Editorial

Diabetic Macular Edema

Diabetic retinopathy is the commonest cause of blindness in the working-age population all over the world.

Poor glycemic control in diabetes is usually associated; with hypertension and increased blood lipid levels hence it is very important to control these risk factors during the management of diabetic retinopathy.

The most frequent cause of significant and progressive visual loss is diabetic macular edema which may start from the very early stage of retinopathy resulting in central vision loss.

With the availability of noninvasive diagnostic instrumentations we can now better diagnose, study, analyse, follow and manage diabetic macular edema keeping the various factors into consideration like:

- Location relevant to fovea
- Duration (recent or chronic)
- Signs of ischaemia
- Any vitreoretinal traction
- State of pigment epithelium
- Status of diabetic and B.P control
- Presence of vascular leakage

Based on above factors we can now offer more appropriate management of diabetic retinopathy and macular edema with the availability of recent therapeutic modalities like:

1. PKC enzyme inhibition with Ruboxistaurin.
2. Intravitreal steroids
3. Intravitreal injections of VEGF inhibitors like Pegaptanib sodium (Macugen), Ranibizumab (Lucentis), Bevacizumab (Avastin) alone or with traditional laser applications.

Laser treatment is still the mainstay in management of diabetic retinopathy and macular edema. While stabilizing the visual field and acuity in the long term actual improvement in visual acuity is an exception rather than the rule. Many a times there is some immediate vision loss and some patients keep on complaining of loss of peripheral field and night vision that is why we are looking for better alternatives like pharmacological modalities.

PKC enzyme inhibition with Ruboxistaurin seemed very exciting during the extensive trials as the drug can be given orally in tablet form, is well tolerated and effective in the early stages of diabetic retinopathy when the changes are still reversible and its use over an extended period reduced the loss of vision. However there was one significant drawback that it did not influence the progression of nonproliferative diabetic retinopathy to the proliferative form and also it did not appear to reduce the need for panretinal photocoagulation in diabetic retinopathy. Hence Ruboxistaurin despite having significant potential as a treatment of diabetic retinopathy is not yet approved by FDA for want of further information and evidence regarding its efficacy which might take some further time in exploring, modifying and developing this molecule to an approvable level.

An increase in the vasoendothelial growth factors (VEGF) is reported to be responsible for diabetic retinopathy changes and diabetic macular edema resulting in loss of vision and blindness. There is enough evidence now that the use of VEGF inhibitors like Pagaptanib (macugen), Ranibizumab (lucentis), Bevacizumab (avastin) as intravitreal injections are dramatically effective in regression or disappearance of neovascularisation and macular edema resulting in improvement of visual acuity. The intraocular injections of these VEGF inhibitors are well tolerated and are not associated with any local or systemic adverse effects. The only concern is the rare incidence of endophthalmitis and retinal detachment. As the effect of these injections lasts 4-6 weeks it comes down to repeating these injections for the rest of life which makes the complication of endophthalmitis etc of greater concern in the long run. Hence there are efforts to develop agents with prolonged effect or use them as slow release vitreous inserts or use them in combination with other modalities like steroids and or laser for prolonged and synergistic effectivity. Avastin is already being used as an adjunt in vitrectomy, if the surgery is performed within seven days of intravitreal injection bleeding during cutting and removal of fibrovascular tissues is greatly reduced making the surgery quicker, easier and safer due to reduction or complete resolution of neovascularisation in majority of the cases.

Macugen and Lucentis are already approved by FDA but Avastin being very economical is extensively used all over the world despite not been approved as yet.

There are encouraging results of improved visual acuity after intravitreal injections of steroids (Triamcinolone Acetonide, kenacort, kenalog etc) in diabetic macular edema particularly diffuse chronic variety, the effect again being short term, reported with complications of cataract and glaucoma in addition to chances of endopthalmitis etc. An alternative being a deep subtenon injection of steroids with lesser effectivity and reduced complications.

Diabetic macular edema due to traction of taut posterior hyaloid tends to get reduced with visual improvement following vitrectomy with intraoperative use of kenacort.

As already mentioned

1. The most common cause of progressive visual deterioration in diabetes is macular edema.
2. Laser treatment in macular edema can slow down or stabilize visual loss and any improvement in visual acuity is an exception rather than the rule.
3. Improvement of visual acuity is reported in significant number of patients following intravitreous injections of VEGF inhibitors which is an exciting breakthrough but the beneficial effect is short lived requiring repeat injections at 4-6 weeks intervals for the rest of life exposing the patients to increased risks of complications. We are anxiously waiting for an alternative with prolonged effect.
4. Intravitreal steroids are also beneficial with slightly longer duration specifically for chronic diffuse macular edema with attendant risks of complications, deep subtenon injections are a lesser effective and safer alternative.
5. PKC enzyme inhibitors like Ruboxistaurin would be an ideal therapeutic tool when refined, .approved and available.
6. As the different treatments attack the disease at different stages of development, all the therapeutic modalities if used together intelligently are likely to have an additive and synergistic effect with better outcomes like combining intravitreal injection of avastin with deep subtenon steroids and laser treatment alongwith vitrectomy within intraoperative intravitreal steroids if indicated.
7. We should always keep on stressing the importance of proper diabetic and blood pressure control ,no smoking ,healthy diet and regular exercise.

M Lateef Chaudhry
Editor in Chief
Pakistan Journal of Ophthalmology