Journal of Plastic, Reconstructive & Aesthetic Surgery (2013) **66**, 209—214

JPRAS
An International Journal of Surgical Reconstruction
www.JPRASurg.com

Use of botulinum toxin type A to improve treatment of facial wounds: A prospective randomised study

Makram Ziade [a,*], Sophie Domergue [a], Dominique Batifol [a], Riad Jreige [b], Mustapha Sebbane [b], Patrick Goudot [a], Jacques Yachouh [a]

[a] *Department of Plastic and Reconstructive Surgery, Lapeyronie University Hospital, 371 Avenue du Doyen Gaston Giraud, 34295 Montpellier, France*
[b] *Emergency Department, Lapeyronie University Hospital, 371 Avenue du Doyen Gaston Giraud, 34295 Montpellier, France*

Received 11 January 2012; accepted 13 September 2012

KEYWORDS
Botulinum toxin type A;
Wound healing;
Face injury;
Randomised study

Summary *Background:* The tension vectors acting on the wound edges are transmitted to immature collagen fibres synthesised during the normal healing phase. This accounts for scar widening as well as hypertrophic and hyperpigmented scars. The aim of our study was to evaluate whether early injections of botulinum toxin type A (BTA), which induces temporary muscular paralysis, decreases tension vectors on wound edges and enhances scarring of facial wounds.
Patients and methods: Thirty patients with facial wounds were enrolled in this study and randomised into two groups with or without injection of BTA within 72 h postoperatively. BTA was injected into the facial muscles directly or indirectly involved in scar widening. Scars were assessed at a 1-year follow-up visit by patients using the Patient Scar Assessment Scale (PSAS) scale, by an independent evaluator using the Observer Scar Assessment Scale (OSAS) and the Vancouver Scar Scale (VSS), and by a board of six experienced medical specialists using the Visual Analogue Scale (VAS) with standardised photographs.
Results: At the 1-year visit, 24 patients were reviewed and six patients were lost to follow-up. No statistically significant differences were found between the two groups for the PSAS, OSAS and VSS scores. However, the median VAS rated by the six evaluators was 8.25 for the botulinum toxin-treated group compared with 6.35 for the control group. This result was statistically different, demonstrating improved scarring with BTA.
Conclusions: Thanks to chemoimmobilisation, injections of BTA appear to improve cosmesis of facial wounds. Accordingly, they would be beneficial for use in young patients for wounds without tissue loss, lying perpendicular to the reduced tension lines of the skin of the face.

* Corresponding author. Tel.: +33 4 67 33 80 77; fax: +33 4 67 33 68 41.
E-mail address: m_ziade@hotmail.com (M. Ziade).

1748-6815/$ - see front matter
http://dx.doi.org/10.1016/j.bjps.2012.09.012

Unsightly facial scars have a destructive socio-psychological impact.[1] They often occur in wounds perpendicular to the lines of Langer as defined by Karl Langer in 1861.[2,3] The tension vectors acting on the wound edges are transmitted to immature collagen fibres synthesised during the normal healing phase. This accounts for scar widening[4] as well as hypertrophic and hyperpigmented scars due to increased extracellular collageneous and glycosaminoglycaneous deposits.[5] In 1892, Theodor Kocher, a Nobel laureate in medicine and physiology, was the first to make skin incisions along relaxed skin tension lines.[6] Yet, scar alignment with the lines of Langer does not completely eliminate elastic forces on the wound edges of adjacent skin.[7] Botulinum toxin type A injections induce temporary muscular paralysis, and relieve the tension on wound edges. This relief of tension may help prevent the widening, hypertrophy and hyperpigmentation of facial scars.

The aim of this study is to investigate whether early botulinum toxin type A injections improve scarring of facial wounds.

Patients and methods

This study was designed as a prospective, blinded, randomised, controlled, single-institution trial. The level of evidence is II according to the American Society of Plastic Surgeons rating levels of evidence.[8]

Patients older than 18 years presenting to the emergency room at the Lapeyronie Hospital in Montpellier (France) with a facial wound without tissue loss were enrolled from May to October 2009.

The exclusion criteria applied were allergy to botulinum toxin, current pregnancy or breast feeding, myasthenia, previous injection of botulinum toxin within 6 months prior to enrolment and refusal to participate in this trial. Eligible patients were informed about the study protocol in clear, simple language before their informed consent was obtained.

Patients were randomly assigned to one of two groups: the 'toxin' group or the 'control' group. Patients of the 'toxin' group were injected with botulinum toxin in facial muscles directly or indirectly involved in scar widening within 72 h following the suturing of the facial wound. Patients of the 'control' group were not given injections following the suturing of the facial wound.

Data regarding age, sex, phototype according to the Fitzpatrick scale,[9] treatment delay, cause of lesion, wound location and wound length were obtained at an initial clinical examination.

All patients were sutured by the same surgeon in the emergency department using identical facilities, according to a standardised protocol. For local anaesthesia, a solution of 1% lidocaine (LIDOCAINE® 10 mg ml; Laboratoire Aguettant, Lyon, France) was used. A standardised resterilisable suture kit was used for suturing. Subcutaneous suturing for 'deep wounds' involving the hypodermis was realised using simple inversant Polyglactin 4/0 sutures (VICRYL 4/0®, Ethicon Inc., Somerville, NJ, USA). Cutaneous suturing was realised using simple Polypropylene 5/0 sutures (PROLENE 5/0®, Ethicon Inc., Somerville, NJ, USA).

Patients randomly assigned to the «toxin» group received an injection of Botulinum Toxin Type A (BOTOX®, ALLERGAN, Westport, Ireland) within 72 h after wound closure. All injections were performed by the same physician experienced in botulinum toxin treatment. The study medication was prepared in proper facilities. The vials contained 100 units of Allergan botulinum toxin type A mixed with 10 ml of 0.9% injectable saline, that is, 1 U of Allergan toxin per 0.1 ml. The vials were refrigerated and used within 4 h. Injections were performed with a 1 ml syringe. The physician injected the amount of botulinum toxin he/she considered necessary to induce paresis of the face muscles directly or indirectly involved in scar widening. Patients received daily standardised antiseptic treatment with Chlorhexidine (BISEPTINE®, Bayer Laboratory, Gaillard, France) for 7 days. At the 7-day follow-up visit, patients were seen and examined for stitch removal and clinical assessment.

Patients were instructed to strictly observe adequate protection with sunglasses and hats and SPF 50+ sunscreen for 1 year. They also initiated a course of 20 manual scar massages 10 days after suturing.

Close-up photographs were taken of the wounds at a 1:1 ratio with a Kodak digital camera (KODAK® M1073 IS, Rochester, NY, USA), flash, 10.6-megapixel resolution and blue background prior to wound suturing, following wound suturing, at the 7-day follow-up visit and at the 1-year visit.

At the 1-year visit, the final outcome was evaluated via subjective patient satisfaction rating (very unsatisfied, unsatisfied, satisfied, very satisfied), PSAS completed by patients,[10] OSAS completed by an experienced observer in an independent and blinded fashion,[10] VSS completed by an experienced observer in an independent and blinded fashion[10] and a 1–10 VAS used by a group of three plastic surgeons and three emergency physicians, all experienced in the treatment of facial wounds. VAS scores were determined in a blinded fashion with serialised digital photographs of all patients. The evaluators assessed the scars independently to avoid any influences.

The number of participants to be enrolled in the study was calculated with EPIINFO based on data in a study by Quinn et al.[11] A 30% discrepancy between the 'toxin' group and the 'control' group was expected on the VAS scale. Minimal sample size was estimated at 15 per treatment group assuming a type 1 error level of 5% and an 80% chance of bilateral hypothesis. A 15% loss to the follow-up rate was expected. Data were analysed with the Student *t*-test or the Wilcoxon rank sum test according to the distribution for the quantitative variables, and with a chi-squared test for the qualitative variables. When chi-squared test validity conditions could not be met, the Fisher exact test was used. The minimal significant difference was 5% for all tests. Statistics were analysed in collaboration with the Department of Medical Information at the Montpellier University Hospital with SAS V9 software (SAS Institute, Cary, NC, USA).

Results

Thirty-four patients were assessed for eligibility in this study from May to October 2009. Four patients were