

LETTER

Response to letter: Comments on “Hyaluronidase: an overview of its properties, applications, and side effects”

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First of all, thank you for your interest and comments on this paper.

As you pointed out, hyaluronidase does not break down hyaluronic acid into monosaccharides. Mammalian hyaluronidase produces tetrasaccharides, microbial hyaluronidase produces unsaturated disaccharides, and leech/hookworm hyaluronidase produces tetrasaccharides and hexasaccharides [1]. Secondly, as stated in the paper, hyaluronidase can be classified as mammalian or microbial hyaluronidase according to its production method. Microbial hyaluronidase can be obtained from bacteria such as *Streptococcus agalactiae*, whereas mammalian hyaluronidase is extracted from animal ovaries and testes and needs purification because otherwise it is impure and immunogenic. Therefore, all the mammalian hyaluronidase currently used undergoes a purification process as part of its production [1]. The extraction of bovine hyaluronidase using recombinant technology also requires multiple purification steps before it is ready to be shipped as a product [2].

Thirdly, unfortunately, it was not possible to find a reference about the exact mechanism of hyaluronidase inhibition, but this fact does not mean that a hyaluronidase inhibitor does not exist. A hyaluronidase inhibitor was described as early as the 1940s, and there was also

a later publication stating that the predominant protein with hyaluronidase inhibition activity possesses the characteristics of the inter-alpha inhibitor (IαI) family, which contains plasma protease inhibitors [3,4].

Fourthly, DeLorenzi [5] stated in his unpublished work that he confirmed that polyphasic filler responds better to hyaluronidase. My personal experience also supports his theory. As was stated in this paper; the more cross-linking, the more difficult it is for hyaluronidase to access its binding site inside the hyaluronic acid filler. I think we are on the same page about the fact that hyaluronidase activity is significantly diminished when the density of cross-linking increases, which is a representative modification in the production process of hyaluronic acid filler.

Lastly, I agree that a sufficient amount of hyaluronidase is required for the treatment of filler embolism. I would also like to thank you for again emphasizing the fact that we should take precautions in using hyaluronidase because products contain various amounts of hyaluronidase and the dosage varies accordingly.

Notes

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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