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EDITOR'S INVITED COMMENTARY

Invited Discussion on: Retrobulbar Injection for Hyaluronic Acid Gel Filler-Induced Blindness—A Review of Efficacy and Technique

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I read this article, *Retrobulbar Injection for Hyaluronic Acid Gel Filler-Induced Blindness: A Review of Efficacy and Technique* with extreme personal interest and continued enthusiasm. The concept of utilizing a rapidly administered rescue procedure and technique as an attempt to treat and reverse this devastating event was introduced during an "international coalition committee in 2013" (as mentioned in this article) that I chaired [1]. As I had stated in several prior publications [2–4], I became acutely aware of this escalating problem of vascular occlusion of the ophthalmic circulation, particularly with hyaluronic acid (HA) gels related to facial injectables after reviewing an alarming number of new case reports of this occurrence as a section editor and reviewer for several peer-reviewed journals. I had actually changed my original presentation at the "last minute" while in-flight to this meeting to what I believed was a more prudent report on this topic to an esteemed group of multi-specialty, international injectors whereby I displayed the thesis of retrobulbar (RB)/peribulbar (PB) injection rescue therapy with hyaluronidase. Understanding much of the prior work by others as well as personal experiences with the positive effects of hyaluronidase particularly in its common use for a spectrum of indications including enhancing infiltrative local anesthesia [5, 6] and for HA gel induced vascular occlusions in other areas of the face [7], suggested that it was a plausible yet untried solution. Furthermore, the fact that this substance penetrates the vascular walls and most other soft tissue and oftentimes travels significantly distant beyond the point of injection, it seemed relevant that an effective local orbital dose of hyaluronidase delivered expeditiously might have the potential for reversing an HA gel occlusion of the ophthalmic artery and possibly its branches. Without proof of concept, we quickly published on this idea to alert our colleagues about this emerging problem and thoughts of novel ideas on potential treatments [8]. Then and thereafter, there was no mention by me, despite the presumption of others, of the exact pathway or mechanism whereby this procedure would reverse the occlusion, suffice it to say that it is well known that the effects of hyaluronidase extend quite distant from the point of injection. The concept was met with skepticism at that time and rose to the level of objection by some, including ophthalmologists who relayed their concerns, in part, regarding the potential hazards of non-ophthalmologists performing RB rescue therapy, and those that believed, without good evidence, that such a treatment would not be effective, based on antiquated notions relating to timing and the complexities of the anatomic regions involved. Nonetheless, I was compelled to explore and publish on this in several peer-reviewed journals to alert all injectors worldwide to consider this form of rescue therapy in light of the fact that, up until that time and currently, there is no known proven effective therapy. It was my opinion and that of several others, that until it could be disproven, the benefits of an attempt at RB rescue therapy outweighed the risks. I am also personally delighted that the authors of this article chose to discuss and adopt some of the essential elements for a proper assessment and nomenclature used in my prior publications and, as I have urged the necessity of

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confirming an accurate diagnosis prior to consideration of treatment. I first introduced the new definition of *injection-related visual compromise* (IRVC) [2] since there was no universally accepted way to explain this varied and complex adverse event, yet IRVC also encompassed all of the potential components of accidental intra-arterial injection of filler product with retrograde and distal occlusion of the various branches of the ophthalmic circulation that could result in a host of consequences including visual loss, upper eyelid ptosis, ocular motility disturbances and beyond. Moreover, the article reminds us, as I have also in previous publications [2–4], that it is essential to make the correct diagnosis (prove that there is indeed an IRVC) prior to the consideration of treatment by, not only, a cursory yet accurate ophthalmologic history and examination but also to pay particular attention to associated signs and symptomatology for confirmation. I would however, respectfully disagree with the authors that the presence of functional reading vision itself would suggest against IRVC as an isolated peripheral branch retinal arteriolar occlusion is a potential scenario that might be detected by ophthalmoscopy and confrontational visual field assessment or subjective field loss by the patient that could preserve central (reading) vision also indicating an ophthalmic artery embolization with an occlusion sparing the macula. Since the beginning of these writings and up to the present and despite some anecdotal case reports of its successes [9, 10] and failures [11], weak experimentation attempting to prove or disprove its effectiveness [12, 13] and more recent animal models showing some promise [4], there is still no consensus.

This article illustrates, once again, that this is a growing problem and despite our greater understanding of the causality, these events still occur and amplifies the importance of this updated manuscript that indicates the numbers of reported events have nearly doubled (from prior reporting) and that these issues continue. Also realizing, however, that many incidences perhaps go un-reported and the numbers here are likely much greater. To be critical, this article, however, is more of a review of one technique, not efficacy (as the title suggests), and it also fails to explain or suggest the reasons why or why not the reported treatments may have either failed or have claimed to be successful despite the apparent advocacy of this approach, leaving reasonable doubt and trepidation for anyone not versed with any retrobulbar or peri-bulbar technique to be successful in reversing IRVC understanding the concern of potential risks of the rescue therapy itself. Timing (expeditious) is likely crucial, but many rely on an exact deadline with the critic's position resting on old data and publications that may not be entirely relevant [14]. Furthermore, the authors suggestions of the method of administration (technique, volume, etc.), of which I was also co-author on the original publication introducing this technique [15] (that included my video demonstrating one method of RB administration), which is one of many ways to deliver hyaluronidase into the orbit/periorbita, fail to explain the mechanism of actions of hyaluronidase whereby this treatment might be successful amidst those that refute its efficacy.

There is a pervasive undertone of resistance to accept the potential rescue therapy that also relies on an assumption that the pathway must follow the course of the occlusion rather than a greater understanding of the other ways hyaluronidase might reach the target. The argument of the anatomy of the ophthalmic and central retinal artery protected by the dural or meningeal layers that might prevent the effectiveness (penetration) of hyaluronidase assumes that this is the only pathway for potential success and the premise of much of the flawed research and conclusions yielding to abandonment of consideration of RB rescue therapy in itself is ignorant of so many other factors and I would seriously challenge that this is incorrect [12, 13]. It is also still unclear whether thrombolytic agents need to be administered concurrently, but this is also highly controversial and its adjunctive implementation might add to the delay in treatment [16]. Finally, I have already introduced the concept of the likely requirement for a large volume and high dosing (possibly more than 1000u–2000u of hyaluronidase in most cases and the challenges of only having smaller dose vials available in the US) to facilitate an enhanced hydrostatic pressure for better general tissue penetration/direct mechanical diffusion in the scenario of documented IRVC that likely would address many of the issues that some critics have voiced [1–4]. This concept is also in agreement with others advocating a higher dosage of hyaluronidase (than originally suggested), now known to be generally safe and more effective, in most situations of injection-related vascular occlusions [17].

In summary, IRVC is a serious problem that requires further research and practical solutions with cooperation across the specialties so we can arrive on consensus. The very fact that there appears to be some successes with RB rescue therapy [9–11] suggests that we are on to something, but we simply do not fully understand all of the complexities involved for potentially effective resolve. Despite the current lack of indisputable evidence of the ability to reverse IRVC, safe application of RB or PB technique skills can be taught to most physicians and presently should be considered by all qualified individuals to avoid delay in a potential treatment. Of course, it would be ideal to have a colleague/ophthalmologist well versed and experienced in RB/PB injection as a first resort should an IRVC be encountered, but in the absence of this possibility and to avoid the usual time delay, every filler injector should become familiar with this technique.

I applaud the authors for this updated paper revealing the continued occurrences of IRVC. Now more than ever, the focus must shift from negative baseless opinions, a misunderstanding of mechanism of action and flawed research to effective practical and timely solutions.

Compliance with Ethical Standards

Conflict of interest The author declares that he has no conflict of interest to disclose.

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

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

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