Guidelines on the use of botulinum toxin Type A

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ABSTRACT

Botulinum toxin is available as types A and B. These two different forms need different dosages and hence, the physician needs to be familiar with the formulations. A thorough knowledge of the anatomy and physiology of the muscles in the area to be injected is essential. **Indications for botulinum toxin:** Dynamic wrinkles caused by persistent muscular contractions are the main aesthetic indications for the use of Botulinum toxin. These include forehead lines, glabellar lines, crow’s feet, bunny lines, perioral wrinkles, and platysmal bands. Non-aesthetic indications include hyperhidrosis of the palms, soles and axillae. **Physicians’ qualifications:** Any qualified dermatologist may practice the technique after receiving adequate training in the field. This may be obtained either during post-graduation or at any workshops dedicated to this subject. **Facility:** Botulinum toxin can be administered in the dermatologist’s minor procedure room. **Preoperative counseling and informed consent:** Detailed counseling with respect to the treatment, desired effects, and longevity of the results should be discussed with the patient. The patient should be given brochures to study and adequate opportunity to seek information. A detailed consent form needs to be completed by the patient. The consent form should include the type of botulinum toxin, longevity expected and possible postoperative complications. Pre- and postoperative photography is recommended. **Dosage** depends on the area, muscle mass, gender and other factors outlined in these guidelines. It is **recommended** that beginners should focus on the basic indications in the upper third of the face and that they treat the middle and lower parts of the face only after garnering adequate experience.

**Key Words:** Wrinkles, Dynamic wrinkles, Aging

INTRODUCTION

Since the introduction of botulinum toxin type A more than two decades ago, its use has expanded to include a wide range of clinical applications for the aging face and the technique has emerged as a commonly performed aesthetic procedure. Botulinum toxin type A targets the SNAP-25 protein and is available commercially in two formulations, Botox® (Allergan Inc., Irvine, CA) and Dysport® (Ispen Limited, Berkshire, England). Both are available in a lyophilized form and must be reconstituted with physiological saline before use. The type B toxin targets a vesicle-associated membrane...
protein called synaptobrevin and is available as Myobloc® (Elan Pharmaceuticals, San Diego, CA), an aqueous solution. The doses for Dysport® and Myobloc® are typically 3-6 and 50-100 times higher than typical Botox® doses.

RATIONALE AND SCOPE

The aesthetic use of botulinum toxin type A is governed by general principles as well as specific considerations for each treatment area. Guidelines stated below will include information on the target muscles, injection sites, total starting doses based on gender and amount per injection site, response assessment and potential retreatment intervals. An approach to minimize side effects and maximize efficacy will be suggested. Finally, potential complications accompanying the use of botulinum toxin on the face will be addressed.

Indications for Botox®: Botox® is indicated for all wrinkles produced due to persistent muscular contractions. These include forehead lines, glabellar lines, crow’s feet, bunny lines, perioral wrinkles and platysmal bands. Dynamic wrinkles respond better than fixed wrinkles. A patient may have more than one type of wrinkle and will therefore need combination treatment with other modalities such as fillers, peels, laser resurfacing, threadlift, etc. Non-aesthetic indications include hyperhidrosis (palms, soles, axillae, gustatory), blepharospasm, cervical dystonia, migraine, wound healing and anal fissures.

Contraindications to the use of botulinum toxin type A include:

i. Injections in patients with peripheral motor neuropathic diseases or neuromuscular functional disorders.

ii. Coadministration with aminoglycoside antibiotics or other agents that interfere with neuromuscular transmission.

iii. Treatment of patients with inflammatory skin disorders at the injection site.

iv. Pregnancy and lactation

Physicians’ qualification: Any qualified dermatologist may practice Botox after receiving adequate training in the field. This may be obtained either during postgraduation or at any workshops dedicated to the subject of Botox.

Task force recommendations: It is recommended that beginners focus on the basic indications in the upper third of the face and that they move to the middle and lower parts of the face and other indications only after garnering adequate experience.

Facility: Botulinum toxin can be administered in the dermatologist’s minor procedure room if appropriate sterilization and storage facilities are in place.

PREOPERATIVE COUNSELING AND INFORMED CONSENT

Detailed counseling with respect to the treatment, desired effects, and longevity of the results should be discussed with the patient. The patient should be given brochures to study and adequate opportunity to seek information. A detailed consent form needs to be completed by the patient. The consent form should include the type of botulinum toxin, longevity expected, need for repeated treatments and possible postoperative complications. As in all aesthetic procedures, it is essential that the patient have realistic expectations.

Preoperative photography is mandatory.

1. Set overall aesthetic goals with patients.

2. Develop treatment plan.

3. Establish realistic expectations for treatment outcome.

4. Patients need to receive information about potential adverse effects but they should be aware of the long history of safe use, the low probability of any of these effects occurring, and the fact that most adverse effects are mild and transient.

5. Accurate medical history.

6. Reduce the risk of bruising by asking patients to avoid medications that inhibit clotting such as vitamin E, aspirin, and nonsteroidal antiinflammatory drugs (NSAIDs) for a period of 10-14 days prior to treatment.

Table 1: Recommendations for reconstitution and handling

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diluent</td>
<td>Preserved 0.9% Saline (preferred)</td>
</tr>
<tr>
<td>Dilution</td>
<td>Nonpreserved 0.9% Saline</td>
</tr>
<tr>
<td>Storage</td>
<td></td>
</tr>
<tr>
<td>Before reconstitution</td>
<td>2.5 mL of diluent in 100 U vial. This implies 4 U/0.1 mL or any convenient concentration to deliver required units per injection site.</td>
</tr>
<tr>
<td>After reconstitution</td>
<td>2-8°C for up to 24 months</td>
</tr>
<tr>
<td>Handling</td>
<td>4 h at 2-8°C</td>
</tr>
<tr>
<td></td>
<td>Up to six weeks at 4°C (7)</td>
</tr>
<tr>
<td></td>
<td>Special precautions not required</td>
</tr>
</tbody>
</table>
7. After injection, patients are advised not to massage the treatment area.
8. They should be instructed to contract the injected area for approximately 90 minutes to two hours, which will help in the uptake of the toxin.
9. Patients may be asked to avoid bending for a few hours after treatment to avoid potential diffusion.

**RECONSTITUTION AND HANDLING**

Clostridium botulinum toxin type A (Botox®; Allergan) is supplied in vials containing 50 and 100 units of vacuum-dried neurotoxin complex.

**Key Considerations**

1. Injecting botulinum toxin type A reconstituted with isotonic preserved saline produces less patient discomfort than nonpreserved saline (Evidence level B). [3]
2. Avoid agitating the vial and foaming during reconstitution although some studies suggest they do not impact potency (Evidence level C). [4]
3. Dilutions may vary from 1-3 mL per 100 unit vial for cosmetic use though 2.5 mL appears to be the most common (Evidence level C). [5]
4. Greater the volume for a given number of units, the shorter the duration of effect and the higher the likelihood of diffusion to neighboring muscle groups (Evidence level C). [6]
5. Although the full prescribing information states that botulinum toxin type A should be used within four hours of reconstitution, clinical experience and recently published data suggest that potency can be maintained for up to six weeks with proper storage (Evidence level B). [7]

**PROTOCOL**

1. Follow all usual precautions of sterility and skin preparation before injection.
2. Seat the patient with chin down and head slightly lower than the physician’s.
3. Plastic single use insulin syringes with 30-32 gauge needles are recommended.
4. Topical anesthetics are generally reserved for the very sensitive. Ice could be used as a numbing agent.
5. Preoperative photography is mandatory.

**THE GLABELLAR COMPLEX AND VERTICAL FROWN LINES** (EVIDENCE LEVEL A)

<table>
<thead>
<tr>
<th>Target muscles</th>
<th>Usual number of injection points</th>
<th>Total starting dose (usual range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrugator, procerus depressor supercilii orbicularis oculi frontalis</td>
<td>3-7; men may require more sites</td>
<td>Women: 12-30 U Men: 16-40 U</td>
</tr>
</tbody>
</table>

**DOSAGE RECOMMENDATIONS FOR TREATING GLABELLAR FROWN LINES**

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Location</th>
<th>Origin/Insertion/Orientation</th>
<th>Primary function</th>
</tr>
</thead>
</table>
**Anatomy of the musculature constituting the Glabellar Complex**

**Key Considerations:**
1. Assess facial expression at rest and during animation.
2. Evaluate the range of motion of involved muscles.
3. Palpate muscles during repose and contraction.
5. Evaluate any asymmetries and assess potential effects of botulinum toxin type A injection.
6. Avoid injecting too low over the orbit.
7. Use caution with lateral brow injections; stay well above the superior orbital rim.
8. Recognize the variables that affect required dosage in individuals.
9. Begin with the recommended starting doses and add more units or additional sites if necessary at a two-week evaluation.
10. Do not completely paralyze the muscles.
11. Consider patient expectations in planning the overall effect.
12. Assess the need for treatment with other modalities such as soft tissue augmentation or surgical intervention.

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**Dosage Recommendations for treating horizontal forehead lines**

<table>
<thead>
<tr>
<th>Target muscle</th>
<th>Usual number of injection points</th>
<th>Total starting dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontalis, but consider interactions with procerus, corrugators, and orbicularis oculi in overall facial shape</td>
<td>4-8; more or fewer may be required based on anatomic and aesthetic evaluations</td>
<td>Women: 10-20 U Men: 12-24 U</td>
</tr>
</tbody>
</table>

---

**Dosage recommendations for treating Crow’s feet**

<table>
<thead>
<tr>
<th>Target muscle</th>
<th>Usual No. of Injection points (per side)</th>
<th>Total starting dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral portion of the lateral orbicularis</td>
<td>2-5 (higher in selected cases)</td>
<td>12-30 U divided on either side</td>
</tr>
</tbody>
</table>
The selected approach should be undertaken in the context of the pretreatment aesthetic evaluation.

7. Start with a low dose in the frontalis and avoid using a dose of botulinum toxin type A that will cause forehead immobilization. This may also facilitate a more uniform dissipation of effects to the upper face and accentuate facial harmony throughout the treatment period.

8. Distribute the injection points according to the observed animation and muscle function of the individual patient.

9. A ‘quizzical’ eyebrow shape can result from centralized injections.

10. Centrally focused injection can allow lateral brows to elevate.

CROW’S FEET\textsuperscript{[19-22]} (EVIDENCE LEVEL A)

Anatomy of the Orbicularis Oculi\textsuperscript{[2]}

Key Considerations
1. Ask the patient to animate to enable assessment of the line patterns of the dynamic eyebrow and cheek positions.
2. Treat crow’s feet around the lower third of the canthal area with caution.
3. Evaluate lid laxity with a snap test. Laxity indicates the potential for developing an ectropion, and lower injections may be avoided.
4. Exercise caution in patients who have undergone surgery.
5. Avoid, in most patients, the area below the zygomatic arch and the zygomaticus major muscle. Injection into this area has the potential to cause lip and cheek ptosis.
6. Start with low doses to avoid over-treatment and potential lid ptosis.
7. Asking patients to animate during injection can be helpful, especially in individuals with significant rhytides.
8. Avoid veins, whenever possible, in the lateral canthus; they may be revealed under appropriate lighting and magnification.
9. Proceed with caution when treating patients who have a history of dry eyes.
10. Keep injections superficial; use intradermal or subdermal blebs with the needle oriented away from the orbit.
11. Use ice to help avoid ecchymoses.

BUNNY LINES\textsuperscript{[2,23-24]} (EVIDENCE LEVEL C)

Anatomy of the Nasalis
Bunny lines result from contracting the transverse portion of the nasalis. This portion arises from the maxilla and runs diagonally across the bridge of the nose. It expands into a thin aponeurosis and is continuous with that of the muscle of the opposite side and with the aponeurosis of the procerus.

Key Considerations
1. Ensure that injections avoid the levator labii alaeque nasi and the levator labii superiors to prevent drooping of the upper lip.
2. Do not massage vigorously or in a downward direction, which could result in lip ptosis.
3. Consider including an injection of 1-2 U/side of the upper nasalis when treating the glabellar area to prevent recruitment.
4. Keep injections superficial in this vascularized area to avoid bruising.

PERIORAL WRINKLE LINES\textsuperscript{[2,23-24]} (EVIDENCE LEVEL C)

Key Considerations
1. Patient selection and counseling are critical. Those

Anatomy of the orbicularis oris and associated musculature

<table>
<thead>
<tr>
<th>Location</th>
<th>Origin/ insertion</th>
<th>Primary function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surrounds the orifice of the mouth</td>
<td>Buccinator/ forms deeper strata of orbicularis oris; caninus/ upper lip; depressor anguli oris (trianguli)/ lower lip; quadratus labii superiors, zygomaticus; quadratus labii inferiors; orbicularis oris is also connected to the maxillae and septum of the nose and mandible</td>
<td>Direct closure of the lips; applies lip to alveolar arch; brings lips together and protracts them forward; the depressor anguli oris depresses the angle of the mouth (to express sadness)</td>
</tr>
</tbody>
</table>

Dosage recommendations for treating bunny lines

<table>
<thead>
<tr>
<th>Target muscle</th>
<th>Usual number of injection points</th>
<th>Total starting dose (usual range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasalis</td>
<td>1 per side</td>
<td>2-5 U, divided evenly</td>
</tr>
<tr>
<td>Procerus (for transverse nasal)</td>
<td>1 in midline</td>
<td>1 U, if needed</td>
</tr>
</tbody>
</table>

Dosage recommendations for treating the perioral area

<table>
<thead>
<tr>
<th>Target muscle</th>
<th>Usual number of injection points</th>
<th>The total starting dose (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbicularis oris</td>
<td>2-6; to start: 4 sites, 1 site/lip quadrant</td>
<td>4-10 U, evenly divided among the sites</td>
</tr>
</tbody>
</table>
who rely on their lips in their professions (e.g., some musicians, singers, and public speakers) are not good candidates for botulinum toxin type A treatment. Patients may also have unrealistic expectations about the benefits of the treatment and should be counseled or not treated.

2. Treat conservatively with low doses at a minimum number of injection sites (1-2 sites per side of the upper lip); always inject symmetrically.
3. Avoid treating the corners of the lips, which could result in drooping and drooling.
4. Avoid the midline of the upper lip to avoid flattening the lip.
5. Avoid treating too distantly from the lip margin, i.e., not usually more than 5 mm above the vermilion border.
7. Injections in the lower lip area are more likely to affect function; treat conservatively, if at all.
8. Consider using botulinum toxin type A in conjunction with resurfacing procedures and fillers.
9. Use ice liberally to anesthetize the area as injections in the perioral area can be painful.

**DIMPLED CHIN (PEAU D’ORANGE)**

The dimpled appearance of the chin is the result of the actions of the mentalis muscle coupled with loss of collagen and subcutaneous fat in the chin.

**ANATOMY OF THE MENTALIS**

The mentalis originates from the mandible, covers the chin, and inserts into the skin below the lower lip. The mentalis raises the chin, which can cause wrinkles and dimpling and causes protrusion of the lower lip, which expresses sadness, anger, disdain or doubt.

**Dosage recommendations for treating dimpled chin**

<table>
<thead>
<tr>
<th>Target muscle</th>
<th>Usual Number of injection points</th>
<th>Total starting dose (usual range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mentalis</td>
<td>1-2 (start with 1 midline or 2 symmetrical, lateral injections)</td>
<td>Women: 2-6 U Men: 2-8 U</td>
</tr>
</tbody>
</table>

**Dosage recommendations for treating platysmal bands**

<table>
<thead>
<tr>
<th>Target muscle</th>
<th>Usual number of injection points</th>
<th>Total starting dose (usual range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platysma</td>
<td>Women: 2-12/ band Men: 3-12/ band</td>
<td>Women: 10-30 U Men: 10-40 U</td>
</tr>
</tbody>
</table>

**Key Considerations**

1. Some patients are unaware of their dimpled chin, which appears mainly on animation and can be demonstrated with a mirror.
2. Avoid injecting the toxin too high, which can affect the orbicularis oris and cause lower lip incompetence and possibly, drooling.
3. Care must be taken to avoid the depressor labii, which can cause the lower lip to depress.
4. Be aware that some individuals who present with a dimpled chin, may have hypertrophic mentalis muscles, which may be a sign of predisposition to oral incompetence. Do not treat with botulinum toxin type A if this is the case.

**PLATYSMAL BANDS**

**Anatomy:** The platysma, a broad, thin sheet of muscle, originates in the pectoral and deltoid fascia. It extends upward over the clavicle and inward along each side of the neck and under the skin near the mandible. Anterior fibers may interdigitate with fibers of the opposite side. The platysma depresses the lower jaw and pulls the lower lips and corners of the mouth sideways and down, partially opening the mouth. Banding occurs with aging and changes in the submental space.

**Key Considerations**

1. Select patients with care, as patient selection is critical. This procedure works best with younger patients with good skin elasticity or postoperatively for residual bands.

<table>
<thead>
<tr>
<th>Gummy smile</th>
<th>Target muscle</th>
<th>Usual Number of Injection Points</th>
<th>Total Starting Dose (usual range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levator labii superioris alaeque nasi</td>
<td>1 site/ side</td>
<td>2-4 U divided on either side</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marionette lines</th>
<th>Target muscle</th>
<th>Usual Number of Injection Points</th>
<th>Total Starting Dose (usual range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressor anguli oris</td>
<td>1 site / side</td>
<td>4-10 U divided on either side</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Massetetic Hypertrophy</th>
<th>Target muscle</th>
<th>Usual Number of Injection Points</th>
<th>Total Starting Dose (usual range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massetter</td>
<td>4-5 sites/ side</td>
<td>50-60 U divided on either side</td>
<td></td>
</tr>
</tbody>
</table>
2. Note that botulinum toxin type A injection in this area can also diminish horizontal (“neck-lace”) lines of the neck in selected patients.

3. Counsel patients about the variability of the results in the neck area so that they will have realistic expectations. Platysmal band injections do not substitute for surgical procedures and will not correct skin laxity and fat deposits.

4. Use caution to avoid dysphagia, dysphonia, and neck weakness; the strap muscles should be avoided. Grasping of the bands and direct injection and/or the use of electromyographic guidance should ensure a more accurate injection.

5. Inject multiple sites per band for the most satisfactory results.

**BOTULINUM TOXIN IN THE TREATMENT OF HYPERHIDROSIS[32-45] (EVIDENCE LEVEL A)**

Selective, focal chemodenervation may be achieved by injecting botulinum toxin intradermally to combat localized, but severe sweating in areas such as the palms, soles and axillae. Unlike sympathectomy, which renders > 20% of the body surface anhidrotic, thereby triggering compensatory sweating, treatment with botulinum toxin does not precipitate hyperhidrosis elsewhere as the total body surface area treated is < 3%.

The extent of excessive sweating can be documented by employing the simple starch-iodine test. This should be carried out prior to regional nerve blocks or the use of topical anesthetics. The test can also help determine the approximate amount of the drug needed.

**INJECTION TECHNIQUE**

The bevel should face upwards as the needle penetrates the skin almost parallel to it, and is then advanced for about 2 mm before injecting intradermally. The thumb is taken off the syringe plunger for a second or two before withdrawal. These measures help prevent backflow of botulinum toxin and its wastage. Avoid subcutaneous injections to prevent diffusion into intrinsic muscles of the palms and soles or beyond the targeted glands in the axillae.

**Key considerations**

**Palms and soles:**

1. Injections are placed about 1.5 cm apart. The total dose is dependent on the surface area and may range from 50-150 units per palm. Doses on the soles exceed those on the palms.

**Axillae:**

1. Injections are placed between 1.5 and 2.5 cm apart in 10-20 sites totaling approximately 50 units per axilla.

2. Tiny intradermal wheals are raised beginning at the periphery of the hair-bearing skin and circling into the center of the axillary vault.

3. Response times for duration of anhidrosis in the axillae range from 4-10 months.

**COMPLICATIONS WITH THE USE OF BOTULINUM TOXIN[2,6,46]**

The treatment of hyperfunctional dynamic facial creases with botulinum toxin type A is safe, effective and largely devoid of serious side effects. Properly carried out, the incidence of complications is low and their severity mild.

Sequelae that can occur at any site because of injection of botulinum toxin include pain, edema, erythema, ecchymosis, headache and short-term hypesthesia.

**GLABELLAR REGION**

The most common complication in the treatment of the glabellar complex is ptosis of the upper eyelid. Eyelid ptosis is a significant risk if injections are placed at or under the middle part between the eyebrows in the region of the midpupillary line. This is caused by diffusion of the toxin through the orbital septum, where it affects the upper eyelid levator muscle. This can occur as early as 48 hours or as late as 7-10 days following injection and can persist for 2-4 weeks. If ptosis occurs, it can be treated with alpha-adrenergic agonists, apraclonidine 0.5% and phenylephrine hydrochloride (2.5%) eyedrops. These mydriatic agents cause contraction of Muller’s muscle, thereby producing 1-2 mm elevation of the eyelid. The treatment is symptomatic and 1-2 drops three times a day must be continued until ptosis resolves.

**FOREHEAD**

The most significant complication of treatment of the frontalis is brow ptosis. This often results from overaggressive treatment with injections being placed too low on the...
forehead or from poor patient selection. Treatment of the brow depressors (glabellar complex) can elevate the brow from 1-2 mm. Be conservative while treating forehead expression lines.

**CROW’S FEET**

Complications in this area are bruising, diplopia, ectropion or a drooping lateral lower eyelid and an asymmetric smile caused by injection of the zygomaticus major. In this area, stay at least 1 cm outside the bony orbit and inject superficially. Do not inject close to the inferior margin of the zygoma to avoid lip ptosis.

**LOWER FACE AND NECK**

Many of the muscles in the lower central face, especially those used in facial expression, are also involved in the functions of the mouth and cheeks. An asymmetric smile, cheek bite or incompetence of the mouth manifesting as drooling or dribbling, are potential complications resulting from the use of botulinum toxin in the treatment of the complex musculature of the lower face. Platysmal injections in large doses to treat prominent vertical bands and horizontal neck lines, may cause weakness of the neck flexors and dysphagia.

**SUMMARY**

In a short span of time, Botulinum toxin has established its role in the nonsurgical management of ageing skin. Its use in a number of non-aesthetic indications has also been well documented. The technique is a safe, simple and effective modality when used by a properly trained physician. Proper knowledge of the anatomy and physiology of muscles, and proper patient selection are essential. Botox can also be combined with other aesthetic treatments such as fillers, micordermabrasion, peels, threadlifts and Laser resurfacing. As with all aesthetic techniques, proper patient counseling with respect to achievable results is important.

**REFERENCES**


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Appendix

Consent form for botulinum toxin injection

I ………………………..aged ………years and residing at …………………………………………………have requested that Dr. ……………………….. improve my facial expression lines with Botox. This is the trademark for purified botulinum toxin type A marketed by Allergan.

Although the results are usually dramatic, I have been informed that the practice of Medicine is not an exact science and that no guarantees can or have been made concerning expected results in my case. I understand that repeat treatments and dose titrations may be necessary as advised by the doctor to complete the treatment.

I am aware that when small amounts of purified Botox are injected into a muscle, it causes weakness of that muscle. This takes 4-6 days and usually lasts four months, but can be shorter or longer.

I understand that the muscles injected will not function while the injection is taking effect, but that this will reverse itself after a period of months at which time, retreatment is appropriate.
Shetty MK: Use of botulinum toxin Type A

Risks and side effects:
Botox treatment of facial expression lines can sometimes cause minor, temporary droop of an eyelid or eyebrow. This could last 2-3 weeks. Occasionally, slight swelling or bruising can occur and last for a few days.

Pregnancy and Neurologic disease:
I am not aware that I am pregnant and I do not have any significant neurological disease.
I have read the above details and understand them. I certify that I have had sufficient opportunity for discussion and to ask questions.

Patient…………………….............................................. Date…………........

Doctor…………………….............................................. Date…………........

Author Help: Reference checking facility

The manuscript system (www.journalonweb.com) allows the authors to check and verify the accuracy and style of references. The tool checks the references with PubMed as per a predefined style. Authors are encouraged to use this facility before submitting articles to the journal.

- The style as well as bibliographic elements should be 100% accurate to get the references verified from the system. A single spelling error or addition of issue number / month of publication will lead to error to verifying the reference.
- Example of a correct style
- Only the references from journals indexed in PubMed would be checked.
- Enter each reference in new line, without a serial number.
- Add up to a maximum 15 reference at time.
- If the reference is correct for its bibliographic elements and punctuations, it will be shown as CORRECT and a link to the correct article in PubMed will be given.
- If any of the bibliographic elements are missing, incorrect or extra (such as issue number), it will be shown as INCORRECT and link to possible articles in PubMed will be given.