

A Retrospective Study Supporting the Importance of Individualizing the Dose of Botulinum Toxin According to the Age

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Abstract

Background: Botulinum toxin type A injection remains the leading nonsurgical cosmetic procedure worldwide with a high rate of efficacy and patient satisfaction. **Objective:** This study aims to demonstrate the importance of individualization of botulinum toxin doses to treat the upper face according to the age of the patients, considering the muscles particularities and the specificities of each face area. **Materials and Methods:** A retrospective study with 389 female patients treated with botulinum toxin type A in the upper third of the face (forehead, glabellar, and periorbital lines). Statistical analysis of the data was performed. **Results:** The mean age was 47.49 years old and the median total dose of botulinum toxin type A was 53.76 units, whereas the median dose in the glabella was 26.28 U, the mean forehead dose was 12.23 U, and in the periorbital area was 14.79 U, adding both sides. It is possible to observe that the doses are negatively correlated with age, except in the periorbital area, where an increase in the dose was observed. **Conclusion:** It is important to highlight that although there is consensus on pre-established dose suggestions, the treatment should be individualized, respecting the individual characteristics of each patient.

Keywords: Aging process, botulinum toxin, dose, upper face

INTRODUCTION

Botulinum toxin injection remains the leading nonsurgical cosmetic procedure worldwide with a high rate of efficacy and patient satisfaction.^[1]

According to Botox® (Allergan) prescribing information, the doses to aesthetic use of botulinum toxin may vary according to the treated area and the muscle contraction.^[2] The global aesthetics consensus recommends a total dose range from 27 U to 86 U for the treatment of the upper face (glabellar, horizontal forehead, and orbicular lines).^[3]

This study aims to demonstrate the importance of individualization of botulinum toxin doses to treat the upper face according to the age of the patients, considering the muscles particularities and the specificities of each face area, by evaluating if patients' age is statistically significant to explain the dosage on the areas being treated, verifying and regarding the first visit and the review.

MATERIALS AND METHODS

A retrospective, single-center study was conducted from April 2017 to April 2019, by medical record review of 389 female patients from 27 to 74 years old who were treated with upper face botulinum toxin with dilution of 100 units to 1mL (Botox®, Allergan) injection. All patients provided written informed consent before treatment and the study was conducted in compliance with the ethical principles for clinical research in Brazil. Statistical analysis of the data was performed.

RESULTS

The sample comprised 389 female patients from 27 to 74 years old. The mean age was 47.49 years old and

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How to cite this article: Bravo BSF, Carvalho RdM, Gallo BF, Bravo LG. A retrospective study supporting the importance of individualizing the dose of botulinum toxin according to the age. *J Cutan Aesthet Surg* 2021;14:88-92.

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10.4103/JCAS.JCAS_20_20

50% were between 38 and 58 years old. According to exploratory analysis and tests of statistical significance, reports of the mean, the coefficient of variation (CV) in percentage, the first and third quantiles for each of the dose injected in each area, and the total dose for the 389 patients considered in the analysis and their age are demonstrated in Table 1.

While the botulinum toxin dose in the glabellar complex presents a higher mean than the others, the dosage injected in the frontalis area is the one with the highest variability.

Lower and upper panels of Figure 1 present, respectively, the scatterplot and the sample Pearson correlation for the administered dose in each area, the total dose, and the age of the 389 patients considered in the analysis.

It was fitted with normal regression models to measure the significance of the effect of the age in the doses injected in each area being treated considering all patients and Figure 2 shows the scatterplots, with these estimates.

For the doses administered in the frontalis, there is a significant negative effect of age (P -value < 0.05), with a

decrease of 15% in the dose injected for each year added. For the doses administered in the glabellar area, the effect of age is not significant at the 10% level, with a decrease of 5% in the injected dose for each year of the patient. On the other hand, for the periorbital area, there is a significant positive effect of age (P -value < 0.05) with an increase of 7% in the dose injected for each year the patient gets older. For the total dose on the upper face, there was a decrease of 12% in the injected dose for each added year (P -value < 0.06).

Forty-one patients had a follow-up consultation (10.5%). The mean complementary dosage was 10 U.

The total mean dose of botulinum toxin type A was 53.76 U, of the glabellar complex was 26.28 U, of the forehead was 12.23 U, and of the periorbital area was 14.79 U on both sides [Figure 3].

DISCUSSION

This is a large retrospective single-center study and the injections were performed by one treatment provider.

Table 1: Mean, coefficient of variation (CV) in percentage, first and third quantiles for the dose of botox in the three areas being treated, the total dose and the age for the 389 patients considered in the analysis

	Frontalis	Glabellar complex	Periorbicular	Total	Age
Mean	12.23	26.28	14.79	53.76	47.49
CV (%)	0.63	0.30	0.52	0.28	0.26
Q1	7	21	10	45	38
Q3	16	30	20	62	58

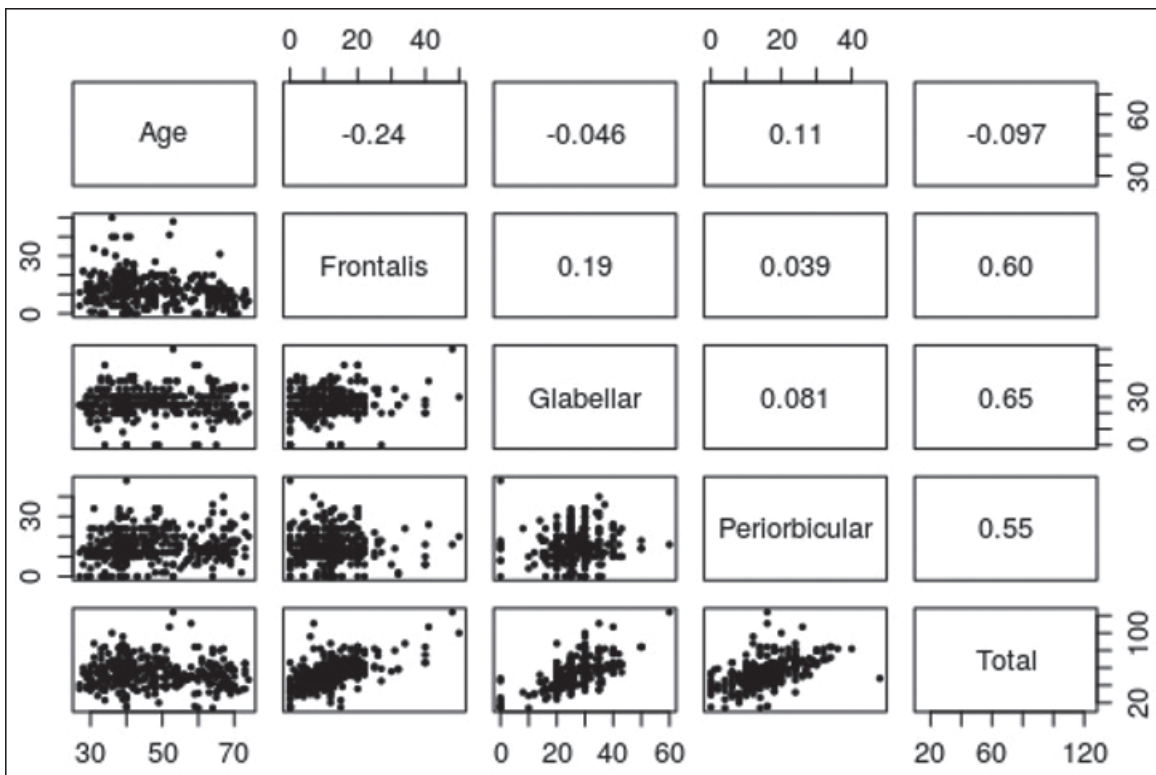


Figure 1: Scatterplot and the sample Pearson correlation for dose injected in each area, the total dose, and the age of the patients

Concerning the correlation between doses and age, it is possible to observe that the doses are negatively correlated with age, except in the periorbital area, where an increase in the dose was observed.

There was an estimated decrease of 15 and 5% in the injected dose in the forehead and glabellar areas, respectively, for each year added in age. In the total dose, a decrease of 12% is also estimated for each year added to age.

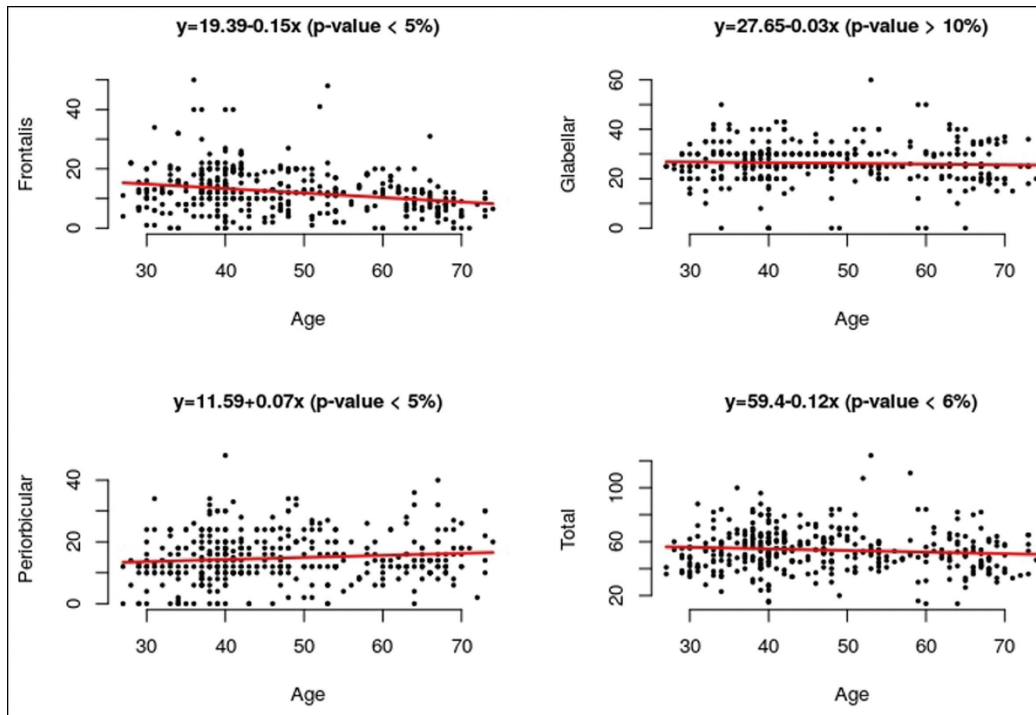


Figure 2: Scatterplots of doses injected in each area considered and the total dose versus age for 389 patients. The P-values are calculated for the linear coefficient of the regression line fitted



Figure 3: Total mean dose of botulinum toxin type A per area

In assessing doses by area, we found that the glabellar complex and especially the forehead doses decreased with age. However, the periorbital area had an oppositely proportional dose/age relationship, requiring higher doses over the years. In relation to the orbicularis muscle, our results are compatible to the findings in the study by Kane *et al.*,^[3] which shows that the frequency of full fan also increased with age. A study by Yun *et al.*^[4] evaluated the activity of the frontalis muscle, the corrugator supercilii muscle, and the orbicularis oculi muscle according to eyebrow movement and aging, for the strained movements (opening eyes maximally, closing eyes maximally, and frowning maximally), motor recruitment of the frontalis and corrugator supercilii muscles was significantly higher for the younger group ($P < 0.05$), whereas in the older group, orbicularis oculi muscle recruitment was significantly higher ($P < 0.05$).

In relation to the other muscles, our results are compatible with the Global Aesthetics Consensus of Botulinum Toxin Type A, which cites that lower doses may be appropriate to older patients, due to changes in muscle mass and function with age.^[5] The treatment of the forehead, for example, should be individually tailored, considering the patient's sex, age, forehead size, distribution of frontal wrinkles, and position of the eyebrow.^[5]

In the authors' experience, higher doses bring longer-lasting outcomes, but in older patients already with muscle weakness, there is usually a contraindication to total muscle block to maintain eye-opening and lymphatic drainage function. Therefore, if we follow an "age \times dose rule," the dose would decrease with age, we would inject low doses, and often it is not enough to obtain a satisfactory result. At the review visit, some patients still complained about crow's feet. It happens because, with the aging process, dynamic wrinkles became static wrinkles and loss of subcutaneous support occurs, leading to a deeper wrinkle during muscle contraction.

The objective to prevent rhytides is most applicable to younger patients. Loss of volume and consequent deflation of the soft tissues and underlying, supportive bone are cardinal features of facial aging.^[3,6-13] The experts considered it critical to the development of age-appropriate treatment goals to understand that these changes may impact muscular activity as well as facial contours. A greater proportion of rhytides in older patients may be due to loss of skin elasticity.^[3]

There are some study limitations like comparing different patients in a horizontal time frame. Therefore, for these observations, we can realize that increasing the dosage of botulinum toxin is not always the only solution. Skin thickness and texture may also contribute to dosing decisions, as it decreases with aging.^[14] The rhytides can be ameliorated by multiple modalities, including botulinum toxin, but probably not toxin alone.^[3]

We should complement the treatment by combining intradermal and subcutaneous hyaluronic acid injections to increase the resistance of the skin to muscle contraction.

Firstly, before any toxin treatment, it is mandatory to carefully assess the patient. The treatment of the forehead, for example, should be individually tailored, considering the patient's sex, age, forehead size, distribution of frontal wrinkles, and position of the eyebrow.

CONCLUSION

- The dose of botulinum toxin to be injected depends on the specific area of the face and the characteristics of the involved muscles, including their masses. In turn, muscle mass is influenced by gender, age, and individual variation. The required dose and the sites to be injected are also based on an assessment of how the muscles behave in rest, in normal animation, and during maximal contraction.
- In older patients, the periorbital area has active muscles and thin dermis, so the treatment of these wrinkles is more difficult and should be associated with fillers.
- All patients in this study who were treated with botulinum toxin A had satisfactory results.
- It is important to highlight that, although there is a consensus on pre-established dose suggestions, we should individualize the treatment, respecting the characteristics of each patient.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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