Commentary: Oral management of diabetic retinopathy

Diabetic retinopathy (DR) ranks fifth among leading global causes of moderate to severe vision impairment and blindness in adults aged 50 years and older.[1] The disease has been observed to show 1-step and 2-step progressions over four years from baseline in 30.2% and 12.6% of patients, respectively.[2] Chronic inflammation is known to play a role in the pathophysiology of type 1 and 2 diabetes mellitus (DM).[3]There also seems to be role of inflammatory processes in the development and progression of DR.[4] Intravitreal anti-vascular endothelial growth factors (VEGF), corticosteroids, and tumor necrosis factor (TNF); alpha inhibitors are known to reduce vascular permeability and suppress inflammation and thereby regress diabetic macular edema (DME).[5-7] Recently, intravitreal anti-VEGF treatment has also been shown to delay the progression of non-proliferative DR to proliferative DR.[8] In diabetic animals, control of inflammation by systemic therapy was found to be associated with amelioration of DR.[9] However, this has not been evaluated in humans. This could be attributed to the requirement of long-term administration of immune-based anti-inflammatory drugs which are associated with unwarranted side effects.

In the current issue of the Indian Journal of Ophthalmology, a prospective observational case-control study has evaluated the role of systemic anti-inflammatory drugs (immunosuppressants) for effect on DR progression.[10] They have utilized the opportunity of evaluating it in diabetic patients who needed immunosuppression for comorbidities such as rheumatoid arthritis and post-renal transplant (PRT) and compared it with matching diabetic patients not requiring immunosuppression. At 1-year follow-up, one-step progression of DR from baseline was seen in 33.3% of patients in the control group only. This small, well-documented study provides initial evidence about the role of systemic anti-inflammatory in the management of DR. The difference in glycemic control between the two groups was 0.4% (worse in the control group) at baseline, which increased to 0.6% at end of the study. This could be a confounding factor and needs to be addressed in future studies. Again, in PRT cases, previous studies have shown that DR status stabilizes in the majority of patients following transplant and in the current study also, PRT cases did not show DR progression.[11] Whether it is related to metabolic control or the effect of prolonged immunosuppressants post-transplant is debatable and needs to be addressed in future studies.

Unlike other anti-diabetic drugs, oral sodium-glucose co-transporter 2 inhibitors (SGLT2i) have a positive effect on cardiorenal functions as well as on vascular endothelium. This also holds promise for delaying the progression of DR.[12] Preliminary data suggests SGLT2i is associated with reduction in central retinal thickness in eyes with chronic DME.[13]

Larger studies are needed for clinical validation of oral therapies for preventing the progression of DR.

Kushal Delhiwala, Bakulesh Khamar

Department of Vitreo Retina, Netralaya Superspeciality Eye Hospital, Ahmedabad, Gujarat, India

Correspondence to: Dr. Kushal Delhiwala, Netralaya Superspeciality Eye Hospital, KD House, 1st Floor, Above Andhra Bank, Parimal Cross Roads, Ellisbridge, Ahmedabad - 380 006, Gujarat, India.
E-mail: kushal.delhiwala@yahoo.co.in

References

1. GBD 2019 Blindness and Vision Impairment Collaborators, Vision Loss Expert Group of the Global Burden of Disease Study. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: The right to sight: An analysis for the Global Burden of Disease Study. Lancet Glob Health 2021;9:e144-60.
2. Raman R, Ganesan S, Pal SS, Gella L, Kulothungan V, Sharma T. Incidence and progression of diabetic retinopathy in urban India: Sankara Nethralaya-diabetic retinopathy epidemiology and molecular genetics study (SN-DREAMS II), report 1. Ophthalmic Epidemiol 2017;24:294-302.
3. Tsalamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis GA, Vogiatzi G, Papaioannou S, *et al*. The role of inflammation in diabetes: current concepts and future perspectives. Eur Cardiol 2019;14:50-9.
4. Rübsam A, Parikh S, Fort PE. Role of Inflammation in diabetic retinopathy. Int J Mol Sci 2018;19:942.
5. Imazeki M, Noma H, Yasuda K, Motohashi R, Goto H, Shimura M. Anti-VEGF therapy reduces inflammation in diabetic macular edema. Ophthalmic Res 2021;64:43-9.
6. Rübsam A, Wernecke L, Rau S, Pohlmann D, Müller B, Zeitz O, *et al*. Behavior of SD-OCT detectable hyperreflective foci in diabetic macular edema patients after therapy with anti-VEGF agents and dexamethasone implants. J Diabetes Res 2021;2021:8820216. doi: 10.1155/2021/8820216.

7. Tsilimbaris MK, Panagiotoglou TD, Charisis SK, Anastasakis A, Krikonis TS, Christodoulakis E. The use of intravitreal etanercept in diabetic macular edema. Semin Ophthalmol 2007;22:75-9.
8. Maturi RK, Glassman AR, Josic K, Antoszyk AN, Blodi BA, Jampol LM, *et al*. Effect of intravitreous anti-vascular endothelial growth factor vs sham treatment for prevention of vision-threatening complications of diabetic retinopathy: The protocol w randomized clinical trial. JAMA Ophthalmol 2021;139:701-12.
9. Eid SA, O'Brien PD, Hinder LM, Hayes JM, Mendelson FE, Zhang H, *et al*. Differential effects of minocycline on microvascular complications in murine models of type 1 and type 2 diabetes. J Transl Sci 2021;7. doi: 10.15761/jts. 1000431.
10. Raman P, Kathare R. The role of concomitant immunosuppressants in impeding the progression of diabetic retinopathy: A pilot study. Indian J Ophthalmol 2021;69:3321-7.
11. Roy R, Das MK, Pal BP, Ganesan S, Raman R, Sharma T. The effects of renal transplantation on diabetic retinopathy: Clinical course and visual outcomes. Indian J Ophthalmol 2013;61:552-6.
12. Lahoti S, Nashawi M, Sheikh O, Massop D, Mir M, Chilton R. Sodium-glucose co-transporter 2 inhibitors and diabetic retinopathy: Insights into preservation of sight and looking beyond. Cardiovasc Endocrinol Metab 2020;10:3-13.
13. Mieno H, Yoneda K, Yamazaki M, Sakai R, Sotozono C, Fukui M. The efficacy of sodium-glucose cotransporter 2 (SGLT2) inhibitors for the treatment of chronic diabetic macular oedema in vitrectomised eyes: A retrospective study. BMJ Open Ophthalmol 2018;3:e000130.

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_2088_21

Cite this article as: Delhiwala K, Khamar B. Commentary: Oral management of diabetic retinopathy. Indian J Ophthalmol 2021;69:3327-8.