The primary mechanism of action of botulinum toxin type A (BoNT-A) is on the vesicle release containing acetyl choline at the neuromuscular synapse. This action of BoNT-A causing muscle relaxation has been used extensively in the cosmetic area to relax muscles causing facial lines and therapeutically in hyper-contraction of muscles causing conditions such as distonias, bruxing and clenching.

Although there are numerous articles documenting the primary mechanism of action of BoNT-A, and its therapeutic use in hyper-muscular contraction, the current literature is extremely scarce with respect to the secondary and tertiary mechanisms of action of BoNT-A and its therapeutic use on pain and the CNS.

This paper presents the results and conclusions of two different research papers on the topic of stress, anxiety and depression: The first paper is a current concept consensus report on the research concluding that stress and depression can cause or exacerbate periodontal disease.

The second paper concludes that BoNT-A placed in the glabella decreases negative mood and depression.

Treatments directed at decreasing stress, anxiety and depression can improve periodontal conditions.

Hypothesis: The Glabella placement of BoNT-A in individuals with periodontal conditions, caused or influenced by stress, anxiety and/or depression can improve the condition of the periodontium.

Background

Numerous practitioners have realized the benefits of treatment with Botulinum Toxin type A (BoNT-A) and have incorporated it into their treatment plans. Others have a mistaken preconception that it is only a cosmetic procedure. This article is intended to bring awareness to the use of BoNT-A into the broad treatment regime for our patients.
Historically the first commercial use of BoNT-A was not for cosmetic purposes. Dr. Scott in the 1960’s was using BoNT-A ‘Octagon®’ for the ophthalmic treatments of blepharospasm and ‘lazy-eye syndrome.’ Serendipitously, the cosmetic use was discovered when injecting to relax the hyper contraction of the lateral rectus, close to orbicularis oculi, resulting in a smoothing of the ‘crow’s feet’.

There are currently only eight FDA approved usages of the medication. However, there are over a hundred off-label uses. In 2007, British Columbia dentists were among the first to utilize BoNT-A for cosmetic treatments, and to subsequently appreciate the potential in dental therapeutic treatments. In the USA, the majority of state boards have approved, or are in the process of approving, the usage.

Clinically, BoNT-A can be integrated in the dental therapeutic treatments and diagnosis of bruxism, clenching, TMD, pain management, myofacial pain, trigeminal neuralgia, periodontics, endodontics, implant surgery, sleep apnea, and their effect on smile design enhancement.
There are numerous articles in the medical literature of which the majority of treatments, as previously stated, are off-label; few of those articles being in the dental literature. Where are the research articles in the periodontal literature illustrating the therapeutic use of BoNT-A?

**Clinical Hygiene Periodontal Protocol** - Part of our diagnosis and treatment for all adult patients is a thorough exam and periodontal probing. Depending on the individual patient’s maintenance requirements, a 3- to 6-month recall program is instituted, as part of our standard maintenance protocol. Often, there is a patient that is following their recall instructions properly and attending their recall appointments, however, various periodontal pockets persist. Another scenario is when a long term ‘normal-hygiene’ patient returns for
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### Fig. 1a-e: PTIFA_RFRP

#### Full Face
- Frontal Non-Retracted View
  - f-9, 1:3m

#### Full Smile
- Frontal Non-Retracted View
  - f-29, 1:3 Magnification

#### Full Smile
- Right Non-Retracted View
  - f-29, 1:3 Magnification

#### Full Smile
- Left Non-Retracted View
  - f-29, 1:3 Magnification

#### Upper & Lower Teeth
- Frontal Retracted View
  - f-29, 1:3 Magnification

#### Upper & Lower Teeth
- Right Retracted View
  - f-29, 1:3 Magnification

#### Upper & Lower Teeth
- Left Retracted View
  - f-29, 1:3 Magnification

#### Maxillary Arch
- Occlusal Retracted View
  - f-29, 1:3 Magnification

#### Mandibular Arch
- Occlusal Retracted View
  - f-29, 1:3 Magnification

#### Maxillary Anterior View
- Frontal Retracted View
  - f-32, 1:1.5 Magnification

#### Maxillary Anterior View
- Right Retracted View
  - f-32, 1:1.5 Magnification

#### Maxillary Anterior View
- Left Retracted View
  - f-32, 1:1.5 Magnification

### Fig. 2A: Full Face Frontal Relaxed - pre Botox treatment

### Fig. 2B: Full Face Frontal Relaxed 2 weeks post Botox Cosmetic (upper face) treatment with increased Mx tooth display

### Fig. 3A: Close up Face Relaxed - pre Botox treatment

### Fig. 3B: Close up Face Frontal relaxed 2 weeks post Botox Cosmetic (upper face) treatment with increased Mx tooth display

### Fig. 4A: Lower Face Relaxed - pre Botox treatment

### Fig. 4B: Lower Face Relaxed 2 weeks post Botox Cosmetic (upper face) treatment with increased Mx tooth display
their recall appointment, only to discover a quick onset of extensive decay or periodontal problems that were not evident 3-6 months prior. What is the cause of these periodontal conditions? Could the origin, perhaps, be stress, anxiety and depression?

In addition to our general dental procedures, we offer Botox® therapy to our patients. We observe that after Botox® therapy of the upper face, including the Glabella frown lines, the patient has a more alert, awake, happier facial presentation. If you look good, subconsciously, you feel good.

We document each BoNT-A patient visit with the Roberts Facial Rejuvenation Photography series of 29 standard photographs (Fig. 1A-D)(Ref. 1). From the patient’s perspective, there is an increase in self confidence and self esteem from the improved facial appearance. At the 2 week Botox® recall appointment, we notice individuals returning for their exam with a changed behavioral pattern, increasing their grooming due to their improved appearance (Fig. 2 to 11). There is an improvement, not only in the biological aspects but, in addition, an improvement in the behavioral aspect. In the June 2009 issue of the Journal of the Canadian Dental Association, an article called ‘Relationship between Stress, Depression and Periodontal Disease.’ by Anthony Iacopino was published (Ref. 2). It reads:

Let us look more closely at this report.

- **Two Critical Areas of Interest:**
  - 1st “individualized medicine” for effective care
  - Variations in the severity of periodontal disease are influenced by many individual factors:
    - Coexisting systemic conditions, genetics, oral hygiene & age
    - Other factors — including psychological factors
  - 2nd Studies indicate strong relationships between stress, depression and periodontal disease (Ref. 6).
Biological link
• Stress and depression can reduce the immune system function and facilitate chronic inflammation
• Mediated through the hypothalamic-pituitary-adrenal axis
• The production of cortisol, a glucocorticoid capable of reducing immunocompetence.
• Cortisol inhibits immunoglobulin A, G, and neutrophil function, which leads to increased biofilm colonization and reduced ability to prevent connective tissue invasion.
• Additionally, after periods of chronic elevation, cortisol loses its ability to inhibit inflammatory responses initiated by immune reactions.
• This leads to sustained inflammatory destruction of the periodontium.

Behavioural link
• Emphasizes that people suffering from stress & depression may increase poor health behaviours:
  • Smoking, drinking, unhealthy diet & neglecting oral hygiene
  • This leads to oral biofilm burden and a resistance of the periodontium to inflammatory breakdown

Currently, patients with stress, anxiety and depression are prescribed a number of psychotropic medications, which can include antidepressants, benzodiazepines, mood stabilizers and antipsychotics (Ref. 7).

There are numerous side effects that can affect individuals on these medications, including interaction with other dental medications, sedation, xerostomia, urinary retention, constipation etc.

Are there medications that we could employ that do not have these negative side effects? Are there individuals that may be treated alternatively with BoNT-A and also have a positive effect on the periodontium?

This article is directed to spark a paradigm shift in periodontal therapy.

In April 2009 Dr. Michael Lewis, an experimental Psychologist at Cardiff University in Wales, published a paper “Botulinum toxin cosmetic...
therapy correlates with a more positive mood” (Ref. 8). In his article Dr. Lewis presents the following:

‘Facial muscles not only express emotions, but they are also involved in the experience or feeling of emotions’ (Ref. 9).

‘Facial-muscular action can affect our mood and perception’ (Ref.10).

‘The corrugator muscles are universally important in the expression of negative emotions including sadness, fear, anger and distress’ (Ref.11).

‘People who have received BoNT-A treatment for frown lines are rated as showing less negative facial expressions’ (Ref. 12).

‘BoNT-A injections into the corrugator frown muscles could be used as a treatment for depression’ (Ref. 13).

‘Anecdotal evidence of a general improvement in the mood of patients having received BoNT-A therapy’ (Ref. 14). ‘This mood effect may help to explain why BoNT-A treatment leads to higher satisfaction ratings than other forms of cosmetic treatment’ (Ref. 15).

Patients who had their frown lines treated with BoNT-A tended to be happier.

There were 25 women in the Lewis study: 12 frown lines treated with BoNT-A only and the control group of 13 with other facial treatments (glycolic peels, laser treatments and Restylane).

Questionnaires were completed after treatment: The attractiveness ratings of the two sets of participants were greater after treatment, than before treatment. The size of the change was small. Appearance did not seem to explain the difference.

The Irritability-Depression-Anxiety-Scale (IDAS) indicated that the BoNT-A group scored consistently lower than the control group. This was significant.

All the women treated with BoNT-A scored “significantly lower” on the anxiety and depression scale.

“Facial feedback” is the cause for happier feelings. Frown muscles are referred to as “negative muscles” and trigger negative responses in the brain. “Positive muscles” used for smiling release endorphins to the brain, and endorphins make you happy.

BoNT-A therapy can relax muscles. When placed in the Glabellar muscles, this therapy prevents you from using your negative muscles and promotes positive muscle use, thereby causing the release of endorphins in your brain, and making you feel happier.

The significance of Dr. Lewis’ research indicates that BoNT-A therapy not only improves a person’s appearance. Additionally, BoNT-A can have a compound therapeutic effect, resulting in less anxiety and depression and, thus, can have an impact on the periodontal health of our ‘risk-factor’ patients.

Risk factors and treatment alternatives

Every one of us has different risk factors that determine which treatments will work on each particular individual (individualized medicine). We now have additions to our armamentarium of standard treatment modalities such as scaling, root planning and curettage. Laser-assisted new attachment procedures (LANAP) have proved beneficial in the periodontal sulcus (Ref.16). On a bacterial level, we can now test for specific microbes. We can now treat the specific bacteria involved in periodontal disease utilizing specific mouth rinses (Ref.17). On a psychological level, we can utilize BoNT-A therapy and have less depression and anxiety leading to an improvement in the patient’s periodontal health thanks to both psychological and behavioral influences.

Allergan is currently working on research to gain FDA approval for the use of Botox® in the treatment of anxiety and depression. Recognizing the connection between BoNT-A and anxiety and depression, should our institutions be researching a possible role for BoNT-A in treating periodontal disease? Some of the current medical literature is often dismissed as unrelated to the practice of dentistry.

A recent research article demonstrated a direct link from extra-cranial nerves to intra-cranial nerves, via the sutures (Ref.18). In the Glabella area (Lewis’s research area), the anterior frontal bone, has the metopic suture. As BoNT-A therapy becomes more mainstream in dentistry we will find other uses of BoNT-A and further unravel the primary, secondary and tertiary mechanisms of action of BoNT-A for additional treatments.

With the increase in elective cosmetic dental procedures such as implants and smile design, we can now include cosmetic BoNT-A into our complete facial aesthetics and, additionally, benefit from the therapeutic uses to improve and maintain our patients’ periodontal health. More research is required to determine the results. I look forward to assisting our academic community in catching up with the beneficial actions of BoNT-A.

Welcome to the world of BoNT-A in dentistry.

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