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The effect of intradermal botulinum toxin on androgenetic alopecia and its possible mechanism

To the Editor: Dihydrotestosterone (DHT) induces transforming growth factor β1 (TGF-β1) in dermal papilla cells (DPCs) to suppress follicular epithelial cell growth. Thus, TGF-β1 is one of the key players in androgenetic alopecia (AGA), and its antagonist may prevent AGA.[1] Botulinum toxin type A (BTX) may inhibit TGF-β1 secretion from DPCs as it does with scar tissue fibroblasts,[2] which share the mesenchymal origin. Recently, BTX has been effective for the treatment of AGA.[3,4]

Here, we evaluated the efficacy and safety of intradermal injection of BTX (Nabota, Daewoong Pharmaceutical Co, Seoul, Korea) in AGA and its relationship with TGF-β1.

Patients with AGA were enrolled according to the basic and specific classification.[5] Patients undergoing treatment with finasteride, minoxidil, or supplements that affect hair growth were excluded. This study was approved by the institutional review board. The participants received intradermal BTX injections every 4 weeks for 24 weeks. A total of 30 units of BTX were injected at 20 different sites on the balding scalp in each treatment session.

The expression of TGF-β1 from cultured DPCs under 10^{-9}mol/L DHT was evaluated by reverse transcription polymerase chain reaction analysis. Suppression of DHT-induced TGF-β1 secretion from DPCs by BTX (2.5 U/10^6 cells) was assessed by immunofluorescence staining. The doses of BTX in the in vitro study were selected on the basis of a previous report investigating the effect of BTX (2.5 U/10^6 cells) on TGF-β1 secretion from the fibroblasts.[2]

This study comprised 18 male patients with a mean age of 49.00 ± 6.50 years. In an unblinded phototrichogram image analysis (Lead M Corp, Seoul, Korea), the mean ± standard deviation of hairs per square centimeter at weeks 0, 12, and 24 were 129.61 ± 28.05, 129.11 ± 28.80, and 136.22 ± 33.05, respectively. The number of hairs significantly increased at week 24 ($P = .012$) but not at week 12 ($P = .803$). Comparison of the pre- and posttreatment photographs showed significant improvement at week 24 ($P = .031$) (Fig 1). DHT upregulated the TGF-β1 expression of DPCs in 96 hours, whereas BTX downregulated the TGF-β1 expression in 96 hours (Fig 2). No serious adverse events or changes in laboratory parameters were reported.

DHT-induced synthesis of paracrine mediators (Dkk-1, interleukin 6, TGF-β1) in balding DPCs may play a role in AGA and represent alternative treatment targets.[1,6] However, clinical studies targeting these paracrine mediators have not been reported. In our in vitro study, BTX successfully abrogated DHT-induced secretion of TGF-β1 from DPC. Intradermal injection of BTX was effective against AGA by inhibiting TGF-β1 secretion in the hair bulb, which is thought to suppress follicular keratinocyte growth and changes in the hair cycle.[1] Previous studies reported the use of intramuscular BTX injections to treat AGA without elucidating the exact underlying mechanism.[3,4] Considering the diffusion of the injected liquid BTX and scalp anatomy, even the intramuscular injection[3,4] may indirectly inhibit the secretion of TGF-β1 from DPCs in the hair bulb. Advanced AGA or older age may have adversely influenced our treatment outcome.

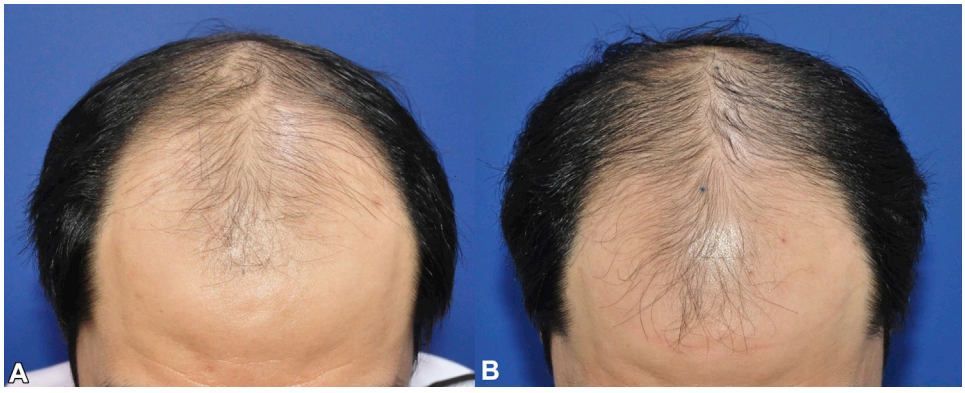

Fig 1. Comparison of pretreatment and posttreatment clinical images. **A**, Baseline photography and (**B**) improvement after 6 months of treatment are shown.

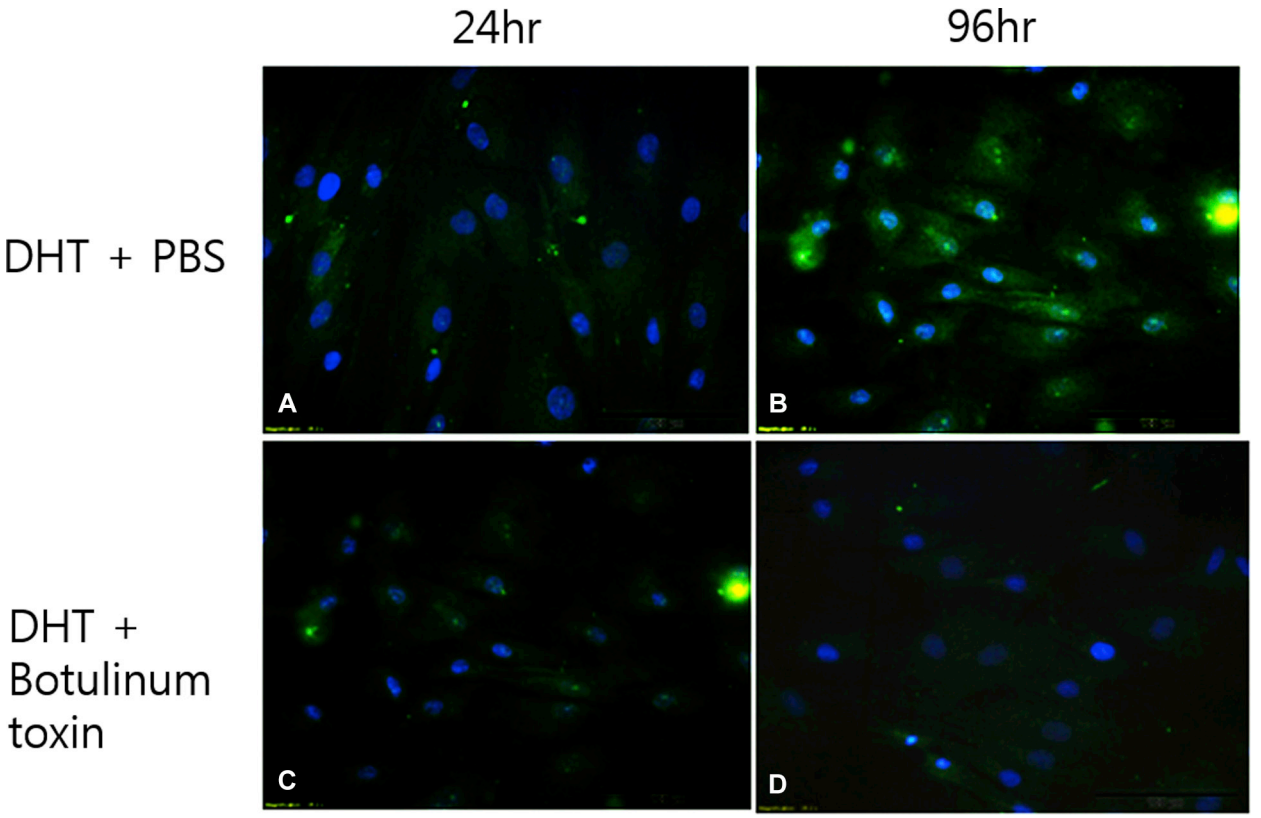

Fig 2. Immunofluorescent assay for TGF-β1 in DPCs. Suppression of DHT (10^{-9} mol/L)-induced secretion of TGF-β1 from DPCs of balding scalps by treatment with botulinum toxin (2.5 U/10^6 cells) compared with control scalps. *DHT*, Dihydrotestosterone; *DPC*, dermal papilla cell; *hr*, hour; *PBS*, phosphate-buffered saline; *TGF*, transforming growth factor.

In conclusion, we suggest that intradermal injection of botulinum toxin could be a possible treatment option for AGA by inhibiting TGF-β1 secretion from the hair follicles. However, further research and long-term follow-up are required.

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Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Reviewed and approved by the Dankook University Medical Center IR (approval 2016-02-001).

Reprints not available from the authors.

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https://doi.org/10.1016/j.jaad.2020.04.082