Letter to the Editor

Vision Loss in Facial Filler Injections: The Necessity of Taking a Critical Look at the Role of Cross-Linkers in Hyaluronic Acid Fillers

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Revised: 2023/05/09
Accepted: 2023/09/09

Please cite this paper as:
Bahadoram M., Shamsaei G., Sharifi Fard M., Akade E., Davoodi S. Vision Loss in Facial Filler Injections: The Necessity of Taking a Critical Look at the Role of Cross-Linkers in Hyaluronic Acid Fillers. World J Plast Surg. 2021;12(2):112-113.
doi: 10.52547/wjps.12.2.112

DEAR EDITOR-IN-CHIEF

Cosmetic procedures have gained widespread popularity in modern society, with an increasing number of individuals incorporating them into their lifestyles. As medical advancements have led to the development of minimally invasive methods, the reliance on invasive surgeries such as rhinoplasty or otoplasty has significantly decreased. However, with the rise in popularity, concerns regarding adverse effects resulting from negligence have emerged.

Facial filler injections, classified as minimally invasive cosmetic procedures, involve the injection of specific substances into the patient's skin to reduce wrinkles, enhance facial volume, and augment features[1]. While complications associated with these injections are rare, it is crucial to acknowledge that they can have significant side effects. One of the most severe complications is the occurrence of blindness, attributed to the accidental injection of filler material into the facial vascular system, leading to the obstruction of critical vessels, including branches of the ophthalmic artery[2]. Although such instances are infrequent, they underscore the potential risks associated with this procedure.

Hyaluronic acid-based fillers have gained popularity due to their favorable characteristics, including minimally painful injections, temporary yet durable outcomes, and minimal probability of immunogenicity[3,4]. However, there have been reported cases of vision loss resulting from the use of hyaluronic acid-based fillers[5].

Hyaluronidase, an enzyme that can break down hyaluronic acid, has been used to address complications associated with hyaluronic acid fillers, such as delayed hypersensitivity and obstruction. However, achieving consistently effective treatment has proven challenging[6]. Hyaluronidase has a relatively short half-life, and effectively delivering the enzyme to the specific site of obstruction remains a considerable challenge[7]. Innovative approaches are needed to effectively address this issue.

The production process of hyaluronic acid-based fillers involves a crucial

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[DOI: 10.61186/wjps.12.2.112]

cross-linking step, where hyaluronic acid chains are interconnected using specific chemicals[8]. This cross-linking provides the desired firmness and longevity to the resulting gel. Instead of solely focusing on breaking down the constituent components of hyaluronic acid molecules using hyaluronidase, a more promising approach could involve targeting the cross-linking that holds these molecules together. Disrupting the intermolecular bonds created during cross-linking may lead to more effective treatments for addressing the blindness resulting from filler injections.

Traditionally, 1,4-butanediol diglycidyl ether (BDDE) and di-vinyl sulfone (DVS) have been used as cross-linkers in hyaluronic acid-based fillers, with BDDE emerging as the industry standard due to its enhanced durability and biodegradability[9]. However, there is a notable absence of research focused on exploring methods to enhance the breakdown of these cross-linkers. Investigating the development of enzymes specifically designed to degrade these cross-linkers is crucial. Interdisciplinary collaboration will be necessary to selectively target and degrade the cross-linking agents, potentially disintegrating the filler material and alleviating obstructions in the vascular system, thereby restoring vision and improving patient outcomes.

In conclusion, while facial filler injections have become increasingly popular, it is essential to acknowledge the potential risks and complications associated with these procedures. Addressing the occurrence of blindness resulting from filler injections requires innovative solutions. By targeting the cross-linking process and exploring methods to enhance the breakdown of cross-linkers, researchers can potentially develop more effective treatments. Further research and interdisciplinary collaboration are necessary to address this issue and improve patient outcomes.

CONFLICTS OF INTEREST

The authors declare that they have no potential conflicts of interest.

REFERENCES

1. Rohrich RJ, Savetsky IL, Avashia YJ. Assessing Cosmetic Surgery Safety: The Evolving Data. *Plast Reconstr Surg Glob Open* 2020;8(5):e2643. Published 2020 May 13. doi:10.1097/GOX.0000000000002643
2. Hwang CJ, Chon BH, Perry JD. Blindness After Filler Injection: Mechanism and Treatment. *Facial Plast Surg Clin North Am* 2021;29(2):359-367. doi:10.1016/j.fsc.2021.02.002
3. Draelos ZD, editor. Cosmetic dermatology: products and procedures. John Wiley & Sons; 2022 Mar 21. ISBN:9781119676867
4. Owczarczyk-Saczonek A, Zdanowska N, Wygonowska E, Placek W. The Immunogenicity of Hyaluronic Fillers and Its Consequences. *Clin Cosmet Investig Dermatol* 2021;14:921-934. Published 2021 Jul 16. doi:10.2147/CCID.S316352
5. Davidova P, Müller M, Wenner Y, König C, Kenikstul N, Kohnen T. Ophthalmic artery occlusion after glabellar hyaluronic acid filler injection. *Am J Ophthalmol Case Rep* 2022;26:101407. Published 2022 Feb 11. doi:10.1016/j.ajoc.2022.101407
6. Putthirangsiwong B, Vongsilpavattana V, Leelawongs S, Chanthanaphak E, Tunlayadechanont P, Chokthaweesak W. Superior Ophthalmic Vein Embolism Following Forehead Augmentation with Autologous Fat Injection. *Aesthetic Plast Surg* 2022;46(1):450-455. doi:10.1007/s00266-021-02414-0
7. Zein M, Tie-Shue R, Pirakitikulr N, Lee WW. Complications after cosmetic periocular filler: prevention and management. *Plast Aesthet Res* 2020;7:44. doi:10.20517/2347-9264.2020.133
8. Paap MK, Milman T, Ugradar S, Goldberg R, Silkiss RZ. Examining the Role of Retrobulbar Hyaluronidase in Reversing Filler-Induced Blindness: A Systematic Review. *Ophthalmic Plast Reconstr Surg* 2020;36(3):231-238. doi:10.1097/IOP.0000000000001568
9. Tezel A, Fredrickson GH. The science of hyaluronic acid dermal fillers [published correction appears in J Cosmet Laser Ther. 2014 Jan;16(1):45]. *J Cosmet Laser Ther* 2008;10(1):35-42. doi:10.1080/14764170701774901

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[DOI: 10.61186/wjps.12.2.112]