Increased Incidence of Rise in Intraocular Pressure after Intravitreous Injection of Aflibercept with Prefilled Syringes

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Background

Intravitreal injections (IVI) with prefilled syringes (PFS) are supposed to reduce procedure time and increase patient safety due to a lower reported incidence of endophthalmitis.[1] Postoperative rise in intraocular pressure (IOP) is suspected to lead to glaucomatous changes.[2] In June 2020, following the introduction of the new aflibercept PFS in our clinic, we observed an unusual incidence of severe spikes in intraocular pressure (IOP), leading to short-term transient visual loss in five eyes of five patients that were reported to Swissmedic. Four of the five patients had diabetic retinopathy with macular edema and one had wet age-related macular degeneration. All eyes have already been treated with intravitreal anti-VEGF therapy with aflibercept vials without any complications. Two of the five eyes had to undergo a paracenthesis as the IOP was above 60mmHg whereas in the remaining three eyes the symptoms and IOP rise normalized spontaneously.
The elaboration of their possible cause was published elsewhere. [3,4,5] Our aim here was to analyze the IOP changes following IVI procedures.

Methods

The IOP was measured pre- and postoperatively using a non-contact tonometer in patients receiving IVI with ranibizumab PFS or aflibercept, either with PFS or manually withdrawn from vials (groups RP, AP and AV, respectively). A random intercept model was run with type of intravitreal injection (IVI) and pre-treatment IOP as fixed factors. A second model was run including other possibly confounding factors (age, sex, pathology, pseudophakia, hyperopia, myopia, and number of IVI). An analysis was performed with a binary outcome, i.e., IOP > 30mmHg post-treatment. A chi-square test and a mixed effects logistic regression were run to test the effect of type of IVI on IOP > 30mmHg.

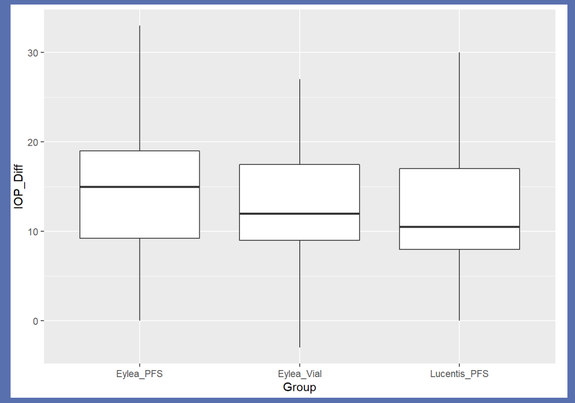

Figure 2. Boxplot of difference of IOP by IVI. The line in the box stands for the median, the lower and upper hinges correspond to the first and third quartile. Mean IOP difference was 14.23, 12.59, and 11.89 for “Eylea_PFS”, “Eylea_Vial”, and “Lucentis_PFS”, respectively. The random intercept model indicates that type of IVI is not greatly affecting post-treatment IOP. The p-values under the blue lines indicate the pairwise comparisons using t-tests with non-pooled standard deviations (SD).

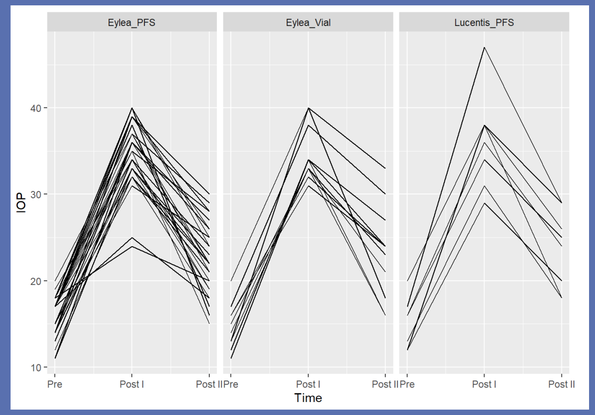

Figure 2. Course of intraocular pressure (IOP). For eyes with three measurements (n=48), IOP first rose after injection for all three types of intravitreal injection before it decreased again, though not to pre-treatment level. Figure 3 and 4 show the correlation between pre and post-treatment IOP.
The random intercept model indicates that pre-treatment IOP has a large effect on post-treatment IOP

Results

We included 173 eyes of 141 consecutive patients in our study undergoing IVI either with RP, AO or AV at our retina outpatient clinic. Mean IOP difference was 14.23 (standard deviation, SD 6.45), 12.59 (SD 6.59), and 11.89 (SD 6.78) mmHg for the AP, AV, and RP groups, respectively. These differences were not statistically significant. The only significant confounding factor identified as a potential risk factor for IOP rise was the pre-treatment IOP. An IOP rise to > 30 mmHg was observed in 40.7% in the AP group versus 31.4% in the AV, and 22.2% in the RP group, respectively (chi-square test p < 0.001, AP vs. RP p=0.060).

Conclusion

We observed a higher incidence of IOP elevations above 30mmHg following IVI with the aflibercept PFS. One reason for this could be the error-proneness of administering the correct volume with the AP, which has a higher diameter compared to the other syringes used for the AV or RP injections. Moreover, preoperative IOP tends to play a role for the degree of postoperative pressure rise. Further prospective studies are warranted in order to elucidate the exact reason behind our observations; till then, caution should be taken when using the APFS in order to prevent optic nerve damage in patients undergoing long-time anti-VEGF therapy.

References

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