Letter to the Editor Re: "Comparison of 20% Autologous Platelet-Rich Plasma Versus Conventional Treatment in Moderate to Severe Dry Eye Patients"

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Dear Editor,

We read with great interest the study by Sachan et al.[1] examining the comparative efficacy of autologous platelet-rich plasma (aPRP) and conventional therapy for moderate-to-severe dry eye disease. The authors should be commended for implementing a robust design with clearly defined outcome measures and a meaningful follow-up period. While the therapeutic benefits of aPRP are compelling, we identified methodological and interpretive issues that affect the strength of clinical inferences, particularly regarding the evaluation of treatment response. Chief among these is the reliance on mean group differences in Ocular Surface Disease Index (OSDI) without reporting the proportion of patients achieving a minimal clinically important difference (MCID). Statistically significant differences in OSDI scores may not equate to symptom relief that is meaningful to patients. For instance, a 15-point OSDI reduction is commonly considered the MCID threshold.[2] Reporting this would have contextualized the patient-perceived benefit and helped guide clinical adoption.

Similarly, while p values are frequently cited for intergroup comparisons of secondary outcomes such as tear break-up time, Schirmer's test, and corneal fluorescein staining, these are time-varying, observer-dependent variables that can be influenced by environmental conditions.[3] However, no stratified variance analysis or adjustment for within-subject correlation appears to have been performed, despite repeated measurements on the same eyes. In studies of bilateral ocular disease, paired-eye statistical models better account for intra-patient correlation than independent-sample t-tests,[4] which were used in this study. The use of inappropriate models increases the risk of type I error, particularly with small sample sizes.

Additionally, the authors did not quantify the platelet concentration in the prepared aPRP drops. Given the direct link between platelet-derived growth factor content and epithelial recovery,[5] the absence of dosage validation introduces uncertainty in replicability. This is clinically relevant because interindividual variability in baseline platelet levels can lead to inconsistent therapeutic effects, especially when generalizing across diverse patient populations.

Notably, the study concluded that aPRP improves visual acuity; however, the data revealed that best-corrected visual acuity (BCVA) changes were not statistically significant at any time point. Including BCVA as a primary outcome when it remained unchanged across groups risks overinterpretation, particularly when no prespecified thresholds were provided to define clinically meaningful change.

Finally, although conjunctival impression cytology data were a novel and welcome addition, the grading system used was not standardized or referenced, limiting the generalizability of the histopathologic interpretation. Without a validated scoring metric, reported cytological improvements should be interpreted with caution.

Keywords: Autologous platelet-rich plasma, dry eye disease, ocular surface health, minimal clinically important difference, statistical modeling, regenerative therapies

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Despite these concerns, this study adds value to the ongoing exploration of biologics in ocular surface disease and reflects a growing interest in patient-specific regenerative therapies. Constructive scrutiny of methodology, particularly outcome reporting and statistical modeling, is essential for translating findings into clinical practice. We appreciate the authors' contributions to this evolving field.

Declarations

Authorship Contributions

Concept: R.M., P.S., R.S., Design: R.M., P.S., R.S., Data Collection or Processing: R.M., P.S., R.S., Analysis or Interpretation: R.M., P.S., R.S., Literature Search: R.M., P.S., R.S., Writing: R.M., P.S., R.S.

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Reply

We would like to thank you for the opportunity to respond to the issues raised in the letter and to clarify aspects of our study[1] related to these concerns. We would also like to thank the authors for their interest in our paper and for taking the time to express their observations.

We totally agree that reporting the proportion of patients achieving a minimal clinically important difference (MCID) would have been better than reporting Ocular Surface Disease Index (OSDI) scores. The problem with MCID is that there is no single universally agreed upon MCID for OSDI. I would like to point out that the study provided as a reference is a neurology article.[2] There is no consensus on the method used to measure MCID. Also, a multitude of factors affect MCID, such as disease severity, study methodology, patient population, and treatment context. A key study published in 2010 established the following MCID ranges for OSDI: improvement of 4.5 to 7.3 points for mild to moderate disease and 7.3 to 13 points for severe disease.[3] However, we completely agree that once a single universally agreed upon OSDI MCID value is obtained, including it for calculation of symptom improvement will be of paramount importance.

We acknowledge the authors' concern regarding the potential for type I error due to repeated measures and intra-patient correlation in bilateral ocular disease. While regression models are more suitable for prediction analyses, in our study we primarily compared mean values between two groups. To address their concern, we re-analyzed the data with Bonferroni correction applied to control for type I error. The mean, standard deviation, and p-values remain unchanged. We appreciate this suggestion, as it has helped strengthen the statistical rigor of our results.

In this study, outcomes from both eyes were used. The results from this analysis are usually unbiased and the variance of estimate is similar to using all of the data with appropriate accommodation of correlation.[4] Regarding the use of a paired-eye statistical model and stratified variance analysis, we will try to incorporate these suggestions in our future studies. Also, we totally agree that platelet concentration should have been quantified in the prepared aPRP drops, especially the stored ones. We are very thankful for the suggestion and will definitely implement this approach going forward.

Regarding best corrected visual acuity (BCVA), I would like to clarify that the phrase "improved visual acuity" appears only once in the article, in a sentence citing references 17 and 18.[5,6] Therefore, it was an observation of other researchers. We clearly stated that the improvement in BCVA in the study group, while potentially relevant, did not reach statistical significance.

The grading system of impression cytology has been referenced as early as 1984[7] and as recently as 2025.[8] Therefore, it is a well standardized and referenced grading system. However, I agree that a scoring metric would have been better for objective quantification.

In summary, we are thankful to receive so much interest in our article. We truly acknowledge the appreciation of our study and will try to incorporate the suggestions in our future research.

Declarations

Authorship Contributions

Analysis or Interpretation: S.S., S.P.S., S.K., V.K.S., K.D., Literature Search: S.S., K.D., Writing: S.S., K.D.

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