Letter to the Editor Re: Evaluation of Medically Reversible Limbal Stem Cell Deficiency

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Keywords

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Dear Editor,

This is a response to a published article titled "Evaluation of Medically Reversible Limbal Stem Cell Deficiency" by Korkmaz et al.[1] This study describes the patients' demographics, etiology, and clinical results, providing important insights into the use of medication for limbal stem cell deficiency (LSCD). However, some aspects must be critically examined. First, the sample size of 29 eyes from 21 individuals is modest, potentially limiting the findings' generalizability. The variety of the underlying causes raises concerns regarding the suitability of a one-size-fits-all treatment strategy. Furthermore, the participants' ages (5 to 71 years) resulted in variations in their biological responses to therapy, implying that age-specific analyses may provide more nuanced insights.

The methodology utilized to assess the LSCD stage adhered to the requirements specified by the International LSCD Working Group and seemed to be effective. However, this study may have benefited from a more in-depth explanation of the medicinal therapy used. The absence of detail makes it difficult to duplicate the study and assess the efficacy of certain treatment techniques. Furthermore, while the results are promising, including a reduction in LSCD severity and an improvement in best-corrected visual acuity, the lack of a control group hinders an evaluation of the effectiveness of medical therapy compared to routine care or allows for limited observation to draw conclusions. Future research should include randomized controlled trials to increase the evidence base for the medical treatment of LSCD.

The reported data raise several questions. For example, how does LSCD's underlying etiology affect response to therapy? What characteristics of patients with complete LSCD regression can be used to guide future therapy decisions? Furthermore, what long-term results can we expect from various medical therapies, particularly for ocular rosacea and blepharitis? Exploring these questions can help us better understand LSCD management and make better therapeutic decisions.

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To promote new research and future approaches, studies should look into the molecular mechanisms driving LSCD and the possibility of targeted therapeutics. Furthermore, investigating the function of adjuvant therapy such as autologous serum ointments and anti-inflammatory medications could provide a more holistic approach to LSCD management. Long-term studies evaluating the durability of therapeutic effects and patient quality of life following therapy would also make valuable contributions to this research. Finally, including patient-reported outcomes in future research may ensure that therapies are more closely aligned with patients' actual experiences and expectations.

Declarations

Authorship Contributions

Concept: H.D., V.W., Design: H.D., V.W., Data Collection or Processing: H.D., V.W., Analysis or Interpretation: H.D., V.W., Literature Search: H.D., V.W., Writing: H.D., V.W.

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Reference

1. Korkmaz İ, Eratılgan NF, Palamar M, Eğrilmez S, Yağcı A, Barut Selver Ö. Evaluation of medically reversible limbal stem cell deficiency. Turk J Ophthalmol. 2024;54:251-256.

Reply

We would like to address the concerns raised in the letter to the editor regarding our article, "Evaluation of Medically Reversible Limbal Stem Cell Deficiency", which was published in Turkish Journal of Ophthalmology.[1] We thank the authors for taking the time to read our article with interest and provide valuable feedback. We are grateful for their contribution to the scientific community.

It is evident that the sample size (29 eyes of 21 patients) of the study was limited. Given the retrospective nature of this study, we included patients with reliable data to assess disease reversal. We expect that prospective studies, ideally including larger numbers of participants, will provide more valuable contributions.

Limbal stem cell deficiency (LSCD) is a sight-threatening ocular surface disease, with underlying mechanisms that vary based on the primary etiology. Direct physical damage to the limbal region leads to LSCD through limbal stem cell aplasia. On the other hand, limbal stem cell dysfunction becomes prominent in LSCD cases where increased inflammation plays a primary role. Chronic ocular surface inflammation leads to limbal niche dysfunction characterized by abnormal microenvironment and inadequate stromal support, resulting in impaired limbal stem cell function.[2] In our previous study, although the numerous underlying causes and age differences, we assessed the etiologies of LSCD involving chronic ocular surface inflammation and disruption of limbal niche homeostasis. As emphasized by the authors in the letter, regardless of the etiology of LSCD, a personalized and stepwise treatment protocol should be adopted instead of a one-size-fits-all strategy. However, our article aimed to highlight that, particularly in certain etiologies, addressing the re-establishment of limbal homeostasis could enable the treatment of LSCD without the need for further surgical intervention. Restoring ocular surface health and controlling inflammation are essential to re-establish homeostasis. Furthermore, if it is possible to eliminate all pathological conditions that may cause LSCD, such as by discontinuing contact lens use or avoiding toxic agents, this constitutes the basic approach. In accordance with the recommendations of the global consensus on the treatment of LSCD, the aforementioned approach should be adopted in all LSCD patients, regardless of whether or not surgical intervention is required.[3,4] Consequently, in our study, eliminating the underlying pathology, which primarily entailed anti-inflammatory and lubrication therapies, was regarded as the optimal medical approach for the specific needs of the eyes in question. Data analysis was conducted in accordance with these considerations.

A review of the literature on best corrected visual acuity (BCVA) reveals that BCVA was previously considered a criterion for the evaluation of the disease, both in diagnosis and treatment, prior to the publication of the global consensus on the diagnosis and treatment of LSCD. However, there is now a global consensus that BCVA is no longer considered a criterion in the evaluation and classification LSCD severity.[3] Consequently, BCVA was not associated with LSCD in this study, given that stromal opacity or other factors that may reduce visual acuity may not be associated with disease severity.

It is of great importance in the field of medicine to conduct controlled studies in order to obtain high-quality evidence. However, LSCD is actually classified under the rare diseases. Therefore, even in pharmacological and related research, phase studies are constrained by the regulations pertaining to orphan diseases.[5] In this study, which involved dependent data, the results were analyzed within this context.

The objective of the study was to draw the attention of clinicians to reversible LSCD, which we aimed to emphasize with a limited number of cases. Furthermore, we aim to pioneer more comprehensive studies on this subject, which also focus on molecular mechanisms, as suggested in the author's letter. Prospective, randomized controlled trials in the future will help answer remaining questions regarding the medical treatment approach to LSCD.

Declarations

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Concept: M.P., Ö.B.S., Design: N.F.E., Ö.B.S., Data Collection or Processing: İ.K., N.F.E., Analysis or Interpretation: S.E., A.Y., Literature Search: İ.K., Writing: İ.K.