# Therapeutic advances in the treatment of diabetic retinopathy and diabetic macular edema.

**Shamim Ahmad\*** 

Department of Ophthalmology, Aligarh Muslim University, Aligarh, India

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## **Description**

DR was the primary cause of blindness and visual impairment in the United States in the 1950s. Photocoagulation had achieved extensive usage in medical care, possibly due to a lack of alternative therapy, despite insufficient evidence of its effectiveness. The landmark Diabetic Retinopathy Study (DRS), which begun in 1971 and was completed in 1975, indicated that scatter laser photocoagulation was advantageous in lowering the probability of progression.

### Anti-VEGF therapy

Pegaptanib, which exclusively targets the 165 isoform of VEGF, was the first anti-VEGF medication used to treat DME (Diabetic Macular Edema). Its potential was overshadowed by greater results found with anti-VEGF medicines that inhibited all VEGF isoforms. In 2010, randomized-controlled clinical studies demonstrated the effectiveness of bevacizumab and ranibizumab, then aflibercept in 2014. Conbercept might be the fifth successful anti-VEGF agent, although a level I randomised clinical trial has yet to be published. A prospective, randomised, comparative efficacy study of bevacizumab, ranibizumab, and aflibercept found no difference in efficacy between the three medicines in eyes with center-involved DME and VA of 20/40 or better after one or two years of follow-up. However, in eyes with VA of 20/50 or worse, aflibercept was superior to ranibizumab and bevacizumab at one year, whereas at two years aflibercept was no longer superior to ranibizumab, but remained superior to bevacizumab.

Intravitreal ranibizumab injections given monthly for DME increase the proportion of eyes with 2 or 3 step improvement in diabetic retinopathy severity, decrease the proportion of eyes with 2 or 3 step worsening in diabetic retinopathy severity, and decrease the proportion of eyes progressing to proliferative diabetic retinopathy. Preliminary findings from the Phase III PANORAMA study showed substantial reduction of DR severity with intravitreal aflibercept versus placebo injections. In addition, a recent subgroup analysis from both the RIDE and RISE trials revealed a substantial advantage in reducing DR severity with ranibizumab treatment in patients with mild and moderate NPDR.

#### Nonsteroidal anti-inflammatory drugs

Nonsteroidal anti-inflammatory medicines for DME have not been well explored, although available research indicates that they play minimal role in its therapy. The DRCR Network Protocol R was a 12-month prospective, masked, randomised clinical study of topical nepafenac 0.1 percent three times per day against placebo in eyes with non-center-involved DME and excellent VA. There were no changes in VA outcomes discovered. Meta-analyses investigating the usefulness of NSAIDs in the prevention of post-cataract extraction cystoid macular edoema in patients without and with diabetes have yielded opposing results. In short-term studies, topical bromfenac resulted in substantial macular thickness reductions but no significant increase in VA. In one small randomised trial, intravitreal diclofenac 500 mg was utilised as one of the treatment arms for individuals with DME. The DME improved, but the VA did not. There was no impact on macular edoema or VA in another small case series. There has been no more testing. As a result, there is presently insufficient data to support the use of NSAIDs in the treatment or prevention of DME.

When to start therapy and when to re-treat will be influenced by new imaging methods and the capacity to detect and quantify features of DR. Pharmacotherapy, both ocular and systemic, has emerged as the predominant method of treatment for DR and DME.

#### Conclusion

Conventional laser treatment has evolved into a secondary intervention in DME, and it is possible that it will play the same role in PDR. Subthreshold laser therapy offers unique properties, but further research is needed. What is still required is the best integration approach for various therapy modalities. The goal remains to obtain the largest decrease in clinical disease in the shortest amount of time, with the fewest side effects, for the longest duration, and at the lowest possible cost.

## \*Correspondence to

Dr. Shamim Ahmad

Department of Ophthalmology

Aligarh Muslim University

Aligarh, India

E-mail: shamimshamim@rediffmail.com

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