Panel Discussion on Management of CSME

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Expert Panel

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Clinically Significant Macular Edema (CSME) is one of the commonest posterior segment pathology which we see in our practice. Continuous research and development of new diagnostic devices and drugs has refined the management of CSME and also increased the productivity of patients with Diabetic Retinopathy. With multiple options available, often we are confused in our choice. Our expert panel incorporating the stalwarts in field have put their views on this pertinent issue. I hope this discussion helps all of us in our day to day practice.

Q.1: For a clinically detectable CSME, you go for FFA, OCT or both?

LV: If I am seeing the patient of CSME for the 1st time – I will go for both FFA & OCT;

Although invasive, FFA is a dynamic procedure & it provides wealth of information in 5-7 mins on the circulatory status of retina , may pick up undetected / undiagnosed neovascularization , helps in picking up non-perfusion areas, tells us about macular ischemia ; Also very useful to pick up focal leaks for laser photocoagulation.

OCT helps the clinician with qualitative as well as quantitative information about the anatomical structure of retina, what is happening at Vitreo-retinal interface; recent models of SS- OCT also helps to study choroidal vasculature.

OCT-A (OCT Angiography) provides information, similar to FFA, without any Fluorescein Injection. Along with OCT, it is becoming an increasingly popular tool in evaluation and follow up.

MN: Only OCT unless there is unexplained loss of vision and I want to look at FAZ

MS: Only OCT unless vision loss is profound and not explained by edema alone – to rule out macular ischemia. If OCTA is available, no FFA even in this situation.

SS: For diabetic macular edema (DME), in the current scenario, SD-OCT evaluation confirms the diagnosis. It also provides macular thickness parameters as well as cross sectional analysis providing status of disorganization of retinal inner layers (DRIL) as well as the ellipsoid zone (EZ). All these parameters have a prognosticating value. OCT angiography through its enface and flow study provides a non invasive evaluation of macula in DME to rule out macular ischemia.

Q.2: How do you decide for Anti VEGF Vs Steroids?

LV: Factors to be considered include : phakic / pseudophakic / about to become pseudophakic ; Associated Glaucoma / Raised IOP ; can patient come for follow up every 4 weeks

; affordability ; Any Cardiovascular event / Neurological disease in recent past ; Pregnancy ; Generally 1st line of treatment for centre-involving DME in phakics with compromised BCVA (< 6/9) is multiple Anti-VEGF Injections. Same is true for patients with Associated Glaucoma / Raised IOP ; IntravitrealOzudrex may be preferable in Pseudophakics / about to become pseudophakic, recent CVA (< 2-3 months), Pregnancy & patient is from far flung area & unable to come for frequent follow ups.

MN: My first line would be anti my first line would be anti VEGF as it takes care of oedema as well as helps overall regression of PDR. Would use steroids if we need frequent injections to treat the condition. Also if the presenting oedema is quite significant and there are lot of lipid deposits in macula, I may prefer initial steroids.

MS: Anti VEGF's are the primary choice unless there is history of cardiovascular or neurological vascular event in the past 3 months.

Primary steroid may be considered if there are hyper reflective dots in the retinal layers in SS-OCT, pseudophakia, other eye having shown better results with steroid. Relative indications for primary steroid are subretinal hard exudate and neurosensory detachment.

Pre-existing glaucoma is a relative contraindication for steroid.

SS: Vascular endothelial growth factor (VEGF) and inflammation have been implicated in the pathogenesis of DME. SD-OCT should rule out any tractional component on the macula. Anti-VEGF therapy is the current therapy of choice. In case the patient is not responding after three one-monthly doses of intravitreal Anti-VEGFs, the anti-VEGF molecule may be changed. Intravitreal triamcinolone or dexamethasone implant may be added in unresponsive patients.

Q.3: What's the first choice of Anti VEGF for you in CSME? Ranibizumab Vs Bevacizumab Vs Aflibercept?

LV: As per available evidence + experience, all the available Anti-VEGF agents work equally well.

This has been substantiated by the recently published report of Protocol T. Taking into account Safety & Cost issues, Ranibizumab is my first choice ; Plus it has the largest number of prospective randomised controlled trials and published data – which increase your confidence in treating a patient.

Bevacizumab (Avastin) also works pretty well, but there are issues of non-availability of single use vials; People use various ways to economise the treatment: multiple prick of same vial , prepare multiple injections under laminar flow , pooling patients on a single day etc. But all these are fraught with complications & cases of cluster endophthalmitis have been reported from all across the world, including India.

Aflibercept (Eylea) also works pretty well but hasn`t become 1st line in India because of cost issues.

MN: Ranibizumab

MS: Preferably ranibizumab unless vision is less than 6/12, aflibercept may be considered. However, affordability plays a major role in selection of the agent, ulimtatelybevacizumab being the most commonly used.

SS: Anti-VEGF therapy, in our country, depends on the financial status of the patient. Each patient requires at least 3 loading doses in each eye at monthly interval followed by as per requirement therapy. Hence, Bevacizumab remains the first choice, followed by Ranibizumab. Ranimizumab biosimilar is also effective. Aflibercept has also now been approved by USFDA.

Q.4: After what time interval would you like to repeat your Anti VEGF?

LV: In centre-involving DME with compromised BCVA, generally end up giving 3 Injections of Ranibizumab at 4 weeks interval between injections. If OCT has improved & become stable after 3 injections, interval between injections may be increased – specially if the metabolic parameters are also controlled & stable.

MN: One month

MS: Monthly injections until total regression of edema, monthly follow-up for the next few months to detect interval to recurrence of edema in an individual patient and re-treat. The new follow-up schedule depends on the time to re-treat, increasing the interval to follow-up and treat in due course of time.

SS: As per standard norms, one monthly three loading doses are required followed by alternate month therapy or as per requirement. This depends on the improvement in visual acuity and macular thickness parameters on SD-OCT. Careful evaluation of EZ is also required. Patient's blood and kidney parameters have to be kept in check for an effective outcome. Usually, upto 7 injections may be required in the first year of treatment. Subsequently, the number of injections decrease, if the patient is kept purely on Anti-VEGF therapy.

Q.5: Under what scenario would you like to change your drug in the next injection?

LV: I prefer to change the class of drug (rather than change to

another drug in the same class) & shift to Ozudrex if there is inadequate response to 3 monthly injections of Ranibizumab. The criteria of inadequate response has varied; I consider < 1 line improvement &/or < 100 u decrease in OCT thickness as inadequate response.

MN: Only if it does not respond on the one month follow up.....shall not wait for three injections to do that.

MS: If there is persistence / inadequate response after 3 injections, I would change to another agent. There is however current evidence to state that continuing the same treatment is not inferior to switcing to another agent (data not available for bevacizumab).

SS: If the patient is not responding after three doses at monthly intravitreal injections, medication may be switched. In unresponsive patients intravitreal steroids may help.

Q.6: After how many days of injection do you laser if needed?

LV: If the leaks on FFA are > 750-1000 u away from centre of fovea, I consider doing focal Argon Laser after 2 weeks of Intravitreal Injection. There are lot of patients of DME, where after few intravitreal injections, do focal argon laser – this helps to decrease the number of injections and may make the treatment finite.

MN: If I have decided to laser a circinate for focal oedema then I would do it at the same sitting. If it's a grid laser I would wait for a month post injection for the oedema to flatten.

MS: Grid laser is not something I do anymore but focal laser to microaneurysms after regression of edema. However literature does not seem to support routine use of laser except in resistant cases.

SS: SD-OCT is helpful in evaluating the improvement in macular thickness after injection(s). Barely visible or subthreshold laser may be performed once central subfield thickness is achieved in the range of around 300 microns.

Q.7: Do you do paracentesis while giving intravitreal injections?

LV: Generally Not; Do consider paracentesis in patients with Glaucoma / compromised disc vasculature (Pale disc)

MN: No

MS: Only when the volume of injection is 0.1ml and / or if the patient has glaucoma.

SS: Paracentesis has been advocated and practised too after intravitreal injection. I do not go for paracentesis after injection.

Q.8: Do you think biosimilars score at par?

LV: Biosimilars are a great boon for developing country like ours. Efficacy wise, there are at par.

MN: I haven't used them yet.

MS: Can't answer this question as I have not used biosimilars.

SS: Biosimilar has been been found to be effective, but drug molecule stability often differs from batch to batch making it unpredictable sometimes.

Q.9: Do you advocate giving anti VEGF with phacoemulsification in cases of cataract with CSME?

LV: If the degree of Cataract is not significant & patient has CSME with centre involving DME, would like to give multiple Intravitreal Anti-VEGF Injections. However, if there is a significant cataract in a patient with centre involving DME & there is a need for early visual rehabilitation, I do give Intravitreal Injection at the conclusion of Phacoemulsification. In such situations, Ozudrex may be preferable to Anti-VEGF.

MN: yes, we routinely give that.

MS: Yes.

SS: Anti-VEGF therapy may be given after an uneventful phacoemulsification surgery. I plan surgery and intravitreal in two sittings at our tertiary care center.

Q.10:What's the place for posterior subtenon injections in your practice?

LV: In the management of centre involving DME, Intravitreal Injections work better than posterorsubtenon injections. Can consider PST if After Cataract surgery in diabetic patient with DME there is worsenenig of macular edema with fall in BCVA.

MN: For diabetic csme we rarely give sub tenon.

MS: Not much in the treatment of DME.

SS: Posterior subtenon injections do hold good at times.