT2 inhibitor, on progression of diabetic microvascular complications in spontaneously diabetic Torii fatty rats. Life Scis. 2016;147:125–31.
16. J. Dziuba, P. Alperin, J. Racketa et al., "Modeling effects of SGLT-2 inhibitor dapagliflozin treatment versus standard diabetes therapy on cardiovascular and microvascular outcomes," Diabetes, Obesity and Metabolism. 2014;16(7) :628–635.
17. S. J. Shin, S. Chung, S. J. Kim et al., "Effect of sodium-glucose co-transporter 2 inhibitor, dapagliflozin, on renal renin-angiotensin system in an animal model of type 2 diabetes,". PLoS One. 2016;11(11) article e0165703.
18. H. Tang, G. Li, Y. Zhao et al., "Comparisons of diabetic retinopathy events associated with glucose-lowering drugs in patients with type 2 diabetes mellitus: a network meta- analysis," Diabetes, Obesity & Metabolism. 2018;20(5):1262–1279.

19. Takatsuna, Y., Ishibashi, R., Tatsumi, T., Koshizaka, M., Baba, T., Yamamoto, S., & Yokote, K. Sodium-Glucose Cotransporter 2 Inhibitors Improve Chronic Diabetic Macular Edema. Case Reports in Ophthalmological Medicine, 2020.
20. Ryan EH Jr, Han DP, Ramsay RC, Cantrill HL, Bennett SR, Dev S, et al. Diabetic macular edema associated with glitazone use. Retina. 2006;26:562–70.
21. Idris I, Warren G, Donnelly R. Association between thiazolidinedione treatment and risk of macular edema among patients with type 2 diabetes. Arch Intern Med. 2012;172:1005–11.
22. Vijay SK, Mishra M, Kumar H, Tripathi K. Effect of pioglitazone and rosiglitazone on mediators of endothelial dysfunction, markers of angiogenesis and inflammatory cytokines in type-2 diabetes. Acta Diabetol. 2009;46:27–33.
23. Tatti P, Arrigoni F, Longobardi A, Costanza F, Di Blasi P, Merante D. Retrospective analysis of rosiglitazone and macular oedema in patients with type 2 diabetes mellitus. Clin Drug Invest. 2008;28:327–32
24. Ambrosius WT, Danis RP, Goff DC Jr., Greven CM, Gerstein HC, Cohen RM, et al. Lack of association between thiazolidinediones and macular edema in type 2 diabetes: the ACCORD eye substudy. Arch Ophthalmol. 2010;128:312–8.
25. Jerums G, Murray RM, Seeman E, Cooper ME, Edgley S, Mar-wick K, et al. Lack of effect of gliclazide on early diabetic nephropathy and retinopathy: a two-year controlled study. Diabetes Res Clin Pr. 1987;3:71–80.
26. Yang YS, Danis RP, Peterson RG, Dolan PL, Wu YQ. Acarbose partially inhibits microvascular retinopathy in the Zucker Diabetic Fatty rat (ZDF/Gmi-fa). J Ocul Pharm Ther. 2000;16:471–9.
27. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352:837–53.
28. The Diabetes Control and Complications Trial Research Group. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. Diabetes. 1995;44:968–83.
29. Monnier L, Mas E, Ginet C, et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA. 2006;295:1681–7.
30. Cavalot F, Petrelli A, Traversa M, et al. Postprandial blood glucose is a stronger predictor of cardiovascular events than fasting blood glucose in type 2 diabetes mellitus, particularly in women: lessons from the San Luigi Gonzaga Diabetes Study. J Clin Endocrinol Metab. 2006;91:813–9.
31. Takao T, Ide T, Yanagisawa H, et al. The effect of fasting plasma glucose variability on the risk of retinopathy in type 2 diabetic patients: retrospective long-term follow-up. Diabetes Res Clin Pract. 2010;89:296–302.
32. Goncalves A, Marques C, Leal E, Ribeiro CF, Reis F, Ambrosio AF, et al. Dipeptidyl peptidase-IV inhibition prevents blood- retinal barrier breakdown, inflammation and neuronal cell death in the retina of type 1 diabetic rats. Biochem Biophys Acta. 2014;1842:1454–63.
33. Maeda S, Yamagishi S, Matsui T, Nakashima S, Ojima A, Maeda S, et al. Beneficial effects of vildagliptin on retinal injury in obese type 2 diabetic rats. Ophthalmic Res. 2013;50:221–6.
34. Kim NH, Choi J, Kim NH, Choi KM, Baik SH, Lee J, et al. Dipeptidyl peptidase-4 inhibitor use and risk of diabetic retinopathy: a population-based study. Diabetes Metab. 2018;44:361–7.
35. Schreur V, van Asten F, Ng H, Weeda J, Groenewoud JMM, Tack CJ, Hoyng CB, de Jong EK, Klaver CCW, Jeroen Klevering B. Risk factors for development and progression of diabetic retinopathy in Dutch patients with type 1 diabetes mellitus. Acta Ophthalmol. 2018 Aug;96(5):459-464.
36. DeFronzo RA, Eldor R, Abdul-Ghani M. Pathophysiologic approach to therapy in patients with newly diagnosed type 2 diabetes. Diabetes Care. 2013;36(Suppl 2):S127–38.

37. Cai J, Boulton M. The pathogenesis of diabetic retinopathy: old concepts and new questions. Eye 2002; 16:242.
38. Yamagashi S. Role of advanced glycation end products (AGEs) and receptor for AGEs (RAGE) in vascular damage in diabetes. Exp Gerontol 2011;46: 217-24.
39. Liu, Y., Yang, J., Tao, L., Lv, H., Jiang, X., Zhang, M., & Li, X. Risk factors of diabetic retinopathy and sight-threatening diabetic retinopathy: a cross-sectional study of 13 473 patients with type 2 diabetes mellitus in mainland China. BMJ open, 2017, 7.9.
40. Matthews DR, Stratton IM, Aldington SJ, Holman RR, Kohner EM. Risks of progression of retinopathy and vision loss related to tight blood pressure control in type 2 diabetes mellitus: UKPDS 69. Arch Ophthalmol 2004; 122: 1631–40.
41. Rasmussen KL, Laugesen CS, Ringholm L, Vestgaard M, Damm P, Mathiesen ER. Progression of diabetic retinopathy during pregnancy in women with type 2 diabetes. Diabetologia 2010; 53: 1076–83
42. CAI X., Chen, Y., Yang, W., Gao, X., Han, X., & Ji, L. The association of smoking and risk of diabetic retinopathy in patients with type 1 and type 2 diabetes: a meta-analysis. *Endocrine*, 2018, 62.2: 299-306.
43. Reiter CE, Gardner TW. Functions of insulin and insulin receptor signaling in retina: possible implications for diabetic retinopathy. Prog Retin Eye Res. 2003 Jul;22(4):545-62.