Egypt, J. Plast. Reconstr. Surg., Vol. 27, No. 2, July: 333-339, 2003

Comparative Clinical Study Between "Botulinum A Toxin" and "Phenol" Injection in Treatment of Hyperfunctional Facial Lines

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ABSTRACT

Some wrinkles and unsightly facial expressions are due to over-activity of the underlying facial musculature. Botulinum A toxin (BTX-A) was proven to be safe and effective in management of these facial lines by reversibly paralyzing selected muscles. Phenol as a peeling agent was used topically to remove wrinkles. BTX-A and Phenol have been used to overcome spasticity, especially in the extremity and neck muscles. The aim of this study was to try phenol injection to treat hyperactive facial lines. Twelve patients have been enrolled in this study to compare the effect of either BTX-A or phenol injection on facial muscles. The preliminary results of phenol injection are promising, compared to that of BOX-A. It gave semi-permanent effects with minor complications.

INTRODUCTION

Excessively prominent facial lines are often cosmetically displeasing and sometimes misinterpreted as anger, fear, sadness, anxiety, etc.. **[1]**.

Botulinum A toxin (BTX-A) is a neurotoxin responsible for food poisoning (botulism). The clinical signs of botulism have been recognized since the 1700s and its association with a toxin produced by anaerobic bacterium had already been made by 1897 **[2]**. At first, the toxin had been used as a poison and its therapeutic use was made in the 1970s, in treatment of strabismus in primates **[3]**. This agent, BTX-A has been investigated in and applied to the treatment of wide range of muscular focal dystonic and spastic disorders and also in neurological disorders **[3-6]**.

During treatment of patients with blepharospasm, it was noted that glabellar frown lines would be improved by BTX-A injection **[7]**. It has since been used to treat hyperfunctional facial lines, which are the result of pull on the skin by underlying facial mimetic musculature **[1,7]**.

Phenol is a caustic agent that produces tissue destruction and has been used to weaken muscles in patients with local spasticity by either; percutaneous nerve block (neurolytic), or motor point block (intra-muscular neurolysis) **[8,9]**. It is currently used for the treatment of spasticity or topically as a "peeling" agent to remove wrinkles **[10]**. No article has mentioned the use of phenol in treatment of hyperfunctional facial lines.

The aim of this study was to try phenol injection in treating hyperfunctional facial lines an to compare its effect with that of "Botox" injection.

PATIENTS AND METHODS

Patients:

From January 1999, to January 2001, a total of 12 patients were included in this study. All were selected randomly, from those attending the Outpatient Clinic of Plastic Surgery Unit at El-Minia University Hospital. The inclusion criteria included demonstrable prominent facial lies at forehead, glabella and crow's feet, with

This work was presented in part at the annual meeting of the Egyptian Society of Plastic & Reconstructive Surgeons on March 2001, and has got the award for best research. It also was presented in the postgraduate course organized by the International Society of Aesthetic Surgery, held in Lebanon, on April 2001.

no ptosis in the medial brow and no history of prior injection of BTX-A. All patients have been evaluated as regard their general condition (ASA status I or II). Exclusion criteria included: pregnancy or lactation, hypersensitivity to human albumin or BTX-A. Patients with contraindications to BTX-A or phenol were not included in this study. Patients were told to discontinue salicylate, aminoglycosides, non-steroidal anti-inflammatory drugs, vitamin E, penicillamine, quinine and calcium channel blockers, at least four weeks before injection, as recommended by some authors [11]. An informed consent was obtained from each patient.

Materials:

Botox (Botulinum A toxin) was obtained from "Allergan Botox Ltd Wesport, Co", Mayo, Ireland. It was kept freeze dried and frozen at -5ºC to -20ºC until ready for use. Each vial contained 100 units of toxin. It was diluted just prior to use with 1-2 ml of normal saline without preservative. Each 0.1 ml of the solution, therefore, contained 5-10 units respectively and should be used within several hours of preparation. Total dose for glabella or crow's feet was 5-15 U and for frontalis muscle was 10-20 U, divided into 2.5-5 U aliquots, representing 0.1-0.2 ml per injection site. Total dose per session for each person did not exceed 50 U. Special precautions for handling used syringes and vials were done to guard against cross-contamination.

Phenol solution was prepared by the author and brought from Department of Chemistry, Faculty of Science (1% weight/volume USP phenol crystals in sterile aqueous solution). Three concentrations were used (3%, 4% and 5%). Injection of 0.4 ml to 0.6 ml at each site was done accounting for a dose of 12.8-19.26 mg of 3% concentration, 17.12-25.68 mg of 4% solution and 21.40-32.10 mg of 5% solution.

Method:

Out of the 12 patients, six (5 females and one male) were injected with Botox and six (3 males and 3 females) were injected with phenol. Prior to injection, all patients were assessed as regards their wrinkles with grading of its severity using a scale of 0 to 3 (Table 1). These assessments were made both in repose and during animation [1].

Table (1): Scale of wrinkles severity at rest or function [1].

0	No	Facial wrinkles
1	Mild	Facial wrinkles
2	Moderate	Facial wrinkles
3	Severe	Facial wrinkles

Pre-injection photographs were taken during the hyperfunctional and relaxed state. Also, post-injection photographs were taken at 2,4,8 and 12 weeks. All photographs were standardized using the same camera, operator, lens system, flash system, films and distance. Patients were treated in the 45º supine position or seated position. The area to be injected was cleaned with an alcohol swab at least 5 minutes before injection. Local anesthetic cream was not used. Sites injected included facial lines in forehead, glabella and crow's feet.

The EMG technique for injection was not used. The needle of the tuberculin syringe was placed tangentially through the skin overlying or adjacent to the facial line and into the hyperfunctional muscle. Before placement of the needle, the patient was asked to accentuate the specific facial expression. Areas near major vessels or nerves were avoided. After the needle was aspirated to assure that no blood vessels have been punctured, the material was injected. The total dose depended on the concentration and the effect desired. Follow-up assessment to determine the duration of block was done at baseline and at weeks 2,4,8 and 12.

The overall response to injection was analyzed by objective and subjective criteria. Objective analysis included cutaneous appearance (smooth-no furrow visible, minimal line, residual but improved line, or no response). Subjective analysis was done by rating patient satisfaction (excellent, good, fair, or disappointed). The results were not subjected to statistical analysis because of the small number of patients.

RESULTS

We had 12 patients, four males and eight females. Their age ranged from 26 to 60 years, with an average age of 40.9 years. The results are statistically insignificant due to the small number of patients and are shown in Table (2).

Table (2): Demographic data.

	Sex		
	Female	Male	Total
Patients injected with Botox	5	1	6
Patients injected with Phenol	3	3	6
Total	8	4	12

The group that was injected with Botox consisted of 6 patients (5 females and one male), their age ranged from 32 to 60 years, with mean age of 43.83±9.81 years. The response started within 7-10 days and was complete within 2 weeks. The median longevity of response was about 14 weeks (range 10-21 weeks). Dose and concentration did not influence duration of response.

Three patients needed second injection within five months of the first injection, 2 patients needed that injection after 3 months, while one patient (a male) needed a second injection within 6 months. Frequent touchup injections were needed (2-3), especially for crow's feet.

As regards complications of this group, one patient (female) had a transient brow ptosis with complete recovery after 2 weeks. Another patient (female) had minimal headache that was gone after few hours of injection. We had three patients with excellent results, 2 patients commented that these were good results and one patient did not respond at all to injections and was totally unsatisfied.

The patients who received phenol injections were six (3 males and 3 females). Their age ranged from 26 to 48 years, with mean age of 38.0±7.24 years. After the first three months period of follow-up had passed, one patient was lost. Three of the other 5 patients who had multiple injections needed a second injection within 6 months of the first. The other two patients needed the second injection within 8 months. The facial lines were improved at rest, but the change was most obvious when the patient is asked to accentuate their expressions (Figs. 3 & 4). The subsequent injections were after interval of 8-10 months.

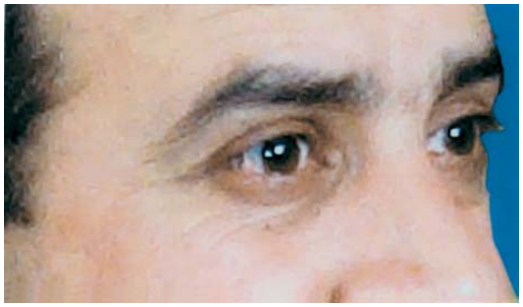
Usually, within 3-4 weeks, the lines of facial expression were softened and it was impossible for the patient to flex the treated muscle. There was severe stitchy pain during injection in 3 patients, while in the other 3, it was mild. It was quite helpful to balance an unopposed muscle resulting from facial palsy in one patient. The active muscle was injected and facial balance returns within 2 weeks (Fig. 2). Younger individuals (usually females) responded extremely well especially for crow's feet (Fig. 5).

Complications after injection were infrequent. Two patients had headache or "tightness" immediately following injection that was gone in the next day. One patient had numbness at the injection site that resolved after a few days and did not recur after subsequent injections. Another patient got occasional bruising around site of injection that resolved subsequently.

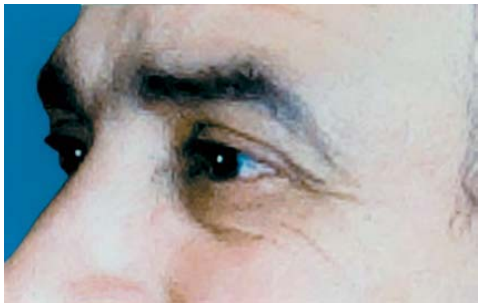
As regards the overall results, two patients were totally satisfied with their results, another 2 patients felt that they had a response that was just over half as good as they felt it would be (Fig. 3) and one patient thought that she did not get a good enough response (Fig. 6).

DISCUSSION

Excessively prominent facial lines are often cosmetically displeasing and sometimes misinterpreted and indicate socially less acceptable emotions as anger, fear, fatigue, sadness, anxiety, pain, or it may be associated with aging [**1**]. It is important to differentiate between rhytids created by loss of collagen or elastic fibers within the dermis causing laxity of the skin (age-induced), wrinkles caused by volumetric loss of fat, redundant folds caused by gravitational pull and those caused by hyperfunctional facial muscles, which are the result of tension and pull of the underlying mimetic facial musculature that cause a pleating of the overlying skin [**12**]. In general, facial rhytids have a myriad of remedies, but these methods do not address the underlying problems [**11-13**]. There is a high incidence of recurrence after myectomy either direct or endoscopically. Filler agents offer only a partial, short-term solution. Rhytidectomy may have unsightly scars [**7**].



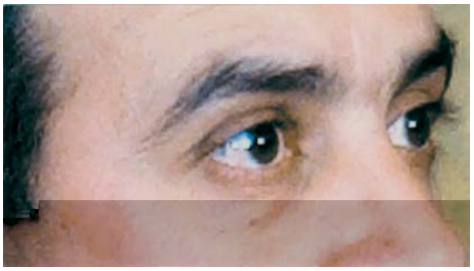
(A)



(B)

Fig. (1-A & B): Forty five-year-old male squinting to demonstrate prominent crow's feet.

(C)



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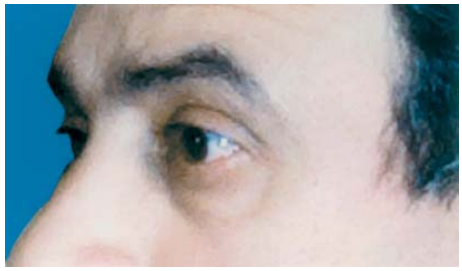


Fig. (1-C & D): The patient squinting 2 weeks after phenol injection. Note marked reduction in crow's feet.

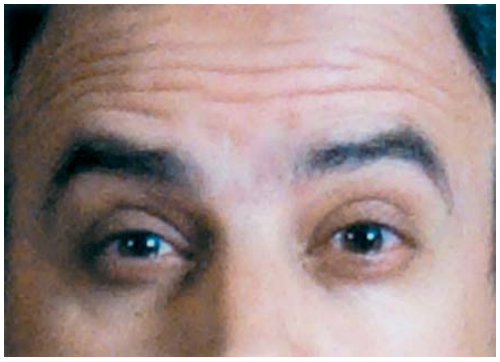


Fig. (2-A): The same patient in Fig. (1) with forehead creases before injection of phenol.

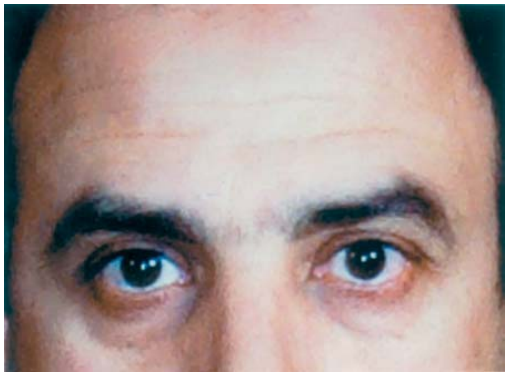


Fig. (2-B): 3 weeks after phenol injection, the patient is unable to produce the forehead lines due to frontalis muscle weakness.

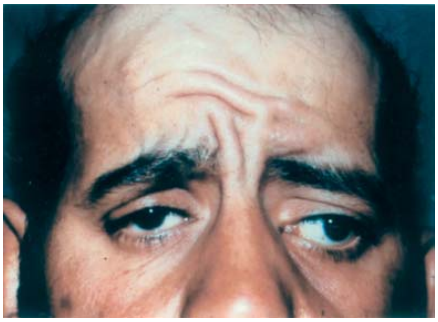


Fig. (3-A): Before phenol injection, during active contraction.

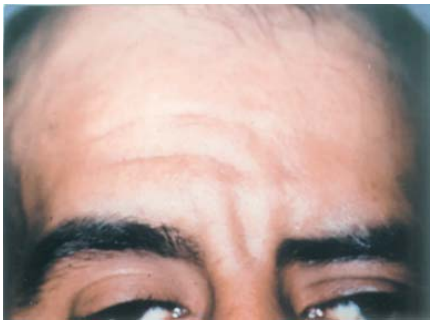


Fig. (3-B): After injection of phenol, during active contraction with almost balanced facial expression and brows.

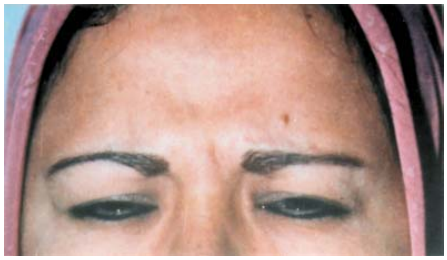


Fig. (4:A): Deep hyperfunctional lines that are formed by active contraction of the corrigator muscle before injection.

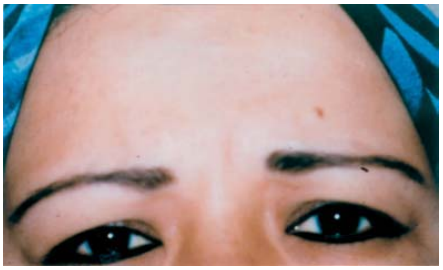


Fig. (4:B): 3 weeks after phenol injection, patient is unable to form any frown lines with attempts at active motion.

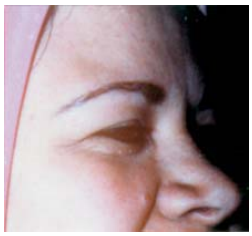


Fig. (5:A)

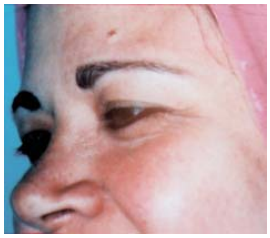


Fig. (5:B)

Fig. (5-A & B): Same patient in Fig. (4) with marked crow's feet before injection.

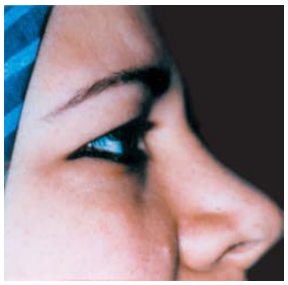


Fig. (5:C)

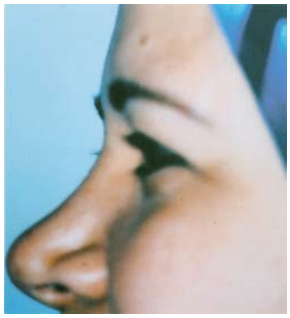
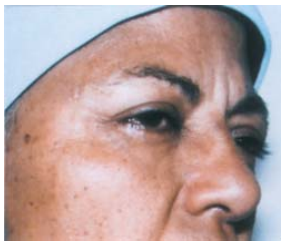
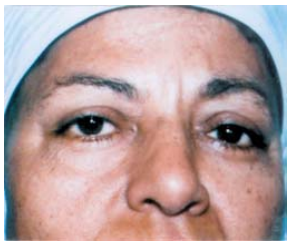


Fig. (5:D)

Fig. (5-C & D): Marked improvement 3 weeks after injection of phenol.



(A)



(B)

Fig. (6: A & B)
Fifty year-old female with prominent crow's feet, before injection.

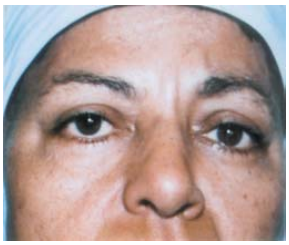


Fig. (6:C)
Same patient with mild improvement after phenol injection.

Several studies showed that BTX-A was effective as a treatment for hyperactive facial lines, when injected into selected muscles particularly in the upper face (forehead, peri-ocular and peri-nasal areas) [7,11,14]. Its clinical effect is due to rapid and strong binding of the toxin to the cholinergic neuromuscular junctions. Muscle function returns to normal after about 4 to 6 months [14,15]. This effect has found widespread application in the treatment of dystonias, hypertonicity, spasticity and spasm in a variety of skeletal and smooth muscles [16,17]. In addition, other cholinergic processes such as parasympathetic innervation of sweat glands, can be specifically blocked locally in cases of hyperhidrosis [18]. Recently, there is an increasing array of medical uses for BTX-A [6,17-20].

We found Botox, aside from being expensive, has several advantages; it can be used during a routine office visit, with minimal discomfort. It is safe and effective with low incidence of complications. It was reported that some patients developed resistance to the toxin [13]. In this study, there was one patient who did not respond at all to Botox injection.

Phenol is a caustic agent that produces tissue destruction. Earlier, it was used as a local anesthetic and disinfectant. Its current therapeutic application is to weaken muscles in patients with local spasticity by either; percutaneous nerve block (neurolytic), or motor point block (intramuscular neurolysis). This action is exerted through two mechanisms: a short-term anesthetic effect and a long-term axonal degeneration from protein denaturation causing denervation of spastic muscles [8,9]. It also has been used as a "peeling agent" topically in treatment of wrinkles [10].

Unlike BTX-A, phenol may be used in both motor point locations and along the larger nerve bundle. In experienced hands, it affords relief for more than a year and does not induce a systemic resistance, although it is more technically demanding [9]. Most of the articles concerning the treatment of spasticity have ignored the superior properties of phenol for long-term treatment [8-10]. There was only a case report of using phenol for intra-muscular neurolysis for managing severe facial muscle spasticity in a post-anoxic encephalopathic patient. To the best of our knowledge, nothing appeared in the literature on its use for management of hyperfunctional facial lines [21].

Applications of phenol, either as intramuscular neurolysis or topically as a peeling agent to remove wrinkles, both have been associated with the occurrence of cardiac arrhythmias, including ventricular tachycardia. These arrhythmias may result from a specific block of cardiac sodium channels. The duration of phenol-induced arrhythmias is shortened by administration of diuretics, suggesting a rapidly reversible action rather than destruction of cardiac tissue [22]. There were no such complications in this study. Another side effect, which was transitory, is the mild erythema and tenderness over the injected site [9]. It was observed that all the patients suffered from burning sensation during injection. Some numbness persists at the site of injection for some time with some bruises.

Although there is considerable concern about the irreversible toxic effects of concentrated solutions of phenol on nerves (6%-10%) [22] a concentration of 3-5% would not be expected to have toxic effects, specially in the manner in which it was injected in this study (small volume). The dose ranged from 12-32 mg per injected site with a total dose per session ranging from 100-150 mg, which was far away from the toxic dose (8-15 gm) [23].

It is a relatively safe, cheap and simple procedure that can offer the patient semi-permanent results, but it is more technically demanding [6]. The use of phenol as intra-muscular neurolysis for managing hyperfunctional facial lines appears to be the first documented cases of such an application. A more documentation and follow-up are warranted to define optimal doses and volumes and establish standard injection guidelines.

Conclusion:

In the logical sequence of managing hyperactive facial wrinkles, phenol block represents a relatively safe, cheap and simple procedure that can offer the patient semi-permanent results. If this promising response is confirmed in a larger series of patients, phenol injection may prove to be an effective treatment for some patients with hyperfunctional facial wrinkles. It also, might be a good alternative to BTX-A in this aspect.

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