

Answers to Audience Questions - WSPOS Worldwide Webinar 10: Retinopathy of Prematurity

WWW 10 Panellists



Wagih
Aclimandos



Dupe
Ademola-Popoola



Kateryna
Fedchuk



Manca
Tekavčič Pompe



Anand
Vinekar



Andrea
Zin



*Manca Tekavčič Pompe (MTP), Kateryna Fedchuk (KF), Dupe Ademola-Popoola (DAP),
Andrea Zin (AZ), Anand Vinekar (AV), Wagih Aclimandos (WA)*

1. I want to ask everyone if you inject or lase AP ROP infants?

MTP: laser or combined if the child is in poor general health

KF: We only do laser in Ukraine but on our way to fix legal aspects using anti-VEGF. Still we strongly believe that approximately 5% patients will benefit more from injection than laser.

DAP: Injection will be my first choice. It can then be followed up with LASER if necessary

AZ: America Latina: 90% anti-VEGF

AV: preference is laser. But I would inject if there is capillary non perfusion in the fovea, posterior zone 1 cases (i.e. zone half APROP) and APROP in cases with severe vascular obliteration / occlusion. We also do FA in our institute before such cases which helps us with better case selection

WA: Inject first and watch carefully for possible need to laser later

2. What is post laser treatment regimen?

MTP: follow up after a week and then until regression

KF: Antibiotic + steroid drops 4 times a day, may prescribe more often (6 times) in aggressive cases. Midriatic drops for day 1-3 postop in case of iris neovascularization and tendency to synechia.

DAP: Antibiotic- steroid combo for 3 days
Discuss need for analgesic with neonatologist

AZ: Antibiotic + steroid drops 4 x / day for 1 week

AV: if the laser is complete and thorough, then 1 week later is sufficient. Usually 2-3 more visits thereafter are sufficient to ensure good outcome. Post that, babies will be needed to be followed up for ocular and vision sequelae which we start at 3 months of corrected age

WA: Review within a week and monitor until clear signs of regression

3. When injecting in APROP in one eye do you see an improvement in the fellow eye?

MTP: haven't seen it

DAP: Mostly both eyes are injected.

AZ: Usually inject OU

AV: we have not had a case like that, since in all our cases we have injected in both eyes

WA: Always injected both eyes so far

4. Could you please start off with the basic staging classification? indication for laser? indication for surgery? what is threshold disease? what is rush disease? what is plus disease? and so on?

KF: I would recommend to strictly follow ETROP recommendations.

For vitrectomy – do as fast as possible if you see the very beginning of detachment (schisis) signs that show no tendency to regression. You may get perfect visual functions even after vitrectomy.

AZ: Please refer to these articles:

- The International Classification of Retinopathy of Prematurity revisited. International Committee for the Classification of Retinopathy of Prematurity. Arch Ophthalmol. 2005;123(7):991-9. Comment in: Arch Ophthalmol. 2006;124(11):1669-70.

- Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol. 2003;121(12):1684-94. Comment in: Arch Ophthalmol. 2003;121(12):1769-71. Arch Ophthalmol. 2005;123(3):406-7; discussion 409-10. Arch Ophthalmol. 2005;123(3):406; discussion 409-10. Arch Ophthalmol. 2005;123(3):407-8; discussion 409-10. Arch Ophthalmol. 2005;123(3):408-9; discussion 409-10.

AV: The ICROP 2005 paper, and the ETROP paper of 2003 would answer all this

WA: Best to refer to Textbooks and Royal College of Ophthalmologists guidelines

5. Curious to know whether in your countries ROP specialists are more of vitreoretinal specialists or paediatric ophthalmologists?

MTP: paediatric

KF: Mostly pediatric ophthalmologists.

DAP: More of Paediatric ophthalmologists screen in Nigeria. In some institutions, we have both group involved. They sometimes alternate screening monthly, or the paediatrician screen and the vitreo-retina do mainly LASER and surgical cases

AZ: Paediatric ophthalmologists

AV: In India predominantly VR specialists. The PO specialists are involved in screening and only rarely treat

WA: In the UK, mostly Paed. Ophthalmologists

6. Does anyone one on the panel use the Panocam device? We have the Retcam II.

MTP: no

KF: No Panocam. We also use RetCam II.

DAP: No. I use mobile smartphone fundoscopy where required

AZ: Not aware of Panocam. Use Retcam portable

AV: We use the RetCam Shuttle, The RetCam 3 (with FA) and the Forus Neo Camera in our KIDROP program

WA: I don't

7. How can we evaluate recurrence after VEGF if there is no angiography?

KF: Vascular reaction: dilation and tortuosity. I believe angiography is a very useful tool but absolutely not a must-have. We do angiography in less than 1% of the patients in case of a very posterior disease to decide which areas may be saved from laser when there is no demarcation. With the experience you will confidently differentiate ischemic areas even in APROP without any demarcations lines. Using green filter on your indirect also helps.

DAP: Same ways as during primary screening mostly comparing the vessels calibre and activity and anterior advancement compared to pre-injection

AZ: Agree with Dr. Fedchuk

AV: clinically there is a reappearance of the plus disease (or worsening if there was never any resolution to begin with), there is also posterior loops, with worsening of the collaterals or even appearance of the classical ridge / FVP tissue. In many cases the media also worsens and the pupil remains rigid

WA: Monitoring for increased PLUS disease, new vessels

8. Does anyone have experience with aflibercept injection in ROP?

MTP: no

KF: Not yet. On our way.

DAP: No, I don't have the experience

AZ: No

AV: No personal experience. There is a paper from India published in the Indian Journal of Ophthalmology

WA: No

9. How does one differentiate between OCT and retcam after laser?

AV: They are two separate modalities. OCT is not routinely used after laser. We have used it to document macular edema of prematurity, the ridge and also have documented persistent neovascularization on OCT-angiography (published)

WA: We don't perform OCT as a routine in the NICU set up

10. Does anyone on the panel have experience using propranolol?

MTP: no

KF: No experience.

DAP: No experience

AZ: No experience

AV: No personal experience.

WA: No

11. What doses do you use for Avastin?

DAP: 0.625 mg

AZ: 1/3 adult dose. But please look at

Wallace DK, Kraker RT, Freedman SF, et al. Short-term Outcomes After Very Low-Dose Intravitreal Bevacizumab for Retinopathy of Prematurity. *JAMA Ophthalmol.* 2020;138(6):698–701. doi:10.1001/jamaophthalmol.2020.0334

Lorenz B., Stieger K., Jager M. et. al. Retinal vascular development with 0.312 mg intravitreal bevacizumab to treat severe posterior retinopathy of prematurity: a longitudinal fluorescein angiographic study. *Retina.* 2017; 37: 97-111

Wallace DK, Kraker RT, Freedman SF, et al. Assessment of Lower Doses of Intravitreal Bevacizumab for Retinopathy of Prematurity: A Phase 1 Dosing Study. *JAMA Ophthalmol.* 2017;135(6):654-656. doi:10.1001/jamaophthalmol.2017.1055

AV: We strive for the 'one-third' of the adult dose. This is about 2 units on the syringe for practical purposes

WA: Half the adult dose

12. What is the anti-VEGF dose after laser in recurrence of APROP?

MTP: 0.12 mg

DAP: Half of 0.625 mg or full dose

AZ: same as for 1st treatment

AV: I have not had the opportunity to encounter a case. Recurrence after laser is first of all rare, and if present, I would manage it with more laser and not anti VEGF. But I guess the dose should be the same as one would use in naïve eyes

WA: Half the adult dose

13. Is there any possibility in regression for AP-ROP before it is given to any laser or anti VEGF treatment?

KF: If it is just a slight vascular reaction and even large avascular zone you probably don't really call it AR ROP, we call it preROP in my centre, still this scenario may sometimes lead to a classic stage 1 or 2 which may eventually regress. AP ROP is a "hurricane" in the eye which, I believe, cannot regress with no treatment.

AZ: Never seen a true APROP regress

AV: Our paper on thrombocytopenia in APROP documented such a case. Although whether this is 'true APROP' or a systemic component driven APROP like disease is a matter of debate.

WA: Not in my experience as we would intervene urgently

14. You are destroying the retina with laser, especially ablating the maximum peripheral retina; What about the future field of View like that needed for driving, etc.?

MTP: peripheral VF can be restricted in some cases, but not all. It depends on patch power

KF: It would be unfair to comment on possible anti-VEGF complications since we aren't using it.

Still if it is zone 2 – nasal retina is usually lasered very safely with very little to no harm to temporal peripheral field and temporal retina function is limited by the face anatomy (nose) so the harm is discussible.

I would leave the answer about zone 1 for my respectable colleagues who have experience in using anti-VEGF in the aspect of recurrence rate and possible additional laser. We work and advocate on the possibility of using anti-VEGF for these extremely posterior cases to give parents a choice to risk with possible remote complications of the injections or aggressive laser damage.

DAP: It's a risk versus benefit decision. If you don't LASER, the child may go blind altogether. That one of the reasons some people prefer to use anti-VEGF

AZ: Treatment is to prevent immediate blindness and best evidence-based treatment future results are aimed for the future.

Graham E. Quinn, Velma Dobson, Robert J. Hardy, Betty Tung, Dale L. Phelps, Earl A. Palmer, Visual Fields Measured with Double-arc Perimetry in Eyes with Threshold Retinopathy of Prematurity from the Cryotherapy for Retinopathy of Prematurity Trial, *Ophthalmology*, Volume 103, Issue 9, 1996, Pages 1432-1437, ISSN 0161-6420, [https://doi.org/10.1016/S0161-6420\(96\)30487-9](https://doi.org/10.1016/S0161-6420(96)30487-9).

(<http://www.sciencedirect.com/science/article/pii/S0161642096304879>)

Abstract: Purpose: To measure monocular visual field extent in very-low birth weight children in whom severe (threshold) acute-phase retinopathy of prematurity (ROP) developed in one or both eyes, and who had random assignment of eyes to cryotherapy or no cryotherapy. A control group of very-low birth weight children in whom ROP did not develop also was tested. Methods: There were 78 children in the severe ROP group from 5 of 23 centers in the randomized trial of cryotherapy for ROP (CRYO-ROP). The comparison cohort consisted of 75 study participants in whom ROP did not develop. All subjects had birth weights of less than 1251 g. At the 5 1/2-year study examination, visual field size was measured using double-arc kinetic perimetry. Testers were masked to treatment status of each eye. Four meridia were tested: superotemporal (ST), inferotemporal (IT), inferonasal (IN), and superonasal (SN). Target size was 6°. Results: When blind eyes were assigned a score of 0°, the no-ROP, treated, and control eyes had an average visual field extent of 62°, 35°, 27° at ST; 73°, 42°, 35° at IT; 510, 30°, 210 IN; and 50°, 26°, 22° at SN, respectively. Among 25 children who had bilateral threshold ROP and measurable fields in each eye, values for treated and control eyes were 59 versus 62 at ST, 69 versus 80 at IT, 44 versus 49 at IN, and 41 versus 48 at SN, respectively. Conclusions: Overall, visual fields in eyes that reached threshold ROP were smaller than those of eyes that did not develop ROP. When only pairs of sighted eyes were considered, visual fields in the treated eyes were 6.4° smaller than those of control eyes. Therefore, it appears that a small loss of peripheral field occurs when cryotherapy prevents the development of retinal detachment.

AV: We have long term follow up of these babies. With the use of 532 nm green (instead of the diode, 810 nm) the field loss is not a big problem. OCT also shows neurosensory retinal preservation after laser with green (compared to diode)

WA: We know from PRP on adult diabetics that they would be expected to maintain adequate binocular field of vision to allow them to drive. Difficult question to answer if someone only ends up with one seeing eye that has had considerable laser ablation.

15. Do you observe more myopia in babies post anti-VEGF injection? or in babies post LIO?

MTP: post LIO

DAP: LIO is known to result in more myopia

AZ: Post laser

AV: Myopia can be noted even in preterms who have never had ROP or never treated as well. We have noted myopia in Anti VEGF as well as laser cases. Contrary to the usual observation, cases of anti VEGF have on occasion shown very high myopia as well. The incidence of myopia in post 532 nm green laser babies in our experience is less than 10% and with diode was over 25%

WA: There seems to be less myopia following injection, but this is just an impression. My numbers of injected babies are too small to draw a scientific conclusion

16. How soon do you do baseline refraction in post treatment babies? 6 months' post gestational age ok or start at 3 months?

MTP: 3 months

KF: 6 months or even later. I see no strong need to examine refraction earlier but never skip if the baby is willing

DAP: I do mostly 3 month

AZ: 6 month corrected age

AV: In our institute we start off at 3 months of corrected age

WA: Not earlier than six months.

17. What about Anti VEGF entering the patient's general circulation? and its effects on other developing vascular areas like neuro circulation and cardiac circulation etc.?

MTP: I believe this is an important issue

KF: I have no personal experience, but there is still a huge global discussion with possible negative general impact of anti-VEGF drugs in infants.

DAP: That's a genuine concern, however, where LASER or the expertise is not available, I consider that the benefit of vision preservation outweighs the possible neurodevelopment challenges.

AZ: Agree with Dr. Fedchuk

AV: Yes, it is a concern and is not adequately addressed. Paediatricians are also worried about this. Hence our personal bias towards laser treatment as the first choice

WA: Very difficult to assess as those babies often have multiple other morbidities. No obvious impact clinically. We also do not know what exactly is the impact of sedating and possibly re-intubating a baby for Laser.

18. Does anyone use WINROP to predict risk of Type-1 ROP?

MTP: we do

KF: We don't.

DAP: Not yet in my centre

AZ: No

AV: We used it in a trial a few years ago. Like Mexico and other countries with similar demographics like India, the sensitivity was not as good as the ones reported in the original Swedish cohort

WA: I looked at it but found no significant benefit compared to the current screening guidelines.

19. We would appreciate if detailed information about viewing with mobile phones is shared later in the experts answers section.

KF: We don't use it for ROP but it is a great technique. Sometimes we use it for other pathology, or to show parents the ocular findings.

You should "play" with it in bigger patients to adjust the distance and method overall. Turn on your camera on video mode with a flash-light on and place it where your eyes usually are, also place a lens as usual, then adjust the image.

DAP: There is some bit of learning curve, best to start with adult eyes, perfect it before trying on the babies. You can use some adapters like the paxoscope to make it easier and to keep one hand free for you to rotate the eye ball if required. Please see this publication for the description

Dupe Ademola-Popoola, Victoria Olatunji. Retinal Imaging with Smartphone. Nigerian Journal of Clinical Practice. 2017;20:341-345 A publication of Medical & Dental Consultants' Association. 23/07/2016. www.njcponline.com

AZ: https://eyewiki.aao.org/Smartphone_Funduscopy-How_to_use_smartphone_to_take_fundus_photographs
<https://www.keelermio.com/>
<https://www.aao.org/clinical-video/how-to-take-retinal-images-with-smartphone>

AV: Please refer to papers on KIDROP on Pubmed and MII RetCam on Pubmed for details

WA: No personal experience

20. We need to know more about angiofibrotic switch in ROP. It could be similar D-Mellitus switch?

KF: Pathogenesis is very similar. Ischemia - aggressive VEGF production – neovascularization + fibrosis proliferation. The etiology of the process is different. I call ROP – a "flash proliferative DRP".

AZ: Kim SJ, Port AD, Swan R, Campbell JP, Chan RVP, Chiang MF. Retinopathy of prematurity: a review of risk factors and their clinical significance. *Surv Ophthalmol.* 2018;63(5):618-637. doi:10.1016/j.survophthal.2018.04.002
Chan-Ling, Tailoi & Gole, Glen & Quinn, Graham & Adamson, Samuel & Darlow, Brian. (2017). Pathophysiology, screening and treatment of ROP: A multi-disciplinary perspective. *Progress in Retinal and Eye Research.* 62. 10.1016/j.preteyeres.2017.09.002.

AV: I am not certain

21. How do you secure the eye under topical anaesthesia laser treatment?

KF: We do general anaesthesia.

DAP: I use a small vectis / spatula

AZ: we treat under general anaesthesia

Jalali S, Azad R, Trehan HS, Dogra MR, Gopal L, Narendran V. Technical aspects of laser treatment for acute retinopathy of prematurity under topical anesthesia. *Indian J Ophthalmol.* 2010;58(6):509-515. doi:10.4103/0301-4738.71689

AV: We use the simple infant wire speculum and the Flynn Infant scleral depressor

WA: My NICU has so far preferred GA whenever possible. Otherwise the baby has sedation and muscle relaxants as well as local anaesthesia.

22. Indirect ophthalmoscope examination becomes difficult in bigger babies; do you have any suggestions on the equipment used in the examination?

MTP: we do it under GA

KF: Talk to the child, if it works. If it doesn't, hold strong and firmly and finish fast.

DAP: You can still use your indirect with the babies well wrapped and made comfortable and topical anaesthetics apply to the eye. We think it's ok for the babies to cry, it expands the lungs. It at least rules out apnoea. Do not forget that we screen primarily to determine if there is a sight threatening disease -Type I. Lots of it happens in zone 1 which you are used to examining. ROP screening personnel also grow experience just as babies grow. Be encouraged

AZ: Totally agree with Dr. Fedchuk!!! Practice practice practice

AV: Use a good wireless headset. Once the baby is held or wrapped securely, you can also tilt the head from one side to the other (gently) to view the periphery. Hold the 20 D more vertically between your fingers for a more peripheral view

WA: I find it helpful to ask the parents to time the feeding of the baby with the time of the examination. Otherwise when the baby is asleep.

23. We need to know more about vasculogenesis in preterm born babies, mainly in posterior ROP.

KF: Use general protocols.

DAP: <https://onlinelibrary.wiley.com/doi/full/10.1111/aos.12049>

AZ: Please see these - Kim SJ, Port AD, Swan R, Campbell JP, Chan RVP, Chiang MF. Retinopathy of prematurity: a review of risk factors and their clinical significance. *Surv Ophthalmol.* 2018;63(5):618-637. doi:10.1016/j.survophthal.2018.04.002

- Chan-Ling, Tailoi & Gole, Glen & Quinn, Graham & Adamson, Samuel & Darlow, Brian. (2017). Pathophysiology, screening and treatment of ROP: A multi-disciplinary perspective. *Progress in Retinal and Eye Research.* 62. 10.1016/j.preteyeres.2017.09.002.

AV: Publications from Hartnett, TaiLoi-Chang-Ling, Louis Smith answer some of these queries.

24. Please advise us regarding the minimum safety and sterilization requirements for the Anti VEGF Administration in any Clinical set up.

MTP: we do it in the OR

KF: We plan to do it in the OR and treat the procedure as an intraocular surgery.

DAP: Typically, we collect sterile supply from the operation room, including speculum, vectis, cotton bud, surgical gloves, sterile gowns and drapes and syringes. They are transported sterile as drum in drum to be opened only besides the baby after scrubbing as in surgery. Clean with Povidone Iodine, instil between 1-2.5% Povidone drops in conjunctiva. If it's at the base hospital, and baby is fit, transport to the OR and give the child there.

AZ: Please see these

Miller JL, Johnson PN, Harkey K, Siatkowski RM. Sedation Protocol During Bevacizumab Intravitreal Injection in Preterm Infants with Retinopathy of Prematurity. *J Pediatr Pharmacol Ther.* 2018;23(1):34-40. doi:10.5863/1551-6776-23.1.34

Eyes are prepared using 5% povidone-iodine and topical antibiotics, anti-VEGF is injected intravitreally via the pars plicata under intravenous sedation. The injection is performed with a 30-gauge needle that was initially directed along an angle perpendicular to the globe 1.5 mm behind the limbus and then redirected slightly toward the optic nerve after the needle had entered the sclera. This technique is used to avoid damaging both the lens and retina

AV: The same protocols that would be used for adults. We do the injection procedure in the OR, and rarely NICU if the baby cannot be shifted in.

WA: Usually in NICU with same process used to inject adults: cleaning, drape, separate syringe for each eye. No routine antibiotics.

25. Could I know what is the protocol for topical anaesthesia treatment?

KF: We perform general anaesthesia.

Sometimes (extremely rarely) to put additional few spots we do topical anaesthetic drops and glucose-sucrose solution orally.

DAP: One drop of proparacaine, repeat after 5 minutes, wait 10 minutes. Wipe of excess from the eye.

AV: Proparacaine HCL Ophthalmic Solution USP: 0.5%

26. What do you do if the pupil is difficult to enlarge in the patient who is scheduled for examination or laser?

MTP: try to use all possible midriatics

KF: Use additional phenylephrine drops, they work very fine. I've done phenylephrine subconjunctival injection very few times with a great mydriasis result (no adverse events). I always get neonatologist's/anaesthesiologist's approval to do that.

DAP: I typically will assume that that child has type 1 ROP and will endure, Instil topical anaesthetic before the dilating drop. Use the dilating drops thrice, 5, 10 and 30 minutes. Alternatively, Insert cotton pledget in the inferior fornix, wet it with mydriatics - cycloplegic drop. The most experience person to examine through the small pupil. Be prepared to give injection. Especially if you found rubeosis iridis.

AZ: Just add more phenylephrine 2.5% drops

AV: Gently depression using the infant depressor will ensure dilatation in most cases, even those that have TVL and zone 1 disease.

WA: The challenge is more for treatment than examination. If there is threshold disease but poor view (eg small pupils, cloudy media, TVL) I have opted for injection and lasered at a later date. Some years ago I used Transcleral Diode laser (published in EYE). Good results.

27. Does anyone from the panel do Laser without general anesthesia?

MTP: not me

KF: We always use general anesthesia. Just a few cases (around 5 overall) when I needed to put few additional spots (up to 5 minutes) I lasered under local anesthesia.

DAP: Yes, I do it under topical anaesthesia

AZ: Never

AV: In India we are trained to do laser under topical anesthesia in most cases

WA: If need be!

28. How about telemedicine or smart phone aided screening in your center for peripheral area (secondary center of hospitals)? Please share your experiences and technique for this.

KF: We use RetCam or “oral presentations” as explained by our skilled colleagues from the remote regions. While time goes by you develop some “professional” language when your colleague’s words are compatible with your eyes. But I strongly recommend this way of telecommunication in cases when you doubt the diagnosis and there is no other affordable retinal imaging device.

DAP: See previous comment. It’s about rotating the eyeball and aligning the lens

AV: Our program KIDROP has been using tele-ROP since 2007. We have screened over 150,000 sessions in over 127 NICUs. Our experience has been published. Request you to kindly PubMed “KIDROP”

29. WRT Bevacizumab, how do you deal with the systemic risk?

MTP: Anti-VEGF is very very rarely our first line treatment

AZ: you can’t control it. Just inform parents and neonatologists

AV: This is difficult to determine and hence the best we can do is to keep the baby under observation for a few hours before they go home (if not already admitted). Long term side effects are also not well reported and are a matter of concern especially neuro development related. Long term studies are awaited

WA: None identified to date

30. How does Retinopathy affect a New born?

KF: If it totally regresses even with the treatment, there is just another happy and healthy kid that simply might need to see ophthalmologist a bit more often.

We deal with the consequences of ROP if they are negative. We treat myopia, amblyopia, anisometropia or blindness as ones that are a result of any other possible pathology.

AZ: suggest reading this article

Rothman AL, Mangalesh S, Chen X, Toth CA. Optical coherence tomography of the preterm eye: from retinopathy of prematurity to brain development. *Eye Brain*. 2016;8:123-133. Published 2016 May 27. doi:10.2147/EB.S97660

AV: ROP pathology is well described in texts. We also have a paper on term and healthy infants who were screened ad retinal diseases in them were reported

31. I had experience of twin patients, one baby developed ROP and the other did not. Do you have any experience or data about ROP in twins?

MTP: they can be fairly asymmetrical, especially if dizygotic

KF: A condition seen quite often and I advocate for the quality of neonatal care or comorbidity.

AZ: suggest reading these articles

Azad R, Chandra P, Patwardhan SD, Gupta A. Profile of asymmetrical retinopathy of prematurity in twins. *Indian J Ophthalmol*. 2010;58(3):209-211. doi:10.4103/0301-4738.62645

Yau GS, Lee JW, Tam VT, et al. Differences in risk factors for retinopathy of prematurity development in paired twins: A Chinese population study. *ScientificWorldJournal*. 2014;2014:212183. doi:10.1155/2014/212183

AV: There are publications on multiple gestations and ROP and yes, asymmetry can exist.

WA: This is not unusual. Often the smaller baby gets worse ROP

32. Do you inject anti-VEGF in ROP stage 4A? And when? During laser treatment? Do you wait to inject combined with a vitrectomy?

MTP: combined with vitrectomy

KF: When we have this opportunity, we'd love to use anti-VEGF prior to vitrectomy for "plus disease" cases. The hemorrhage after vitrectomy may be very aggressive. We would use it 2 to 5 days before the surgery.

DAP: I don't inject in 4A, I will LASER if there are active stage 3 as well

AZ: suggest reading this article

Hansen ED, Hartnett ME. A review of treatment for retinopathy of prematurity. *Expert Rev Ophthalmol*. 2019;14(2):73-87. doi:10.1080/17469899.2019.1596026

AV: I do not use anti VEGF in 4A

33. In view of babies of 36 wks. with >2 kg developing aggressive ROP, what's the current opinion of WSPOS in an attempt not to miss such children? would you advocate screening all babies after 1 month?

MTP: it depends on each region situation, but would be probably wise in certain parts of the world

KF: For over 1000 treated babies in my hospital we've had none older than 36 weeks. It is a matter of neonatal care since there still may be NICUs that keep on "producing" oxygen induced cases. If the neonatal care is equipped enough and follows all the modern recommendations, you won't get cases older and larger that are within screening criteria of high income countries.

DAP: In Nigeria, if the baby is high risk with stormy **postnal (should this be postnatal?)** event, we'll screen at 1 week of life

AZ: Each country/region would have to develop its own screening guideline

AV: In India up to 2000 grams BW and 34 weeks GA are under the ROP protocol and those outside these criteria are covered under the universal screening program

WA: Not in my experience

34. Usually AP-ROP occurs in zone I. Since the BEAT-ROP Study is clear on the advantage of Anti-VEGF over laser treatment, why do you consider to use laser for first line treatment?

MTP: because of much more predictable side effects

KF: We've legal nuances prohibiting usage of anti-VEGF but we work on starting implementing the injections. Nevertheless, we don't treat the eyes separately, we treat the whole baby, laser is a local treatment of a local problem, anti-VEGF comes out to be a general treatment of a local problem. Possible developmental delays due to injections, recurrence rate and follow-up difficulties are leading points against injecting. Still we are very eager to use anti-VEGF in posterior zone 1 and as an additional drug pre-vitreotomy to calm down the vessels and prevent aggressive bleeding postoperatively. We believe laser – is the golden standard.

AV: Laser has a predictable outcome, excellent results if done well. We have a paper in which we compared the two methods of laser in ARPROP and had over 95% success

35. What is proportion of APROP to all ROP?

MTP: In my country about 2-3%

KF: It also depends on the neonatal care. Some centers present more than the others. Approximately 25-35%.

AV: Depends on the country, the region and the NICU setting, In India, up to 30% of treatable ROP has been reported to be APROP

36. Dr. Anand: would you prefer to treat with anti-VEGF injection or Laser for zone-1 ROP?

AV: Preference is laser. But I would inject if there is capillary non perfusion in the fovea, posterior zone 1 cases (i.e. zone half APROP) and APROP in cases with severe vascular obliteration / occlusion. We also do FA in our institute before such cases which helps us with better case selection

37. The APROP is not showing EFP - are these ROP?

KF: Sure! Sometimes after performing laser for APROP you see calming down the vascular reaction, you start getting happy with the result but eventually EFP starts growing within the coagulates, showing the classical stage 3 coarse.

AV: It could be, if there is FVP it is classical ROP and not APROP

38. Dr. Anand: How did the current COVID situation affect your clinical practice in terms of screening and treatment of ROP babies?

AV: We have published the guidelines on the Indian ROP society website. Kindly google the same and it you can download for free.

39. Have you checked any difference in vascular findings between plus and no plus ROP using OCT FA?

KF: Never performed FA in "no plus" cases. It is probably more for the interest of science not the baby.

AV: No we did not attempt to quantify any changes on FA

40. When do we choose anti VEGF in ROP treatment?

MTP: AP ROP in very sick babies, any type 1 ROP: one eye anti-VEGF, the other eye laser in very sick babies

KF: We believe APROP posterior zone 1; 4A plus disease, 4B plus disease – prior to vitrectomy.

AV: Answered above

WA: In APROP or poor fundus visualization

41. What is the preferred treatment for APROP? Ranibizumab or Bevacizumab? And why?

MTP: Ranibizumab, because is approved for eye injections

AZ: in Latin America, what is available

AV: Due to cost considerations most specialists in India are still using Bevacizumab. However, Ranibizumab has better regulatory acceptance

42. Has anyone given bifocals to premature babies due poor accommodation after dynamic retinoscopy?

KF: We've done a few for babies with additional strabismus. This didn't help much somehow. While the child grows up we found the accommodation problem decreasing.

AZ: Sure, some have CP and over plus lens prescription is very helpful

WA: No unless they also have Down's

43. Is there an algorithm (should this be algorithm?) for antiangiogenics?

AV: Similar to indication of anti VEGF mentioned above

44. What is the best technique to do screening of ROP? because all we know is so difficult to screen a premature baby, right?

MTP: camera makes it all easier, but if you don't have it you have to learn some tricks. Above all you have to have enough time

KF: Indirect ophthalmoscopy. First calm down and be pushy. You have same eyes as we do. You'll reach the point eventually!

Practice periphery examination in all your patients regardless age and you'll get more confident.

Personally I don't even use the scleral depressor for screening, only for surgery. But you should take any time and equipment (eyelids retractor, hook, depressor) to be sure you've reached the aimed peripheral retina. The price for mistake is too high.

DAP: Once the pupil is dilated and you have checked the posterior segment for presence of plus disease, identify one of the vessels and follow it through, try to note the branching pattern, once it stops being dichotomous, suspect there is a problem ahead. Gently turn the head / rotate the eyeball through a gentle sliding of conjunctiva towards the fornix while you look and bend a little backwards.

AZ: Agree with Dr. Fedchuk

AZ: In our program KIDROP all our screening sessions are done on wide-field imaging. Approximately 2000+ per month

45. Can you explain the difference between type 1 ROP and threshold ROP?

KF: These are different terms of two studies: BEATROP and ETROP. Please follow the ETROP recommendations.

AZ: Threshold ROP is a term used by CRYO-ROP clinical trial for treatment indication. Threshold ROP was defined as a condition with 50% risk of retinal detachment if left untreated. This includes ROP of more than 5 contiguous or 8 cumulative clock hours of stage 3 plus ROP in zone 1 or zone 2. All eyes with threshold disease were recommended to be treated.

ETROP aimed to treat earlier to achieve better results. Type 1 is defined as zone 1 plus with any stage, zone 1 stage 3 with no plus and zone 2 stage 2 or 3 plus. All eyes with type 1 prethreshold ROP are currently recommended for immediate treatment.

Agarwal K, Jalali S. Classification of retinopathy of prematurity: from then till now. Community Eye Health. 2018;31(101):S4-S7.

AV: Briefly put, Type 1 ROP is the ROP that requires to be treated (based on ETROP guidelines) and Threshold ROP was defined under the CRYO-ROP study. We treat earlier than 'threshold' after the ETROP study gave its guidelines

46. At what distance from the limbus do you inject anti VEGF? 1 mm / 1.5 mm?

MTP 1.5 mm

DAP: I do 1 mm, some people do 1.5 mm

AZ: 1 mm. Also please see

Hansen ED, Hartnett ME. A review of treatment for retinopathy of prematurity. Expert Rev Ophthalmol. 2019;14(2):73-87. doi:10.1080/17469899.2019.1596026

AV: 1.5 mm

47. Could you please list out the Merits / Demerits of transpupillary diode laser (TDL) vis - a - vis argon laser in ROP treatment?

MTP: I only use diode laser (810 nm)

KF: If you have a choice – diode laser for ROP works safer and better.

DAP: TDL is more painful but, it more likely to be available because of the versatility in a low resource setting

AZ: Agree with Dr. Fedchuk

AV: We prefer and use only 532 in our practice

48. When we chose anti VEGF for ROP?

MTP: answered above

KF: Posterior zone I APROP.

DAP: Zone 1 plus, APROP, if that's the only available option

AV: Answered above

WA: Please see Q 40