

## Commentary: All India Ophthalmological Society members' survey: Practice pattern of intravitreal anti-vascular endothelial growth factor injection

This issue of Indian Journal of Ophthalmology (IJO) is publishing the results of a survey conducted by the AIOS on practice pattern of intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF).<sup>[1]</sup>

The survey addresses an important and controversial component in vitreo retinal practice. The survey includes questions related to the informed consent, procurement, aliquoting, storage, administration of the drug, and postinjection follow-up. While the survey is meant to cover use of anti-VEGF drugs in general, the stress appears to be on the off-label use of bevacizumab.

The survey thus does not cover the following points related to the use of anti-VEGF drugs.

1. Choice of the drug in a given case
2. Other than economic criteria, what drives the practitioner to decide on one vs the other
3. Has there been any change in the practice over the last 10 yrs
4. The practice pattern in cases needing bilateral injections—same day vs different days.

The readers should be aware of the limited information that a survey gives. The limitations are caused by

1. The limited number of questions one can pose
2. The structured answers that force one to choose an option that one may not entirely agree with
3. The potential for a different outcome if the number of responders were more.

Most importantly one should not misconstrue the results of a survey as a prescription for standard of care.

India is in an unenviable situation where cost of medical care is an important issue for most people and does dictate the type of treatment that can be offered. The practitioners are caught between providing the best medical care and yet be affordable to everyone.

Arising out of/and related to this survey, the following contentious points need to be discussed.

1. If cost was not a factor, would there be any disagreement on the need to use single dose vials for injection?  
The obvious answer is no. None would favor multidose vial as first choice. The safety in using a single dose vial is obvious.
2. If a compounding pharmacy takes the responsibility for aliquoting the bevacizumab, does it guarantee safety. Again, the answer is no. This is evidenced by the spate of fungal infections that occurred in the United States of America.<sup>[2]</sup>
3. The results of the survey seem to indicate two options when bevacizumab is used.
  - a) Pooling the patients on one day: The drug in one vial is used up entirely or residue is thrown away, thus making it the safest of all techniques. However, the downside is that one should have enough cases that can

be accumulated in one day to utilize one vial and be cost effective. Obviously, this method is not practicable for solo practitioners or small group practices

- b) Aliquoting and storing for later use: The majority of the responders in this survey loaded multiple syringes from single or multiple punctures of the vial and stored them in refrigerator and used the drug up to 1 month from the aliquoting. While perhaps most cost effective, this technique has the risk of contamination. Safety can be improved by adopting some common sense practices.
  - i) The aliquoting should be done under a laminar hood using sterile gloves and gown
  - ii) The 1 ml syringes should be capped with air-tight Luer lock caps (e.g.,: Orange Luer lock round tip cap AD400-OR Adhesive dispensing Ltd). These short Luer lock caps effectively seal the syringe preventing accidental leakage of the drug on one hand and contamination on the other. Capping the syringes with needles (with caps) is not protective
  - iii) Each syringe should be individually placed in plastic bags (one bag for one syringe) and the bags should be sealed before being placed in a container which in turn is placed in the refrigerator
  - iv) The refrigerator should be used exclusively to keep sterile medicines and not one used for general purpose
  - v) The interval between aliquoting and actual administration should be shortest. One cannot be dogmatic about a cut-off time limit but intuitively one month appears too long (personal opinion).
4. Location where injection was administered:  
In most developed countries, the injections are administered routinely in the clinic. Performing the procedure in the operation theatre utilizes the sterile conditions of the operation theatre and involves a change of clothes into operation theatre attire for the surgeon as well as the patient (at least in the Indian circumstances). Performing the procedure in operation theatre may appear ideal but can interfere with the theatre schedules and escalates the cost of administration.<sup>[3]</sup> Evidence indicates that place of injection does not seem to be important in influencing the risk of endophthalmitis after intravitreal injections.<sup>[4]</sup> One perhaps should keep in mind patient-related factors as well (such as level of hygiene, etc.) before deciding on where to administer the injection. Having a separate injection room with semi-sterile conditions should be acceptable. Whether to change the patient's clothes into operation theatre attire or not would be an individual decision.
5. Intraprocedure practices:  
The survey showed that most surgeons use gloves, mask, and eye speculum during the procedure. There is really no controversy on the use of sterile gloves and face mask for the hospital personnel during the procedure (for the surgeon as well as nurses). Using an eye speculum has also been shown to reduce risk of infection by preventing contact of the needle with the eyelashes.<sup>[5]</sup>  
The survey is silent on the use of povidone-iodine as a preprocedure application. Perhaps it is understood that use of povidone-iodine is a must and hence need not be queried. However, there are issues relating to the use of povidone-iodine that need to be discussed.

- a) It can be safely assumed that everyone instills 5% povidone-iodine in the conjunctival cul-de-sac before the injection
  - b) However, is cleaning of the skin of eye lids and eyelashes with povidone-iodine a standard protocol? Sterilizing the eyelashes and skin of eye lids reduces the risk of accidental needle contamination further<sup>[6]</sup>
  - c) What if patient is allergic to iodine?  
0.1% aqueous chlorhexidine has been shown to be a good alternative for preprocedure antiseptics.<sup>[7]</sup> This study also showed that the comfort level appears to be better with chlorhexidine compared to povidone-iodine.
6. Postprocedure practices:

**Patching:** 77.3% of Indian ophthalmologists prefer eye patch immediately after procedure. Many cataract surgeons have given up routine patching after cataract surgery.<sup>[8]</sup> Considering the tiny 30-gauge puncture involved in intravitreal injection, routine patching is probably unnecessary.

**Antibiotic drops:** The survey showed that 89.3% use postprocedure antibiotics. There are some who use antibiotics before and after the procedure as well. Considering the monthly injections some patients receive, this would amount to roughly being 10 days on antibiotic and 20 days off antibiotic every month. One has to consider the epithelial toxicity of such continued use of antibiotic drops in addition to the effect on the normal bacterial flora. Studies have shown the lack of prophylactic value of use of these antibiotics<sup>[9]</sup> and actually an increase in incidence of endophthalmitis with their use.<sup>[10]</sup> Hence, there is need to educate ophthalmologists on the need to avoid routine use of antibiotic drops pre- and postprocedure for intravitreal injections.

**Bilateral simultaneous injections:** The survey unfortunately did not cover this aspect of intravitreal injections. Simultaneous bilateral injections are a norm in most developed countries and have been found to be safe and well tolerated.<sup>[11]</sup> This however may not be an issue for most patients who may not mind a second visit next day for fellow eye injection.

If one opts to inject in both eyes on the same day, one needs to use separate preparation and set up for the two eyes (change of gloves; new pack to be opened, fresh speculum, etc.).

This survey conducted by the AIOS is an important step toward understanding the differences in practice of administering intravitreal injections in India. This commentary attempts to discuss the important points that arose out of this survey and put them in a perspective to facilitate a potential consensus approach.

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