Video Commentary

Commentary on: High-Dose Neuromodulators: A Roundtable on Making Sense of the Data in Real-World Clinical Practice

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Rather unusually, the paper reads as a summary of a roundtable discussion between experts on the use of botulinum toxin for aesthetic facial rejuvenation, with a specific focus on whether changes to the existing dose-concentration standards might deliver more durable effects given that the current manufacturer guidelines are based on commercial and regulatory factors rather than optimized clinical standards (Video). The first important point raised by the paper is evidence in the literature to suggest that, when aliquots are administered at a higher concentration, the median time to return to baseline seems to be prolonged. In other words, the typical formulae for administration have not been optimized. This being the case, they go on to debate 6 key questions. These are:

1. Whether there exists a linear relationship between the durability of results and dose given?
2. Whether increasing the dose is to the detriment of natural-looking results?
3. Whether increased durability of result is an important consideration for patients?
4. Whether these dose-relationship observations are product specific?
5. Whether an increase in dose is associated with an increased complication profile?
6. What are the economic implications for a practice that adopts a new dosing strategy?

The authors concede that the interpretation of clinical trials data is complicated by the lack of methodological standardization across different trials. They also raise, and I find this to be a key point here, the issue of lack of a standardized unit of activity for botulinum toxin formulations. Rather, formulae are based on the proprietary median lethal dose provided by the manufacturer. Thus, a comparison of one formulation with another based on units of activity is essentially meaningless. They also revisit the need to tailor the dose to the muscle mass of the patient with higher

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doses needed for those with greater muscle mass. This is not particularly controversial as I think most people would agree with this.

These caveats aside they conclude that increasing the dose does not come at the expense of natural-looking results as reported by the patients to a point. Similarly, there does appear to be a linear relationship between dose and durability of result up to a certain point, where upon the duration of effect levels off. In many ways, this is what we would have expected and does indeed suggest that some clinical optimization of the dose regimen is needed. Of crucial importance here is that more concentrated formulations delivered a more durable result than the same total dose delivered at a lower concentration in a higher volume of solvent. The dose-response relationship does not appear to be product specific as different manufactured botulinum toxins demonstrated similar results.

In terms of safety, higher concentrations were not associated with an increase in the complication profile (eg, blepharoptosis). The authors also discuss immune responses to botulinum toxin. They present the only reasonable conclusion they could, given the lack of data, which is that we simply do not know if higher concentration of aliquots given less often is more or less immunogenic than standard protocols.

The authors conclude the discussion with an evaluation of the economic implications of this work on the clinical practice. Specifically, they ask the question about whether patients would be prepared to pay more for higher doses given at higher concentrations on the understanding that they may be given less frequently. I think the authors were wise to raise this point and, if they could be accused of sitting on the fence in terms of the conclusions drawn, it is merely that we genuinely do not know if there will be a demand among patients or an appetite among providers to change practice in this way.

**Supplemental Material**
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**REFERENCE**
1. Fabi SG, Carruthers J, Joseph J, et al. High-dose neuromodulators: a roundtable on making sense of the data in real-world clinical practice. Aesthet Surg J Open Forum. 2021;3(4):1-7. doi:10.1093/asjof/ojab036