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ROLE OF BOTULINUM TOXIN TYPE A IN DENTAL IMPLANTOLOGY: A REVIEW.

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ABSTRACT

Immediate loading of implant has become a hot topic in implant dentistry. It shortens the treatment time and makes it possible to provide the patient with an aesthetic reconstruction during the whole treatment period. The clinical role of Botulinum toxin as a therapeutic agent is expanding. Botulinum toxin is a neurotoxic protein produced by the bacterium Clostridium Botulinum. It is one of the most poisonous naturally occurring substances in the world. Though it is highly toxic, it is used in minute doses both to treat dental conditions and as a cosmetic treatment. This article reviews the prophylactic and therapeutic role of Botulinum toxin A in immediate loading of dental implant therapy.

***KEY WORDS*: Botulinum Toxin A, immediate loading implant, Osseo-integration.**

INTRODUCTION

The clinical role of Botulinum toxin as a therapeutic agent is expanding.[1] Increasing functional and aesthetic challenges have prompted implantologist to reduce the treatment period by loading the implant immediately at the time of placement. The immediate loading of dental implant clearly represents the change in dogma, therefore to achieve this goal, the stress-free healing period had to be considered as an absolute prerequisite to achieve osseointegration.[2] Controlling functional forces has been suggested as one of the ingredients for obtaining success with immediate implant loading.[1] Our purpose of this article is to review the prophylactic and therapeutic role of Botulinum toxin A in immediate loading of dental implant therapy.

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Botulinum Toxin (BTX) is a natural protein. It is produced by the gram negative anaerobic bacterium *clostridium Botulinum*. It is harvested form a culture medium after fermentation of a toxin-producing strain of C. Botulinum, which lyses and liberates the toxin into the culture. The toxin is then extracted, precipitated, purified, and finally crystallized with ammonium sulfate. Administration of the toxin results in a reduction of tone in the integrated muscle. The toxin inhibits the release of acetylcholine. There are seven serotypes of BTX (A, B, C, D, E, F, and G) [3] where, BTX-A is the most potent and commonly used in dental conditions.[4]

BTX-A produces partial chemical denervation of the muscle resulting in localised reduction in muscle activity. Injections are made by adding 4 ml of 0.9% normal saline solution without preservative and preparation should be used within four hours. The Potency of BTX is expressed as mouse units equivalent to the median lethal dose (LD 50) for mice, and each 0.1 ml contains 2.5 U of BTX-A. It is dispensed in small vials containing 100 U or 500 U. The lethal dose of Botox in humans in not known. Although is has been estimated to be about 3000 U, the usual maximum total recommended dose at an injection session in the dental office is about 80-100 U. It is marketed worldwide under the name Botox (Allergan inc, Irvine, CA, USA.) [Figure 1] and in Europe as Dysport (Speywood Pharmaceuticals Ltd, Maidenhead, UK).[3] Botox has been approved by the US Food and Drug Administration (FDA) for the treatment of strabismus, blepharospasm,[5] focal spasms including hemifacial spasm,[6] cosmetically for the facial glabellar lines,[7] and more recently for the treatment of cervical dystonia and axillary hyperhydrosis.[8]

BTX is synthesized as a large single-chain peptide. Activation requires a two-step modification in the tertiary structure of the protein. This process converts the single-chain neurotoxin to a di-chain neurotoxin comprising a 100,000-Da heavy chain (HC) linked by a sulfide bond to a 50,000-Da light

chain (LC). BTX acts at the neuromuscular junction where it exerts its effect by inhibiting the release of ACH from the presynaptic nerve terminal[3]

Role of Botulinum Toxin-A in dental implants:

Jaw volume, bone quality, and overload are the three major determinants for late implant failures.[9] Since Osseo-integration represents a dynamic process both during its establishment and its maintenance, implants initially well integrated may occasionally show unexpected mobility when the bone/implant/restoration system is in actual function. This mobility can be the result of increasing muscular forces or a changing occlusal situation after an unexpected repositioning of the temporomandibular joints. If the mobility is not the result of infection, the implant may be treated and protected without an invasive removal procedure.[1]

If implants are placed in bone areas where tensile forces dominate,[10] these forces may enhance bone resorption by creating unfavorable conditions for implant integration, especially if the implant it not yet firmly integrated (e.g., immediate load conditions). To avoid detachment of the bony interface from the implant and overload in areas that have been subject to minor loads preoperatively, the prophylactic reduction of masticatory forces through the use of Botulinum toxin therapy appears to be a sensible therapeutic adjunct.[1]

There are alternative treatment strategies to decrease the loads on the bony interface, such as the use of interceptors, splint therapies, and TENS devices.[1] Interceptors and splints tend to change the location and the time pattern of increased masticatory forces, whereas TENS devices provide relaxation for a very limited time period but these strategies do not provide enough protection against deleterious involuntary nocturnal mandibular excursions or nocturnal changes in the mandibular position. Therefore, prophylactic administration of Botulinum toxin close to the time of implantation for immediately loaded implants has been reported to control functional forces. Even therapeutic administration of Botulinum toxin in patients exhibiting instability after implant placement for the purpose of preserving an implant/restoration system unrelated to infection has also been reported.

The use of Botulinum Toxin has become routine practice both prophylactically and therapeutically when basal (lateral) implants are used. When cases with extreme bone atrophy are treated with this implant therapy, long prosthetical cantilevers are often required to establish correct restoration of the vertical dimension. These cantilevers may in addition increase the risk of overload. Comprehensive insertion of implants and immediately loaded restorations can change all parameters of masticatory function; the newly created occlusal surfaces will be included in the masticatory process and the vertical dimension is often changed. This results in considerable changes in the patterns of muscular function, which in turn influences the morphology of the jawbone and thus the relative position of the dental arches. Most patients are able to position and move their dental arches congruently during the day. During phases in which voluntary control is absent (i.e., during the night), the jaws may approximate in positions that greatly deviate from their daytime positions. If this happens, balance is lost. Muscular dynamics during the patient's sleep are unique and differ from those during voluntary clenching exerting a greater mechanical load on the temporomandibular joint on the balancing side[11]

The prophylactic administration of Botulinum toxin may reduce the risk of damage being exerted to the bony interface by gradual or sudden changes in mandibular position on the interface of immediately loaded implants. Especially in early phases of the implant therapy, such forces may mobilize the implants. The extent and sequence of these changes cannot be predicted, which is why the inserted restorations must be monitored and adjusted at regular intervals. Even more unpredictable are the morphological changes which can have a variety of effects in the implanted jawbone. Changes in the integrated implants and thus the functional surfaces of the restorations will passively follow. In addition to masticatory force and masticatory function, age, hormonal status and genetic dispositions as well as habits and other factors will play a role in determining the nature and extent of this changes.[12-15] Collectively, these changes often exceed the extent of what dentists know and expect from their daily experience with tooth-supported restorations.

The bilateral medication of the masseter muscles (without treating the temporalis muscles) will generally suffice to achieve satisfactory results both prophylactically and therapeutically; however, no studies have been conducted to support this

clinical anecdote. In cases of severe preoperative atrophy, the surgeon may want to medicate both muscles. Administered a full dose of 200-250 U for each masseter muscle in order to provide an adequate reduction of chewing forces for up to eight weeks, These recommendations are based on the principles of bone physiology and healing, clinical experience and its application in other maxillofacial conditions.[1]

It is necessary to address premature contacts and unilateral loading at the outset of Botulinum toxin therapy to ensure the stabilization of the bone/implant system will be a lasting success. However, it is conceivable, in principle, that this medication can be used as an adjunct in treatment concepts including either root-form implants or a combination of root-form and lateral implants. To establish the scientific safety and efficacy of Botulinum toxin use in dental implantology, more studies need to be published on this topic.

Future Direction

A focus on discovering the appropriate doses for therapeutic and prophylactic indications while considering the bone physiology for increasing the chances of successful integration in immediate load protocols for root-form dental implants would be useful.

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Limitation of Botulinum Toxin A

Relative contraindications to the use of BTX are pregnancy and lactation, neuromuscular disease (myasthenia gravis, Eaton-Lambert syndrome), motor neuron disease [3] and concurrent use of amino glycosides. Botulinum toxin therapy is not indicated in cases where the heavily remodeled intrabony overload areas have become infected.[1]

One might be concerned that though the therapeutic approach using Botulinum toxin will inhibit masticatory function temporarily, the masticatory forces will eventually return to previous levels once the effect of the drug has subsided, once again exercising their potential deleterious functions. However, a permanent reduction of masticatory forces is not the therapeutic goal. Rather, the objective is to create a more favorable load situation during a phase of higher elasticity in the region of the bony interface for a limited time to allow the bone to remineralize and the implant to reintegrate in the bony interface region.

If sufficient bone is available in the upper jaw to allow the placement of eight or more implants (with a diameter of 10 mm or more), the need for Botulinum toxin therapy is less imminent.[1]

CONCLUSION

In particular, patients with reduced bone supply as well as patients suspected of delivering high masticatory forces present special challenges to the implantologist. Prophylactic administration of Botulinum toxin may facilitate a reduction of the strength of the masseter and temporalis muscles after implantation, especially with immediate load.

Bone/implant/restoration systems can become mobile due to overload on the peri-implant bone during the treatment phase. Botulinum toxin can reduce the indirect influence of the masticatory load on the bone/implant interface which may in turn protect the Osseo -integration process.

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