

Sir, Reply to Grzybowski and Ascaso

We thank Drs Grzybowski and Ascaso¹ for their interest in and comments on our recent article.² We agree that in our paper there is a lack of details concerning the statistical tests used (which were omitted for the sake of brevity). In the study, we proved that each variable group was normally distributed using the Kolmogorov-Smirnov normality test. Then we applied the ANOVA for repeated measures test, which best fitted for our analysis. Please note, the Kruskal-Wallis test is valuable only for a two-group comparison. We also agree that the lack of a control group is crucial, and this was acknowledged as a limitation of our study. We also acknowledged the unmasked design of the study as a limitation of our analysis. Regarding the evaluation of posterior hyaloid peeling, our method to describe the intrasurgical findings has been already published by Azzolini et al³ in a study investigating autologous plasmin enzyme for diabetic macular oedema, and, to our knowledge, no other classification systems are available in the literature.

In the conclusion section, we stated that a single intravitreal autologous plasmin enzyme injection seemed to be insufficient to induce a complete posterior vitreous detachment in patients affected by focal vitreomacular traction syndrome, as in our case series, we did not obtain any complete posterior vitreous detachment with a single injection. We thank the authors for the opportunity to clarify this important aspect, which we do not find contradictory. As per our ethical committee approved protocol (reported in the Methods section), we were allowed to perform just one single intravitreal injection for each study patient, with a 24-hour waiting time before vitrectomy. Although we could not ascertain if a greater time gap could have influenced the rate of posterior vitreous detachment occurrence, we remarked that the single injection appeared as a useful tool in vitreoretinal surgery by obtaining an easier-to-peel posterior hyaloid.

Finally, during the revision process of our paper, we preferred to exclude the comparison of our results with the MIVI-IIT study,⁴ as the MIVI-IIT study has a very different study design and uses a different drug. Particularly, we believe that our impossibility (per protocol) to re-inject patients preclude any comparison between the two studies.

Conflict of interest

The authors declare no conflict of interest.

References

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- 2 Codenotti M, Maestranzi G, De Benedetto U, Querques G, Della Valle P, Iuliano L *et al*. Vitreomacular traction syndrome: a comparison of treatment with intravitreal plasmin enzyme *vs* spontaneous vitreous separation without treatment. *Eye* 2013; 27: 22–27.

- 3 Azzolini C, D'Angelo A, Maestranzi G, Codenotti M, Della Valle P, Prati M et al. Intrasurgical plasmin enzyme in diabetic macular edema. Am J Ophthalmol 2004; 138: 560–566.
- 4 Stalmans P, Delaey C, de Smet MD, van Dijkman E, Pakola S. Intravitreal injection of microplasmin for treatment of vitreomacular adhesion: results of a prospective, randomized, sham-controlled phase II trial (the MIVI-IIT trial). *Retina* 2010; 30: 1122–1127.

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Sir,

Comment on 'Vitreomacular traction syndrome: a comparison of treatment with intravitreal plasmin enzyme *vs* spontaneous vitreous separation without treatment'

In some patients, incomplete posterior vitreous detachment leads to symptomatic vitreomacular adhesion or vitreomacular traction syndrome. This is a medico-surgical problem in which new therapy is interesting due to the potential prognosis of the untreated disease and its only actual therapy being surgery. Several studies^{1,2}, have reported the use of intravitreal proteases such as plasmin, which is able to degrade biochemical glue composed of proteoglycans, including laminin and fibrinectin. The microplasmin is a truncated derivative of plasmin. The product thus obtained has a significantly reduced size and maintains native proteolytic activity. Stalmans et al.¹ report that intravitreal injection of microplasmin was superior to injection of placebo in altering the vitreoretinal interface significantly, with the resolution of more vitreomacular tractions and the closure of more macular holes, than that accomplished by placebo treatment of the affected eyes. Therefore, Codenotti et al³ should wait longer to conclude that 'a single intravitreal APE (autologous plasmin enzyme) injection seems insufficient to induce a complete posterior vitreous detachment in these patients'. In previous studies, there was no statistically significant difference between placebo and microplasmin before 7 days, but it was significant for all comparisons after 7 days, especially as there seemed to be a marked difference during surgery in the adhesion of the posterior hyaloid between autologous plasmin enzyme and placebo treatment in their study.3

Conflict of interest

The authors declare no conflict of interest.

References

1 Stalmans P, Benz MS, Gandorfer A, Kampik A, Girach A, Pakola S *et al.* MIVI-TRUST Study Group. Enzymatic