



# **Best Practice Intravitreal injections in a safe and sustainable way**

Author: Project Group Sustainable Ophthalmology, Redmer van Leeuwen

Approved by the Working Group on Medical Retina and chair of the Quality Committee of the Dutch Ophthalmology Society, March 2021

Final version, approved by the Medical Retina working group

1. Introduction

2. What do the current guidelines say?

3. Advice

4. Conclusion

5. Worked out example

6. References

7. Figure

1. Introduction

The injection of medication into the vitreous humor of the eye, the intravitreal injection (IVI), was developed in 2003, later the number of injections has exploded worldwide. In the Netherlands, the number of IVIs has increased from 100,000 injections in 2012 to 300,000 injections in 2019 (NZa figures). For the time being, there seems to be no alternative for this successful labour-intensive therapy.

The first guideline for the IVI procedure in 2004 (Aiello, 2004), which was revised in 2014 (Avery, 2014). In Dutch practice, this guideline appears to have been worked out well in essence. There does appear to be a diversity in the materials used (see Figure 1).

## **1 Introduction**

The main complications of an IVI are endophthalmitis, lens perforation, corneal erosion, and conjunctival hemorrhage. Endophthalmitis is the most serious complication and has an incidence of 0.01 – 0.26% (Menchini, 2018). An IVI guideline should aim to prevent this complication. This requires optimal disinfection of the eye and rapid and sterile introduction of the needle into the eye.

The aim of this Best Practice is to advise on how ophthalmologists in the Netherlands can perform the IVIs as safely and sustainably as possible. Not using unnecessary materials has the most impact on sustainability, fully through reuse and finally recycling waste from (reduce-reuse-recycle principle). Given the enormous quantities, a small saving per procedure can lead to significant gains in terms of costs, waste, and carbon footprint (see point 5). Therefore, the aim should be to use only the essential parts with an IVI and to leave unnecessary gestures.

## **2. What do the current Guidelines say?**

This Best Practice is based on the 'Updated Guidelines of an Expert Panel' from the US (Avery 2014, see Figure 2), the 'Euretina Expert Consensus Recommendations' from 2018 (Gryzbowski 2018, see Figure 3) and the Dutch guideline AMD from 2014. In these recommendations by American and European experts, all steps of the IVI procedure are substantiated with the most recent scientific literature and the opinion of retina experts. The text below quotes from these recommendations. In exceptional cases, references are made to specific publications. Sometimes reference is made to other guidelines or literature.

### *Setting/Space*

The legal requirements in this regard differ between countries and so does clinical practice. In the US and Canada, most IVIs are performed in the doctor's office, while in other countries the OR or treatment room is used. The question is this difference is reflected in the risk of endophthalmitis. Studies in the US report incidence rates of 0.029% to 0.057%. In countries where the IVI takes place in the OR, an incidence of 0.009% to 0.021% is found. Comparative studies could not find any difference in risk between office-based and OR-based procedures. The effect of air control was also not demonstrable (Dossarps 2015).

Euretina expert panel: “In conclusion, operating theatre, adequate room or in-office settings are recommended for IVI.”

### *Anesthetics*

Usually proparacaine or lidocaine drops are used. There is no evidence for superiority of any particular type of anesthetic. The added value of a cotton swab soaked in anesthetic has also not been demonstrated. A retrospective analysis of a US clinic found that the use of lidocaine gel was associated with an increased risk of endophthalmitis (Stern et al 2019).

### *Topical antiseptics*

It is recommended by both guidelines to disinfect the fornix and conjunctiva with povidone iodine eye drops, preferably 2 times, and leave on for 30 seconds. Usually the 5% concentration is used. Brushing the eyelids is not recommended because this can release bacteria from the meibomian glands. Dropping povidone iodine on the eyelids is recommended by some. Chlorhexidine is a safe alternative.

### *Perioperative antibiotics*

A systematic review and meta-analysis showed that antibiotic prophylaxis is not associated with a reduction in endophthalmitis risk (Benoist d'Azy et al, 2016). Also, a recent large study from Japan showed again that topical antibiotic prophylaxis does not reduce the risk of endophthalmitis (Morioka et al 2020). Unnecessary use of antibiotics will lead to resistance. For this reason, the use of antibiotic drops is not recommended, both before and after the IVI procedure.

### *Pupil dilation*

In some countries, ophthalmologists want the pupil to be dilated to allow visualization of the lens and papilla. However, this is not essential and is not recommended as standard procedure. Informing the patient about light perception is a good alternative.

### *Injection location*

There is agreement on the location of the injection: 3.5 to 4 mm from the limbus. In the US, only 56% of respondents measured this distance for the IVI, mostly using a marker. No statement is made about the necessity of using a compass or marker.

### *Eyelid spreader*

The usefulness of an eyelid dilator has been demonstrated in a prospective, placebo-controlled trial with pegaptanib, in the early years of the IVIs (Mansour et al 2012). Alternatives have been studied, but there seems to be a consensus about the standard use of an eyelid dilator in IVIs. No statement is made about the type of spreader or the choice between reusable or disposable spreader.

### *Gloves, clothing, and drapes*

The WHO prescribes the use of surgical gloves in surgical interventions in general (WHO guidelines on hand hygiene in health care, 2009). There are no prospective randomized studies on the use of sterile or non-sterile gloves or drape in an IVI.

The US expert panel (Avery 2014) stated that the use of sterile or non-sterile gloves fits into modern clinical practice, in combination with hand washing. In addition, these experts argued that the use of a sterile drape is optional. Applying a hole cloth to the face can cause stress and discomfort, takes time, and was found to even lead to more infections in a Cochrane review of 5 randomized trials (Tailor 2011; Webster 2013). For this reason, it seems better not to use a drape.

US expert panel: “Although the use of gloves has not been shown to reduce the risk of endophthalmitis, sterile or nonsterile gloves may be used as consistent with modern office practice. There is no evidence to support the routine use of a drape when performing IVT injections.”

Euretina expert panel: “In summary, there is no significant evidence that the use of sterile gloves or drape reduces endophthalmitis rates or adverse events, as prospective and randomized controlled trials are lacking. From the available data we conclude to consider gloves, sterile or nonsterile, appropriate for IVI; draping, however, may not be essential. Appropriate clothing depending on the IVI setting is advised.”

### *Face mask*

Several studies have shown that wearing a mask as well as being silent by the surgeon significantly reduces the spread of bacteria from the oral flora. It is therefore recommended that the doctor and nurse wear a mask during the IVI procedure. Recently, through experimental research has shown that wearing a mouth mask by the patient can actually increase the risk of endophthalmitis (Hadayer et al, 2020).

No statement is made about hat and jacket, but there seems to be no hard indication to recommend this personal protection in this setting.

### *Eye bandage/eye pad*

In the guidelines of the American and European experts, no statement is made about an eye bandage after the IVI. There doesn't seem to be any medical argument for this either. The wound is closed and does not leak. Patient comfort could well be an argument.

### **3. Advice**

Based on the above, the following advice applies to the requirements for an IVI:

Essential: Mouth mask (operator and assistant) Gloves (sterile or non-sterile, operator only) Anesthetic eye drops Povidone iodine drops Sterile eyelid spreader (single use or reusable)

Optional: Compass/marker (preferably reusable) Cotton swabs for iodine fornix Non-sterile gauze and non-sterile fluid for removing iodine Eye ointment (usable for several patients)

Not necessary:

Hole cloth Swab for anesthesia and massage

Tweezers

Hat

Jacket (for doctor and patient)

Tablecloth

Antibiotics Pre and Post Injection

Savings can be made by omitting optional and unnecessary parts (Reduce). An option that needs further investigation is the reuse of gloves (Reuse), for example by washing the hands with alcohol while wearing gloves between procedures.

Tips:

- Use a non-sterile tray of iodine for multiple patients
- Iodine can also be poured into the packaging/bag of the cotton swabs, instead of in a container
- Bottles of oxy/tetracaine/cocaine instead of minims
- Use sterile (crepe) paper wrapping paper, instead of plastic coated paper

### **4. Conclusion**

In order to realize savings in costs, waste and CO<sub>2</sub> emissions, it makes sense to critically assess the material you are currently using for the IVI and to adjust it if necessary. This Best Practice, based on the literature, can help with that.

Given the large numbers of IVIs, the use of only essential materials during this procedure leads to significant savings in costs, waste and CO<sub>2</sub> emissions. Based on this Best Practice, based on the literature, you can critically assess your IVI procedure: you can omit optional and unnecessary parts. Finally, the choice of materials from which the IVI set is built can also contribute to a saving in costs and CO<sub>2</sub> emissions.

## **5. Saving example**

In the UMC Utrecht, a disposable IVI set has been used for many years with a plasticized tablecloth, metal spreader, 2 plastic swabs for iodination of the fornix, 1 plastic swab for anaesthesia, a plastic measuring stick, a container for the iodine, and a plastic container. for the sturdiness. All together this set weighs 135.5 grams. This IVI set was adapted on the basis of the above Best Practice. After removing the two plastic containers, replacing the plasticized tablecloth with a much smaller crepe paper sheet, and a much smaller packaging, this weight had decreased to 66.5 grams. In combination with recycling of the clean paper and plastic, a reduction in the carbon footprint from 0.68 kilograms of CO<sub>2</sub> to 0.17 kilograms of CO<sub>2</sub> could be achieved. See Figure 4 for the exact dates. If this reduction of 75% is extended to the 300,000 injections that take place annually in the Netherlands, based on approximately identical disposable IVI sets, a gain of 153,000 kg CO<sub>2</sub> is possible. This carbon footprint corresponds to 695,461 kilometers of driving.

## **References**

- Menchini et al. Antibiotic prophylaxis for preventing endophthalmitis after intravitreal injection: a systematic review. *Eye* 32:1423-1431, 2018
- Aiello et al, Evolving guidelines for intravitreal injections. *Retina* 24:S3-S19, 2004

- Avery et al, Intravitreal injection technique and monitoring. Updated guidelines of an expert panel. *Retina* 34:S1-S18, 2014
  
- Mansour et al, Insight into 144 patients with ocular vascular events during VEGF antagonist injections. *Clin Ophthalmol* 2012;6:343-363
  
- Grzybowski et al, 2018 Update on intravitreal injections: Euretina expert consensus recommendations. *Ophthalmologica* 2018 (<http://dx.doi.org/10.1159/000486145>)
  
- Webster et al. Use of plastic adhesive drapes during surgery for preventing surgical site infection. *Cochrane Database Syst Rev* 2013;1:CD006353
  
- Hadayer et al. Patients wearing face masks during intravitreal injections may be at a higher risk of endophthalmitis. *Retina* 40(9):1651-1656, 2020
  
- Siu et al. Systematic review of reusable versus disposable laparoscopic instruments: costs and safety. *ANZ J Surg* 87 (2017) 28-33
  
- Dossarps D, et al. Endophthalmitis after intravitreal injections: incidence, presentation, management, and visual outcome. *Am J Ophthalmol* 2015;160:17-25
  
- Morioka et al. Incidence of endophthalmitis after intravitreal injection of an anti-VEGF agent with or without topical antibiotics. *Scientific Reports* 2020; 10:22122



- Nederlandse Zorgautoriteit <https://www.opendisdata.nl/msz/zorgactiviteit/039810>
  
- WHO guidelines on hand hygiene in health care 2009  
[https://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906\\_eng.pdf?sequence=1&isAllowed=y&ua=1](https://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906_eng.pdf?sequence=1&isAllowed=y&ua=1)
  
- Benoist d'Azy et al. Antibio prophylaxis in prevention of endophthalmitis in intravitreal injection: a systematic review and meta-analysis. PLoS One 2016 <https://doi.org/10.1371/journal.pone.0156431>
  
- Stern et al. Predictors of endophthalmitis after intravitreal injection. A multivariable analysis based on injection protocol and povidone iodine strength. Ophthalmology Retina 2019;3:3-7



Figur 1. Various IVI sets in the Netherlands.

8

Table 2. Areas of General Agreement by Committee Members

---

Povidone-iodine (5–10%) should be the last agent applied to the intended injection site before injection. If a gel anesthetic is used, povidone-iodine should be applied both before and after application of gel, as retained gel may prevent povidone-iodine from contacting the conjunctival surface of the injection site

Pre-, peri-, or postinjection topical antibiotics are unnecessary

There is no evidence to support the routine use of a sterile drape

Avoid contamination of the needle and injection site by the eyelashes or the eyelid margins

Avoid extensive massage of the eyelids either pre- or postinjection (to avoid meibomian gland expression)

Use adequate anesthetic for a given patient (topical drops, gel, and/or subconjunctival injection)

Use of sterile or nonsterile gloves as consistent with modern office practice, combined with strong agreement regarding the need for handwashing before and after patient contact

Either surgical masks should be used or both the patient and providers should minimize speaking during the injection preparation and procedure to limit aerosolized droplets containing oral contaminants from the patient and/or provider

Monitor IOP both pre- and postinjection

Routine anterior chamber paracentesis is not recommended

---

Table 3. Areas With No Clear Consensus by Committee Members

---

Need for povidone-iodine application to the eyelids, including the eyelashes and eyelid margins. All agreed that when povidone-iodine is applied to the eyelashes and eyelid margins, eyelid scrubbing or eyelid pressure adequate to express material from the meibomian glands should be avoided

Use of a speculum (some prevent contact between the needle/injection site and the eyelashes and eyelids with manual lid retraction)

Need for pupillary dilation and postinjection dilated examination of the posterior segment (although some viewed the return of formed vision as sufficient, others routinely dilate the pupil and examine the posterior segment after injection)

Use of povidone-iodine flush (most preferred drops only and saw no benefit to allowing the povidone-iodine to dry before injection)

---

Figur 2. From Avery et al., 2014

9

**Table 1.** Expert consensus recommendations on intravitreal injections (IVI)

Subject	Recommendations
Clinical setting for IVI	Operating theater, adequate room or in-office setting
Anesthetics	Topical anesthesia No recommendation for a specific substance or technique
Topical antisepsis	Topical administrations of 5% povidone-iodine over at least 30 s into the conjunctival sac. Chlorhexidine for patients with local irritation due to povidone-iodine
Perioperative antibiotics	Not recommended
Pupil dilation	No concluding recommendation, but it might be advisable for beginners in order to be able to immediately examine the retinal vessel perfusion after IVI
Globe softening	No recommendation Might be considered in vulnerable eyes
Lid speculum	Sterile speculum is recommended
Needle gauge and length	30-gauge or thinner needles are recommended for liquid injections whereas larger needles should be used when necessary
Injection location	Inject through the pars plana, between 3.5 and 4 mm from the limbus Switch injection sites if patients receive repeated IVI
Feasibility of bilateral injections	Handle each injection as separate procedure
Gloves/draping	Gloves are recommended Draping may not be essential
Use of facial masks	Face masks recommended

Figur 3. From Grzybowski et al, 2018

10

	Totaal afval	Restafval	CO <sub>2</sub> footprint
Baseline	135,5 g	135,5 g	0,68 kg CO <sub>2</sub>
Na reductie en reuse	66,5 g	66,5 g	0,36 kg CO <sub>2</sub>
Na recycle	66,5 g	34,5 g	0,17 kg CO <sub>2</sub>
Afname per injectie	69 g (-50,9%)	101 g (-74,5%)	0,51 kg CO <sub>2</sub> (-75%)
Afname per 50 injecties	3,45 kg	5,05 kg	25,5 kg CO <sub>2</sub>
Afname per 300.000 injecties	20.700 kg	30.300 kg	153.000 kg CO <sub>2</sub> *

Figuur 4. Waste from disposable intravitreal sets at UMC Utrecht, broken down by weight of total waste, residual waste (hospital specific waste) and CO<sub>2</sub> emissions.