Aesth Plast Surg
https://doi.org/10.1007/s00266-023-03807-z

RESPONSE TO LETTER TO THE EDITOR

Reply to "Letter on Lipofilling Enriched with Adipose-Derived Mesenchymal Stem Cells Improves Soft Tissue Deformities and Reduces Scar Pigmentation: Clinical and Instrumental Evaluation in Plastic Surgery"

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Received: 20 November 2023 / Accepted: 4 December 2023

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I would like to thank the authors Zuguang Hua and Peng Wei for their positive feedback and particular attention to "Letter on Lipofilling Enriched with Adipose-Derived Mesenchymal Stem Cells Improves Soft Tissue Deformities and Reduces Scar Pigmentation: Clinical and Instrumental Evaluation in Plastic Surgery [1]".

I'm pleased to see that the scientific data reported in my paper [1] has been read with great interest by other authors. For this reason, I have been invited by the Aesthetic Plastic Surgery (APS) journal, to perform a "Reply", and, as already done previously for other articles published, I would like to thank the APS journal for this opportunity and for the possibility to share scientific information with several colleagues and permit a constructive comparison also to build new partnerships or to develop a new protocol and/or research.

I have read with attention the "Letter on" performed by the authors Zuguang Hua and Peng Wei, and I would like to reply regarding the following observations performed:

> This prospective clinical controlled study holds a degree of persuasiveness and offers valuable insights for the enhancement of atrophic scars and scar-related epidermal pigmentation, paving the way for future clinical treatments and research endeavors.
>
> Thank you very much.
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> Regarding the affirmation "First, although existing research has indicated that fat grafting can ameliorate scar-related pigmentation, the precise molecular mechanisms underlying these effects remain elusive. (2) Further research is necessary to explore the molecular mechanisms involved, particularly in relation to the immunomodulatory properties of ASCs and their ability to mitigate inflammation and, consequently, improve pigmentation."

I agree with this affirmation. Several papers were published analyzing the role of fat grafting enhanced with ASCs or not enhanced in different kinds of scars, (post-traumatic scars, outcomes of burns, hemifacial atrophy) as reported in my paper [1] improving not only the pigmentation but also the volume, not only in the face but also in breast soft tissue defects [2, 3].

Additionally, the methods of ASC isolation (mechanical or enzymatic) and preparation (minimal manipulation) as already summarized [3], should be better investigated in terms of the immunomodulatory properties of ASCs and their ability to mitigate inflammation and, consequently, improve pigmentation.

At the same time, regarding their affirmations "Second, the results presented by the authors suggest that ASCs enhance the improvement of pigmentation following fat grafting. However, from a clinical perspective, it is worth noting that pigmentation often naturally lightens over time. In other words, time itself can serve as a confounding factor in assessing pigmentation outcomes. To address this concern and enhance the persuasiveness of the research results, we suggest that the authors introduce a blank

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Published online: 02 January 2024

control group to control for the impact of time on pigmentation outcomes".

Really, the investigation was built as a case–control study aiming to strictly evaluate if there were statistically significant differences between fat grafts enhanced with ASCs (study group) and fat grafts not enhanced (control group) in terms of scar pigmentation. The follow-up analysis was the same. In this case, the "eventual time effect" that we can consider as a confounding factor or more precisely a bias, influenced both groups. All people who underwent the treatments (fat grafts enhanced with ASCs and fat grafts not enhanced) were satisfied with the improving pigmentation, texture, and volume contours with some differences. However, the results reported displaying a better trend in patients treated using fat grafts enhanced with ASCs to be more satisfied than patients treated with fat grafts not enhanced ($p < 0.0001$). In every case, the suggestion of the authors, about the time effect is attractive and it is valuable in the next study to consider a blank control group to control for the impact of time on pigmentation outcomes.

Regarding the affirmation "Third, the figures provided by the authors depict patients with relatively mild preoperative epidermal pigmentation in their scars. As a result, when comparing preoperative and postoperative images, the differences in pigmentation do not appear prominently significant. We kindly suggest that the authors provide cases with more conspicuous differences in preoperative and postoperative pigmentation. More pronounced before-and-after comparison images can better illustrate treatment efficacy, enabling readers to more readily comprehend the research findings".

The results shown in the pictures, clearly demonstrate the differences in terms of pigmentation improvement between the study and control groups, as also documented by instrumental analysis.

Regarding the affirmation "In conclusion, this study holds substantial promise in the field of scar management".

I'm pleased to thank the authors Zuguang Hua and Peng Wei for their positive feedback, particular attention to my paper, and for their constructive suggestions.

Declarations

Conflict of interest The author declared no potential conflicts of interest concerning the research, authorship, and publication of this article.

Informed Consent For this type of study informed consent is not required.

Statement of Human and Animal Rights, or Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors

References

1. Gentile P (2023) Lipofilling enriched with adipose-derived mesenchymal stem cells improves soft tissue deformities and reduces scar pigmentation: clinical and instrumental evaluation in plastic surgery. Aesthet Plast Surg 47(5):2063–2073
2. Fiaschetti V, Pistolese CA, Fornari M, Liberto V, Cama V, Gentile P, Floris M, Floris R, Cervelli V, Simonetti G (2013) Magnetic resonance imaging and ultrasound evaluation after breast autologous fat grafting combined with platelet-rich plasma. Plast Reconstr Surg 132(4):498e–509e
3. Gentile P, Kothari A, Casella D, Calabrese C (2020) Fat graft enhanced with adipose-derived stem cells in aesthetic breast augmentation: clinical, histological, and instrumental evaluation. Aesthet Surg J 40(9):962–977
4. Trivisonno A, Alexander RW, Baldari S, Cohen SR, Di Rocco G, Gentile P, Magalon G, Magalon J, Miller RB, Womack H, Toietta G (2019) Intraoperative strategies for minimal manipulation of autologous adipose tissue for cell- and tissue-based therapies: concise review. Stem Cells Transl Med 8(12):1265–1271