

## Review Article

### **Botulinum Toxin: A Peek at a Wonder Drug for Dentistry**

Anand Farias<sup>1</sup>, Sushma R<sup>2\*</sup>, Dr. Manoj Varma<sup>3</sup>

<sup>1</sup>Associate Professor, <sup>2</sup>Assistant Professor, <sup>3</sup>Dean, Prof and HoD Department of Prosthodontics, Srinivas Institute of Dental Sciences, Srinivas Integrated Campus, Mukka, Mangalore, India

#### **\*Corresponding author**

Dr. Sushma R

Email: [anandffarias@gmail.com](mailto:anandffarias@gmail.com)

---

**Abstract:** Botulinum toxin for therapeutic use has been available in India since 1994. The general perception of this “wonder drug” in the field is that its role is limited to esthetic and cosmetic enhancements. This review is an attempt to bring to light the true medical and specifically dental benefits of this deadly neurotoxin as a minimally invasive treatment option. Continuing research worldwide and the isolation of newer strains of *Cl. Botulinum* could place this once deadly neurotoxin in a key position for an even wider application of use in both medical and dental conditions in the near future.

**Keywords:** Botox; Bruxism; Esthetics; Dystonia; Temporomandibular Joint Disorders.

---

#### **INTRODUCTION**

The Botulinum toxin is a neurotoxin produced by the bacterium *Clostridium botulinum*. It is the most potent naturally occurring toxin known, with as little as 30–100 ng being potentially fatal. Consumption of just a few milligrams of neurotoxin-containing food is likely to be sufficient to cause illness and potential death. It is responsible for botulism, a severe neuromuscular disease that affects humans, animals, and birds [1,2]. *Cl. botulinum* is responsible for foodborne botulism, infant botulism, and wound botulism, adult infectious botulism and inadvertent botulism following botulinum toxin injection [3]. *Cl. botulinum* produces heat resistant endospores that are commonly found in soil and allow for survival in adverse conditions.

*Clostridium botulinum* was first recognized and isolated in 1895 by Emile van Ermengem following an incident of severe neuromuscular illness that included three fatalities among 34 musicians in Belgium that year. He named the organism *Bacillus Botulinus* [4,5]. Justinus Kerner described botulinum toxin as a “sausage poison” and “fatty poison”, because the bacterium caused poisoning by growing in improperly handled or prepared meat products [6,7,8]. Ida A. Bengtson placed the organism into the genus *Clostridium* [9].

Since the second half of the 20<sup>th</sup> century research has been conducted into the use of botulinum toxins for clinical therapy [10,11,12].

#### **Classification and Mechanism of Action of Botulinum Neurotoxin**

Present day *Cl. Botulinum* are evolved forms of the organism isolated by van Ermengem (13). *Cl. Botulinum* is classified into four phenotypes (I to IV). Botulinum neurotoxin production (BoNT) is the unifying characteristic of the phenotypes. There are eight types of BoNT. The most recent was described in January 2014. [14,15,16].

Structurally the BoNT is a non-covalently bound complex with two or more protein complexes which include haemagglutinating proteins as well as a non-toxic non-haemagglutinating proteins. The non-toxic proteins enhance the toxin potency and stabilize the BoNT in the gastrointestinal tract.

The neurotoxin acts by preventing acetylcholine (ACh) release in the target muscles causing clinically visible muscle paralysis. Out of eight known BoNT serotypes, types A, B, E, F and H have been documented to cause Botulism in humans [13,15,16,17]. BoNT A has been shown to have the highest rate of mortality in humans [1,2,18].

#### **Silver Linings - Clinical Applications of the Botulinum Toxin**

Genetic sequencing of *Cl. Botulinum* and extensive studies on the BoNT have allowed its use in controlled doses to treat a variety of disorders utilizing the ability of the BoNT to produce muscle relaxation when administered in *Controlled Titrated Doses*. Table-1 presents a summary of disorders where administration

of BoNT has been shown to have clinically successful results. [19,20,21,22,23,24,25,26].

Commercially only two serotypes of BoNT are used in the treatment of medical and dental conditions – BoNT/A (Onabotulinumtoxin A, Abobotulinumtoxin A and Incobotulinumtoxin A) and a BoNT/B (Rimabotulinumtoxin B) [14, 27, 28, 29, 30, 31]. The formulations are prepared using different processes which determined by different biological assays based on their clinical use. The potency of a single unit varies greatly among the commercial types. (Table II)

Therapeutic BoNT doses have to be adjusted according to multiple factors such as severity of the hyperactive muscle, number of muscles involved, age, and previous response to BoNT therapy. The duration of BoNT effect is variable depending upon the type of neurotoxin, dose, site of injections, and clinical applications. In the disease state, BoNT A has a longer paralysis than BoNT B; likewise, formulations of BoNT/A have shown to have a longer duration of action than BoNT/B formulations in muscle dystonia [32,33]. Both however have a similar duration of action when used in treating sialorrhea secondary to neurological diseases [34].

#### **Facial Esthetics**

The general public's view of the use of "Botox®" is for correction and enhancement of esthetics. In terms of micro- (dental) esthetics, the use of BoNT/A finds its place in the correction of gummy smiles[35]. lip augmentation [36]. and reduction of facial wrinkles contributing to an overall improvement in a macro-esthetic treatment plan[37,38]. Correction of these conditions is brought about by a temporary paralysis of a specific muscle or muscles caused by the action of BoNT.

Gummy smiles due to hyper-functional upper lip elevator muscles when paralyzed by the BoNT/A, fall inward and downwards, reducing the amount of gingival display changing the smile type [39]. Results are generally noticeable in 2 weeks and last up to 3 to 6 months.

Only those facial wrinkles which are due to muscle contractions can be treated by BoNT therapy. Wrinkles due to degenerative processes are not treatable by BoNT therapy. Noticeable improvement is seen within 1 to 3 days after injection with maximum improvement seen in 1 to 2 weeks. Repeat injects may be carried out at this period during a review and the effects can last up to 8-12 weeks.

Complications following injection of botulinum neurotoxin for esthetic purposes are well documented and can range from bruising to severe life threatening conditions if not administered correctly[40,41].

#### **In the Management of Sialorrhoea**

BoNT/A has been successfully used in the treatment of hypersalivation *secondary* to neurological and otolaryngologic conditions such as in infant cerebral palsy, Parkinson's disease and amyotrophic lateral sclerosis, and oral cancers. Complications documented are dysphagia, xerostomia and chewing difficulties[22,42,43,44,45].

#### **In the Management of Temporomandibular Disorders (TMD), Oro-Facial Pain and Oromandibular Dystonias**

Non-Surgical management of TMD, oro-facial pain and oromandibular dystonias using BoNT has shown promising results due to its muscle relaxing properties [46,47]. BoNT/A therapy primarily targets the muscles of mastication. It is administered at multiple sites of the affected muscles depending on the amount of muscle tenderness and pain reported by the patient to achieve the desired clinical results [48].

Good outcome has been cited for the treatment of habitual dislocation of the TM-Joint secondary to neurological diseases with BoNT/A. Single doses have been shown to be satisfactory in treating the dislocations [49,50,51]. It has also been hypothesized that BoNT/A may be useful in preventing trauma induced TMJ ankylosis. Injection of BoNT/A into the lateral pterygoid muscle causes temporary immobilization of the TMJ and thus prevents the traumatic TMJ ankylosis [52].

Parafunctional habits of the jaws associated with muscle hypertrophy can be treated with BoNT/A injections [53,54]. Bruxism has been associated with neurological disorders and dystonias[55,56]. Single dose injections of BoNT/A have been reported to completely abolish severe bruxism behaviors. It is thought that jaw muscle paralysis induced by BoNT/A disrupts the feedback loop from the trigeminal motor nucleus and inhibits the central bruxism generator or may deactivate periodontal mechanoreceptors during mastication, which may have a facilitatory effect on jaw closure motoneurons[57].

#### **BoNT in the treatment of Tetanus**

Reports in literature show that Botulinum neurotoxin may be useful in treating Tetanus, if administered into the masseter and temporalis muscles early in the course of the disease to reduce the risk of pulmonary aspiration, involuntary tongue biting, anorexia allowing for dental care. [58].

Tetanus is caused by the toxin released by *Clostridium Tetani*. The tetanus toxin moves trans-synaptically into inhibitory nerve terminals, where vesicular release of inhibitory neurotransmitters becomes blocked, leading to disinhibition of lower motor neurons resulting in characteristic symptoms of the disease - muscle rigidity and spasms.

Botulinum toxins enter nerve terminals of lower motor neurons where toxins attack synaptic vesicle proteins differentially. Compared to tetanus toxin, the botulinum toxins undergo less axonal and trans-synaptic transport. Therefore, the effects of botulinum toxins remain fairly confined to the nerve terminals of lower motor neurons, inhibiting release of acetylcholine and activation of voluntary muscles[59,60,61]. This may be the reason why BoNT could have a role in reducing the muscular hyperactivity in Tetanus.

Administration into the trapezius, splenius capitis, levator scapulae and sternocleidomastoid muscles, which are also involved in tetanus should be avoided due to proximity to vital structures such as the carotid artery, during injection of the toxin and also to avoid possible spread of the BoNT effects to the larynx [58].

### **In Maxillo-facial Surgery**

Correction of maxillofacial trauma usually requires multiple fixation sites and hardware to overcome strong forces of masticatory musculature. The muscular relaxation achieved with BoNT A injections to the masticatory muscles may be beneficial by allowing ease in operating and healing following fixation[62].

### **Contra-Indications and Complications of Botulinum Toxin Therapy**

Currently available Botulinum Toxin formulations are safe and effective. Cited complications associated with the use these formulations are minor such as pain at the injection site, flu-like symptoms, non-targeted muscle weakness. Dysphagia and hematomas may occur though rare [37,63]. The adverse events associated with chronic, periodic exposure to BoNT type A or B injections are generally minor and self-limiting, and even decrease over time [64].

### **Are Dentists Allowed to Administer Botulinum Toxin as Part of Dental Therapy?**

Different dental councils world over have varied policies regarding whether licensed dental surgeons should be allowed to administer botulinum toxin as part of dental therapy. The American Dental Association poses a neutral stand on the issue. Individual state councils in the USA have their own policies. Some states in the USA allow board certified oral and maxillofacial surgeons to practice BoNT therapy as training is included in their curriculum. General dentists and other specialists are allowed to practice only after completing accredited training programs and obtaining board certification[65,66].

Administration of BoNT for cosmetic procedures in settings other than a certified medical center is not allowed [67].

In India, there are currently no regulations regarding the use and administration of Therapeutic Botulinum Neurotoxin by dentists.

**Table -1: Conditions for which treatment with botulinum toxin may be used [19-26]**

- I. Cosmetic Applications
  - a. Muscular facial lines
  - b. Facial asymmetries
- II. Dystonias
  - a. Bruxism
  - b. Oromandibular Dystonia (OMD)
  - c. Cervical Dystonia (CD)
  - d. Cranio-cervical Dystonia
  - e. Focal Hand Dystonia (FHD)
  - f. Hemifacial spasm
  - g. Tremors
  - h. Tics
  - i. Re-innervation Synkinesias
  - j. Myokymia
  - k. Neuromytonia
  - l. Stiff Person Syndrome
- III. Spasticity and Muscle Disorders
  - a. Masseteric hypertrophy
  - b. Mandibular spasm
  - c. Chronic low back pain
- IV. Hypersecretory Disorders
  - a. Sialorrhea
  - b. Hyperhidrosis
  - c. Hyper-lacrimation
  - d. Rhinorrhea
- V. Ophthalmic disorders

- a. Strabismus, Nystagmus
  - b. Exotropia, esotropia, entropium
  - c. Protective ptosis
  - d. Blepharospasm
- VI. Pain
- a. Temporomandibular Disorders (TMD)
  - b. Myofacial pain and neckpain
  - c. Trigeminal neuralgia
  - d. Tension headache
  - e. Migraine
- VII. Pelvic floor and Gastrointestinal disorders
- a. Achalasia
  - b. Anal fissures
  - c. Detrusor-Sphincter Dyssynergia
  - d. Vesicle sphincter spasm
  - e. Sphincter Odii spasm
  - f. Anismus
  - g. Vaginismus
- VIII. Lower urinary tract disorders
- IX. Miscellaneous
- a. Wound healing and diabetic neuropathy
  - b. Eyelid opening
  - c. Tetanus
  - d. Stuttering
  - e. Perioperative fixations in orthopedic surgeries.
  - f. Facial Trauma and Reconstructive surgery
  - g. Non-Surgical Correction Gummy Smiles

**Table-2: Commercially Available Botulinum Toxin Formulations**

Contents	Trade Name	Manufacturer	Presentation		Available in India
			Form	Packing	
Clostridium Botulinum Type A	BOTOX® (Onabotulinumtoxin A)	Allergan India Private Ltd.	Powder for Injection	50 IU x 1's 100 IU x 1's	Yes
	NEURONOX® (Onabotulinumtoxin A)	Ranbaxy Laboratories Ltd.	Powder for Injection	100 IU x 1's	Yes
	DYSPORT® (Abobotulinumtoxin A)	Ipsen Biopharm Ltd.	Powder for Injection	300 IU x 1's 500 IU x 1's	No
	XEOMIN® (Incobotulinumtoxin A)	Merz Pharma GmbH & Co KGaA	Powder for Injection	50 IU x 1's 100 IU x 1's	No
Clostridium Botulinum Type B	MYOBLOC® (Rimabotulinumtoxin B)	Solstice Neurosciences	Powder for Injection	2,500 Units/0.5 mL 5,000	No
	NEUROBLOC® (Rimabotulinumtoxin B)	Eisai Europe Ltd.	Powder for Injection	Units/1 mL 10,000 Units/2 mL	

**CONCLUSION**

Botulinum toxin therapy is a safe and promising option for patients suffering from a variety of dental conditions and esthetic concerns. It is a minimally invasive option that will ease operative procedures, enhance patient satisfaction and treatment results. Minimal post-operative complications occur provided basic procedural guidelines are followed – individualized doses to the patients based on muscle size, pain and activity, injecting the toxin into

established tender muscle points, using the smallest needle size possible, use of adjunctive topical local anesthesia and monitoring of EMG activity during further associated procedures.

The isolation of newer strains of *Cl. Botulinum* and continuing research worldwide could place this once deadly neurotoxin in a key position for an even wider application in both medicine and dentistry. Current costs of the drug restrict its use to a minority of

the patients who would benefit from its therapeutic advantages. A need for research and production of the drug in India is paramount if it has to be made viable for therapeutic use in our country.

## REFERENCES

1. Peck MW; Biology and Genomic Analysis of *Clostridium botulinum*. *Adv Microb Physiol*, 2009; 55:183-265.
2. Peck MW, Stringer SC, Carter AT; *Clostridium botulinum* in the post-genomic era. *Food Microbiol*, 2011; 28(2):183-91.
3. Nantel AJ; *Clostridium Botulinum* - International Programme on Chemical Safety Poisons Information – Monograph 858. WHO; 1999.
4. Van Ermengem E; Übereinenneuenanaeroben *Bacillus* und seine Beziehungen zum Botulismus. *Zentralbl. Hyg. Infektionskr*, 1987; 26(1): 1-56.
5. Van Ermengem E; Classics in infectious diseases. A new anaerobic bacillus and its relation to botulism. E. van Ermengem. Originally published as "Uebereinenneuenanaeroben *Bacillus* und seine Beziehungen zum Botulismus" in *Zeitschrift für Hygiene und Infektionskrankheit. Rev Infect Dis.*, 1979; 1(4):701-19.
6. Kerner J; Neue Beobachtungen über die in Württemberg so häufig vorfallende tödliche Vergiftung durch den Genuss geräucherter Würste. Tübingen. Osiander, 1820.
7. Kerner J; Das Fettgift oder die Fettsäure und ihre Wirkungen auf den thierischen Organismus, ein Beitrag zur Untersuchung des in verdorbenen Wurstengiftig wirkenden Stoffes. Stuttgart Cotta, 1822.
8. Erbguth FJ; Historical notes on botulism, *Clostridium botulinum*, botulinum toxin, and the idea of the therapeutic use of the toxin. *Mov Disord*. 2004; 19(Suppl 8):S2-6
9. Bengtson IA; Studies on organisms concerned as causative factors in botulism. *Hygiene Laboratory Bulletin* 136. Washington DC: US Public Health Service, 1924.
10. Dressler D; Pharmakologische Aspekte therapeutischer Botulinum-Toxin-Präparationen. *Der Nervenarzt*, 2006; 77(8): 912-21
11. Pasricha PJ, Ravich WJ, Kalloo AN; Botulinum toxin for achalasia. *The Lancet*. 1993; 341(8839):244-45
12. Bushara KO, Park DM; Botulinum Toxin and Sweating. *J Neurol Neurosurg Psychiatry*. 1994; 57(11): 1437–1438.
13. Collins MD, East AK; Phylogeny and taxonomy of the food-borne pathogen *Clostridium botulinum* and its neurotoxins. *J Appl Microbiol*. 1998; 84(1):5-17
14. Chen ZP, Morris JG, Rodriguez RL, Shukla AW, Tapia-Nunez J, Okun MS; Emerging opportunites for serotypes of Botulinum Neurotoxins. *Toxins*, 2012; 4(11): 1196-1222.
15. Dover N, Barash JR, Hill KK, Xie G, Arnon SS; Molecular characterization of a novel botulinum neurotoxin type H gene. *J Infect Dis.*, 2014; 209(2):192-202.
16. Barash JR, Arnon SS. A novel strain of *Clostridium botulinum* that produces type B and type H botulinum toxins. *J Infect Dis.*, 2014; 209(2):183-91.
17. Shapiro RL, Hatheway C, Swerdlow DL; Botulism in the United States: A clinical and epidemiologic review, 1998, 129(3): 221-228.
18. Schantz EJ, Sugiyama H; Toxic proteins produced by *Clostridium botulinum*. *J. Agric. Food Chem.*, 1974, 22 (1), 26–30.
19. Dressler D, Saberi FA, Barbosa ER; Botulinum toxin: Mechanisms of Action. *Arq Neuropsiquiatr*. 2005; 63(1):180-5.
20. Ramirez-Castaneda J, Jankovic J; Long-Term Efficacy and Safety of Botulinum Toxin Injections in Dystonia. *Toxins (Basel)*. 2013; 5(2):249-66.
21. Rao LB, Sangur R, Pradeep S; Application of Botulinum Toxin Type A: An Arsenal in Dentistry. *Indian J Dent Res*. 2011; 22(3):440-5.
22. Fuster Torres MA, Berini Aytés L, Gay Escoda C; Salivary gland application of botulinum toxin for the treatment of sialorrhea. *Med Oral Patol Oral Cir Bucal*, 2007; 12(7): 511-7.
23. Chen S; Clinical uses of botulinum neurotoxins: current indications, limitations and future developments. *Toxins (Basel)*, 2012; 4(10): 913-39.
24. Schwartz M, Freund B; Treatment of temporomandibular disorders with botulinum toxin. *Clin J Pain*, 200; 18(6 Suppl):198-203.
25. Freitag FG; Botulinum toxin type A in chronic migraine. *Expert Rev Neurother*, 2007; 7(5):463-70
26. van Zandijcke M, Marchau MM; Treatment of bruxism with botulinum. *J Neurol Neurosurg Psychiatry*, 1990; 53(6):530.
27. Hasler WL; The expanding spectrum of clinical uses for botulinum toxin: Healing of chronic anal fissures. *Gastroenterology*, 1999; 116(1):221-3.
28. Dykstra DD, Sidi AA; Treatment of detrusor-sphincter dyssynergia with botulinum A toxin: A double-blind study. *Arch Phys Med Rehabil*, 1990; 71(1):24-6
29. Snow BJ, Tsui JK, Bhatt MH, Varelas M, Hashimoto SA, Calne DB; Treatment of spasticity with botulinum toxin: a double-blind study. *Ann Neurol*, 1990; 28(4):512-5.
30. Brashear A; Clinical comparisons of botulinum neurotoxin formulations. *Neurologist*, 2008; 14(5):289-98.
31. Lew MF; Botulinum toxin type B (Myobloc, NeuroBloc): A new choice in cervical dystonia. *Expert Rev Neurother*, 2001; 1(2):143-52.
32. Keller JE; Recovery from botulinum neurotoxin poisoning in vivo. *Neuroscience*, 2006; 139(2): 629-37.

33. Comella CL, Jankovic J, Shannon KM, Tsui J, Swenson M, Leurgans S, Fan W; Dystonia Study Group. Comparison of botulinum toxin serotypes A and B for the treatment of cervical dystonia. *Neurology*, 2005; 65(9):1423-9.
34. Guidubaldi A, Fasano A, Ialongo T, Piano C, Pompili M, Mascianà R, Siciliani L, Sabatelli M, Bentivoglio AR; Botulinum toxin A versus B in sialorrhea: a prospective, randomized, double-blind, crossover pilot study in patients with amyotrophic lateral sclerosis or Parkinson's disease. *MovDisord*. 2011; 26(2):313-9.
35. Polo M; Botulinum toxin type A (Botox) for the neuromuscular correction of excessive gingival display on smiling (gummy smile). *Am J Orthod Dentofacial Orthop*, 2008; 133(2):195-203.
36. Moragas JSM, Verduyze HJ, Mommaerts MY; "Non-filling" procedures for lip augmentation: A systematic review of contemporary techniques and their outcomes. *J Craniomaxillofac Surg*. 2014; 42(6):943-52.
37. Dastoor SF, Misch CE, Wang HL; Botulinum Toxin (Botox) to enhance facial macroaesthetics: a literature review. *J Oral Implantol*, 2007; 33(3):164-71
38. Huijing MA, van der Palen J, van der Lei B; The effect of upper eyelid blepharoplasty on eyebrow position. *J Plast Reconstr Aesthet Surg*, 2014; 67(9):1242-7.
39. Philips E; The classification of smiles. *J Can Dent Assoc*. 1999; 65(5):252-4.
40. Gadhia K, Walmsley AD; Facial aesthetics: is botulinum toxin treatment effective and safe? A systematic review of randomised controlled trials. *Br Dent J*, 2009; 207(5):216-7.
41. Chertow DS, Tan ET, Maslanka SE, Schulte J, Bresnitz EA, Weisman RS, Bernstein J, Marcus SM, Kumar S, Malecki J, Sobel J, Braden CR; Botulism in 4 Adults Following Cosmetic Injections With an Unlicensed, Highly Concentrated Botulinum Preparation. *JAMA*, 2006; 296(20):2476-9.
42. Corradino B, Di Lorenzo S, Moschella F; Botulinum Toxin A for Oral Cavity Cancer Patients: In Microsurgical Patients BTX Injections in Major Salivary Glands Temporarily Reduce Salivary Production and the Risk of Local Complications Related to Saliva Stagnation. *Toxins (Basel)*, 2012; 4(11):956-61.
43. Ellies M, Laskawi R, Tormahlen G, Gotz W; The Effect of Local Injection of Botulinum Toxin A on the Parotid Gland of the Rat: An Immunohistochemical and Morphometric Study. *J Oral Maxillofac Surg*, 2000; 58(11):1251-6.
44. Banerjee KJ, Glasson C, O'Flaherty SJ; Parotid and submandibular botulinum toxin A injections for sialorrhoea in children with cerebral palsy. *Dev Med Child Neurol*, 2006; 48(11):883-7.
45. Tighe D, Gok G, Moody A, Howlett D; Dysphagia as a complication of botulinum toxin injection to treat drooling. *Br J Oral Maxillofac Surg*, 2014; 52(7): 673-4.
46. Maestre-Ferrín L, Burguera JA, Peñarrocha-Diago M, Peñarrocha-Diago M; Oromandibular dystonia: A dental approach. *Med Oral Patol Oral Cir Bucal*, 2010; 15(1):25-7.
47. Møller E, Werdelin LM, Bakke M, Dalager T, Prytz S, Regeur L; Treatment of perioral dystonia with botulinum toxin in 4 cases of Meige's syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 2003; 96(5):544-9.
48. Song PC, Schwartz J, Blitzer A; The emerging role of botulinum toxin in the treatment of temporomandibular disorders. *Oral Dis.*, 2007; 13(3):253-60
49. Fu KY, Chen HM, Sun ZP, Zhang ZK, Ma XC; Long-term efficacy of botulinum toxin type A for the treatment of habitual dislocation of the temporomandibular joint. *Br J Oral Maxillofac Surg*, 2010; 48(4):281-4.
50. Moore AP, Wood GD; Medical treatment of recurrent temporomandibular joint dislocation using botulinum toxin A. *Br Dent J*, 1997; 183:415-7.
51. Ziegler CM, Haag C, Mühling J; Treatment of recurrent temporomandibular joint dislocation with intramuscular botulinum toxin injection. *Clin Oral Investig*, 2003; 7(1):52-5.
52. Dai J, Yu H, Zhu M, Shen SG; Injection of botulinum toxin A in lateral pterygoid muscle as a novel method for prevention of traumatic temporomandibular joint ankylosis. *Journal of Medical Hypotheses and Ideas*, 2014; 9: 5-8
53. Baş B, Özan B, Muğlalı M, Çelebi N; Treatment of masseteric hypertrophy with botulinum toxin: A report of two cases. *Med Oral Patol Oral Cir Bucal*, 2010; 15(4):49-52
54. Castro WH, Gomez RS, da Silva Oliveira J, Moura MDG, Gomez RS; Botulinum Toxin Type A in the Management of Masseter Muscle Hypertrophy. *J Oral Maxillofac Surg*, 2005; 63(1):20-4.
55. Watts MW, Tan EK, Jankovic J; Bruxism and cranial-cervical dystonia: is there a relationship? *Cranio*, 1999; 17(3):196-201.
56. Tintner R, Jankovic J; Botulinum toxin type A in the management of oromandibular dystonia and bruxism. In: Brin MF, Hallett M, Jankovic J, editors. *Scientific and therapeutic aspects of botulinum toxin*. Philadelphia: Lippincott Williams & Wilkins, 2002 :343-50
57. Tan EK, Jankovic J; Treating severe bruxism with botulinum toxin. *J Am Dent Assoc*, 2000; 131(2):211-6
58. Hassel B; Tetanus: Pathophysiology, Treatment, and the Possibility of using Botulinum Toxin against Tetanus-Induced Rigidity and Spasms. *Toxins (Basel)*, 2013; 5(1):73-83.
59. Schiavo G, Matteoli M, Montecucco C; Neurotoxins affecting neuroexocytosis. *Physiol Rev*. 2000; 80(2):717-66.

60. Antonucci F, Rossi C, Gianfranceschi L, Rossetto O, Caleo M; Long-distance retrograde effects of botulinum neurotoxin A. *J Neurosci*, 2008; 28(14):3689-96.
61. Matak I, Bach-Rojecky L, Filipović B, Lacković Z; Behavioral and immunohistochemical evidence for central antinociceptive activity of botulinum toxin A. *Neuroscience*, 2011; 186:201-7.
62. Kayıkçıoğlu A, Erk Y, Mavili E, Vargel I, Özgür F; Botulinum toxin in the treatment of zygomatic fractures. *Plast Reconstr Surg*, 2003; 111(1):341-6.
63. Blumenfeld A; Botulinum toxin type A in the treatment of Dental conditions. *Inside Dentistry*, 2007;3(6).
64. Colosimo C, Tiple D, Berardelli A; Efficacy and safety of long-term botulinum toxin treatment in craniocervical dystonia: A systematic review. *Neurotox Res.*, 2012; 22(4):265-73.
65. Benninger B, Ross A; Should Dentists be Allowed to Administer Botulinum Toxin? *Dentistry*, 2012; 2(5): 135,
66. Commonwealth of Massachusetts. Policy Advisory on the Use of Botulinum Toxins Adopted by the Board of Registration in Dentistry, March 6, 2013. Certification, Licensure & Registration, Health and Human Services; 2013.
67. Fletcher V; Beauticians and hairdressers to be banned from giving Botox jabs in bid to cut botched procedures. Mail Online [newspaper on the internet], 2013, March 31 [cited 2014, October 17]. Available from <http://www.dailymail.co.uk/news/article-2301761/Beauticians-hairdressers-banned-giving-Botox-jabs-bid-cut-botched-procedures.html>