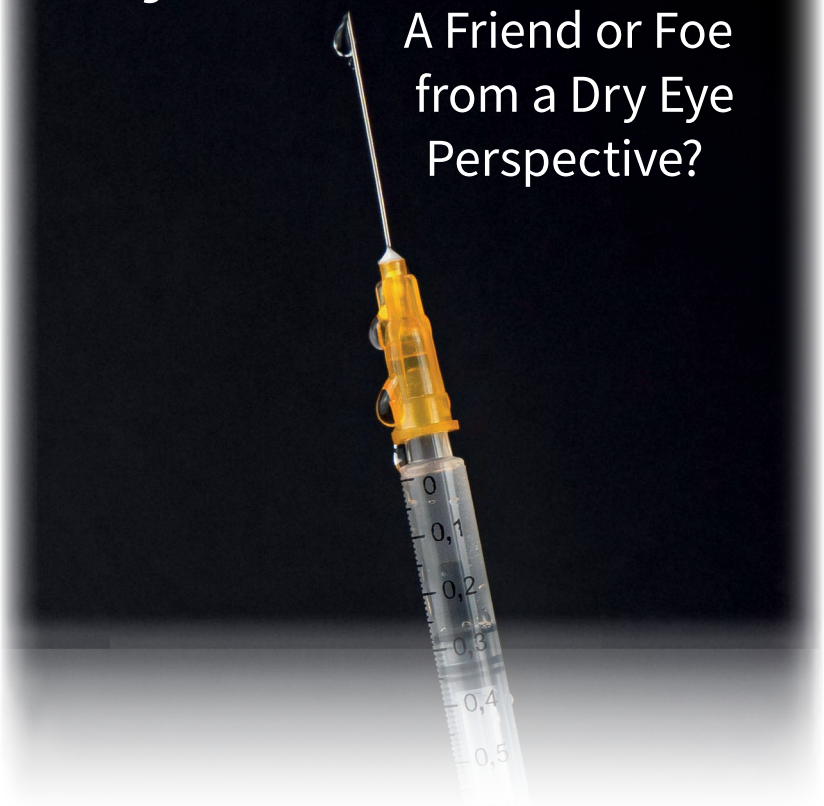
Serial Intravitreal Injections — A Friend or Foe from a Dry Eye Perspective?



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This is a summary of our recent study published in Ophthalmology. We investigated the effects of repeated intravitreal injections with anti-vascular endothelial growth factor (anti-VEGF) on dry eye parameters and found a healthier ocular surface, including reduced meibomian gland loss, in injected eyes compared to non-injected fellow eyes. You can find the full article here: Malmin A, et al. Associations between Serial Intravitreal Injections and Dry Eye. Ophthalmol. *2023 May;130(5):509-515. doi: 10.1016/j.ophtha.2023.01.009.*

Intravitreal injections with anti-vascular endothelial growth factor (anti-VEGF) appear to benefit ocular surface health in patients with neovascular age-related macular degeneration.[1] Our study at the University Hospital of Stavanger included 90 patients who had received on average 30 intravitreal injections with anti-VEGF in one eye. Before the injection, patients underwent a standard antiseptic procedure with povidone–iodine 5% (**Figure 1**). In injected eyes, we found a higher concentration of meibomian glands in the upper and lower eyelids and lower conjunctival redness compared to the fellow non-injected eyes (**Figure 2**). Patients with meibomian gland dysfunction are known to harbor a more diverse bacterial community on the ocular surface than healthy controls.[2–4] Povidone–iodine, with its broad antimicrobial action,[5] may have a beneficial effect on meibomian glands and conjunctival inflammation through the limitation of ocular surface microbes. Povidone–iodine is known to produce corneal epitheliopathy shortly after its application.[6] In our study, we found no differences in corneal fluorescein staining between injected and non-injected eyes at four weeks after treatment. Thus, we suggest that the potential povidone–iodine-related epitheliopathy is temporary, resolving within weeks after its application.

VEGF stimulates the release of pro-inflammatory cytokines, and their concentrations in the tear fluid correlate positively with the severity of dry eye disease.[7–9] Anti-VEGF injected into the meibomian glands has been shown to improve dry eye parameters such as lid margin vascularity, conjunctival redness, and tear break-up time.[10] A potential explanation behind the paler conjunctivas (**Figure 3**) and healthier meibomian glands in injected eyes

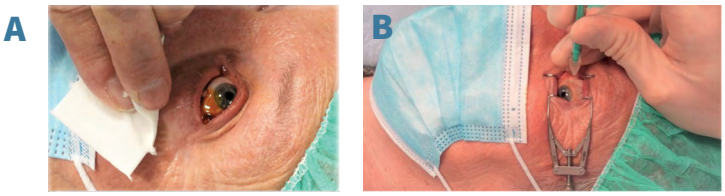

Figure 1. Antiseptic procedure. A) Application of one drop of povidone–iodine to the ocular surface. B) Cleaning of margin, lashes, and periocular skin with povidone–iodine. Photographs by Agni Malmin, with patient approval.

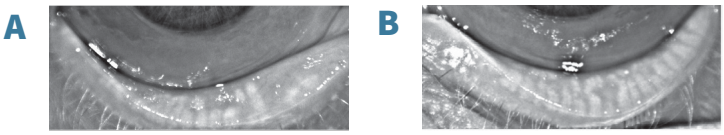

Figure 2. A) Meibomian glands in the lower eyelids of a 75-year-old patient who had received 0 intravitreal injections with anti-VEGF in her right eye and B) 15 intravitreal injections in her left eye. Images by Agni Malmin, with patient approval.

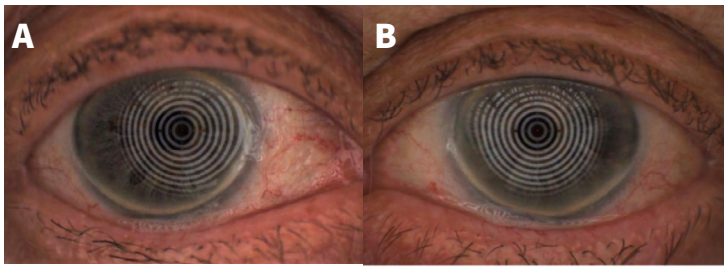

Figure 3. A) Conjunctival redness in a 75-year-old patient who had received 0 intravitreal injections with anti-VEGF in her right eye and B) 85 injections in her left eye. Photographs by Agni Malmin, with patient approval.

found in our study could be a blockage of ocular surface VEGF and thus a reduction in cytokine-mediated inflammation. The mechanism of action could be a reflux of anti-VEGF through the scleral injection canal, leading to a deposition of anti-VEGF in the subconjunctival space. This would allow for diffusion into the tear fluid and meibomian glands lining the eyelids. We hope that our future work may uncover potential mechanisms behind a healthier ocular surface in eyes receiving multiple intravitreal injections with anti-VEGF. To this end, we will examine the level of pro-inflammatory cytokines in the tear fluid of these patients, followed by extended protein analyses (proteomics).

Key points:

- Eyes receiving intravitreal injections with anti-VEGF show healthier meibomian glands.
- Conjunctival redness was lower in eyes receiving intravitreal injections with anti-VEGF.
- Pre-injection povidone–iodine application did not produce long-term corneal epitheliopathy.

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