
BACKGROUND: Cosmetic procedures, particularly those that are minimally invasive, are in demand. The physician specialties performing these procedures are not well-characterized. 

OBJECTIVE: To examine changes in the frequency of cosmetic dermatologic procedures performed in the United States from 1995 to 2010 and the physician specialties performing them. 

METHODS: The volume of cosmetic procedures performed by physician specialties and the types of cosmetic procedures performed were determined from data from the National Ambulatory Medical Care Survey (NAMCS) from 1995 to 2010. 

RESULTS: Cosmetic procedures constituted 8.7% of all skin procedures and have increased since 1995 (p < .001). Botulinum toxin injections were the most frequently performed cosmetic procedure and increased at the greatest rate over time. Plastic surgeons performed the largest proportion of cosmetic procedures (36.1%), followed by dermatologists (33.7%), but other specialties have been performing an increasing proportion of cosmetic procedures. This study was limited to the provision of outpatient procedures, and the nationally representative data of the NAMCS is subject to sample bias. 

CONCLUSIONS: Plastic surgeons and other physicians performed the majority of outpatient cosmetic procedures. Dermatologists performed one-third of ambulatory cosmetic procedures from 1995 to 2010. This broadening spectrum of physicians and nonphysicians providing cosmetic procedures may have important implications for patient safety.


INTRODUCTION: Botulinum toxin (BTX) and dermal fillers (DFs) are considered as quick and effective non-surgical solutions for enhancing facial appearance. 

OBJECTIVE: To evaluate dentists' knowledge and attitude towards using Botulinum toxin and DFs in dental treatment in Riyadh, Saudi Arabia. 

METHODS: Five hundred questionnaires were distributed in Riyadh city to government and private sectors to determine awareness and attitude towards using Botulinum toxin and DFs in dental clinics for therapeutic and aesthetics uses. 

RESULTS: Botulinum toxin: A total of 1.2% is practising it. Only 34.8% could recognise its composition. Use of Botulinum toxin in wrinkle reduction was the most reported (73.7%). A total of 81.1% believed that Botulinum toxin has side effects; allergic reaction was the most reported (57.5%). A total of 47.8% reported that higher doses are more toxic, and that males need higher doses than females (10.2%). Dermal fillers: A total of 0.9% is practising it. The most reported type (47.8%) was Fat transfer. Filling of wrinkles was the most reported use (57.8%). A total of 69% believed that DFs has side effects; allergic reaction was the most reported (53.4%). Attitude: A total of 37.8% would like to practise Botulinum toxin/DFs, mostly for aesthetic dental reason. However, 60.2% rejected the idea, mainly due to lack of knowledge and experience (44%). 

CONCLUSION: Limited knowledge regarding Botulinum toxin and dermal fillers is found among dentists in Riyadh, Saudi Arabia.


BACKGROUND: Legacy recommendations suggest that vials of botulinum toxin be used within 24 hours of reconstitution and in a single patient. Current standard of care is consistent with storage after reconstitution and use of a single vial for several patients. 

OBJECTIVE: To develop expert consensus regarding the effectiveness and safety of storage and reuse of botulinum toxin. 

MATERIALS AND METHODS: The American Society for
Dermatologic Surgery authorized a task force of content experts to review the literature and provide guidance. Data extraction was followed by clinical question review, a consensus Delphi process, and validation of the results by peer review. RESULTS: After 2 rounds of Delphi process, the task force concluded by unanimous consensus and with the highest level of confidence that a vial of toxin reconstituted appropriately can, for facial muscle indications, be (1) refrigerated or refrozen for at least 4 weeks before injection without significant risk for contamination or decreased effectiveness and (2) used to treat multiple patients, assuming appropriate handling. CONCLUSION: The standard of care, which allows for use of botulinum toxin more than 24 hours after reconstitution and in more than 1 patient per vial, is appropriate and consistent with the safe and effective practice of medicine.

4. Alaraj, A. M., et al. (2013). "Variable ptosis after botulinum toxin type a injection with positive ice test mimicking ocular myasthenia gravis." J Neuroophthalmol 33(2): 169-171. We describe a patient who received cosmetic botulinum toxin type A injections to the brow and subsequently developed unilateral ptosis that was variable during examination and was transiently improved after the ice pack test. Ptosis gradually resolved spontaneously over approximately 3 months. This is the third patient to have variable ptosis documented after botulinum toxin type A injection to the brow and the second to have a positive ice test. The ice test is not completely specific for myasthenia gravis but may, at times, improve ptosis resulting from other defects at the neuromuscular junction. Wound botulism now is much more common because of illicit drug use, and the ice test also might be positive in this setting.

5. Alimohammadi, M., et al. (2013). "Correlation of Botulinum Toxin Dose with Neurophysiological Parameters of Efficacy and Safety in the Glabellar Muscles: A Double-blind, Placebo-controlled, Randomized Study." Acta Derm Venereol. Despite the extensive use of botulinum toxin type A (BoNT-A) in cosmetic treatments for glabellar frown lines; the europhysiological dose-response effect in the glabellar muscles remains unknown. The aim of this randomized, double-blind, placebo-controlled prospective study was to characterize the neurophysiological parameters that correlate with the effect of BoNT-A in the glabellar muscles and its diffusion to surrounding ocular muscles. Sixteen healthy women were recruited and randomized to 3 different dose-groups of onabotulinumtoxin A (Vistabel) or placebo and followed 24 weeks by neuro-physiological examinations. Efficacy of treatment on corrugator superciliii muscles was measured by compound motor action potential (CMAP) and electromyography (EMG). Photographs were used to score glabellar frown lines according to a previously described scoring scale. Diffusion of the drug to surrounding muscles was assessed by CMAP of the nasalis muscle, EMG and concentric needle electrode jitter analysis (CNE) of the orbicularis oculi muscle. CMAP reduction correlated well with intramuscular BoNT-A dose. Muscle paralysis, measured by EMG, began from 2 weeks and was not entirely reversed at 24 weeks in individuals who received high dose of onabotulinumtoxin. All subjects receiving BoNT-A were satisfied with the aesthetic results. Limited diffusion of orbicularis oculi was detected with CNE. In conclusion, we developed a novel neurophysiological strategy for effect evaluation of BoNT-A in glabellar muscles. CMAP and EMG correlated with given BoNT-A dose and are more defined effect measures than clinical glabellar photo scales. This study provides better understanding of the glabellar dose-response and safety effect of BoNT-A.

Background IncobotulinumtoxinA was approved in Argentina in 2007 for the treatment of moderate to severe glabellar lines. Objective The authors evaluate real-world changes in facial aesthetic treatment patterns and patient satisfaction following the introduction of incobotulinumtoxinA in Argentina. Methods This multicenter, retrospective chart review conducted in Argentina included women who had received at least 2 treatment cycles of onabotulinumtoxinA (Allergan, Irvine, California) for glabellar lines (period 1) prior to switching to incobotulinumtoxinA (Merz Pharma, GmbH, Frankfurt, Germany (period 2)). Subjects were given the option to continue with incobotulinumtoxinA treatments (captured in period 2) or switch back to onabotulinumtoxinA (documented as period 3). Medical records were reviewed for demographics, dosing, reason for switching between products, treatment satisfaction, and interval between injection cycles. Results One hundred ten women were enrolled and collectively received 662 treatment cycles with botulinum toxin. Subjects were switched to incobotulinumtoxinA at unit doses that were numerically and statistically similar to the onabotulinumtoxinA doses they received in period 1. Most subjects (92%) initially switched to incobotulinumtoxinA because of lower cost. Ninety-two subjects (84%) switched back to onabotulinumtoxinA in period 3, most commonly due to insufficient duration of effect with incobotulinumtoxinA (61/92; 66%). Subjects reported satisfaction with treatment in >90% of their onabotulinumtoxinA visits and in 34% of their incobotulinumtoxinA visits. Median interinjection intervals with onabotulinumtoxinA were 180.3 days (period 1) and 176.9 days (period 3) and 144.3 days with incobotulinumtoxinA in period 2. Conclusions In this real-world setting, subjects did not appear to perceive the same facial aesthetic benefits from incobotulinumtoxinA as onabotulinumtoxinA when the products were administered at comparable doses. Level of Evidence: 3.


Botulinum toxin type A is a 150 kD protein produced by Clostridium botulinum, which exists in a complex with up to six additional proteins. The ability of botulinum toxin to inhibit acetylcholine release at the neuromuscular junction has been exploited for use in medical conditions characterized by muscle hyperactivity. As such, botulinum toxin is widely recommended by international treatment guidelines for movement disorders and it has a plethora of other clinical and cosmetic indications. The chronic nature of these conditions requires repeated injections of botulinum toxin, usually every few months. Multiple injections can lead to secondary treatment failure in some patients that may be associated with the production of neutralizing antibodies directed specifically against the neurotoxin. However, the presence of such antibodies does not always render patients non-responsive. The reported prevalence of immunoresistance varies greatly, depending on factors such as study design and treated indication. This review presents what is currently known about the immunogenicity of botulinum toxin and how this impacts upon patient non-response to treatment. The complexing proteins may act as adjuvants and stimulate the immune response. Their role and that of neutralizing and non-neutralizing antibodies in the response to botulinum toxin is discussed, together with an assessment of current neutralizing antibody measurement techniques. Botulinum toxin preparations with different compositions and excipients have been developed. The major commercially available preparations of botulinum toxin are Botox (onabotulinumtoxin A; Allergan, Inc., Ireland), Dysport (abobotulinumtoxin A; Ipsen Ltd, UK), and Xeomin (incobotulinumtoxin A; botulinum toxin type A [150 kD], free from complexing proteins; NT 201; Merz
Pharmaceuticals GmbH, Germany). The new preparations of botulinum toxin aim to minimize the risk of immunoresistance in patients being treated for chronic clinical conditions.


PURPOSE: To assess the long-term results of the treatment of oculofacial asymmetries using a combined injection schedule for injections of hyaluronic acid, with a specific micro cannula and botulinum toxin. METHOD: A retrospective study was conducted from January 2009 to January 2010. Patients were treated in the Alcazar Eye Clinic and Oculoplastic Department in Princess Grace Hospital, Monaco. We selected patients complaining of asymmetrical periorbital features who received treatment with hyalurostructure and botulinum toxin injection in one or more sessions. Nine patients were selected and presented with the following symptoms: asymmetry of eyebrow position (2 patients), superior orbital hollow (2 patients), tear trough (2 patients) and orbital volume (ocular prosthesis) (3 patients). The objective was to evaluate the efficiency of combined treatment in one or more sessions on these oculofacial asymmetries. Hyaluronic acid injections were done using hyalurostructure. Hyaluronic acid gel (Restylane Lidocaine) was used with a 25 gauge reinforced micro-cannula (pixl +, Thiebaud). This was combined with injections of botulinum toxin (azzalure*) to areas of muscular hyperaction. Follow-up was done at 1 year by clinical examination, photography and patient satisfaction. Complications of this combined treatment have been identified. RESULTS: At 1-year follow-up, 88% of patients were satisfied or very satisfied with their results. There were no more complications secondary to both treatments in the same session. It was not noticed more hematomas and bruises than in classical injection method. The action of toxin is constant over time despite the association of hyaluronic acid injections. CONCLUSION: Combined treatments with toxin and hyaluronic acid in oculofacial asymmetries are efficient and can be proposed in the same session. These treatments must be repeated to maintain and optimize muscle contraction and volume loss. Use of hyalurostructure and botulinum toxin injection in the same session is effective and safe.


Despite its ubiquity in cosmetic circles and broad general awareness, a literature search of botulinum neurotoxin in JPRAS and BJPS yielded a mere 4 articles germane to cosmesis. A pair each detailing its application in masseteric hypertrophy(1,2) and the use of cryoanalgesia.(3,4) Given that botulinum neurotoxin A is the most commonly used cosmetic treatment, with American figures being most accurate,(5) a review of the background, development and scientific evidence would be perhaps useful, if not overdue, as Plastic Surgeons increasingly incorporate non-surgical interventions into their practices as part of a comprehensive facial rejuvenation strategy.


BACKGROUND: This article is a review of the literature and the authors' experience in managing patients seeking facial and nonfacial rejuvenation procedures with budgetary constraints., OBJECTIVE: To provide readers with an approach to the cosmetic patient with financial limitations., METHODS AND MATERIALS: This article is written from a review of the
literature and the authors' experience. RESULTS: The readers should learn how to better manage a patient with financial limitations seeking cosmetic procedures. CONCLUSION: Because patients seeking cosmetic procedures are often faced with budgetary constraints, it is important for the cosmetic physician to educate patients about available treatment options and their costs. Giving patients realistic expectations and tailoring treatment plans to the patient's primary goals and financial limitations can help maximize overall patient satisfaction. 

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BACKGROUND: Botulinum toxin A is a commonly used biological medication in the field of facial plastic surgery. Currently, there are three distinct formulations of botulinum toxin A, each with their purported benefits and advantages. However, there is considerable confusion as to the relative efficacy and side-effects associated with each formulation. Therefore, the purpose of this paper is to systematically assess published studies and perform a meta-analysis to determine if there is a significant advantage of any of the individual formulations. METHODS/DESIGN: A systematic literature search was performed for all relevant English language randomized controlled trials using Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL), MEDLINE, World Health Organization (WHO) International Clinical Trials Registry Platform, European Union (EU) Clinical Trials Register, Cochrane Library databases of clinical trials, and ClinicalTrials.gov. Inclusion criteria included any randomized controlled trial (RCT) that assessed the use of botulinum toxin for cosmetic purposes. The included articles were also analyzed for bias using the Cochrane Collaboration's tool for assessing the risk of bias in RCTs. DISCUSSION: The results of this review will provide clinicians with an unbiased, high level of evidence of the comparative efficacy of individual preparations of botulinum toxin A.


BACKGROUND: Three formulations of botulinum toxin are available for facial rhytides. It is unclear which formulation offers the greatest balance of benefits and harms. The objective of this study was to conduct a systematic review with meta-analyses to compare formulations of botulinum toxin for reduction of facial rhytides at the glabella. METHODS: The authors' protocol was registered with the International Prospective Register of Systematic Reviews (CRD4201200377). A systematic literature search was performed identifying double-blind studies. The authors assessed 1-, 3-, and 4-month follow-up. The authors performed pairwise meta-analyses using random effects models to compare response rates among the three botulinum formulations and a network meta-analysis. RESULTS: A total of 18 studies (3082 patients) were included. At 30-, 90-, and 120-day follow-up, all medications with available data showed statistically significantly increased treatment response versus placebo. Only high-dose onabotulinum toxin (compared to standard-dose onabotulinum toxin) offered additional benefit at 30 days. Exploratory analysis using network meta-analysis mostly suggested insufficient evidence of incremental benefits when comparing specific formulations. CONCLUSIONS: Evidence supporting
benefits versus placebo of the different formulations was clear over time. Comparisons between active formulations were rare and typically based on single trials of small to moderate sample size. The data suggest some gains with high-dose onabotulinum toxin (relative to standard dose), whereas exploratory indirect comparisons between active formulations were largely associated with inconclusive findings. Future studies should undertake head-to-head comparisons of the different formulations and ensure longer follow-up to best inform the accumulating evidence base. CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.


Seven distinct strains of Clostridium botulinum (type A to G) each produce a stable complex of botulinum neurotoxin (BoNT) along with neurotoxin-associated proteins (NAPs). Type A botulinum neurotoxin (BoNT/A) is produced with a group of NAPs and is commercially available for the treatment of numerous neuromuscular disorders and cosmetic purposes. Previous studies have indicated that BoNT/A complex composition is specific to the strain, the method of growth and the method of purification; consequently, any variation in composition of NAPs could have significant implications to the effectiveness of BoNT based therapeutics. In this study, a standard analytical technique using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and densitometry analysis was developed to accurately analyze BoNT/A complex from C. botulimum type A Hall strain. Using 3 batches of BoNT/A complex the molar ratio was determined as neurotoxin binding protein (NBP, 124 kDa), heavy chain (HC, 90 kDa), light chain (LC, 53 kDa), NAP-53 (50 kDa), NAP-33 (36 kDa), NAP-22 (24 kDa), NAP-17 (17 kDa) 1:1:1:2:3:2:2. With Bradford, Lowry, bicinchoninic acid (BCA) and spectroscopic protein estimation methods, the extinction coefficient of BoNT/A complex was determined as 1.54 +/- 0.26 (mg/mL)(-1)cm(-1). These findings of a reproducible BoNT/A complex composition will aid in understanding the molecular structure and function of BoNT/A and NAPs.

BACKGROUND: The U.S. Food and Drug Administration has approved four distinct formulations of botulinum toxin (BoNT) serotypes A and B (BoNTA and BoNTB) for medical use. These four products are indicated for many medical applications, but the three BoNTA formulations are the most widely used worldwide and are the only products approved for aesthetic use. The latest approval of a BoNTA with no complexing proteins (incobotulinumtoxinA) necessitates a review and discussion of differences between available formulations and the effect that these differences may have on clinical practice. OBJECTIVES: To review the history, science, safety information, and current and emerging applications of BoNT in clinical and cosmetic practice and to compare commercially available BoNTA formulations. METHODS AND MATERIALS: Publications, clinical trials, and author experience were used as a basis for an up-to-date review of BoNT and its use in human medicine. The similarities and differences between formulations are presented, and diffusion, spread, equivalency ratios, stability, and storage are discussed. RESULTS: Each commercial formulation has unique characteristics that may influence its use in aesthetic
medicine. Familiarity with the similarities and differences between products will aid physicians in making patient care decisions. CONCLUSION: New formulations, emerging uses, and continued research into the science and uses of BoNTA will lead to increasingly refined therapeutic approaches and applications. Continued education is important for physicians to optimize use of the agent according to the most current evidence and approaches.


BACKGROUND: The new world of safe aesthetic injectables has become increasingly popular with patients. Not only is there less risk than with surgery, but there is also significantly less downtime to interfere with patients' normal work and social schedules.

Botulinum toxin (BoNT) type A (BoNTA) is an indispensable tool used in aesthetic medicine, and its broad appeal has made it a hallmark of modern culture. The key to using BoNTA to its best effect is to understand patient-specific factors that will determine the treatment plan and the physician's ability to personalize injection strategies. OBJECTIVES: To present international expert viewpoints and consensus on some of the contemporary best practices in aesthetic BoNTA, so that beginner and advanced injectors may find pearls that provide practical benefits. METHODS AND MATERIALS: Expert aesthetic physicians convened to discuss their approaches to treatment with BoNT. The discussions and consensus from this meeting were used to provide an up-to-date review of treatment strategies to improve patient results. Information is presented on patient management and assessment, documentation and consent, aesthetic scales, injection strategies, dilution, dosing, and adverse events. CONCLUSION: A range of product- and patient-specific factors influence the treatment plan. Truly optimized outcomes are possible only when the treating physician has the requisite knowledge, experience, and vision to use BoNTA as part of a unique solution for each patient's specific needs.


BACKGROUND: Facial aging is multifactorial, including changes in all the anatomical layers of the face including bone, fat, connective tissues and skin., METHODS: An evaluation of the multifactorial causation of facial aging pointed to the need for a multifactorial approach to restoration and rejuvenation of the aging human face., RESULTS: The varied aetiologies of the expressions of facial aging require more interventions than a unipolar approach. Combinations of neuromodulators, three and two-dimensional fillers and energy based devices were discussed. Surgical interventions were also discussed but were not addressed in this paper. CONCLUSIONS: A multimodal approach to lower facial rejuvenation and restoration is discussed as the most effective and appropriate method to achieve noninvasive aesthetic treatment success., (C) 2016 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. All rights reserved.


Although the mechanism of action of botulinum toxin (BTX) has been intensively studied, many unanswered questions remain regarding the composition and clinical properties of the two formulations of BTX currently approved for cosmetic use. In the first half of this review, these questions are explored in detail, with emphasis on the most pertinent and
revelatory studies in the literature. The second half delineates most of the common and some not so common uses of BTX in the face and neck, stressing important patient selection and safety considerations. Complications from neurotoxins at cosmetic doses are generally rare and usually technique dependent.


21. Chen, J. J. and K. Dashtipour (2013). "Abo-, inco-, ona-, and rima-botulinum toxins in clinical therapy: a primer." Pharmacotherapy 33(3): 304-318. Botulinum neurotoxin (BoNT) is an acetylcholine release inhibitor and a neuromuscular-blocking agent used for the treatment of a variety of medical and cosmetic indications. Currently, in the United States, there are four BoNT formulations licensed for use: abobotulinumtoxinA, incobotulinumtoxinA, onabotulinumtoxinA, and rimabotulinumtoxinB. These revised name designations were established to reinforce the understanding that each BoNT product has an individual potency and is not interchangeable with any other BoNT product. The therapeutic use of BoNTs is expanding and new formulations are on the horizon. This article is a primer that describes distinctions among currently available, licensed BoNT formulations. Toxin pharmacology, product characteristics, storage, handling, preparation, and dosages will be reviewed. In addition, issues related to dose equivalency ratios, immunogenicity, potency, and toxin spread will be discussed. Therapeutic indications and safety are discussed briefly. Knowledge of the available and licensed BoNT formulations and the ability to make distinctions in toxin pharmacology, product characteristics, and indications are vital for product selection, preparation, drug information, avoidance of drug errors, quality assurance, and patient safety.

22. Chen, S. (2012). "Clinical uses of botulinum neurotoxins: current indications, limitations and future developments." Toxins (Basel) 4(10): 913-939. Botulinum neurotoxins (BoNTs) cause flaccid paralysis by interfering with vesicle fusion and neurotransmitter release in the neuronal cells. BoNTs are the most widely used therapeutic proteins. BoNT/A was approved by the U.S. FDA to treat strabismus, blepharospam, and hemifacial spasm as early as 1989 and then for treatment of cervical dystonia, glabellar facial lines, axillary hyperhidrosis, chronic migraine and for cosmetic use. Due to its high efficacy, longevity of action and satisfactory safety profile, it has been used empirically in a variety of ophthalmological, gastrointestinal, urological, orthopedic, dermatological, secretory, and painful disorders. Currently available BoNT therapies are limited to neuronal indications with the requirement of periodic injections resulting in immune-resistance for some indications. Recent understanding of the structure-function relationship of BoNTs prompted the engineering of novel BoNTs to extend therapeutic interventions in non-neuronal systems and to overcome the immune-resistance issue. Much research still needs to be done to improve and extend the medical uses of BoNTs.

23. Cigna, E., et al. (2013). "The use of botulinum toxin in the treatment of plunging nose: cosmetic results and a functional serendipity." Clin Ter 164(2): e107-113. INTRODUCTION: Muscles of the nose are active in facial movements both with the other facial muscles. An active depressor septi muscle (DSN) can accentuate a drooping nasal tip and shorten the upper lip on animation, especially during smiling. Paralysis of the DSN allows the tip of the nose to be lifted up. MATERIALS AND METHODS: Between January and June 2011 a double blinded, randomized study was performed on 40 patients for nasal
defects as "plunging" tip. 20 patients underwent Botulinum toxin injection (B), 20 patients were treated with placebo such as saline solution (S). Both aesthetic and functional results were evaluated using objective and subjective parameters at time 0, after 7, 15 and 30 days and values were compared using t Student test. RESULTS: S group results were not significant from an objective point of view. In botulinum group, patients showed an increase in columellar-lip distance. Satisfaction of the Group B patients was an average of 6.3 on VAS (range from 4 to 9). VAS mean values were studied with t Student test and were found significant. DISCUSSION: Several authors recommend the incision of DSN muscle during rhinoplasty to correct the plunging tip. In patients with no needs for rhinoplasty this procedure is unnecessary and a quick and targeted injection of Botulinum toxin is the most convenient choice to improve aesthetic of the plunging tip.


BACKGROUND: Throughout the literature, investigators have assessed the cosmetic efficacy of botulinum toxin (BT) treatment by using various subjective, qualitative measures, including the Facial Wrinkle Scale (FWS) and Subject Global Assessment (SGA). The widely used FWS and SGA attempt to quantify both the magnitude and duration of cosmetic outcomes as assessed by physician and patient. We sought to determine the interobserver validity of these scales relative to the level of observer experience. METHODS: Botulinum toxin injections were performed to cosmetic effect in 6 patients recruited as part of an institutional review board-approved investigation. Subjects were photographed at rest and during animation (raising eyebrows, frowning, and blinking) before treatment and at 1, 2, 4 weeks, and monthly with follow-up to 6 months. Standardized digital 8"x10" prints were scored using the FWS by board-certified plastic surgeons (n=5), general surgery residents (n=3), and medical students (n=4). Photographs at each time point were then compared to baseline using the SGA. Statistical analysis of observer data was performed using SPSS v19. Cohen kappa (FWS) and Spearman rho (SGA) were calculated for each pairwise comparison of observer data, with a conservative alpha of 0.01. RESULTS: The FWS observer scores for the upper face overall were generally in agreement, with no negative kappa values. The distribution, even among members of a single group, was highly variable. Agreement among plastic surgeons was the greatest (kappa, 0.194-0.609). Resident concordance was moderate, and medical students displayed the most variable agreement. Spearman rho for SGA scores was much higher, with surgeons approaching excellent agreement (kappa, 0.443-0.992). In comparisons between members of different groups, agreement was unpredictable for both the FWS and SGA. Comparisons using scores from individual areas of the face were least concordant. CONCLUSIONS: The FWS and SGA represent the current standard of cosmetic outcomes measures; however, when subjected to scrutiny they display relatively unpredictable agreement even among plastic surgeons. Compared to the FWS, the SGA has a more acceptable user concordance, especially among plastic surgeons accustomed to using such scales. The interobserver variability of FWS and SGA scoring underlines the need to explore objective, quantitative cosmetic outcomes measures.


Facial rhytides represent a widespread aesthetic concern. In particular, glabellar lines are perceived as a sign of aging and may give an erroneous impression of negative emotions. The onset of glabellar lines is closely related to the movements of the underlying muscles. Botulinum toxins inhibit the release of acetylcholine into the synaptic cleft and therefore result in temporary muscle paralysis. The observation that botulinum toxin (BTX) smoothed facial lines when used therapeutically led researchers to study the toxin effect on glabellar lines. Nowadays, the use of BTX to smooth glabellar frown lines represents the leading procedure in aesthetic facial treatments and an increasing number of BTX formulations are becoming available. This article provides a comparative evaluation of currently available BTX options for the treatment of glabellar lines. Toxins have been divided into three groups, based on whether they have obtained approval for cosmetic use (approved treatments) or not (off-label treatments), or whether they are still under investigation (experimental treatments). We examine the basic similarities and differences between available botulinum toxins, and summarize the pharmacokinetics and dosing. All approved treatments consist of BTX type A (BTX-A) and differ in their molecular weight, as some formulations are made of a BTX-A complex of 900 kDa while the latest option on the market is a 150 kDa BTX-A that is free from complexing proteins. As for the dosage, the important aspect that emerges from this comparison is that even within a given serotype, such as BTX-A, formulations are not interchangeable as each possesses distinctive characteristics that are attributed to the unique toxin purification and manufacturing processes. There is a substantial body of published evidence on the use of these approved treatments for facial enhancement, proving efficacy and safety. We investigate the methods of evaluation used for each toxin and review the safety and efficacy data reported in the literature. Minor adverse effects, such as headache, blepharoptosis, and injection-site reactions, are relatively frequent but transient, whilst major adverse effects are rare. Some botulinum toxins, i.e. BTX type B, that are approved for therapeutic applications are used off-label for cosmetic indications, thus without the approval of the health regulatory committees and without sufficient published evidence on safety and efficacy. As for experimental treatments, a number of BTX products are currently in development or have been recently launched for aesthetic applications. These products have been specifically designed to overcome some of the limitations present in the older generation of products. However, some of these toxins may be easily purchased via the Internet, without having any license or approval for cosmetic or therapeutic indications; these products must be considered unsafe and are potentially a severe health risk for patients.


Botulinum toxin (BT) is injected intramuscularly and may produce injection site pain (ISP). We wanted to explore whether the pH value of the reconstituted BT drug contributes to ISP and, if so, what strategies can be applied to reduce it. In part 1 of the study, pH values of different reconstitution solutions and of major BT drugs reconstituted with different reconstitution solutions were assessed. In part 2, the effects of reconstitution with normal saline (NS) and Ringer acetate (RA) were compared intraindividually and in a double blind fashion in 34 patients with blepharospasm. pH values of reconstitution solutions were 5.52 +/- 0.02 for NS, 6.98 for RA, 6.31 for Ringer lactate, 6.56 for electrolyte and 5.31 for bacteriostatic solution. pH values for NS-reconstitution were 6.09 +/- 0.20 for Botox(R), 5.95 +/- 0.24 for Dysport(R) and 5.81 +/- 0.18 for Xeomin(R). pH values for RA-reconstitution were 6.95 +/- 0.03 for Botox(R), 7.01 +/- 0.02 for Dysport(R) and 6.87 +/- 0.06 for Xeomin(R). By using RA instead of NS the pH could be increased by 0.86 for Botox(R), by 1.06 for Dysport(R) and by 1.06 for Xeomin(R). 47% of the patients
experienced less ISP when Botox(R)-RA was given rather than Botox(R)-NS, 76 % when Xeomin(R)-RA was given rather than Xeomin(R)-NS. None of the patients reported a difference in efficacy between NS- and RA-reconstitution. Despite previous reports, reconstituted BT type A drugs show acidic pH values. Normalising these pH values by use of RA instead of NS reduces ISP considerably without sacrificing clinical efficacy.


BACKGROUND: A microfocused ultrasound system with visualization (MFU-V) is currently indicated for use as a noninvasive dermatological aesthetic treatment to lift the eyebrows, lax submental and neck tissue, and improve lines and wrinkles of the decollete., OBJECTIVE: To determine the existence of any safety signals when combining MFU-V with botulinum toxin-A and/or semipermanent and temporary dermal fillers., MATERIALS AND METHODS: A retrospective chart review was performed using subjects who received aesthetic treatments including incobotulinumtoxinA injection, cohesive polydensified matrix hyaluronic acid (CPM HA) dermal fillers, and calcium hydroxylapatite (CaHA) dermal fillers within 6 months of treatment with MFU-V in the same or different anatomic areas., RESULTS: All subjects (N = 101; 96 female; 25-70 year old) received MFU-V, 18% received incobotulinumtoxinA injections, and 81% were treated with CPM HA and/or CaHA fillers. Seven adverse events (7%) were reported: bruising/purpura (n = 4), swelling (n = 1), paresthesia (n = 1), and herpes simplex virus (HSV) outbreak (n = 1). Only the HSV outbreak was considered to be related to combined treatments., CONCLUSION: Although limited by relatively few subjects, the results of the present study suggest that the safety profile of MFU-V combined with other aesthetic products is consistent with the safety profiles of the individual treatments., (C) 2016 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. All rights reserved.


Botulinum toxin A has a wide variety of clinical applications in medical and dermatologic sciences. Nowadays, researchers introduce some other indications for botulinum toxin in cosmetic and especially noncosmetic aspects of dermatology such as medical rhinoplasty, hypertrophic scar, chemical brow lift, supraciliary wrinkles, pompholix, eccrine angiomatosis, Hailey-Hailey, dermatomalasis, lichen simplex, nosthalgia parestetica, and granulosis rubra nasi. In this general overview of the use of botulinum toxin in dermatology, an extensive literature search was carried out to updates of all dermatology-oriented experiments and clinical trials on the mentioned aspect of botulinum toxin.


Botulinum neurotoxin serotype A (BoNT/A), a potent therapeutic used to treat various disorders, inhibits vesicular neurotransmitter exocytosis by cleaving SNAP25. Development of cell-based potency assays (CBPAs) to assess the biological function of BoNT/A have been challenging because of its potency. CBPAs can evaluate the key steps of BoNT action: receptor binding, internalization-translocation, and catalytic activity; and therefore could
replace the current mouse bioassay. Primary neurons possess appropriate sensitivity to develop potential replacement assays but those potency assays are difficult to perform and validate. This report describes a CBPA utilizing differentiated human neuroblastoma SiMa cells and a sandwich ELISA that measures BoNT/A-dependent intracellular increase of cleaved SNAP25. Assay sensitivity is similar to the mouse bioassay and measures neurotoxin biological activity in bulk drug substance and BOTOX(R) product (onabotulinumtoxinA). Validation of a version of this CBPA in a Quality Control laboratory has led to FDA, Health Canada, and European Union approval for potency testing of BOTOX(R), BOTOX(R) Cosmetic, and Vistabel(R). Moreover, we also developed and optimized a BoNT/A CBPA screening assay that can be used for the discovery of novel BoNT/A inhibitors to treat human disease.


AIM: To present the latest findings and future developments in the cosmetic use of botulinum neurotoxin. METHODS: Review of recent literature and new scientific developments. RESULTS: Botulinum neurotoxin type A preparations onabotulinumtoxinA (BOTOX(R)) Cosmetic/Vistabel(R), Allergan Inc.) and abobotulinumtoxinA (Dysport((R))/Azzalure((R))/Reloxin((R)), Ipsen Pharma,) have been used for many years and are effective and well tolerated for facial esthetic procedures. However, advances are continually made in the esthetics field. New formulations that may exhibit reduced antigenicity are becoming available, such as incobotulinumtoxinA (Xeomin(R))/Xeomeen(R)/Bocouture(R); formerly known as NT 201, Merz Pharma), which is a botulinum neurotoxin type A free from complexing proteins. In addition, lower facial procedures using botulinum toxin combined with fillers are becoming increasingly popular. Injection techniques and patterns are also evolving, with the aim of creating a more natural result and avoiding a "frozen" appearance. Moreover, the diversity of individuals requesting esthetic procedures is increasing, with growing interest from men and patients with a variety of skin types and colors. CONCLUSIONS: The uses of botulinum toxins for facial esthetics procedures continue to expand, with new techniques and formulations. The availability of products such as incobotulinumtoxinA may reduce the risk of neutralizing antibody development while maintaining the good efficacy and safety of existing formulations.


INTRODUCTION: Botulinum toxin (BoNT) is the treatment of choice for many neurologic movement disorders, including blepharospasm, hemifacial spasm, and cervical dystonia. There are two serotypes approved for use by the US Food and Drug Administration: three brands of serotype A and one of serotype B. Many attempts have been made at establishing dose conversion ratios between brands and serotypes. This review focuses on the existing data comparing different formulations of the same BoNT serotypes as well as that comparing different serotypes with one another. We focus on existing data regarding switching from one formulation or serotype to another and will also discuss the issue of immunogenicity of BoNT. With this information as a foundation, recommendations on safety of switching agents are addressed. METHOD: Literature review searching PubMed and Google Scholar using the search terms "switching botox", "dosing equivalency in
botox", and "comparing botox". RESULTS/CONCLUSION: Overall, there are many studies that demonstrate the efficacy and safety of each of the brands of BoNTs used in clinical practice. However, determination of dosing equivalencies among these brands and serotypes is complex with inconsistencies among the studies. When switching from one brand to another, the clinician should be aware of these issues, and not make the assumption that such ratios exist. Tailoring the dosage of each brand of BoNT to the clinical situation is the most prudent treatment strategy rather than focusing closely on conversion factors and concerns for immunogenicity.

There is a potential use for intradermic or hypodermic drug delivery in skin surgery or aesthetic surgery. Hypodermic delivery with the use of a noninvasive device can be a more useful, reliable, and effective administration route to obtain higher compliance. The authors developed a microneedle device composed of three fine needles (three-microneedle device). The tip of each needle was fabricated with a bevel angle to release a drug broadly into the tissue in a horizontal fashion. In this study, the authors investigated the usefulness of this newly developed three-microneedle device for hypodermic liquid injection, focusing on the optimum insertion depth and the diffusion of injected materials to the tissue. The authors also assessed the efficacy of and patient satisfaction with three-microneedle device injections of botulinum toxin type A for wrinkle reduction in patients with glabellar rhytides. The three-microneedle device yielded consistent results in hypodermal diffusion. On India ink diffusion test and ultrasonographic imaging, three-microneedle device injection showed a broad diffusion in horizontal extension, as compared with usual 31-gauge needle injection. The efficiency and satisfaction of the patients receiving botulinum toxin type A with the three-microneedle device were highly rated. Three-microneedle device delivery enables accurate and broad diffusion of injected substances, thus reducing the total dose and/or injection number of drugs. CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

BACKGROUND: Duration of effect of aesthetic treatments with botulinum toxin potentially influences subject satisfaction, treatment frequency, and annual costs, but quantitative outcomes for measuring duration of effect and correlations with subject satisfaction have yet to be fully elucidated. METHODS AND MATERIALS: Phase III clinical trials with similar designs were identified and their data pooled to ascertain duration of clinical effect of onabotulinumtoxinA in glabellar muscles. Duration was calculated using the Kaplan-Meier method for investigator-rated Facial Wrinkle scale (FWS) scores and subject global assessment (SGA) of glabellar lines. Responders were determined according to FWS score at maximum contraction and at repose 30 days after injection. RESULTS: Data from four trials with 621 onabotulinumtoxinA-treated (20 U) subjects were analyzed, 523 of these (84.2%) were identified as day-30 responders on the FWS at maximum contraction. Pooled median duration of effect for day-30 responders was 120 days for FWS at maximum contraction and 131 days for FWS at repose. Higher day 30 SGA scores were correlated with a greater duration of effect on dynamic, but not static lines. CONCLUSION: Treatment of glabellar lines with 20 U of onabotulinumtoxinA resulted in sustained clinical benefit for 4 months in more than 50% of responders; subject satisfaction increased with duration of effect.
Two patients under the authors' care developed facial herpes zoster that erupted soon after cosmetic treatment with botulinum toxin type A (BTA). Both patients received typical doses of BTA in the glabella, forehead, and lateral periorbital areas. Within one week after treatment, each patient began experiencing symptoms of herpes zoster in one of the dermatomes supplied by the trigeminal nerve. Since the resolution of the herpes zoster, both patients have gone on to receive further treatments of BTA with prophylactic oral antivirals without sequelae.

Botulinum neurotoxins (BoNTs) are among the most poisonous substances known to man, but paradoxically, BoNT-containing medicines and cosmetics have been used with great success in the clinic. Accidental BoNT poisoning mainly occurs through oral ingestion of food contaminated with Clostridium botulinum. BoNTs are naturally produced in the form of progenitor toxin complexes (PTCs), which are high molecular weight (up to ~900 kDa) multiprotein complexes composed of BoNT and several non-toxic neurotoxin-associated proteins (NAPs). NAPs protect the inherently fragile BoNTs against the hostile environment of the gastrointestinal (GI) tract and help BoNTs pass through the intestinal epithelial barrier before they are released into the general circulation. These events are essential for ingested BoNTs to gain access to motoneurons, where they inhibit neurotransmitter release and cause muscle paralysis. In this review, we discuss the structural basis for assembly of NAPs and BoNT into the PTC that protects BoNT and facilitate its delivery into the bloodstream.

INTRODUCTION: Botulinum toxin is widely used in glabellar musculature. The authors express the need to individualize the approach by means of muscular identification to improve effectiveness. Despite these guidelines, the fixed-point technique is still used. OBJECTIVE: Comparison of effectiveness of botulinum toxin administration in the glabellar zone by using fixed-site application versus objective-muscle-identification. MATERIALS AND METHODS: Prolective dynamic cohort study. Patients (after previous informed consent) were assessed on their facial expressions, level of satisfaction, re-interventions, adverse effects, dosage, dilution, and number of injections. All patients who experienced either of both techniques of botulinum toxin administration (fixed-site or objective-muscle-identification) were subjected to followup by the following parameters: statistical analysis: student’s t Test (inter-group mean comparisons), paired student’s t test (intra-group mean comparisons), chi (2) with Fisher exact text. RESULTS: Sixty-two patients were evaluated (31 fixed-site approach, 31 objective-muscle-identification). No patient abandoned the trial during followup. Fixed-site injections required larger doses (16 vs 12 U, p = 0.001), greater volume (0.48 vs. 0.37 ml, p = 0.001), and more application sites (4 vs 2, p = 0.001), compared to the objective-muscle-identification approach. Under the objective-muscle-identification technique, facial expressions were better attenuated (52 vs 65 %, p = 0.001), with a higher initial satisfaction level (6 vs 9, p = 0.001) and final satisfaction level (9 vs 9.9, p = 0.001). CONCLUSIONS: Botulinum toxin application is more effective when administered through the objective-muscle-identification approach (less frowning, lower doses, less fixed sites injected, and patients more satisfied at the end). LEVEL OF EVIDENCE III: This journal
requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.


BACKGROUND: A prospective, randomized, double-blind, multicenter, Phase III trial of incobotulinumtoxinA using new Food and Drug Administration endpoints. OBJECTIVE: To investigate the efficacy and safety of a single dose of incobotulinumtoxinA for the treatment of glabellar frown lines. MATERIALS AND METHODS: Two hundred seventy-one subjects with moderate to severe glabellar frown lines at maximum frown-as assessed by an investigator according to the facial wrinkle scale (FWS)-were randomized 2:1 to receive one treatment of 20 U of incobotulinumtoxinA or placebo, respectively, and assessed over 120 days. The primary efficacy variable was a composite endpoint consisting of patients who were 2-point or more responders at maximum frown on Day 30 according to the investigator's rating on the FWS, and 2-point or more responders at maximum frown on Day 30 according to the patient's assessment on a 4-point scale. Safety analyses were performed throughout the study. RESULTS: IncobotulinumtoxinA was statistically significantly more efficacious than placebo using a new rigorous composite endpoint (p < .0001). CONCLUSION: A single dose of 20 U of incobotulinumtoxinA is superior to placebo in the treatment of glabellar frown lines at Day 30 and is well-tolerated.


Botulinum neurotoxin type A injection to correct and/or reverse the physical effects of aging process has become one of the most frequently requested cosmetic procedures at an outpatient setting. Careful clinical evaluation together with proper use of the techniques, including pre- and post-procedures recommendations, reconstitution of the products, techniques, and doses, are described in this article. This article also covers the main indications of botulinum neurotoxin type A for aging face and other aesthetic uses, as well as some possible adverse reactions and their management.


BACKGROUND: Botulinum toxin type A (BoNT-A) injection has become the most popular cosmetic nonsurgical procedure, and it has been suggested that BoNT-A injections may improve emotional states when frown lines are treated. OBJECTIVES: To evaluate symptoms of depression and self-esteem before and after onabotulinumtoxinA (ONA) injections in the glabella in subjects with and without depression. METHODS: Twenty-five subjects with depression were allocated into one group and 25 subjects without depression were matched to those according to demographic characteristics. The Beck Depression Inventory (BDI) and Rosenberg Self-Esteem Scale (RSES) were used to assess depression
symptoms and self-esteem, respectively. Patients were assessed up to 12 weeks after the intervention. RESULTS: Patients with depression had significant improvement in depression symptoms after ONA injections. The maximum effect occurred within the first 8 weeks after treatment. A significant reduction from baseline in BDI score and significant improvement in self-esteem were also observed in patients with depression. CONCLUSION: This research presents new data regarding BoNT-A as a potential treatment to improve depression symptoms in patients with Major Depressive Disorder. Self-esteem scores alone cannot explain the improvement in depression symptoms.

BACKGROUND: Facial aging in the midface reflects cumulative results of multiple intrinsic and extrinsic factors over time. Midfacial rejuvenation procedures can make a positive impact on facial attractiveness and patient satisfaction. OBJECTIVE: To review evidence and clinical experience using combination treatments for midfacial rejuvenation to achieve optimal outcomes. MATERIALS AND METHODS: This article provides a review of published scientific evidence supporting the use of combination therapy in midfacial rejuvenation. In addition, the authors share their cumulative clinical experience and best practices for combination treatments in the midface. RESULTS: Clinical experience and evidence shows that combining multiple aesthetic therapies targeting multiple aspects of the aging process provides optimal results, with greater overall efficacy and a higher level of patient satisfaction. (C) 2016 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. All rights reserved.

A new technique for the treatment of diplopia secondary to cosmetic botulinum toxin A use is described. In this interventional case reports, two consecutive patients who developed diplopia after periorcular cosmetic use of botulinum toxin A were treated with intramuscular botulinum toxin A injection into the antagonist extraocular muscle. Diplopia resolved in both patients in less than 1 week with no side effects or complications. In conclusion, the injection of intramuscular botulinum toxin A is an encouraging option for treatment of diplopia secondary to botulinum toxin A use for facial lifting.

Chemoimmobilization with botulinum toxin A is an ideal biochemical agent that allows near-total elimination of muscle pull on the healing facial wound. The goal of chemoimmobilization of facial cutaneous wounds is to eliminate dynamic tension on the healing tissues to improve wound healing and minimize scarring for optimal aesthetic results.

BACKGROUND: It is accepted that the three commercially available type A botulinum toxins (BoNT-As) are different, their units of potency are not interchangeable and no fixed dose conversion ratio exists between them. To date, there is no clear evidence demonstrating the superiority of one toxin over another clinically. OBJECTIVE: The study aims to identify evidence confirming the equivocal efficacy of the formulations and to justify that attention can therefore be reasonably turned to their differing costs as a means of aiding choice of
treatment. This is achieved via the development of the cost calculator presented herein, to enable direct economic comparisons to be made between the three commercially available BoNT-A formulations licensed for aesthetic indications in the UK. METHODS: An online literature search using PubMed was undertaken and the latest available information on the cost for each BoNT-A treatment was accessed via the British National Formulary (BNF). Predicated on the evidence review, a cost calculator was developed which takes into account for the glabella: the number of treatments needed per patient with each product over a year and the number of treatments available with differing dilutions of each vial of each product over a year. A range of cost prices can also be introduced allowing a direct cost-comparison to be made for treating the glabella of a set number of patients over a year between different products. RESULTS: Azzalure((R)) (abobotulinumtoxinA) was the most cost-effective in almost all scenarios tested, whilst Vistabel((R)) (onabotulinumtoxinA) was the least cost-effective. Of the two products with published non-inferiority with respect to each other, onabotulinumtoxinA and Bocouture((R)) (incobotulinumtoxinA), incobotulinumtoxinA offered a lower overall cost to treat the glabella of the same number of patients when compared with Vistabel. CONCLUSION: In most scenarios, BoNT-A treatment with abobotulinumtoxinA will result in significant annual cost savings when compared with onabotulinumtoxinA or incobotulinumtoxinA.


Botulinum neurotoxin-A (BoNT-A) has become widely used in aesthetic applications over the past 20 years with several formulations now available. Although widely assumed to be equipotent, recent claims that the original commercial formulation, onabotulinumtoxinA (Botox(R)/Vistabel(R), Allergan UK, Marlow, UK) is more potent than incobotulinumtoxinA (Bocouture(R)/Xeomin(R), Merz Pharma, UK) have raised concerns that clinicians may be persuaded to increase doses to the potential detriment of their patients. To investigate this further, a review of the clinical evidence for the commercially available cosmetic formulations of BoNT-A was undertaken alongside a meta-analysis, carried out using mixed treatment analysis (MTA) methodology, of the available clinical data in the aesthetic setting. This demonstrated that at a dose of 24 units, there was a 94% likelihood that incobotulinumtoxinA was more effective than onabotulinumtoxinA in achieving a response as defined in the included studies; however, the scale of this advantage was not clinically meaningful. Of 11 clinical and preclinical studies identified comparing incobotulinumtoxinA and onabotulinumtoxinA directly, the weight of evidence suggested that there was no difference in the relative potency of the two products. As such, clinicians should continue to consider the formulations to be equipotent until such time that compelling clinical evidence to the contrary becomes available.


BACKGROUND: Despite the escalating number of patients undergoing aesthetic BoNT-A procedures, a standardized, objective means of setting treatment goals and measuring the success of treatment is lacking. Treat-To-Goal (TTG) is a new approach to consent that utilizes the Merz Aesthetics Scale to set objectively defined start points and treatment goals to better inform the consent process and provide a means of measuring the success of treatment. OBJECTIVE: To evaluate the TTG approach vs standard consent procedures in terms of patient understanding of the risks and benefits of treatment. METHODS: This study was undertaken in 2 phases among consecutive patients presenting for BoNT-A
treatment. Phase 1 consisted of a crossover comparison of patient satisfaction with standard consent vs the TTG approach (n=20). Patient understanding of the likely outcomes and risks associated with treatment following consent and their overall preference were assessed using 10-point visual analog scales (VAS). Phase 2 assigned patients to receive no treatment (n=10) or treatment with BoNT-A (n=54) following consent with the TTG approach. Patients were followed up with 28 days later to assess whether the goals defined during consent had been met. RESULTS: The TTG approach significantly improved patient understanding of likely outcomes of BoNT-A treatment compared with standard consent (P=.004 when standard consent assessed first, and P=.002 when TTG assessed first). All patients assessed preferred the TTG approach (median VAS score in favor of TTG: 7.0, P<.0001). Target improvements were successfully met or exceeded in at least one treatment area (forehead, glabellar lines, crow’s feet) in all patients treated with BoNT-A. In contrast, none of the untreated patients met their target improvements unless the target was defined as no change. CONCLUSION: The TTG approach represents a significant improvement over standard consent in terms of the information it provides to patients. Further investigation of this concept is warranted.


Over the past decade, facial cosmetic procedures have become more commonplace in dentistry and oral and maxillofacial surgery. An increasing number of patients seek minimal invasive procedures. One of the most requested procedures is treatment with botulinum toxin type A (BoNTA). Treatment of dynamic rhytids and lines with BoNTA is effective and produces high rates of improvement with rapid onset and long duration of action (longer than 4 months for some patients) compared with placebo. This paper considers the history and pharmacology of this neurotoxin, and focusses on the literature concerning the treatment of different facial areas with BoNTA. It also presents clinical guidelines on the treatment of glabellar lines, the frontalis muscle, peri-orbital lines, gummy smile and masseter muscle hypertrophy. Knowledge about the mechanisms of action and the ability to use BoNTA as an adjunctive treatment are mandatory for those working in the field of cosmetic facial surgery.


BACKGROUND: Different diffusion of different botulinum toxin type A (BoNTA) preparations may account for differences in outcomes in cosmetic clinical practice. OBJECTIVES: A double-blind, randomized, self-controlled study was performed to evaluate the diffusion characteristics of onabotulinumtoxinA and a Chinese type A botulinum toxin (CBTX-A). MATERIALS AND METHODS: Healthy volunteers (N = 20) were recruited to receive a 0.05-mL (2 U) injection of BoTNA at four forehead sites (medial forehead (subcutaneous (SC)) and temporal forehead (intradermal (ID))). On day 14, the Minor’s iodine starch test was performed and photographs were taken for calculating the area and dimensions of anhydrotic area. RESULTS: When BoNTAs were different, the anhidrosis ID area was significantly greater with CBTX-A than onabotulinumtoxinA, the vertical dimension was significantly longer with CBTX-A ID than onabotulinumtoxinA ID and the horizontal dimension was significantly greater with CBTX-A ID than onabotulinumtoxinA ID. The area of anhidrosis SC was significantly greater with CBTX-A than onabotulinumtoxinA. When injection depths were different, the mean horizontal dimension was significantly greater with onabotulinumtoxinA SC than ID. Comparing the dimension of the same BoNTA and injection method, the vertical dimension was significantly greater than the horizontal
dimension. CONCLUSION: OnabotulinumtoxinA diffuses less than CBTX-A. ID injection technique may result in less diffusion than SC.


CONTEXT: Botulinum neurotoxins (BoNTs) are popularly used to treat various diseases and for cosmetic purposes. They act by blocking neurotransmission through specific cleavage of soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins. Recently, several polyphenols were shown to interfere with SNARE complex formation by wedging into the hydrophobic core interface, thereby leading to reduced neuroexocytosis.

OBJECTIVE: In order to find industrially-viable plant extract that functions like BoNT, 71 methanol extracts of flowers were screened and BoNT-like activity of selected extract was evaluated. MATERIALS AND METHODS: After evaluating the inhibitory effect of 71 flower methanol extracts on SNARE complex formation, seven candidates were selected and they were subjected to SNARE-driven membrane fusion assay. Neurotransmitter release from neuronal PC12 cells and SNARE complex formation inside the cell was also evaluated. Finally, the effect of one selected extract on muscle contraction and digit abduction score was determined. RESULTS: The extract of Potentilla chinensis Ser. (Rosaceae)(Chinese cinquefoil) flower inhibited neurotransmitter release from neuronal PC12 cells by approximately 90% at a concentration of 10 mug/mL. The extract inhibited neuroexocytosis by interfering with SNARE complex formation inside cells. It reduced muscle contraction of phrenic nerve-hemidiaphragm by approximately 70% in 60 min, which is comparable to the action of the Ca(2)(+)-channel blocker verapamil and BoNT type A. DISCUSSION AND CONCLUSION: While BoNT blocks neuroexocytosis by cleaving SNARE proteins, the Potentilla chinensis extract exhibited the same activity by inhibiting SNARE complex formation. The extract paralyzed muscle as efficiently as BoNT, suggesting the potential versatility in cosmetics and therapeutics.


Botulinum neurotoxin (BoNT) is composed of the heavy chain with the receptor-binding site and the translocation domain and the light chain with endopeptidase activity that cleaves the SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) complex, an essential molecule for membrane fusion. Its extraordinarily high toxicity depends on the affinity of the receptor-binding site to the receptor located inside the synaptosome. The membrane fusion mechanism is important not only in neurotransmitter release at the nerve terminals but also in the expression of pain receptors on the cell surface. Based on these mechanisms, BoNT is increasingly used for varieties of conditions including cosmetic uses, muscle hyperactivity, hyperhidrosis, pain, overactive bladder and epilepsy. It will become a major arm of neuromodulating treatments for neurological diseases. A part of this toxin, such as the heavy chain, may become a novel drug-delivery system for neurodegenerative diseases.

BACKGROUND: Several scales have been employed for evaluating the effects of cosmetic treatments in the periorbital area. The Food and Drug Administration (FDA) has recently issued new recommendations specifying a rigorous process to validate new aesthetic scales. OBJECTIVES: The authors describe and validate a new clinical rating scale: the Investigator’s Global Assessment of Lateral Canthal Line (IGA-LCL) severity scale. METHODS: The new FDA recommendations were utilized to validate the new scale. The first step was concept elicitation (based on direct input from clinicians, patients, and literature) and evaluation of content validity (appropriateness of concepts). The resulting five-point scale provided detailed descriptions of the lateral canthal lines (LCL), including quantitative assessment of LCL length and depth. Performance parameters, including intra- and interrater reproducibility and construct validity, were then evaluated in clinical studies. Finally, the scale’s threshold for clinically-meaningful benefit and the ability of the scale to detect change were confirmed in two Phase 2b clinical studies involving a total of 270 subjects. RESULTS: Content validity was established and the IGA-LCL scale showed excellent interrater reliability (weighted Kappa = 0.89) and interrater reliability (weighted Kappa = 0.77; Kendall’s coefficient of concordance = 0.89). In clinical trials, the scale was sensitive enough to detect clinically-meaningful one- and two-point changes in LCL severity following treatment with topical botulinum toxin type A (BoNT-A). The authors observed statistically-significant correlations between the physician-rated IGA-LCL results and patient-reported outcomes. CONCLUSIONS: The IGA-LCL scale was shown to be reliable, appropriate, and clinically meaningful for measuring LCL severity.


There have been no long-term complications or life-threatening adverse effects related to botulinum toxin treatment for any cosmetic indications. Nevertheless, there are well-known, mild side effects of botulinum toxin treatment on the upper face, though most of them are self limited with time. However, excluding brow ptosis, reports about site specific side effects are few and anecdotal. We experienced cases of exaggeration of wrinkles after botulinum toxin injection for forehead horizontal lines, and report them here. In our cases, new appearance of a noticeable glabellar protrusion following botulinum toxin injection on the forehead was observed in 2 patients. Also, a new deep wrinkle on one side of the forehead just above the eyebrow appeared in another 2 patients. The exaggerated wrinkles nearly disappeared without treatment by week 4 in all subjects. These exaggerations of wrinkles may be caused by hyperactivity and overcompensation of untreated muscles. With the increasing availability of diverse botulinum toxin for cosmetic purposes, physicians and patients should be aware of this temporary change after therapeutic injections. We recommend explaining this possible effect prior to injection, for better understanding of treatment for cosmetic indications.


Aesthetic practitioners prefer various reconstitution volumes for botulinum toxins (BoNTAs). Some injectors prefer larger volumes of bacteriostatic normal saline (NaCl) to achieve a larger diffusion in certain areas and a smaller volume for more precise administration of the BoNTA. Some practitioners believe dilution volumes do not matter at all in relation to spread or diffusion, asserting the diffusion area is simply dose-related.
can get confusing when there is more than one injector in an office, different volumes of saline, and more than one type of syringe to administer the neurotoxin. This leaves possibilities for confusion and dosage errors. This article explores four steps to take the confusion out of reconstituting BoNTAs and delivering accurate and consistent doses within a medical office.

60. Katona, P. (2012). "Botulinum toxin: therapeutic agent to cosmetic enhancement to lethal bioterror." Anaerobe 18(2): 240-243. The clinical effects of Clostridium botulinum and its extremely potent neurotoxin have been known for two centuries. The disease threat and the clinical uses are now well established. What's changed is the potential for botulinum neurotoxin to be used as a biological threat agent. The recent upsurge of illegal trafficking of reagent-grade toxin could, if bought in large enough quantities, be as serious a threat as other biothreat agents such as anthrax and smallpox, which have received much more attention. Fortunately, effective countermeasures are available.

61. Keaney, T. (2015). "Male aesthetics." Skin Therapy Lett 20(2): 5-7. Men are a fast growing segment of the aesthetic industry. A review was performed for publications on gender differences in facial anatomy, behavior, and the use of minimally invasive aesthetic procedures in men. There are substantial facial anatomical differences between genders with men having a larger but unique cranial shape, increased skeletal muscle mass, unique subcutaneous fat distribution, and more severe facial rhytides. Men also exhibit poor behavior that can accelerate aging including poor utilization of preventive health care services, higher rates of smoking, and increased ultraviolet light exposure. Despite gender differences in facial anatomy and behavior, few studies have examined the role of gender in cosmetic procedures. Men require a unique injection technique with botulinum toxin and dermal fillers due to differences in facial anatomy.

62. Keaney, T. C. and T. S. Alster (2013). "Botulinum toxin in men: review of relevant anatomy and clinical trial data." Dermatol Surg 39(10): 1434-1443. BACKGROUND: Botulinum toxin is widely used for facial aesthetics, and its use in men continues to increase. OBJECTIVE: To provide a review of pertinent male anatomic features and updated clinical information on the use of botulinum toxin in men. METHODS: A Medline search was performed for publications on sex differences in facial anatomy and on clinical studies examining the role of sex in botulinum toxin treatment. RESULTS: There are substantial facial anatomic differences between the sexes, with men having increased cranial size, unique cranial shape, greater skeletal muscle mass, higher density of facial blood vessels, and more-severe facial rhytides. A review of sex and botulinum toxin treatment identified 17 clinical studies with 5,646 total participants, of whom 629 (11.1%) were male. Only two studies accounted for sex in study design or subgroup analysis. Both studies found abobotulinumtoxinA to be less effective in men. An additional study examining onabotulinumtoxinA dosing in men found that higher doses than typically used in women were more efficacious. There were not more adverse events in male participants in any study. CONCLUSION: Despite sex differences in facial anatomy, the use of botulinum toxin in men is inadequately studied with regard to dosing, efficacy, and safety.

63. Kerscher, M., et al. (2012). "Comparison of the spread of three botulinum toxin type A preparations." Arch Dermatol Res 304(2): 155-161. Botulinum toxins are frequently used in esthetics to improve the appearance of facial wrinkles. In this setting, precise localization of the neurotoxin is required to produce the...
desired clinical effects. Unwanted effects can occur if the neurotoxin diffuses into untargeted muscle. Therefore, a neurotoxin with low and predictable spread would be preferable for esthetic applications. The aim of this study was to investigate the spread of three approved botulinum toxin type A preparations, with and without complexing proteins, by measuring and comparing the size of the anhidrotic halos they produced following injection of equivalent doses in an identical volume into the forehead of patients. The results showed that incobotulinumtoxinA and onabotulinumtoxinA displayed comparable spread at 6 weeks (maximal area of anhidrosis within 6 weeks) and area under the effect curve (AUEC) over 6 months. However, abobotulinumtoxinA, when assuming a 1:2.5 injection volume ratio, produced a statistically significantly greater maximal area of anhidrosis within 6 weeks and AUEC over 6 months compared with incobotulinumtoxinA. All preparations were well tolerated. The results of this study demonstrate that incobotulinumtoxinA and onabotulinumtoxinA have comparable spread, while abobotulinumtoxinA has significantly greater spread than incobotulinumtoxinA.

IncobotulinumtoxinA (Xeomin(R)/Xeomeen(R)/Bocouture(R)/XEOMIN Cosmetic) is a botulinum toxin type A that differs from other commercially available botulinum toxin type A preparations in that it is free from complexing proteins ([150 kDa]/NT 201). The proven efficacy of incobotulinumtoxinA in various therapeutic indications preceded its use in the field of esthetic medicine, where it is widely approved for the treatment of glabellar frown lines on the basis of positive efficacy and safety findings from a number of clinical trials. Here, we discuss the characteristics of incobotulinumtoxinA and review the clinical data supporting its use in esthetics.

BACKGROUND: The effect of perceived facial blanching with neurotoxin therapy has been described in the literature and has been used to treat the undesirable facial flushing of Frey's syndrome. Patients rarely report it as a complication after cosmetic injection, but it can be distressing. OBJECTIVES: To elucidate the proposed mechanism(s) of this unusual vasculocutaneous phenomenon, we reviewed normal physiologic responses to heat stress and the role of cholinergic neurotransmission in modulating cutaneous vascular tone in the context of the literature. MATERIALS/METHODS: We report a case of a 32-year-old woman who complained of white patches on her forehead at sites of a botulinumtoxinA injections administered 2 weeks before presentation. RESULTS: Acetylcholine is a primary mediator of cutaneous vasodilatation; certain co-transmitters modulate its effect. Chemical denervation by botulinum toxin (BoNT) appears to interfere with these normal signaling pathways and can provide symptomatic relief to patients with undesirable facial flushing. Conversely, it may create an unwanted cosmetic effect in patients who desire isolated muscle paresis. CONCLUSIONS: Skin sites injected with BoNT type A may not experience the expected decrease in cutaneous vessel tone associated with higher body temperature. The exact mechanism remains unclear.

Background: The injection of botulinum toxin is now commonly used for many therapeutic and cosmetic purposes but because of its increased use more adverse events are being
reported. Objective: To retrospectively evaluate and analyze the safety of botulinum toxin injections in terms of purpose and the type of toxin administered. Materials and methods: Data were collected on 1819 patients who underwent a total of 5310 treatments between 2005 and 2011 at a single tertiary medical center. Information on the dosage, treatment purpose, type of botulinum toxin, and any adverse events associated with these treatments were collected and analyzed. The generalized estimating equation (GEE) with the logistic link function was used to estimate the overall frequencies of adverse events. A multivariable GEE with the logistic link function was used to identify the factors associated with adverse events. Results: Among the 5310 botulinum toxin treatments in our study cohort, 2258 of which (42.5%) were used to treat hemifacial spasm, 184 adverse events (3.73%) were recorded, 114 (2.26%) muscle-related, and 71 (1.47%) muscle-unrelated. The highest number of adverse events (8.29%) was associated with the treatment of blepharospasm and the lowest (1.07%) with masseter hyperplasia. By multivariate analysis, the odds ratio for females was 1.577 (95% confidence interval [CI] = 1.052-2.364; p = 0.027) and for the dose was 1.006 (95% CI = 1.002-1.010; p = 0.002). When compared with upper face wrinkles, the odds ratio was 2.510 (95% CI = 1.400-4.499; p = 0.002) for blepharospasm, 0.375 (95% CI = 0.202-0.695; p = 0.002) for cervical dystonia, and 0.114 (95% CI: 0.015-0.862; p = 0.035) for masseter hyperplasia. Conclusion: When injecting botulinum toxin for cosmetic purposes, practitioners should be cautious, especially when targeting the areas around the eyes, as these treatments are prone to cause adverse events.


BACKGROUND: The injection of botulinum toxin is now commonly used for many therapeutic and cosmetic purposes but because of its increased use more adverse events are being reported. OBJECTIVE: To retrospectively evaluate and analyze the safety of botulinum toxin injections in terms of purpose and the type of toxin administered. MATERIALS AND METHODS: Data were collected on 1819 patients who underwent a total of 5310 treatments between 2005 and 2011 at a single tertiary medical center. Information on the dosage, treatment purpose, type of botulinum toxin, and any adverse events associated with these treatments were collected and analyzed. The generalized estimating equation (GEE) with the logistic link function was used to estimate the overall frequencies of adverse events. A multivariable GEE with the logistic link function was used to identify the factors associated with adverse events. RESULTS: Among the 5310 botulinum toxin treatments in our study cohort, 2258 of which (42.5%) were used to treat hemifacial spasm, 184 adverse events (3.73%) were recorded, 114 (2.26%) muscle-related, and 71 (1.47%) muscle-unrelated. The highest number of adverse events (8.29%) was associated with the treatment of blepharospasm and the lowest (1.07%) with masseter hyperplasia. By multivariate analysis, the odds ratio for females was 1.577 (95% confidence interval [CI] = 1.052-2.364; p = 0.027) and for the dose was 1.006 (95% CI = 1.002-1.010; p = 0.002). When compared with upper face wrinkles, the odds ratio was 2.510 (95% CI = 1.400-4.499; p = 0.002) for blepharospasm, 0.375 (95% CI = 0.202-0.695; p = 0.002) for cervical dystonia, and 0.114 (95% CI: 0.015-0.862; p = 0.035) for masseter hyperplasia. CONCLUSION: When injecting botulinum toxin for cosmetic purposes, practitioners should be cautious, especially when targeting the areas around the eyes, as these treatments are prone to cause adverse events.

BACKGROUND: Botulinum toxin type A has been widely used to correct unwanted hyperfunctional facial lines. Most forms of botulinum toxin type A currently used require reconstitution, which is very inconvenient for users. The authors compared the efficacy and safety of a newly developed liquid-type botulinum toxin type A (MT10109L) and onabotulinumtoxinA (Botox) for moderate to severe glabellar lines. METHODS: A double-blind, randomized, active drug-controlled, phase III study with 168 enrolled subjects was performed. The primary efficacy endpoint was the improvement rate at maximum frown at week 4 by the investigators' live assessment. The secondary efficacy endpoint included the improvement rate at maximum frown at week 16 and at rest at weeks 4 and 16 by live assessment, and the improvement rate at maximum frown and at rest based on photographic assessment at week 4. Self-assessment and self-satisfaction with glabellar line improvement were also evaluated. RESULTS: The improvement rate at maximum frown by live assessment was not significantly different between the MT10109L and Botox groups. In addition, the improvement rate of glabellar lines at rest based on the investigators' live assessment and photographic assessment was similar in both treatment groups. However, the improvement rate at maximum frown by live assessment at week 16 was significantly higher in the MT10109L group compared with the Botox group. There were no severe adverse events. CONCLUSIONS: The efficacy and safety of MT10109L were comparable to those of Botox for the management of glabellar frown lines. MT10109L provides greater convenience because it does not require dilution and has long-lasting effects. CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.


BACKGROUND: The demands for cosmetic procedures are increasing. Dermatologists perform many of these procedures, therefore adequate education and training during residency is important. Surveys demonstrate dermatology residents desire more training even while faculty members believe this has already become a more prominent feature of resident education. OBJECTIVE: We sought to assess the time and methods dedicated to education and training of cosmetic procedures in dermatology residency. METHODS: A 26-question survey was developed and electronically distributed in May 2010 to dermatology program directors via the Association of Professors of Dermatology list-serve with their approval. Program directors were asked to forward the e-mail to their instructors of cosmetic/procedural dermatology, and chief residents. Responses were anonymous. RESULTS: A total of 86 responses were collected. In all, 67% (n = 54) of respondents had formal lectures focusing on cosmetic dermatology. Lecture topics reported by more than 50% of respondents included botulinum toxin injection, lasers, soft tissue augmentation, chemical peels, and sclerotherapy. Topics such as dermabrasion, liposuction, and scar revision were less commonly taught. The most commonly encountered and performed procedures were botulinum toxin injection and lasers (100%, n = 86); 98.8% (n = 85) encounter soft tissue augmentation and 95.4% (n = 82) encounter both chemical peels and sclerotherapy. Resident experience performing procedures as the first assistant or as the first surgeon varied widely. LIMITATIONS: The limitations of this study are that the data were subjectively reported so results may differ from the true amount of time spent in any activity. The data may be biased by the population that responded as they may have strong opinions supporting or opposing training in cosmetic procedures. The data also may have been skewed by the small percentage of participants who were instructors of cosmetic
dermatology (21%), chief residents (20%), and others respondents (8% total). CONCLUSION: The results demonstrate the variability of training in cosmetic procedures. The challenge for programs is to find the balance between insufficiency and overemphasis. The results of this study will hopefully assist programs in determining the quantity and methods of resident training in cosmetic procedures.

A retrospective analysis was performed to assess efficacy and patient satisfaction associated with AbobotulinumtoxinA for the treatment of dynamic periocular rhytides. When keeping the total dose of ABA the same for each side of the face, one injection point yielded the same efficacy and safety as three separate injection points into the lateral periorcular areas.

Botulinum toxin was shown to be effective in treatment of chronic migraine. We wanted to explore its efficacy and tolerability in chronic application under real-life conditions. For this, 27 consecutive patients (age 45.6 +/- 10.8 years, 25 females, 2 males) received altogether 176 injection series (IS) with 189.7 +/- 45.8MU onabotulinumtoxinA (Botox(R)) according to the PREEMPT scheme. During the study period altogether 6.5 +/- 2.9 (min 4, max 13) IS were applied per patient (total treatment time of 73.1 +/- 36.9 weeks). 96 % of the patients reported benefit. Monthly headache days were reduced from 18.9 +/- 3.9 to 8.7 +/- 4.5 (p < 0.001, -53.7 %), migraine days from 16.8 +/- 4.9 to 7.4 +/- 4.6 (p < 0.001, -55.1 %), autonomic days from 8.6 +/- 7.5 to 2.7 +/- 4.2 (p < 0.001, -71.9 %) and medication days from 14.2 +/- 4.6 to 8.3 +/- 4.2 (p < 0.001, -71.1 %). Health-related quality of life improved by 0.6-1.5 standard deviations (SD) (Short Form Health Survey), migraine-related quality of life by 1.4-2.0 SD (Migraine-Specific Quality of Life Questionnaire) and by 1.9 SD (Headache Impact Test), depression by 1.1 SD (Beck Depression Inventory). Subjective global clinical improvement was 2.6 +/- 0.6 (Global Clinical Improvement Scale). All improvements were stable throughout the entire study period. Adverse effects were infrequent, mild and transient. Botulinum toxin provides highly effective and safe long-term treatment of chronic migraine.

BACKGROUND: Botulinum neurotoxin (BoNT) has diverse cosmetic and therapeutic applications, spanning multiple medical specialties. Recent lawsuits alleging complications from its clinical use have raised significant questions about medicolegal risk. OBJECTIVE: To identify and assess legal cases related to clinical complications of BoNT products. METHODS AND MATERIALS: Using the LexisNexis Academic online database, a search of U.S. federal and state cases between 1985 and 2012 was performed. A second search of U.S. newspapers and wires was also completed. In all but one case, the plaintiffs' legal complaints were obtained for review. RESULTS: Twenty-four relevant legal cases were found, mostly in state courts. All cases alleged adverse effects from onabotulinumtoxinA, and each named its manufacturer, Allergan, Inc., as a defendant. Most lawsuits against Allergan, Inc. were dismissed or settled. In three cases, physicians were codefendants, including one dermatologist. In two cases, jury verdicts resulted in multimillion-dollar
judgments in favor of the plaintiffs. None of the lawsuits named a dermatologist when the complication arose from on-label indications and cosmetic use. CONCLUSION: Lawsuits related to complications from BoNT products are uncommon, are more likely to result from therapeutic than cosmetic applications, and typically involve product liability claims against the manufacturer.

73. Koshy, J. C., et al. (2012). "Effect of dietary zinc and phytase supplementation on botulinum toxin treatments." J Drugs Dermatol 11(4): 507-512. PURPOSE: To determine whether oral zinc supplementation might affect the efficacy and duration of botulinum toxin treatments. METHODS: In a double-blind, placebo-controlled, crossover pilot study, we examined the efficacy of three botulinum toxin preparations (onabotulinumtoxinA, abobotulinumtoxinA, and rimabotulinumtoxinB) following oral supplementation with zinc citrate 50 mg and phytase 3,000 PU, zinc gluconate 10 mg, or lactulose placebo in individuals treated for cosmetic facial rhytids, benign essential blepharospasm, and hemifacial spasm. RESULTS: In seventy-seven patients, 92% of subjects supplemented with zinc 50 mg and phytase experienced an average increase in toxin effect duration of nearly 30%, and 84% of participants reported a subjective increase in toxin effect, whereas no significant increase in duration or effect was reported by patients following supplementation with lactulose placebo or 10 mg of zinc gluconate. The dramatic impact of the zinc/phytase supplementation on some patients' lives clinically unmasked the study and prompted an early termination. CONCLUSIONS: This study suggests a potentially meaningful role for zinc and/or phytase supplementation in increasing the degree and duration of botulinum toxin effect in the treatment of cosmetic facial rhytids, benign essential blepharospasm, and hemifacial spasm.

74. Kouris, A., et al. (2014). "Muscle weakness in treatment of palmar hyperhidrosis with botulinum toxin type a: can it be prevented?" J Drugs Dermatol 13(11): 1315-1316. BACKGROUND: Palmar hyperhidrosis is a chronic disorder, resistant to conventional treatment. Clinical studies suggest the effectiveness of botulinum toxin A in the treatment of primary palmar hyperhidrosis. OBJECTIVE: To evaluate the efficacy of botulinum toxin A in the therapy of palmar hyperhidrosis and the frequency of incurred muscle weakness. MATERIALS AND METHODS: Four hundred seventy-four patients with palmar hyperhidrosis were enrolled in the study. The Hyperhidrosis Disease Severity Scale (HDSS) and the Minor-iodine starch test were chosen to assess the disease severity. In addition, a physician's global assessment scale was used to evaluate the effectiveness of the treatment with BTX-A. RESULTS: There were 312 females and 162 males aged 19-48 (mean 29 years). The improvement following the injection at two weeks and at one, three, six and nine months, as evaluated by physicians, was 82%, 83%, 74%, 48% and 28%, respectively. Two hundred and seventy five patients reported local pain and muscle weakness occurred in 102 patients. CONCLUSIONS: BTX-A led to the reduction of disease severity while transient side effects were reported.

75. Kucuker, I., et al. (2016). "The Effect of Chemodenervation by Botulinum Neurotoxin on the Degradation of Hyaluronic Acid Fillers: An Experimental Study." Plast Reconstr Surg 137(1): 109-113. BACKGROUND: Early degradation is a common complaint for hyaluronic acid fillers. Although the combination of hyaluronic acid fillers with botulinum neurotoxin type A presented improved clinical results, objective measurement of hyaluronic acid volumes has not been previously assessed. METHODS: In this study, the authors have split the calvaria of the rabbit to mimic the glabellar region in humans. In this model, the authors applied
hyaluronic acid alone to one side and hyaluronic acid combined with botulinum neurotoxin type A to the contralateral side. Two days and 3 months after the filler injection, magnetic resonance imaging was performed to assess the filler volumes. RESULTS: Average initial volume of filler only and filler combined with botulinum neurotoxin type A was 0.61 cm on both sides, and there was no difference between initial volumes of the two sides (p = 0.735). At the end of 3 months, average degraded volumes of filler-only and filler combined with botulinum neurotoxin sides were 0.33 cm and 0.19 cm, respectively, and the degradation difference was significant between the two groups (p = 0.001). End volumes for the filler-only and filler combined with botulinum neurotoxin sides were 0.28 cm and 0.42 cm, respectively, and end volumes between two sides were also statistically significant (p < 0.001). CONCLUSION: This study showed that hyaluronic acid filler application in combination with botulinum neurotoxin type A significantly decreases the degradation process and increases the remaining volume of the hyaluronic acid fillers at the end of the paralyzed period.


OBJECTIVE: In general, needling and injection are painful procedures, especially when the face is the target. Although local anesthetics (cream or tape) can be used to reduce the pain, they are not sufficiently effective. It has been suggested that vibration can reduce pain. The aim of this case study was to determine whether application of a vibration device to an area adjacent to the facial target area to be injected/needled would relieve pain.

METHODS: Consecutive women scheduled to undergo facial injection with hyaluronic acid or botulinum toxin were recruited. Half of the face was injected with concomitant vibration, whereas the other half was injected without vibration. The pain experienced by the women during both procedures was assessed using the Numeric Rating Scale. The safety of injection with vibration was also assessed.

RESULTS: Of the 32 patients, 28 indicated that vibration relieved the pain, 3 stated that it had no effect, and 1 (who received deep botulinum toxin injections to the masseter muscle) complained that it made the pain worse. Vibration did not affect the safety of the injections. The average Numeric Rating Scale scores for the no-vibration and vibration injections were 4.5 +/- 1.5 and 2.3 +/- 0.9, respectively (P < .001). CONCLUSIONS: The Gate Control Theory of Pain explains why vibration reduces pain.


Understanding the role of volume loss in the aging face has resulted in a paradigm shift in facial rejuvenation techniques. Injectable materials for volume restoration are among the most widespread cosmetic procedures performed. A new approach to the aesthetics of facial aging is necessary to allow the greatest improvement from volumetric techniques while maintaining natural appearing results. Examining the face in terms of facial frames and facial shadows provides the fundamental basis for our injectable analysis.


BACKGROUND: The upper face and periocular region is a complex and dynamic part of the face. Successful rejuvenation requires a combination of minimally invasive modalities to fill dents and hollows, resurface rhytides, improve pigmentation, and smooth the mimetic muscles of the face without masking facial expression. METHODS: Using review of the
literature and clinical experience, the authors discuss our strategy for combining botulinum toxin, facial filler, ablative laser, intense pulsed light, microfocused ultrasound, and microneedle fractional radiofrequency to treat aesthetic problems of the upper face including brow ptosis, temple volume loss, A-frame deformity of the superior sulcus, and superficial and deep rhytides.

RESULTS: With attention to safety recommendations, injectable, light, laser, and energy-based treatments can be safely combined in experienced hands to provide enhanced outcomes in the rejuvenation of the upper face.

CONCLUSION: Providing multiple treatments in 1 session improves patient satisfaction by producing greater improvements in a shorter amount of time and with less overall downtime than would be necessary with multiple office visits.

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BACKGROUND: Botulinum toxin type A (BoNT-A) is widely used to improve the lower facial contour. OBJECTIVE: To determine the difference in the changes in the lower facial contour achieved with 1 and 2 sessions of BoNT-A injections using 3-dimensional (3D) laser scanning. MATERIALS AND METHODS: Twenty volunteers were randomly divided into 2 groups. Group I (n = 10) received a single injection, whereas Group II (n = 10) received 2 sessions of injections, the second being administered 4 months after the first. Each injection comprised of 25 U of BoNT-A and was administered to the masseter muscle bilaterally. Evaluation of the effect of BoNT-A injection was performed using 3D laser scan images obtained before the injection and 6 months thereafter in Group I, and before the first injection and 6 months thereafter in the Group II. RESULTS: The mean changes in the volume and thickness in Group I were -1.186 mm and -1.52 mm, respectively; the corresponding changes were -4.072 mm and -3.84 mm in Group II. The reductions were significantly greater in Group II than in Group I. CONCLUSION: The administration of a second BoNT-A injection is effective for better aesthetic results for the lower facial contour.


BACKGROUND: Incobotulinum is a newly developed botulinum toxin A in which the complexing proteins had been removed. OBJECTIVE: The aim was to compare the efficacy and safety of incobotulinum with onabotulinum in treating periocular rhytides and masseteric hypertrophy. METHODS: A randomized, double-blind, split-face study was planned. Fifty-six patients were treated for periocular rhytides and the other 56 patients were treated for masseteric hypertrophy. Onabotulinum was injected on one side of the face and incobotulinum was injected on the other side of the face. The degree of periocular rhytides and masseteric hypertrophy was rated using Fitzpatrick Wrinkle Classification System (FWCS) and 10-point visual analogue scale (VAS) (0: the minimum to 10: the maximum). Objective and subjective rating was performed at pretreatment and every posttreatment follow-up visit by investigators and subjects. RESULT: The efficacy and safety of incobotulinum were not inferior to those of onabotulinum in treating periocular rhytides and masseteric hypertrophy up to 16 weeks after injection. There were no noteworthy differences in the onset time of effect between two botulinum toxins for periocular wrinkles and masseteric hypertrophy. No adverse event was reported. CONCLUSION:
Incobotulinum provided non-inferior efficacy and safety for the treatment of periocular rhytides and masseteric hypertrophy compared with classic onabotulinum.


BACKGROUND: Botulinum toxin A (BTA) responders have elevated levels of calcitonin gene-related and vasoactive intestinal peptides, which are potent vasodilators. We aimed to investigate neurovascular features as a predictor of BTA treatment response in patients with chronic migraine.

METHODS: We prospectively recruited South Korean patients who were diagnosed with chronic migraine and underwent BTA injection at a university hospital from December 2013 to January 2015. Intercital transcranial Doppler (TCD) test was performed before BTA treatment when patients did not experience moderate-to-severe headache attacks. Botulinum toxin A was injected per the Phase III REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) protocol. Treatment response was determined after 4-6 weeks of follow-up. Pretreatment clinical and neurosonologic features of responders and non-responders were analyzed.

RESULTS: Of the 83 enrolled patients, 70 who completed initial and follow-up evaluations were included for this study. Forty-two (60.0%) patients were classified as responders. 50% responders were 31 (44.2%). Longer disease duration was associated with poor treatment outcome (p=0.019). The ratio of the mean velocity of middle cerebral artery to that of ipsilateral internal carotid artery (MCA/ICA index) was significantly higher in responders than non-responders (p=0.027) and remained significant after controlling for covariates (p=0.025).

CONCLUSIONS: Shorter disease duration and higher pretreatment MCA/ICA index on TCD are associated with good early outcomes of BTA treatment.


Masseter muscle hypertrophy has been treated for cosmetic purposes using several modalities, including injection of type A or type B botulinum toxin into the masseter muscle. In this report, we compared the efficacy and safety of abobotulinum toxin A with onabotulinum toxin A treatment for masseteric hypertrophy in 25 Korean patients with a conversion factor of 2.5:1 through a controlled, split-face, and evaluator-blinded study. The mean grade of clinical improvement based on clinical assessment was 2.8 +/- 0.9 for abobotulinum toxin A and 2.7 +/- 0.8 for onabotulinum toxin A at 8 weeks after the injection. At 12 weeks after the injection, the mean grade of clinical improvement based on clinical assessment was 2.9 +/- 0.9 for abobotulinum toxin A and 2.7 +/- 0.8 for onabotulinum toxin A. More pronounced improvement was observed with abobotulinum toxin A than onabotulinum toxin A in three (12%) patients at 8 weeks and five (20%) patients at 12 weeks. We believe that our data can be used as an essential reference for determining the dose of type A botulinum toxin in the treatment of masseteric hypertrophy.


Since the first introduction of botulinum toxin in cosmetic surgery, techniques and indications using botulinum toxin, mainly intramuscularly, have expanded greatly. Some of cosmetic surgeons are trying to inject the toxin intradermally and, anecdotally or through clinical studies, they sometimes show positive cosmetic results. The mechanism of which is unclear but we should not always belittle the results of this technique. Also there are lots of confusing terms for this intradermal technique, so I propose a new descriptive term...
"multiple intradermal small bolus injection of botulinum toxin (MISBIB)". In this article, I reviewed important papers on this topic including my own experiences and summarized possible mechanism of action and, finally, discussed the limitations and potential of MISBIB.

Over the past decade, facial rejuvenation procedures to circumvent traditional surgery have become increasingly popular. Office-based, minimally invasive procedures can promote a youthful appearance with minimal downtime and low risk of complications. Injectable botulinum toxin (BoNT), soft-tissue fillers, and chemical peels are among the most popular non-invasive rejuvenation procedures, and each has unique applications for improving facial aesthetics. Despite the simplicity and reliability of office-based procedures, complications can occur even with an astute and experienced injector. The goal of any procedure is to perform it properly and safely; thus, early recognition of complications when they do occur is paramount in dictating prevention of long-term sequelae. The most common complications from BoNT and soft-tissue filler injection are bruising, erythema and pain. With chemical peels, it is not uncommon to have erythema, irritation and burning. Fortunately, these side effects are normally transient and have simple remedies. More serious complications include muscle paralysis from BoNT, granuloma formation from soft-tissue filler placement and scarring from chemical peels. Thankfully, these complications are rare and can be avoided with excellent procedure technique, knowledge of facial anatomy, proper patient selection, and appropriate pre- and post-skin care. This article reviews complications of office-based, minimally invasive procedures, with emphasis on prevention and management. Practitioners providing these treatments should be well versed in this subject matter in order to deliver the highest quality care.

The platysma muscle acts as a major depressor in the lower face with subsequent anaesthetic implications. Botulinum toxin-A can be very useful to reverse some of these and this chapter describes how to (1) sharpen the jawline with the Nefertiti Lift, (2) treat anterior neck bands, and (3) soften necklace lines.

The facial feedback effect (e.g., Strack et al., 1988) is explored in three experiments. It was found that when someone lowers their eyebrows, following instructions, their mood becomes more negative. If, however, they are instructed to raise their eyebrows they become more surprised by facts. Finally, if people are instructed to wrinkle their noses, then odors are evaluated as more unpleasant. While providing further diverse evidence for facial feedback, the experiments are also considered in the context of facial muscular paralysis induced as part of cosmetic treatments using botulinum toxin. The research presented here supports the previously suggested idea that such treatments could reduce depression, but other possible psychological impacts of such treatments are considered.

Botulinum toxin (BoNTA) has become the modern generation's treatment of choice for facial aging. Advanced uses of neurotoxin have treated specific areas of the face, in addition
to the glabella, which is the only site for injection approved by the Food and Drug Administration. This article suggests that BoNTA has replaced surgical procedures that treat oral commissures, mild brow ptosis and brow asymmetries, and hypertrophic orbicularis oculi muscles. It is becoming increasingly used for lip asymmetry, platysmal banding, and necklift, although it has not replaced traditional procedures for the correction of these areas.

Facial wrinkles are the most visible morphological change of the aging process. Therefore, several rejuvenation methods have been developed to cure these unloved signs of the times, such as botulinum toxin, laser treatments as well as topical active ingredients. Recently, dermal fillers have become a popular means of addressing contour defects and soft-tissue augmentation. Although this aesthetic treatment is considered to be relatively safe, the use of injectable dermal fillers is a minimally-invasive treatment, and as with any medical procedure, there is a risk for unwanted side effects.

The amount and complexity of scientific and clinical evidence for aesthetic use of botulinum neurotoxin type A (BoNT-A) has expanded rapidly in recent years, especially for abobotulinumtoxinA, necessitating reassessment of current knowledge about aesthetic use of abobotulinumtoxinA and other BoNT-A preparations. A committee of 13 plastic surgeons, facial plastic surgeons, and dermatologists engaged in a live discussion of information from a systematic literature review and an Internet-based survey of their beliefs and practices. The committee achieved consensus on most issues. It was concluded that doses of different BoNT-A preparations cannot be interconverted with a fixed ratio. The size of the "field of effect" is difficult to measure, and comparisons between preparations have yielded equivocal results. Nonresponse due to neutralizing antibodies appears exceedingly rare with currently available BoNT-A preparations and of little concern clinically. BoNT-A dose, injection depth, and injection technique should be adjusted according to the anatomic area being treated and each patient's individual characteristics and goals. Aesthetic use of BoNT-A has a good safety profile. Most adverse events are minor and related to the trauma of injection, although special care is needed in certain anatomic areas. Detailed recommendations for treatment of different anatomic areas are presented. BoNT-A products are often used in conjunction with other treatment modalities (eg, fillers and resurfacing), but little agreement was reached on best practices. The findings reported in this consensus document may serve as a practical guide for aesthetic practitioners as they apply the latest knowledge about BoNT-A in providing their patients with optimal care.


Facial expressions convey emotions that form the foundation of interpersonal relationships, and many of these emotions promote and regulate our social linkages. Hence, the facial aging symptomatological analysis and the treatment plan must of necessity include knowledge of the facial dynamics and the emotional expressions of the face. This approach aims to more closely meet patients' expectations of natural-looking results, by correcting age-related negative expressions while observing the emotional language of the face. This article will successively describe patients' expectations, the role of facial expressions in relational dynamics, the relationship between facial structures and facial expressions, and the way facial aging mimics negative expressions. Eventually, therapeutic implications for facial aging treatment will be addressed.


BACKGROUND: Although application of botulinum toxin type A (BTX-A) for the treatment of forehead rhytides has become very popular, the effects of its intramuscular injections on the skin mechanical properties remain unclear. OBJECTIVES: We prospectively investigated the alterations in the mechanical properties of the skin of patients who received intramuscular injections of botulinum toxin A (BTX-A) for forehead rhytides and compared two injection doses. METHODS: Of the 42 enrolled patients, one randomly assigned half received intramuscular injections of two units (group I), and the other half received four units (group II) of BTX-A in each injection point. The baseline and post-treatment skin mechanical parameters, including gross elasticity (R2), net elasticity (R5), viscoelastic ratio (R6) and biological elasticity (R7), were measured using the Cutometer(R) and compared. RESULTS: Treatment with BTX-A resulted in significant overall alterations in the mechanical properties of skin at the injection sites of both treatment groups during the 16-week period, and no significant differences were observed between groups. Significant decreases in biological elasticity, net elasticity and viscoelasticity properties were observed at 2 weeks follow-up and began to recover at that time. All of the skin mechanical properties recovered to baseline levels by 16 weeks of follow-up in both dosage groups, which indicates that the higher dosage (4 units) did not delay relapse compared to the two-unit dosage. CONCLUSIONS: We concluded that intramuscular injections of BTX-A significantly regulated the gross elasticity, net elasticity, functional elasticity and viscoelasticity at the injection point over a radius of 1.5 cm at 2, 4 and 8 weeks follow-up. The alteration in the skin measurements had completely diminished by the 16-week follow-up. LEVEL OF EVIDENCE IV: This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.


BACKGROUND: Biological activity data indicate that the units of incobotulinumtoxinA are not equivalent to those of onabotulinumtoxinA. Objective: This study compared 20 units of onabotulinumtoxinA with 30 units of incobotulinumtoxinA in the treatment of glabellar lines. METHODS AND MATERIALS: In this multicenter, randomised, double-blind study, subjects with moderate or severe glabellar lines received a single treatment with 20 units of onabotulinumtoxinA (n = 112), or 30 units of incobotulinumtoxinA (n = 112). The primary endpoint was the percentage of subjects with a reduction of >/= 1 point on the Facial
Wrinkle Scale at maximum contraction as rated by injectors on day 28 post injection. The same variable was evaluated on days 84, 98, and 112. RESULTS: At the primary endpoint, 20 units of onabotulinumtoxinA was as effective as 30 units of incobotulinumtoxinA (96% vs. 95% responders, respectively; difference in proportion of responders = 0.02, 95% confidence interval [CI] - 0.04, 0.07). At subsequent time points, a trend towards a higher percentage of responders was observed in the group treated with 20 units of onabotulinumtoxinA. Given that the 95% CI surpassed the upper equivalence margin at these time points, equivalence was not established. CONCLUSION: These data support the non-interchangeability of units of onabotulinumtoxinA and incobotulinumtoxinA, and the absence of a fixed dose ratio in clinical practice.

97. Monheit, G. (2015). "Neurotoxins: Current Concepts in Cosmetic Use on the Face and Neck-Upper Face (Glabella, Forehead, and Crow’s Feet)." Plast Reconstr Surg 136(5 Suppl): 72S-75S. There are 3 Food and Drug Administration-approved botulinum toxin formulations now being successfully used for treatment in the upper face. The most common areas for botulinum toxin treatment are the upper face, including the glabella, forehead, brows, and lateral canthal lines or crow’s feet. The frozen look is no more desired in patients. Thus, physicians are more commonly individualizing dosage based on the patient's variation in anatomy, muscle mass, asymmetry, and, most importantly, desired outcome.

98. Montaser-Kouhsari, L., et al. (2014). "Comparison of intradermal injection with iontophoresis of abobotulinum toxin A for the treatment of primary axillary hyperhidrosis: a randomized, controlled trial." J Dermatolog Treat 25(4): 337-341. BACKGROUND: Botulinum neurotoxin type A (BTX-A) injection is the treatment of choice for idiopathic axillary hyperhidrosis (IAH) refractory to conventional treatments. OBJECTIVE: This study compared the efficacy of BTX-A injection and iontophoresis for treatment of IAH in a randomized controlled trial. METHODS: In eleven patients with the diagnosis of IAH, one axilla was randomly treated with injections of 1.5 mL (250 MU) of BTX-A, and the other side was treated with BTX-A administered by iontophoresis. The amount of sweating, skin hydration, transepidermal water loss, pain, and patient satisfaction on both axilla were compared with baseline levels, and also between both sides 1 week, 1 month, and 6 months after treatment. RESULTS: The injection side had significantly less sweat production than the iontophoresis side 1 week, 1 month, and 6 months after treatment (84%, 76%, and 50% vs. 73%, 22%, and 32%, respectively). The response to iontophoresis was more stable than that to injection. Participants' pain perception during the procedure score was significantly less on the iontophoresis side compared with the injection side (15.0 vs. 20.0, p < 0.05). CONCLUSION: This study has shown that injection is a more effective method for the administration of BTX-A, though iontophoresis can also be considered a non-invasive and painless method in some patients.

99. Nahabet, E., et al. (2015). "Neurotoxins: Expanding Uses of Neuromodulators in Medicine--Headache." Plast Reconstr Surg 136(5 Suppl): 104S-110S. Over the course of the past 17 years, since the initial discovery of the association between botulinum toxin-A (BT-A) and the reduction of headache symptoms, the use of this neurotoxin has greatly evolved. BT-A has emerged as an alternative to prophylactic pharmacological therapies in the prevention of chronic migraine headaches, with an excellent safety profile and proven efficacy, and is Food and Drug Administration-approved for on-label use since October 2010. The mechanism of BT-A involves its effect at the neuromuscular junction, inhibition of neuropeptide and neurotransmitter release in
peripheral sensory neurons, and retrograde axonal transport allowing for its direct effect on inhibiting central sensitization. Through its diagnostic and therapeutic utility, BT-A has proven to be an integral part in the treatment of chronic headache disorders.


101. Narurkar, V. A. M. D., et al. (2016). "A Comprehensive Approach to Multimodal Facial Aesthetic Treatment: Injection Techniques and Treatment Characteristics From the HARMONY Study." Dermatologic Surgery 42 Supplement(2): S177-S191. BACKGROUND: The HARMONY study is the first clinical trial to assess the impact of a global approach to facial rejuvenation with several minimally invasive modalities, using patient-reported outcome measures., OBJECTIVE: Provide details of this treatment approach and describe investigators' experiences and recommendations based on this study., METHODS: This multicenter, 4-month study evaluated subject satisfaction with and psychological impact of combined treatment with VYC-20L (Juvederm Voluma XC), HYC-24L (Juvederm Ultra XC), HYC-24L+ (Juvederm Ultra Plus XC), onabotulinumtoxinA (Botox), and bimatoprost 0.3% ophthalmic solution (Latisse). Treatment-naïve adults with moderate-to-severe facial lines and folds and eyelash hypotrichosis received on-label, staged treatment with fillers. Bimatoprost was self-administered once daily for 17 weeks from day 1. OnabotulinumtoxinA was administered for glabellar lines, crow's feet lines, or both at month 3., RESULTS: Overall, 100 subjects received bimatoprost for eyelash hypotrichosis, 96 received onabotulinumtoxinA for glabellar lines and/or crow's feet lines, and 96 received VYC-20L for midface volume deficit. From 17 to 96 subjects received HYC-24L and/or HYC-24L+ for nasolabial folds, oral commissures, marionette lines, perioral lines, or radial cheek lines. Injections of filler generally progressed from cranial to caudal, with midface injected first. Investigator-reported factors that may have contributed to the potential benefits of this approach include the critical role of the midface in facial aesthetics, use of lower volumes of filler in individual facial areas, and anesthetic effects., CONCLUSION: The investigators' perspectives and experience with the injection pattern, sequencing, volumes, and techniques may provide valuable guidance for a multimodal approach to facial aesthetic treatment., (C) 2016 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. All rights reserved.

102. Naumann, M., et al. (2013). "Immunogenicity of botulinum toxins." J Neural Transm 120(2): 275-290. Botulinum neurotoxins are formulated biologic pharmaceuticals used therapeutically to treat a wide variety of chronic conditions, with varying governmental approvals by country. Some of these disorders include cervical dystonia, post-stroke spasticity, blepharospasm, migraine, and hyperhidrosis. Botulinum neurotoxins also have varying governmental approvals for cosmetic applications. As botulinum neurotoxin therapy is often continued over many years, some patients may develop detectable antibodies that may or may not affect their biological activity. Although botulinum neurotoxins are considered "lower risk" biologics since antibodies that may develop are not likely to cross react with endogenous proteins, it is possible that patients may lose their therapeutic response. Various factors impact the immunogenicity of botulinum neurotoxins, including product-related factors such as the manufacturing process, the antigenic protein load, and the presence of accessory proteins, as well as treatment-related factors such as the overall toxin dose, booster injections, and prior vaccination or exposure. Detection of antibodies by laboratory tests does not necessarily predict the clinical success or failure of treatment. Overall,
botulinum neurotoxin type A products exhibit low clinically detectable levels of antibodies when compared with other approved biologic products. This review provides an overview of all current botulinum neurotoxin products available commercially, with respect to the development of neutralizing antibodies and clinical response.

Botox has been primarily used in cosmetic treatment for lines and wrinkles on the face, but the botulinum toxin that Botox is derived from has a long history of medically therapeutic uses. For nearly 13 years, until the introduction of Botox Cosmetic in 2002, the only FDA-approved uses of Botox were for crossed eyes (strabismus) and abnormal muscle spasms of the eyelids (blepharospasm). Since then botulinum A, and the seven other forms of the botulinum toxin, have been continuously researched and tested. Botox is a neurotoxin derived from bacterium clostridium botulinum. The toxin inhibits the release of acetylcholine (ACH), a neurotransmitter responsible for the activation of muscle contraction and glandular secretion, and its administration results in reduction of tone in the injected muscle. The use of Botox is a minimally invasive procedure and is showing quite promising results in management of muscle-generated dental diseases like Temporomandibular disorders, bruxism, clenching, masseter hypertrophy and used to treat functional or esthetic dental conditions like deep nasolabial folds, radial lip lines, high lip line and black triangles between teeth.

BACKGROUND: Studies on the pharmacodynamics of abobotulinumtoxinA (ABO) and onabotulinumtoxinA (ONA) have produced inconsistent results. This may be due to the lack of objective measurement methods. OBJECTIVE: To assess and compare pharmacodynamic attributes, including onset of action, spread and efficacy of ABO and ONA using a novel Frontalis Activity Measurement Standard (FMS) and 4-point Frontalis Rating Scale (FRS).
METHODS: Twenty subjects with severe frontalis lines at maximum elevation received equal volumes of ABO or ONA using a dose ratio of 2.5:1 in five injection points on contralateral sides of the frontalis (statistical n=40). Subjects were evaluated using the FMS and FRS for 30 days using pre-defined endpoints for onset and effectiveness. Other assessments included areas of effectiveness and injection pain. RESULTS: For ABO vs. ONA, the FMS revealed a median Initial Onset of 12 vs. 48 hours (P is less than 0.001), Full Onset of 24 vs. 72 hours (P is less than 0.001) and Complete Onset of three vs. five days (P=0.01). The FRS indicated an Initial Onset for ABO and ONA of 18 hours vs. two days (P=0.002), Full Onset of two vs. three days (P=0.001) and Complete Onset of four days vs. eight days (P=0.01). The FMS showed 90 percent of ABO treatment achieved Complete Efficacy vs. 75 percent for ONO, while 90 percent of ABO treatments reached Complete Efficacy using the FRS vs. 65 percent for ONO. No differences in area of effectiveness or spread were observed. Most subjects (80%) reported ABO injections were less painful than ONA injections (P< 0.05). CONCLUSION: The FMS appears to be a sensitive, objective tool for measuring ABO and ONA pharmacodynamics. Using a dose ratio of 2.5:1, ABO displayed significantly earlier onset of effect and less injection pain than ONA but similar areas of effectiveness.

OBJECTIVE: To measure and compare the duration of action of abobotulinumtoxina and onabotulinumtoxina. DESIGN: Randomized, double-blind, contralateral (split-face) study. SETTING: Two United States clinical sites. Participants: Twenty subjects with severe frontalis lines at maximum elevation. Measurements: Subjects randomly received equal volumes of abobotulinumtoxina or onabotulinumtoxina (0.2mL) in five injection points on contralateral sides of the frontalis (N=40) using a dose ratio of 2.5:1.0 (total 25U abobotulinumtoxina:10U onabotulinumtoxina), respectively. Subjects were evaluated using a 4-point Frontalis Rating Scale and a new objective Frontalis Activity Measurement Standard for 210 days using predefined endpoints for efficacy. RESULTS: Using the Frontalis Activity Measurement Standard, the median duration of "complete efficacy" was 72 days for abobotulinumtoxina and 56 days for onabotulinumtoxina (p=0.01), "full efficacy" was 103 days for abobotulinumtoxina and 87 days for onabotulinumtoxina (p<0.003), and "partial efficacy" was 105 days for abobotulinumtoxina and 99 days for onabotulinumtoxina (p=0.006). Using the Frontalis Rating Scale, the median duration of "complete efficacy" was 63 days for abobotulinumtoxina and 44 days for onabotulinumtoxina (p=0.006), "full efficacy" was 119 days for abobotulinumtoxina and 77 days for onabotulinumtoxina (p=0.005), and "partial efficacy" was 160 days for abobotulinumtoxina and 145 days for onabotulinumtoxina (p=NS). Adverse events included local bruising and occasional headache, but no significant inter-group differences. CONCLUSION: The contralateral Frontalis Activity Measurement Standard is well-suited for assessing the pharmacodynamic and clinical attributes of botulinum toxin type A and can be used to measure differences in the clinical properties of abobotulinumtoxina and onabotulinumtoxina. Using a dose ratio of 2.5:1.0, abobotulinumtoxina displayed significantly longer duration of action than onabotulinumtoxina.


BACKGROUND: There are conflicting data regarding the specific attributes of botulinum neurotoxin type-A (BoNTA) products including onset of action, duration and spread because accurate, objective methods for assessing their clinical activity are lacking. OBJECTIVE: To refine definitions for BoNTA activity utilizing the frontalis muscle and describe the Frontalis Activity Measurement Standard (FMS), an objective method for measuring changes in frontalis muscle activity as a metric for assessing BoNTA pharmacodynamics. METHODS: As part of a study to assess BoNTA activity, 20 subjects with severe frontalis lines at maximum elevation were injected with two BoNTA products at five points on contralateral sides of the frontalis. Changes in maximum baseline frontalis elevation were measured by a blinded investigator using the previously-validated Frontalis Rating Scale (FRS) and the FMS. Frontalis activity endpoints were redefined to include Initial, Full and Complete Onsets of action and Partial, Full and Complete efficacy. RESULTS: Differences in the onset of effect of the BoNTA products were detected with both the FRS and FMS; however, the FMS detected changes in frontalis activity earlier than the FRS. A significant correlation between the FRS and FMS was documented. CONCLUSION: The frontalis muscle activity allows for enhanced assessment of BoNTA activity and attributes. The FMS appears to be a sensitive and objective tool for measuring pharmacodynamic parameters of BoNTA. Refining definitions of BoNTA activity provides a more accurate means for describing the clinical effects of BoNTA.

Neuromodulators have risen to the forefront of aesthetic medicine. By reversibly relaxing target muscles, neuromodulators exhibit their effect by softening hyperfunctional lines. An understanding of their physiology, relevant facial anatomy, and current agents is imperative for a successful aesthetic practice.


Botulinum neuromodulators and injectable dermal fillers have become part of the armamentarium in the treatment of facial aging. Their successful use requires a fundamental knowledge of anatomy and physiology and a sound understanding of their risks and complications. Although neuromodulators and fillers continue to demonstrate a strong record of safety, several notable risks exist.


**LEARNING OBJECTIVES:** After studying this article, the participant should be able to: 1. Describe the most common options available for minimally invasive facial rejuvenation. 2. Identify key elements essential to each treatment option. 3. Know how to avoid and manage complications for these procedures. **SUMMARY:** Minimally invasive cosmetic procedures continue to increase in popularity. This article is intended to provide a broad and practical overview of common minimally invasive cosmetic techniques available to the plastic surgeon.


Injection site pain (ISP) reduces compliance of botulinum toxin (BT) therapy considerably. We wanted to study whether nitrous oxide/oxygen (NOO, Livopan(R), Linde Gas Therapeutics, Unterschleissheim, Germany) can reduce ISP in patients receiving intracutaneous BT injections for axillary or palmar hyperhidrosis (HH). The study followed an open-label design comparing intraindividually ISP in both axillae and/or both palms when NOO was applied or not during BT injections. BT efficacy was measured by the Hyperhidrosis Disease Severity Scale (HDSS) and by a 4-point Self-Assessment Scale. ISP was documented by a Visual Analogue Scale (VAS) and the Verbal Scale of Pain Intensity (VSPI), adverse effects by a Structuralised Interview (SI). Altogether 13 patients (age 34.1 +/- 12.4 years, 9 females, 4 males) were studied. 11 BT treatments were for biaxillary and 3 for bipalmar HH. BT reduced biaxillary HH from HDSS 3.7 +/- 0.5 to 1.0 +/- 0 and bipalmar HH from 3.6 +/- 0.6 to 1.0 +/- 0. All patients reported ISP reduction by NOO. In axillary HH, NOO reduced ISP from 55.7 +/- 12.7 to 12.8 +/- 7.5 on the VAS (p < 0.05) and from 4.1 +/- 0.3 to 0.7 +/- 0.5 on the VSPI (p < 0.05), in bipalmar HH from 60.0 +/- 10.0 to 13.3 +/- 5.8 on the VAS (p < 0.05) and from 5.0 +/- 0 to 1.3 +/- 0.5 on the VSPI (p < 0.05). Adverse effects were not identified. NOO is a potent, non-sedative, quickly reversible and safe inhalative analgesic which reduces ISP considerably in patients receiving BT therapy for axillary and palmar HH thus substantially improving compliance of BT therapy.

BACKGROUND: One of the earliest signs of aging is the appearance of wrinkles in the skin at the outer corners of the eyes (lateral canthal rhytids). The purpose of this study was to divide the lateral canthal rhytids into classified groups and describe their clinical characteristics and suitable treatments. METHODS: A total of 525 patients were included in the study. These patients were groups according to age and sex. Digital photographs of the subject’s lateral canthal rhytids (lateral view) were taken and classified as to type (upper, lower, and bidirectional) and degree of direction. RESULTS: A total of 425 patients (81 %) exhibited the bidirectional type of lateral canthal rhytids. The lower directional type was noted on 75 patients (14.3 %), while only 25 patients (4.7 %) exhibited the upper directional type. In the 30s age group, only 50 % exhibited the bidirectional type. However, this rate increased to a 100 % in the 60 year-old and above group. There seems to be no relationship between the type of lateral canthal rhytids and sex. The degrees of the angle of wrinkles were statistically significant only in the 30s and 40s age groups. CONCLUSIONS: We classified lateral canthal rhytids into three groups. This classification helps to decrease the complications of botulinum toxin by associating different treatments with the type of lateral canthal rhytids. LEVEL OF EVIDENCE IV: This journal requires that authors assign a level of evidence to each article.


Botulinum neurotoxins are the most poisonous substances known to humankind, but also are the bacterial toxins most frequently used as pharmaceuticals to benefit humans. The discovery of botulinum toxins and development into a useful drug is unique and fascinating, dating back to the early 19th century, when Justinus Kerner first recognized that botulism was caused by a biological toxin and suggested its use for medicinal purposes. This was translated into reality in 1980, when Alan Scott for the first time used the toxins to successfully treat strabismus. Now a subset of botulinum toxins are widely used for cosmetic applications, treatment of various movement disorders, pain and many other syndromes, and further developments using other botulinum toxins or recombinant molecules engineered from subdomains are promising.

Botulinum toxin (Botox) is an exotoxin produced from Clostridium botulinum. It works by blocking the release of acetylcholine from the cholinergic nerve end plates leading to inactivity of the muscles or glands innervated. Botox is best known for its beneficial role in facial aesthetics but recent literature has highlighted its usage in multiple non-cosmetic medical and surgical conditions. This article reviews the current evidence pertaining to Botox use in the head and neck. A literature review was conducted using The Cochrane Controlled Trials Register, Medline and EMBASE databases limited to English Language articles published from 1980 to 2012. The findings suggest that there is level 1 evidence supporting the efficacy of Botox in the treatment of spasmodic dysphonia, essential voice tremor, headache, cervical dystonia, masticatory myalgia, sialorrhoea, temporomandibular joint disorders, bruxism, blepharospasm, hemifacial spasm and rhinitis. For chronic neck pain there is level 1 evidence to show that Botox is ineffective. Level 2 evidence exists for vocal tics, trigeminal neuralgia, dysphagia and post-laryngectomy oesophageal speech. For stuttering, 'first bite syndrome', facial nerve paresis, Frey's syndrome, oromandibular
dystonia and palatal/stapedial myoclonus the evidence is level 4. Thus, the literature highlights a therapeutic role for Botox in a wide range of non-cosmetic conditions pertaining to the head and neck (mainly level 1 evidence). With ongoing research, the spectrum of clinical applications and number of people receiving Botox will no doubt increase. Botox appears to justify its title as 'the poison that heals'.


Botulinum toxin is composed of 7 botulinum toxin antigenic subtypes. It is produced by Clostridium botulinum bacterial fermentation. Several botulinum toxin subtypes are under investigation for clinical use, but only botulinum toxin type A (BTX-A) is currently approved for cosmetic use because of its clinical safety profile and efficacy. The use of BTX-A in cosmetic facial procedures is a reliable way to enhance aesthetics in the face and is becoming commonplace in oral and maxillofacial surgery. This article reports an uncommon complication after Botox injection in the upper lip, for cosmetic reasons, originating a mass in the anterior region of the maxilla, which leads to failure in orthodontic treatment. Knowledge of the site anatomy, pharmacology, and dose of BTX-A before its use in cosmetic surgery should be strengthened.


OBJECTIVES: This review examines the pharmacologic and clinical characteristics of incobotulinumtoxinA (Xeomin(R)/Xeomeen((R))/Bocouture((R))/XEOMIN Cosmetic; botulinum toxin type A [150 kDa]), which is free from complexing proteins, and discusses its efficacy and safety in the treatment of glabellar frown lines. Differences between incobotulinumtoxinA and other commercially available botulinum neurotoxin type A (BoNT/A) products that have been approved by the European Medicines Agency, US Food and Drug Administration, and other regulatory agencies for this indication are also discussed. FINDINGS: IncobotulinumtoxinA differs from other commercially available BoNT/A preparations, in that it is free from complexing proteins and contains only active neurotoxin, minimizing foreign protein load. IncobotulinumtoxinA is commonly used at a 1:1 dose ratio with onabotulinumtoxinA and displays comparable efficacy and safety; furthermore, it is associated with early onset and long duration of effect, and high levels of subject satisfaction. In terms of practical considerations, incobotulinumtoxinA does not require cold storage and demonstrates low spread, enabling precise treatment and good tolerability. CONCLUSION: IncobotulinumtoxinA is an efficacious and well-tolerated treatment for glabellar frown lines. It differs from other BoNT/A preparations, in that it is free from complexing proteins and contains only active neurotoxin, which is relevant clinically, as this reduces the foreign protein load and minimizes the risk of neutralizing antibody production. In practical terms, incobotulinumtoxinA has a long shelf-life, remaining stable without the need for refrigeration, and due to its limited spread is a precise localized treatment.


BACKGROUND: For the first time, the effectiveness of Xeomin(R), and Dysport(R) in an dose-ratio of 1:3 treating crow's feet (FWS 2-3) was evaluated in a double-blind randomized
pilot study. PATIENTS AND METHOD: Xeomin(R) (12 units) was compared to Dysport(R) (36 units) in an intra-individual split-face technique in 22 patients over a period of 4 months. According to the facial-wrinkle-scale (FWS) patients were rated as responders with an improvement of at least 1 point in FWS. RESULTS: One month after treatment significantly more than 80% of patients were rated as responders. The different products proved to be equivalent in response rate and effectiveness with no significant difference after 4 weeks and 4 months in statistical analysis. Surprisingly the decrease in FWS of crows' feet at rest was more pronounced. CONCLUSION: The different botulinum toxin type A formulations proved to be equivalent in effectiveness and tolerability in a dose ratio of 1:3 (Xeomin(R): Dysport(R)). The more pronounced decrease of crows feet at rest points out the importance of muscle insertion into the skin for the cosmetic result in the periorbital region.


Despite the extensive use of Botulinum toxin A (BoNTA) in medical and cosmetic treatments, the potential spreading of BoNTA to surrounding tissues remains unknown. A patient with hemi-facial paralysis upon blepharospasm treatment with low dose of BoNTA, prompted us to investigate the spreading effect. A randomised, double-blind study was conducted in which 5 healthy women (33-52 years) were treated with different doses of onabotulinum toxin unilaterally in the corrugator muscle. Parameters of efficacy and diffusion (CMAP; EMG and jitter analysis) in both glabellar and frontalis muscles were assessed at baseline, 2 and 4 weeks following BoNTA injection. CMAP of the treated glabellar muscles was reduced to approximately 40% in all dose groups. Additionally, contralateral CMAP reduction was observed in 3 of 5 subjects. These data confirm regional diffusion of BoNTA in facial muscle application, which raises question on the reliability of split-face models in BoNTA studies.


Botulinum toxin (BoNT) is an acetylcholine release inhibitor and a neuromuscular blocking agent used for the treatment of a variety of neurologic and medical conditions. The efficacy and safety of BoNT depends on accurate selection and identification of intended targets but also may be determined by other factors, including physical spread of the molecule from the injection site, passive diffusion, and migration to distal sites via axonal or hematogenous transport. The passive kinetic dispersion of the toxin away from the injection site in a gradient-dependent manner may also play a role in toxin spread. In addition to unique properties of the various BoNT products, volume and dilution may also influence local and systemic distribution of BoNT. Most of the local and remote complications of BoNT injections are thought to be due to unwanted spread or diffusion of the toxin's biologic activity into adjacent and distal muscles. Despite widespread therapeutic and cosmetic use of BoNT over more than three decades, there is a remarkable paucity of published data on the mechanisms of distribution and its effects on clinical outcomes. The primary aim of this article is to critically review the available experimental and clinical literature and place it in the practical context. (c) 2013 Movement Disorder Society.

To review indexed literature concerning adverse ocular effects of the most common aesthetic facial procedures (light-emitting therapy, dermal fillers injection, and botulinum toxin). Literature search using three online databases - PubMed, SciELO, and Capes - selecting case reports, series of cases and reviews, with no language restriction, published in a period of the last twenty years (1995-2015). After reviewing 48 case reports and most recent reviews, the authors found the most common ocular adverse effects of dermal fillers were related to vascular occlusion; light-emitting therapy was associated with pigmented tissue damage leading to anterior uveitis and iris atrophy, and ptosis presented the higher relative risk associated with botulinum toxin. Even though ocular adverse effects are not very frequent, some of them can lead to permanent ocular dysfunction and visual impairment. Professionals involved in cosmetic procedures should be aware of the risks.


The botulinum neurotoxin (BoNT) product Azzalure (manufactured by Ipsen Biopharm Limited, Wrexham, UK; distributed by Galderma), measured in Speywood units (s.U) has been available since 2009 for temporary improvement in the appearance of moderate to severe glabellar lines. Although we know much about the use of Azzalure for aesthetic indications, some aspects of product use in the clinic still require an update based on continuing and prevailing misconceptions and new clinical data. Therefore, a group of experts experienced with the use of Azzalure convened to formulate the following recommendations: (1) The key to an optimal effect is adequate dosing per injection point. Ten s.U are indicated for strong muscular activity, 5 s.U for medium activity, and approximately 2 s.U for minor activity. (2) The main factor that influences the area of effectiveness is the dosage per injection point. (3) In contrast to former beliefs, we know now that Azzalure works very fast, with some patients reporting initial drug activity after hours. (4) Various volumes can be used for dilution. However, the first choice is the recommended volume, 0.63 mL per vial of 125 s.U. Nevertheless, for clinicians changing products, keeping the volume they are used to might be an option. (5) Clinicians changing products have to be very careful not to confuse the units between different products. (6) In aesthetic BoNT-A usage, the development of antibodies is very rare and is not the common reason for insufficient results. (7) Probably the most common reason when BoNT-A is not working is the absolute or relative underdosage. The present adjunctive recommendations elaborated in an informal expert meeting should help physicians to optimize their treatment with Speywood unit products.


125. Scaglione, F. (2016). "Conversion Ratio between Botox(R), Dysport(R), and Xeomin(R) in Clinical Practice." Toxins (Basel) 8(3).

Botulinum neurotoxin has revolutionized the treatment of spasticity and is now administered worldwide. There are currently three leading botulinum neurotoxin type A products available in the Western Hemisphere: onabotulinum toxin-A (ONA) Botox(R), abobotulinum toxin-A (ABO), Dysport(R), and incobotulinum toxin A (INCO, Xeomin(R))). Although the efficacies are similar, there is an intense debate regarding the comparability of various preparations. Here we will address the clinical issues of potency and conversion
ratios, as well as safety issues such as toxin spread and immunogenicity, to provide guidance for BoNT-A use in clinical practice. INCO was shown to be as effective as ONA with a comparable adverse event profile when a clinical conversion ratio of 1:1 was used. The available clinical and preclinical data suggest that a conversion ratio ABO:ONA of 3:1 or even lower could be appropriate for treating spasticity, cervical dystonia, and blepharospasm or hemifacial spasm. A higher conversion ratio may lead to an overdosing of ABO. While uncommon, distant spread may occur; however, several factors other than the pharmaceutical preparation are thought to affect spread. Finally, whereas the three products have similar efficacy when properly dosed, ABO has a better cost-efficacy profile.


BACKGROUND: Because abobotulinumtoxinA treatment for glabellar lines must be repeated regularly to prevent recurrence, understanding the safety and effectiveness of long-term, repeated administration of abobotulinumtoxinA is important. OBJECTIVE: To report the long-term safety and efficacy of abobotulinumtoxinA in patients with moderate to severe glabellar lines. METHODS AND MATERIALS: AbobotulinumtoxinA was administered to 1,415 patients in multiple cycles over 24 months as a fixed dose of 50 U or as a dose based on muscle mass and sex (women: 50-70 U; men: 60-80 U). Adverse events were assessed after each visit on days 7, 14, and 30 and monthly thereafter; monitoring continued every 3 months for a total safety monitoring duration of 36 months or less. RESULTS: Nine hundred ninety-one (70%) patients reported treatment-emergent adverse effects (TEAEs); most events were mild (70%) or moderate (20%) in severity. The rate of TEAEs did not increase over 24 months of repeated treatment (mean 5.6 cycles; range 1-9). Treatment-related eyelid ptosis followed 53 of 7,938 (0.7%) treatments, all of which resolved spontaneously. CONCLUSIONS: Multiple cycles of abobotulinumtoxinA treatment over 24 months were well tolerated and effective for the correction of glabellar lines, with no evidence of cumulative safety problems.


BACKGROUND: Many analgesic modalities have been employed with limited success to alleviate the pain associated with botulinum toxin type A (BTX-A) injections. Vibration is an effective method of reducing pain during facial cosmetic injections, but it has not been previously studied in the context of clinical cosmetic procedures. OBJECTIVES: The authors evaluate the safety and efficacy of vibration-assisted anesthesia for reducing pain associated with BTX-A injections. METHODS: In this prospective study, 50 patients received BTX-A injections for cosmetic rhytid reduction. Injections were given in a split-face design that was randomly assigned. A vibration stimulus was coadministered with BTX-A injections on one side, while the other side of each patient's face received BTX-A injections alone. Patients completed a questionnaire immediately posttreatment and were contacted for follow-up three to four weeks later. RESULTS: Patients reported less injection pain on the vibration-treated half of the face as compared to the control side (an average of 1.3 vs 2.4 on a five-point scale; P = .000). Overall, 86% of patients preferred to receive vibration with their next BTX-A treatment. There was no significant difference between first-time and repeat BTX-A patients in terms of preference for vibration. Five of 50 patients experienced
transient side effects perceived to be associated with vibration, including tingling teeth, increased bruising, and headaches. Of the patients who did not request vibration with subsequent BTX-A injections, none cited decreased BTX-A efficacy as the reason for their preference. CONCLUSIONS: Vibration is a safe and effective means of reducing patient discomfort during BTX-A injections for cosmetic rhytid reduction and may have applications in other cosmetic procedures.


Botulinum toxin A (Botox, Allegan) is a potent neurotoxin that blocks the release of acetylcholine at the neuromuscular junction of cholinergic nerves. Botulinum toxin was introduced to clinical medicine in 1980. Since then it has become a major therapeutic drug in many medical sub-specialties and its use for facial rejuvenation has become increasingly popular. Diplopia after botulinum toxin injection for facial rejuvenation is a rare and transient complication which is related to chemodenervation of adjacent muscle groups. We would like to report 3 cases of double vision related to extra-ocular muscle paresis after an injection of botulinum toxin for facial rejuvenation and blepharospasm. In all 3 cases recovery occurred, without any treatment, over 3 to 4 months (apparently from regeneration of inactivated proteins necessary for degranulation of acetylcholine vesicles). The clinicians engaged in botulinum toxin injections for facial rejuvenation or blepharospasm, should be aware of the possible complications, and inform the patients about the risk of developing double vision. The clinicians should take into account and ask about Botox when treating patients complaining of diplopia.


AIM: To critically appraise current literature regarding the management of plantar hyperhidrosis in the form of a structured review. METHOD: A literature search was conducted using various databases and search criteria. DISCUSSION: The literature reports the use of conservative, medical and surgical treatment modalities for the management of plantar hyperhidrosis. However, long-term follow-up data are rare and some treatment modalities currently available are not fully understood. CONCLUSION: There is a considerable dearth in the literature on the management of plantar hyperhidrosis. Further study in larger populations with longer follow-up times is critical to access the long-term effects of treatment. Nonetheless, iontophoresis, botulinum toxin injection and lumbar sympathectomy are promising treatment modalities for this disorder.


Botulinum toxin type A (BTX-A) preparations are widely used nonsurgical treatments for facial wrinkles. Higher doses of BTX-A are also used for therapeutic purposes in the treatment of conditions involving increased muscle tone, such as cervical dystonia. The phenomenon of antibody-induced treatment failure is well known in the therapeutic setting, but reports are also emerging following cosmetic use of BTX-A. We describe the case of a 41-year-old female nurse who developed secondary treatment failure during 6 years of BTX-A treatment for glabellar lines. After a good response to the first BTX-A injection, the intensity and duration of effect decreased after subsequent treatments. Antibody tests revealed a high titer of neutralizing anti-BTX-A antibodies. This case shows secondary treatment failure due to the production of neutralizing antibodies following administration of BTX-A formulations for cosmetic purposes and demonstrates that
immunogenicity of BTX-A preparations is an important consideration, even in the cosmetic setting.


This article outlines practice routines, clinical techniques, applications, and complications of botulinum toxin type A treatment of mimetic facial and neck muscles. Detailed descriptions are provided for each clinical indication that maximize the treatment of the intended muscle groups while minimizing potential complications.


**BACKGROUND:** There is no consensus in the literature about the ideal technique for precisely placing botulinum toxin in the frontal facial regions for the most natural posttreatment appearance. **OBJECTIVES:** The authors describe a safe and effective dosage template for botulinum toxin injection (a "dose disc," which makes it possible to estimate the approximate area to which the action of the toxin dose will reach, thereby guiding the positioning of the injection in a very practical way) for frontal wrinkle effacement, preserving residual movement whenever possible. **METHODS:** Fifty adult patients who presented to the authors' private clinic between January 2009 and May 2010 with aesthetic concerns about cutaneous expression wrinkles in the frontal region of their faces were selected for this study. Patients were sequentially divided into two groups: Group 1 included the first 15 patients, who underwent injections in the frontal region on the first visit and glabellar injections 15 days later; Group 2 included the subsequent 35 patients, who underwent frontal and glabellar treatment simultaneously. All pretreatment markings in both groups were made with the authors' "dose disc, which allows for overlap of the "halos" of effect. **RESULTS:** In the 50 patients included in the study, 317 injections were performed with the dose disc. Two treatment failures occurred (etiology unknown), and five patients presented with failure due to irregular technical positioning of the discs. The latter patients were treated at the beginning of the study and exhibited residual wrinkles. Only one case of complete toxin inactivity was observed. All patients with treatment failures underwent successful correction with additional injections. There was no evidence of palpebral ptosis, eyebrow ptosis, or any other serious diffusion or positioning side effects. **CONCLUSIONS:** A fixed dose disc template can be a useful tool for botulinum toxin injections in the frontal region of the face. Future studies assessing other disc models for different doses and different injection methods are needed, with the goal of establishing a longer duration of the effect and devising similar templates for other facial areas.


RT002, an injectable form of botulinum neurotoxin type A (BoNTA), comprised of a purified 150 kDa neurotoxin formulated in a novel formulation, is designed to limit the extent of diffusion and permit safe administration of longer acting doses. The aim of this study was to evaluate the degree of diffusion of RT002 in comparison to another commercially available BoNTA product, Botox(R) Cosmetic (OnabotulinumtoxinA, Allergan, Inc., Irvine, CA, USA), and establish the relative duration of effect for diffusion matched doses of the two BoNTA formulations using quantitative measurements in mice. Measurement of muscle paralysis by muscle force generation (MFG) in mice at the injected gastrocnemius muscles indicated that RT002 and Botox are equipotent. Measurements of MFG inhibition in an adjacent muscle, the tibialis anterior muscle, indicated significantly less diffusion for RT002 as
compared to Botox. When RT002 and Botox were dosed using the established diffusion matched doses, RT002 treatment resulted in an extended duration of drug effect as compared to Botox by 58-100% as assessed by either partial or complete recovery endpoints. Use of a daily voluntary running activity model provided confirmation that the two BoNTA formulations are equipotent by daily running distance and further confirmed the diffusion matched dose ratio assessed by degree of drug effect on body weight gain. Using these diffusion matched doses, RT002 treatment resulted in an extended duration of drug effect as compared to Botox (100-126% increase in duration) as assessed by either partial or complete recovery endpoints. Use of this model provides further evidence that the RT002 formulation limits diffusion with equipotency and thereby may permit safe administration of higher and more efficacious doses. In summary, data from two murine models suggest that RT002 may represent a next generation of BoNTA drug formulation offering superior degree and duration of effect at the intended target while controlling the unwanted diffusion and accompanying adverse effects of BoNTA at neighboring muscles and distal systemic targets.


BACKGROUND: Combination of fillers and botulinum toxin for aesthetic applications is increasingly popular. Patient demographics continue to diversify, and include an expanding population receiving maintenance treatments over decades. METHODS: A multinational panel of plastic surgeons and dermatologists convened the Global Aesthetics Consensus Group to develop updated guidelines with a worldwide perspective for hyaluronic acid fillers and botulinum toxin. This publication considers strategies for combined treatments, and how patient diversity influences treatment planning and outcomes. RESULTS: Global Aesthetics Consensus Group recommendations reflect increased use of combined treatments in the lower and upper face, and some midface regions. A fully patient-tailored approach considers physiologic and chronologic age, ethnically associated facial morphotypes, and aesthetic ideals based on sex and culture. Lower toxin dosing, to modulate rather than paralyze muscles, is indicated where volume deficits influence muscular activity. Combination of toxin with fillers is appropriate for several indications addressed previously with toxin alone. New scientific data regarding hyaluronic acid fillers foster an evidence-based approach to selection of products and injection techniques. Focus on aesthetic units, rather than isolated rhytides, optimizes results from toxin and fillers. It also informs longitudinal treatment planning, and analysis of toxin nonresponders. CONCLUSIONS: The emerging objective of injectable treatment is facial harmonization rather than rejuvenation. Combined treatment is now a standard of care. Its use will increase further as we refine the concept that aspects of aging are intimately related, and that successful treatment entails identifying and addressing the primary causes of each. CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, V.


BACKGROUND: Botulinum toxin type A injection remains the leading nonsurgical cosmetic procedure worldwide, with a high rate of efficacy and patient satisfaction. METHODS: A multinational, multidisciplinary group of plastic surgeons and dermatologists convened the Global Aesthetics Consensus Group to develop updated consensus recommendations with a worldwide perspective for botulinum toxin and hyaluronic acid fillers. This publication on
botulinum toxin type A considers advances in facial analysis, injection techniques, and avoidance and management of complications. RESULTS: Use of botulinum toxin has evolved from the upper face to also encompass the lower face, neck, and midface. The Global Aesthetics Consensus Group emphasizes an integrative, diagnostic approach. Injection dosage and placement are based on analysis of target muscles in the context of adjacent ones and associated soft and hard tissues. The indication for selection of botulinum toxin as a primary intervention is that excessive muscular contraction is the primary etiology of the facial disharmony to be addressed. Global Aesthetics Consensus Group recommendations demonstrate a paradigm shift toward neuromodulation rather than paralysis, including lower dosing of the upper face, more frequent combination treatment with hyaluronic acid fillers, and intracutaneous injection where indicated to limit depth and degree of action. CONCLUSIONS: The accumulation of clinical evidence and experience with botulinum toxin has led to refinements in treatment planning and implementation. The Global Aesthetics Consensus Group advocates an etiology-driven, patient-tailored approach, to enable achievement of optimal efficacy and safety in patient populations that are rapidly diversifying with respect to ethnicity, gender, and age. CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, V.


The muscular anatomy of the face is complex. Animation patterns of facial muscles vary significantly among individuals. Activity of facial muscles determines expression and emotion and affects the eyes aperture and the amount and extent of facial rhytids. Injection of botulin toxin for facial rejuvenation has become a very popular procedure and allows the practitioner the ability to modulate facial expression and to decrease the amount of facial rhytids. A thorough knowledge of the variant facial anatomy is necessary to maximize the efficiency of botulin toxin injection. This knowledge will also aid in minimizing complication an untoward side effect.


BACKGROUND: A paucity of research exists on the safety and efficacy of aesthetic medicine products in patients with skin of color (SOC). OBJECTIVE: To compare the effectiveness and tolerability of abobotulinumtoxinA (BoNTA-ABO) for glabellar lines in a subpopulation of patients with SOC with that in white patients. MATERIALS AND METHODS: This post hoc analysis considered pooled safety data from six clinical trials from which were derived a safety population (n = 1,869 white, n = 472 SOC), an efficacy population for a comparison of fixed-dose BoNTA-ABO 50 U in white patients (n = 216) and patients with SOC (n = 117), and an efficacy population for a comparison of BoNTA-ABO adjusted to muscle mass in white (n = 555) and patients with SOC (n = 160). RESULTS: Adverse event rates were similar in white patients and patients with SOC. Onset of effect was similar in patients with SOC and white patients, but the response rate 30 days after treatment was greater in patients with SOC than in white patients. CONCLUSION: Tolerability and effectiveness of treatment BoNTA-ABO for glabellar lines was similar in patients with SOC and white patients.

**CONTEXT:** Standards for an aesthetic face are dynamic. The current trend is towards a leaner looking face with preservation of the inverted triangle of youth. Procedures that have been reported to be employed for correction of a chubby face include buccal fat pad excision, facial liposuction and injection lipolysis. In addition to giving the face an aesthetic triangular cut, chin and malar augmentation may be performed. The rounded appearance at the angles may further be reduced by injection of Botulinum toxin into the masseter.

**MATERIALS AND METHODS:** Forty patients who presented to us for correction of chubby (round) faces were analysed and treated by facial sculpting surgery, which included at least two of the procedures in combination. The procedures included facial liposuction, buccal fat pad excision, chin augmentation, malar augmentation and injection lipolysis. All cases were followed-up for a minimum of 6 months after surgery. **RESULTS:** Aesthetic expectations of the patients were met in 39 cases, one patient complained of facial asymmetry following facial liposuction and was subjected to a touch-up injection lipolysis. **CONCLUSIONS:** A combination of procedures is necessary to give the face an attractive contour. All the individual procedures have stood the test of time and are safe, proven and are put in mainstream. However, a thorough analysis of the face preoperatively and then subjecting the patient to a combination of these procedures in a single surgical sitting has yielded good results as seen in this study.


Botulinum toxin A (BT) is used therapeutically for the treatment of primary focal hyperhidrosis, a chronic debilitating condition characterised by over-activity of the eccrine sweat glands. Systemic toxicity concerns require BT to be administered by local injection, which in the case of hyperhidrosis means multiple painful intradermal injections by a skilled clinician at 6-monthly intervals. This study investigates the potential of a liquid-loaded pocketed microneedle device to deliver botulinum toxin A into the human dermis with the aim of reducing patient pain, improving therapeutic targeting and simplifying the administration procedure. Initially, beta-galactosidase was employed as a detectable model for BT to (i) visualise liquid loading of the microneedles, (ii) determine residence time of a liquid formulation on the device and (iii) quantify loaded doses. An array of five stainless steel pocketed microneedles was shown to possess sufficient capacity to deliver therapeutic doses of the potent BT protein. Microneedle-mediated intradermal delivery of beta-galactosidase and formaldehyde-inactivated botulinum toxoid revealed effective deposition and subsequent diffusion within the dermis. This study is the first to characterise pocketed microneedle delivery of a liquid formulation into human skin and illustrates the potential of such systems for the cutaneous administration of potent proteins such as BT. A clinically appropriate microneedle delivery system for BT could have a significant impact in both the medical and cosmetic industries.


The use of botulinum toxin in the lower face is more complex and less reliable than its use in the upper face. Use in the lower face is also fraught with more adverse events. The anatomy of the lower face is complex, as the muscles of this region are very close together and interface at different levels and depths to perform heterogeneous functions, such as talking, eating, drinking, and expressivity of the face. This article, based on the anatomical knowledge of each muscle of the lower face, provides recommendations and guidelines to
perform botulinum toxin injection safely. The review of each muscle with its relevant anatomy and relationship of this three-dimensional anatomy with the cutaneous plane gives the exact position of injectable locations. For each muscle, the number of points related to the motor end plate location and the exact dose related to the muscular mass are indicated. Summary tables are provided.


**BACKGROUND:** Botulinum toxin (BoNT) has been in use since the late 1970s, and over the last 20 years, its use has been extended to new indications in various areas of medicine. During these years of clinical use, some of the initial ideas have changed, and others have remained stable along with increasing experience with and knowledge about BoNTs. **OBJECTIVE:** To review the literature and prescribing information on all of the available products and to update the concept of handling toxins (preparations, reconstitution, storage, sterility, and dilution). **METHODS:** A review (not Cochrane type analysis) of the medical literature based on relevant databases (MEDLINE, PubMed, Cochrane Library, specialist textbooks, and manufacturer information) was performed. **CONCLUSIONS:** Many of the precautions around BoNT use, often recommended by the manufacturers, are described in the clinical literature as too restrictive. The literature suggests that toxins may be sturdier and more-resistant to degradation than previously understood.


**BACKGROUND:** Aging of the neck is characterized by changes that include skin dyspigmentation, laxity, rhytides, loss of the mandibular contour, widening of the cervicomental angle, accumulation of submental fat, volume loss and prominence of the platysmal bands. Many cosmetic options exist to address these changes individually, but little literature exists about the safety and efficacy of combining such procedures and devices. **OBJECTIVE:** To review the existing literature and the authors' experience in safely and effectively combining aesthetic rejuvenation modalities for the neck. **METHODS:** A Medline search was performed on combination treatments for neck rejuvenation, and results are summarized. Practical applications for combining these procedures are discussed. **RESULTS:** Studies examining the efficacy and safety of intense pulsed light, ablative fractional lasers, nonablative fractional lasers, microfocused ultrasound with visualization, thermistor-controlled subsurface monopolar radiofrequency, cryolipolysis, ATX-101, liposuction, laser lipolysis, neuromodulators, and hyaluronic acid dermal fillers in the neck were found. The authors review their experience in combining these techniques. **CONCLUSION:** Review of the literature revealed options for non- and minimally-invasive rejuvenation of the skin and volume restoration of the neck, but little literature was found on the safety and efficacy of combining such procedures. The authors' experience in clinical practice is that many neck rejuvenation techniques can be combined safely. A combination approach often produces the most optimal outcome for the patient seeking neck rejuvenation.


Botulinum toxin A was Food and Drug Administration approved in 2002 for the temporary correction of glabellar frown lines. Since that time, a variety of neuromodulators have established a convincing profile for both safety and efficacy in the treatment hyperdynamic rhytides of the upper face. With increasing clinical experience and expertise, these applications have been expanded to include targeted treatment of muscles in both the mid and lower face. This article details common techniques using botulinum toxin to treat orbicularis oris, depressor anguli oris, mentalis, and masseter muscles for the temporary correction of unwanted lower face hyperdynamic rhytides and facial contouring. Although we detail our suggested quantity of units per injection site based on onabotulinumtoxinA, all neuromodulators can be used in all of these suggested treatment areas with adjustment of the quantity of units based on the efficacy of the specific neuromodulator. A more compete discussion on the relative efficacy of all neuromodulators is beyond the scope of this article.


A variety of non-invasive techniques have been utilized for the enhancement of cutaneous changes seen with photoaging. Such methods include chemical peels, microdermabrasion, ablative and nonablative lasers, and various rejuvenating light sources. However, the most widely used minimally invasive cosmetic procedures for the correction of undesired rhytides and enhance facial features through contouring and volumization are injections with botulinum toxin and soft tissue fillers. Their extensive long term safety and relative ease of procedural techniques have led to high satisfaction levels worldwide. Nonetheless, proper training of the fundamentals in injection technique, the choice of the appropriate candidate, and knowledge of potential adverse events are imperative to ensure an excellent and safe outcome.


Although botulinum toxin is generally considered safe, its widespread use and the constantly expanded indications raise safety issues. This study aimed to review the serious and long-term adverse events associated with the therapeutic and cosmetic use of botulinum toxin. Serious adverse events included dysphagia, respiratory compromise, generalized muscle weakness, marked bilateral ptosis, pseudoaneurysm of the frontal branch of the temporal artery, necrotizing fasciitis, sarcoidal granuloma, Fournier gangrene, and cervical kyphosis. Death was attributed to botulism or anaphylactic shock. In conclusion, botulinum toxin may cause serious adverse events, which are more common after its therapeutic use, but can also be noticed after its cosmetic use. Thorough knowledge of the anatomy of the treated muscles and of the pharmacology of the drug is imperative to avoid serious adverse events.


OBJECTIVE: To report and discuss the outcome of a prospective, internally controlled, randomized, double-blind, split-face study comparing the onset of action of 2 commercially available botulinum neuromodulators. METHODS: Ninety individuals with moderate-to-severe lateral orbital rhytids were treated with onabotulinumtoxinA, 10 U, and abobotulinumtoxinA, 30 U, for the treatment of lateral orbital rhytids. Participants were
assessed live with a validated 5-point photographic scale before treatment and on days 2, 4, and 6 after treatment. Photographs were taken at each encounter. Statistical analysis was applied to evaluate for any significant difference in onset of action between the 2 products. RESULTS: AbobotulinumtoxinA and onabotulinumtoxinA demonstrated statistically significant change from baseline at day 2 in the treatment of lateral orbital rhytids at maximal contraction and rest when evaluated independently by investigator and participant (P<0.001). Also at day 2, the improvement with abobotulinumtoxinA was better than that with onabotulinumtoxinA for the primary end point of maximal contraction graded by the investigator, although this did not reach statistical significance (P=0.21); by day 4, the greater improvement achieved with abobotulinumtoxinA reached statistical significance (P<0.02) and remained superior at day 6 (P<0.02). The primary findings were strengthened by similar results in the secondary end points of patient self-grade at maximal contraction and at rest and of investigator grade at rest. CONCLUSIONS: In conclusion, both abobotulinumtoxinA and onabotulinumtoxinA achieved statistically significant onset of action at day 2. This improvement was seen in all end points, with abobotulinumtoxinA demonstrating a trend toward greater improvement than onabotulinumtoxinA at day 2 and a statistically significant greater improvement at days 4 and 6 when looking at maximal contraction.


Objective. We evaluated synergistic efficacy and safety of combined topical application of Botulinum Toxin Type A (BTX-A) with fractional CO2 laser for facial rejuvenation. Methods. Twenty female subjects were included for this split-face comparative study. One side of each subject's cheek was treated with fractional CO2 plus saline solution, and the other side was treated with fractional CO2 laser plus topical application of BTX-A. Patients received one session of treatment and evaluations were done at baseline, one, four, and twelve weeks after treatment. The outcome assessments included subjective satisfaction scale; blinded clinical assessment; and the biophysical parameters of roughness, elasticity, skin hydration, transepidermal water loss (TEWL), and the erythema and melanin index. Results. BTX-A combined with fractional CO2 laser sides showed higher physician's global assessment score, subject satisfaction score, roughness, skin hydration, and skin elasticity compared to that of fractional CO2 plus saline solution side at 12 weeks after treatment. TEWL and erythema and melanin index showed no significant differences between two sides at baseline, one, four, and twelve weeks after treatment. Conclusion. Topical application of BTX-A could enhance the rejuvenation effect of fractional CO2 laser.