

## Long-Term Effects of OnabotulinumtoxinA on Facial Lines: A 19-Year Experience of Identical Twins

In 2002, the Food and Drug Administration approved botulinum toxin Type A (BoNTA, onabotulinumtoxinA; Allergan Inc., Irvine, CA) for the temporary improvement in the appearance of glabellar frown lines. Its cosmetic use, however, was the most common non-surgical rejuvenation procedure performed during the 10 years before its approval and continues to be so today.

Hyperfunctional lines in the skin are produced by repeated contraction of the underlying muscles. By inhibiting the release of acetylcholine from the presynaptic terminal of the neuromuscular junction, BoNTA inhibits the contraction of muscles, and as such, may serve to prevent or limit the formation of new wrinkles. To date, however, there have been no prospective studies conducted on wrinkle prevention with repeated use of BoNTA. Binder<sup>1</sup> published a unique case report of twins, one regularly treated with onabotulinumtoxinA, whereas the other twin had only had 2 treatments over the course of 13 years. In Binder's report, photographic documentation showed that the treated twin did not exhibit forehead or glabellar lines at rest, whereas mild resting lines were evident in the sporadically treated twin. This article is a 6-year follow-up of the same twins, as in Dr. Binder's case study. This case report describes the effects of long-term repeated treatment with onabotulinumtoxinA over a 19-year period. The authors provide a photographic evaluation to assess whether repeated treatments of onabotulinumtoxinA may prevent the formation of hyperfunctional wrinkles or delay the onset of atrophic rhytides that may become permanent.

The twins are now 44 years old, and neither twin has had any invasive or noninvasive rejuvenation procedures other than onabotulinumtoxinA treatment. The treated twin lives in Los Angeles, CA, the sporadically treated twin lives in Munich, Germany. The treated twin has been undergoing onabotulinumtoxinA treatments in the forehead and glabella regularly every

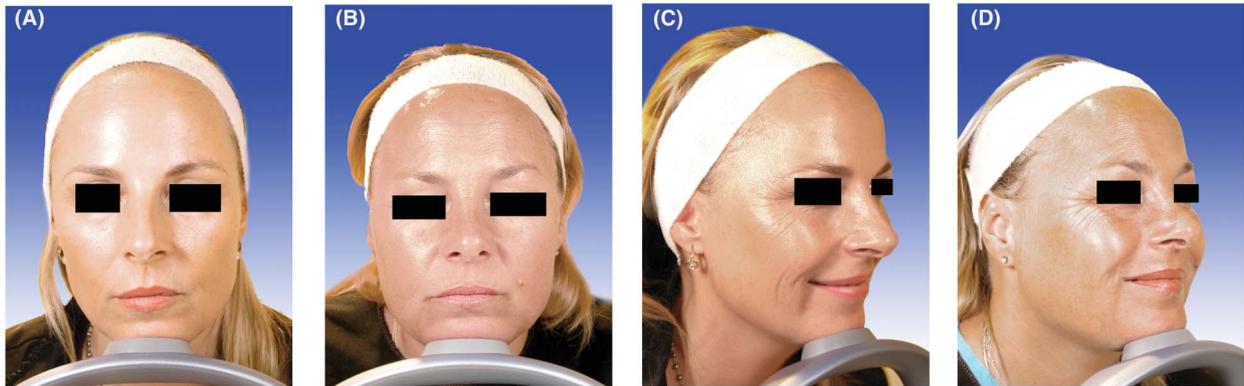
4 to 6 months for the last 19 years. For the last 8 of those years, she added her crow's feet to the areas treated. The dose administered has remained consistent for a number of years, with doses of 20, 10, and 16 U for the glabella, forehead, and bilateral crow's feet, respectively. The dose has decreased over the last few years to 16, 8, and 16 U for the glabella, forehead, and bilateral crow's feet, respectively.

The sporadically treated twin has received 4 onabotulinumtoxinA treatments in the forehead, glabella, and crow's feet over the last 19 years, with treatments administered 2, 9, and 13 years ago. The dose administered to the sporadically treated twin was 20, 10, and 12 U for the glabella, forehead, and bilateral crow's feet, respectively.

Photographs of the treated twin were taken 6 months after onabotulinumtoxinA treatment. Photographic documentation shows that forehead and glabellar lines are not evident at rest in the treated twin (Figure 1A). In contrast, static lines in the forehead have become visible at rest in the forehead of the sporadically treated twin (Figure 1B).

Differences in crow's feet severity at rest also exist between the treated and sporadically treated twin (Figure 1C,D). Whereas the treated twin exhibits mild dynamic crow's feet (Figure 1C), deeper lines are evident in the sporadically treated twin (Figure 1D). Additionally, the skin texture of the treated twin looks smooth with small pores, whereas skin of the sporadically treated twin shows signs of aging with a greater number of wrinkles and visible pores (Figure 1).

Administration of onabotulinumtoxinA inhibits muscular contraction for several months, thus reducing the appearance of dynamic facial lines. Binder<sup>1</sup> previously published photographic documentation that long-term repeated treatment with



**Figure 1.** The treated twin exhibits virtually no forehead rhytides at rest (A), whereas static forehead rhytides are visible in the sporadically treated twin (B). Similarly, the crow's feet are mild in the treated twin (C), deeper in the sporadically treated twin (D).

onabotulinumtoxinA seems to prevent the formation of permanent facial wrinkles. Six years after Binder's publication, the current results further support the contention that repeated treatment with onabotulinumtoxinA continue to diminish the signs of facial aging and delay the appearance of hyperfunctional facial lines.

As the sporadically treated twin lives in Munich, Germany, the changes in skin morphology cannot be explained by differences in sun exposure between the twins. In Munich, the UV index is low moderate ( $\leq 5$ ) for 8 months of the year. In Los Angeles, the UV index is high (6–7) to very high (8–10) for 7 months of the year.<sup>2</sup> Both twins use 45 to 50 SPF sunblock on a daily basis and both lead active outdoor lifestyles. Neither twin smokes, both adhere to a relatively healthy diet, and both work in an indoor office setting. Neither twin has had any laser, light, or skin-tightening procedures, and both use glycolic-based topical skincare products on a daily basis. Neither twin uses any other topical skincare products, including retinol-based products. Regarding the aesthetic quality of their skin, consistent long-term treatment with onabotulinumtoxinA seems to be the only major difference in the lives of these twins. Limiting facial muscular movement over the years with onabotulinumtoxinA seems to have reduced the number and the severity of both static and dynamic wrinkles in the treated twin compared with the sporadically treated twin.

There are relatively few published reports of the long-term effects of onabotulinumtoxinA when used for

cosmetic purposes. Bowler<sup>3</sup> presented 2 case studies of patients who had received onabotulinumtoxinA for cosmetic treatment of the forehead, glabella, and periorbital areas over a 7-year period. Both the patients and the treating physician reported that posttreatment skin quality was significantly improved compared with pretreatment in terms of wrinkle reduction and skin smoothness. Additionally, onabotulinumtoxinA treatment demonstrated reproducible results over the course of 7 years, with no reduction in efficacy, or need to increase the dose to maintain the effect.

Dailey and colleagues<sup>4</sup> published a 2-year prospective study investigating wrinkle reduction and extended duration of efficacy with repeated onabotulinumtoxinA treatments. Patients were injected every 4 months with 20 U onabotulinumtoxinA in the glabellar region for 5 treatment sessions. After the last treatment at 20 months, patients were evaluated at Months 24, 25, and 26. Results demonstrated improvements in wrinkle severity, as the number of onabotulinumtoxinA treatment cycles progressed. Additionally, the study found that the duration of effect increased beyond 4 months with consistent repeated treatment of onabotulinumtoxinA, with 87% of patients reporting sustained satisfaction with the results 6 months after the last treatment session.

Botulinum toxin treatments have repeatedly been the most frequently performed cosmetic procedure in the United States for more than 10 years. Numerous

studies have examined both patient and investigator satisfaction with onabotulinumtoxinA, with most patient satisfaction rates reported in the mid-80% to more than 90%.<sup>4</sup> The continued popularity of BoNTAs as the most frequently requested cosmetic procedure is most likely multifactorial. In addition to patients perceiving themselves as looking younger, studies have shown that mood, self-esteem, and quality of life are also enhanced with onabotulinumtoxinA treatment.<sup>5</sup>

OnabotulinumtoxinA has been used for decades to treat therapeutic conditions and cosmetically to reduce the appearance of facial wrinkles. The findings of this report, continuing on the results of Binder, indicate that dermal and epidermal remodeling may occur with long-term, consistent, onabotulinumtoxinA treatment. The results of this case study provide evidence that onabotulinumtoxinA prevents the formation of hyperfunctional wrinkles, delays the onset of atrophic rhytides that may become permanent, and may improve the overall quality of the skin.

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