Original Article

Efficacy of EMLA Cream in Pain Reduction during Botulinum Toxin Injections for Facial Dystonias

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Purpose: To determine the efficacy of EMLA cream (Eutectic Mixture of Local Anesthetics) in pain reduction while injecting botulinum toxin in patients with hemifacial spasm and blepharospasm.

Study Design: Quasi Experimental Study.

Place & Duration of Study: Yaqin Vision Eye center from January 2015 to December, 2018.

Material & Methods: Patients undergoing routine treatment of Blepharospasm and Hemifacial spasm since 2010 were offered pre-injection EMLA cream application to reduce the pain during injections. A total of 74 Botulinum A toxin injections were given for blepharospam and hemifacial spasm, half of which were administered without the use of any topical analgesia while other half were given to same patient on next visit using EMLA cream 15 minutes prior to injection. Pain was assessed as mild, moderate and severe in all the patients by the consultant administering the medication.

Results: Among 37 cases of facial dystonias, 17 (45.9%) were males and 20 (54.1%) were females. It was observed that when EMLA was not used, severe pain was observed during 8 injections (21.6%), moderate pain in 17 (45.9%), and mild pain in 12 (32.4%) sessions. However when EMLA was used mild pain was observed during 33 (89.2%) injections, moderate pain in 3 injections and severe pain in 1 (2.7%) case. There was a statistically significant difference in pain control during the sessions involving use of EMLA.

Conclusion: Use of topical EMLA cream dramatically reduces the pain and makes the administration of botulinum toxin A injection easier in patients with hemifacial spasm and blepharospasm.

Keywords: Topical anesthetia, Blepharospasm, Hemifacial spasm, Botulinum Toxin.

Facial dystonias is a disease which causes significant disability to the patient as it progresses over time. The time tested and most reliable therapy for hemifacial and blepharospasm is repeated botulinum toxin (Botox, Allergan) injection given subcutaneously. It is also very effective in the reduction of deep creases and wrinkles formed by weakening of the facial muscles with age[1]. The treatment requires injection of botulinum toxin just beneath the skin so that it can diffuse to the targeted facial muscles. Although the injection is given with a 30 gauge needle the patients can feel varying degree of pain and anxiety while receiving this treatment in the very sensitive periocular region[2]. An effective alternate method to avoid this pain and discomfort is by using eutectic mixture of local anaesthetics.

EMLA cream is available as an emulsion which is a eutectic mixture containing 2.5% prilocaine and 2.5% lidocaine established to numb the skin surface. Both the drugs which anesthetise the skin have been mixed in such a way that the cream does not melt at room temperature and the ingredients are present as liquid oil instead of crystals. Indications of EMLA cream include topical pain relief for needle pricks, especially in children, and minor surgery involving superficial skin. The depth of anaesthesia is proportional to the duration of application of the cream on the skin. Skin is anesthetised 1-2 mm after 60 minutes of application while after 3-4 hours the depth of anaesthesia increases to 6 mm[3,4].

For minor surgical procedures involving needle insertion the recommended concentration of EMLA cream is the most effective and safe agent which can anesthetise the skin[5] (including blood testing, intravenous cannulation, lumbar puncture and botulinum A toxin injections). It is also very useful for minor procedures used in dermatology such as removal of warts, biopsy of skin and laser treatment[6]. Adequate anaesthesia of skin is attained after the cream has been applied for 1 hour. It reaches its peak in 2-3 hours and remains present for 1-2 hours after the cream has been removed.

The rationale of our study was to find an effective drug to relieve pain in patients receiving Botulinum toxin injections for the treatment of facial dystonias. Review of literature shows studies on this topic but no local literature was found. The purpose of the study was to determine the usefulness of EMLA cream (Eutectic Mixture of Local Anesthetics) in pain reduction while injecting botulinum toxin in patients with hemifacial spasm and blepharospasm.

MATERIAL & METHODS

The study was conducted at Yaqin Vision Center, Lahore from Jan 2015 to Dec 2018 as a Quasi experimental study. Ethical Approval of the study was taken from the Ethical review committee of Lahore General Hospital, Lahore. Patients included in the study were > 25 years of age of both genders who presented with hemifacial spasm and essential blepharospasm. Only those patients were selected who had already undergone botulinum toxin A injection (Botox, Allergan) without use of EMLA cream previously, as it was not readily available before. Patients who were excluded from the study had blepharospasm due to secondary reasons such as drugs, ophthalmic and neurological conditions. Intracranial pathology was ruled out in all patients before start of treatment using Computed tomography or Magnetic resonance imaging.

Patients undergoing routine treatment of Blepharospasm and Hemifacial spasm since 2010 were offered pre-injection EMLA cream application to reduce the pain during injections. The sample size (n) was calculated by 95% confidence level, with anticipated population proportion (P) 74% and keeping absolute precision (d) 10%. A total of 74 Botulinum A toxin injections were given for routine treatment of blepharospam and hemifacial spasm, half of which were administered without the use of any topical analgesia while other half were offered EMLA cream treatment prior to injection. The cream was applied for 15 minutes before the procedure. Each Botox injection was carefully administrated in the area where EMLA cream was applied. We used Botulinum Toxin-A 100 Units (Botox, Allergan) diluted in 2 ml normal saline. The injections were given using a 1 ml insulin syringe, with a 30G needle (microlance 30G × ¾ 0.4 × 19 mm).

Pain was assessed as mild, moderate and severe without and later with EMLA cream application by the consultant administering the medication. Pain grading was modified from the Visual Analog Scale which is a reliable tool used worldwide[7].

Data entry and analysis was done using SPSS Statistics for Windows package, version 25.0 (IBM, USA). Categorical variables such as pain scoring was analysed using the chi square test. The study reported on the effects of EMLA with regard to the mean difference in pain between the group that received EMLA for Botox injection and the control group with no intervention previously.

RESULTS

Among 37 cases of facial dystonias, 17 (45.9%) were males and 20 (54.1%) were females with a male to female ratio of 1:1.8 (Table 1).

Table 1: Comparison of gender distribution between groups.

Gender	Use of EMLA		Total
	Not Used	Used	
Male	17 45.9%	17 45.9%	34 45.9%

Female	20 54.1%	20 54.1%	40 54.1%
Total	37 100.0%	37 100.0%	74 100.0%

Categorizing the patients into three age groups revealed that majority of the patients 81.1% (60 patients) were above 45 years of age (Table 2).

Table 2: Comparison of age groups distribution between groups.

Age Groups	Use of EMLA		Total
	Not Used	Used	
19-30 years	4 10.8%	4 10.8%	8 10.8%
31-45 years	3 8.1%	3 8.1%	6 8.1%
>45 years	30 81.1%	30 81.1%	60 81.1%
Total	37 100.0%	37 100.0%	74 100.0%

Blepharospasm was present in 46 patients (62.2 %) and 28 patients (37.8%) were diagnosed with Hemifacial spasm (Table-3).

Table 3: Comparison of diagnosis between groups.

Diagnosis	Use of EMLA		Total
	Not Used	Used	
Blepharospasm	23 62.2%	23 62.2%	46 62.2%
Hemifacial Spasm	14 37.8%	14 37.8%	28 37.8%
Total	37 100.0%	37 100.0%	74 100.0%

Patients were categorized in three groups according to pain: mild pain, moderate pain and severe pain. It was seen that in patients in which EMLA was not used, 21.6% (8 patients) had severe pain, 45.9% (17) had moderate pain, and 32.4% (12) had mild pain. However EMLA cream was used 89.2% (33) patients had mild pain, 8.1% (3 patients) had moderate pain and only 2.7% (only 1 patient) had severe pain. (Table 4). This demonstrates a significant reduction in pain during the procedure with use of topical EMLA cream (Figure 1).

Table 4: Comparison of pain scale between groups.

Pain Scale	Use of EMLA		Total	p-value
	Not Used	Used		
Mild Pain	12 32.4%	33 89.2%	45 60.8%	0.000004
Moderate Pain	17 45.9%	3 8.1%	20 27.0%	
Severe Pain	8 21.6%	1 2.7%	9 12.2%	
Total	37 100.0%	37 100.0%	74 100.0%	

*A small **p-value** (typically ≤ 0.05) indicates strongest evidence of results being significant.

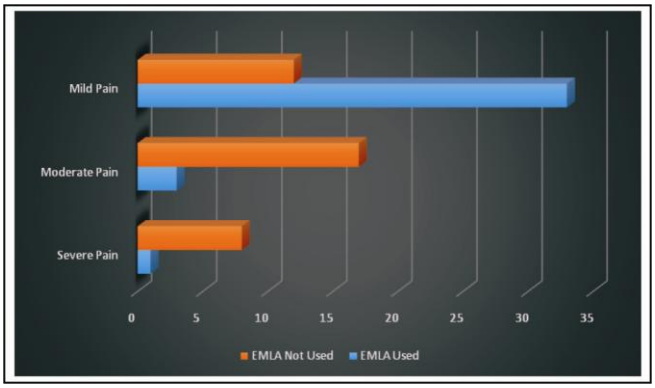

Fig. 1: Comparison of pain with and without the use of EMLA cream.

The effectiveness of the Botox injections among these patients was also noted on follow up by categorizing them into 3 groups: No effect, Fair effect and Good effect. It was seen that there was no significant difference in results and effectiveness of Botulinum toxin A injections on facial dystonias among patients with EMLA, and without use of topical EMLA cream (Table 5).

Table 5: Comparison of effect of Botox on spasm.

Effect of Botox on Spasm	Use of EMLA		Total	p-value
	Not Used	Used		
No Effect	5 13.5%	5 13.5%	10 13.5%	0.356
Fair Effect of Botox	2 5.4%	0 0.0%	2 2.7%	
Good effect of Botox	30 81.1%	32 86.5%	62 83.8%	
Total	37 100.0%	37 100.0%	74 100.0%	

DISCUSSION

Topical anaesthetics are commonly used for routine minor procedures like subcutaneous injections, intravenous cannulisation, catheterization and removal of superficial skin lesions. EMLA has been shown to be tolerated well by the patients. In our study no patients experienced any side effect. Small sample size and experienced injector could be the reason for this. EMLA cream has not been found to show any toxicity except in infants. Local side effects which have been reported by other physicians include contact dermatitis, erythema, oedema and increased pigmentation of the skin[8]. One case report has shown that respiratory depression and seizures can occur**.** The worst complication reported was Methaemoglobinaemia which can be potentially fatal but only infants develop this condition[9,10].

Soylev MF et al**[11]** demonstrated that percutaneous anaesthesia produced by using EMLA cream is quite adequate and it is a safe technique to enhance the patient comfort when repeated botulinum toxin injections are required for facial dyskinesia**.** Applying a dot of EMLA cream is easy, convenient, and inexpensive way of anesthetizing the site of injection.

Many other methods of lowering pain in Botox injections are suggested. Using a small gauge needle as demonstrated by Flynn TC et al[12], is an obviously a preferred intervention, combined with a minimal number of pricks, also helps ensure proper management of discomfort. Using an isotonic mixing solution (preservative-containing saline solution) for reconstitution of the drug and reducing the temperature of the skin with the use of various cooling techniques (eg, ice, aerosol sprays) have also been reported to reduce injection discomfort in a study done by Alam M et al[13]. Same results were obtained by Linder JS et al[14], by using various skin cooling techniques. However, Kuwahara RT et al[15] reported that cold sponging with ice, is inconvenient and the pain control it affords is only partially effective. Essential blepharospasm is an involuntary spasm of eyelid muscles affecting patients in fifth and sixth decade of life and predominantly affect females than male with 3:1[16]. Hemifacial spasm is a neuromuscular movement disorder characterized by brief or persistent involuntary contractions of the muscles innervated by the facial nerve**[17]**. Botox injections are effective treatment for both these facial dystonias i.e. for blepharospasm as shown by Hellman A et al[18] in a recent study, and also for hemifacial spasm as demonstrated by Singh S et al[19] with a success rate of 95%. Botulinum A toxin inhibits cholinergic transmission at neuromuscular synapses and relaxes muscles. Clinical effects are usually observed after 2–5 days and last for 16–24 weeks as reported by Basaret al**[20]**. The pain during this procedure can be measured by a standardized system or scale, like Visual Analogue Scale (VAS), that we modified for reliable measurement of pain and its relief[21].

In our study, we applied Botulinum toxin A (Botox) injections in 74 eyes, among 34 (45.9%) males and 40 (54.1%) females. Among these patients 46 (62.2%) presented with blepharospasm and 28 (37.8%) had hemifacial spasm.

We grouped the patients according to pain suffered, into three categories: mild pain, moderate pain and severe pain. It was seen that in 89.2% (33) patients in which EMLA was used had only mild pain, 8.1% (3 patients) had moderate pain and 2.7% (only 1 patient) had severe pain. However, among the patients in which EMLA was not used, 21.6% (8 patients) had severe pain, 45.9% (17 patients) had moderate pain, and 32.4% (12 patients) had mild pain. All these results clearly indicated that topical EMLA cream can be used as an effective tool in management of pain among patients having Botox injections for their facial dystonia treatments. Similar results were seen in a comprehensive study done on anaesthetic effectiveness of EMLA cream during Botulinum A injections in eyelids by Soylev MF et al**[11]**. Another recent study by Elibol Oet al[22] reported that EMLA applications significantly decrease the pain associated with periocular botulinum toxin injections. It also demonstrated that patients had a slight preference for EMLA cream over skin cooling for pain relief. In a study done by Barry L. Eppley, MD**[23]** on twenty patients, receiving 200 Botox injections in the glabellar area, it was seen that patients experienced a 60% reduction in pain in EMLA pre-treated sites compared with that in matched control sites. Similar dose of botulinum toxin can usually be repeated to get stable results of the injection[24]. The use of EMLA, however, did not have any significant effect on efficacy of botulinum injection in relieving the spasm itself, apart from reduction in pain.

The limitation of our study was the limited number of patients in our study. Moreover it was also performed at a single centre. A multi-centre study is needed to find the efficacy in large sample of population.

CONCLUSION

Use of EMLA cream can dramatically reduce pain, make administration of botulinum toxin A injection easier in patients with blepharospasm and hemifacial spasm. This can improve the therapeutic relationship of the patients with health professionals.

Disclosure

The authors have no financial benefit or conflicts of interest in this work.

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