



State of the art of orofacial harmonization: a review

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DOI: <https://doi.org/10.54448/mdnt23S403>

Received: 08-24-2023; Revised: 10-28-2023; Accepted: 10-30-2023; Published: 11-08-2023; MedNEXT-id: e23S403

Abstract

Nowadays, a harmonious smile depends on several factors ranging from the aesthetic to the functional, but it is known that a smile opens doors and is also known as a business card for anyone. The present study aims to discuss the issue of orofacial harmonization nowadays, the existing indications, and the contraindications of this treatment modality, through a literature review. This study is a systematic literature review and for its realization, a bibliographical survey of articles in the main internet databases was carried out. It is worth remembering that, like any procedure, it is necessary to carry out an evaluation, to plan well how the procedure will be carried out, to know the indications, the contraindications, the places that can be applied, the way to dilute the product, when using botulinum toxin. However, this study made it possible to understand that orofacial harmonization, in addition to being an aesthetic procedure, has characteristics that are linked to the question of the biomechanics of the smile, forgetting the question of the person's self-esteem.

Keywords: Orofacial harmonization. Botulinum toxin Type A. Aesthetic.

Introduction

Nowadays, a harmonious smile depends on several factors that range from aesthetic to functional, but it is known that a smile opens doors and is also known as anyone's business card. Facial appearance plays an important role in self-esteem and can positively and negatively influence the patient's psychological and social appearance. However, with technological

advances and the influence of the media, the population is increasingly critical and demanding, the high quality of dentistry allows dentists to improve the harmony of the face, applying orofacial techniques that complement a beautiful smile and improve aesthetics [1].

Faced with the search for facial harmony, consists of aesthetics as a whole, acquiring transformations and increasing over the years. Therefore, the dental professional must obtain the necessary knowledge to know how to deal with the different individual conceptions of aesthetics, taking into account the patient's personality, the population that surrounds them, and the environment in which they are inserted [2].

Over time, the facial harmonization technique began to use other components that help in the process, such as botulinum toxin, and hyaluronic acid, to improve the final result. Recently, there have been several treatment techniques to improve aesthetics that are closely linked to the search for a concept of beauty, where, due to the influence of digital media, there has been an increase in demand, resulting in well-being and self-confidence. Therefore, when discussing oral aesthetics, the entire stomatognathic system and the relationship between the risks and benefits that these procedures can generate for the patient must be taken into account [2].

However, it can be said that beauty is subjective for each personal profile, and when aesthetics is used beneficially, it brings a satisfactory increase, thus generating a good quality of life. The oral health professional has as a reference the standard of normality of the Brazilian biotype and can diagnose an aesthetic disharmony of the face of skeletal, dental, or anatomical origin, which may or may not be corrected

with conventional non-surgical or surgical aesthetic therapies [1]. However, facial analysis is a tool used to evaluate the patient's facial characteristics, defining proportions, volume, appearance, symmetry, and visible deformities. It consists of analyzing the face with photographs associated or not with imaging tests [1].

Until recently, this area was an exclusive area of medical competence, but on January 29, 2019, the Federal Council of Dentistry officially recognized orofacial harmonization as a specialty and took other measures. However, the dental surgeon's training is focused on the head and neck and can work on the area of the face that goes from the tricheal point to the hyoid bone in the cranial-caudal direction and from tragus to tragus in the anterolateral direction. Also knowing the fundamentals of facial analysis, based on references of the normality standard, being able to diagnose an aesthetic disharmony of skeletal, dental origin, and anatomical changes [3].

According to facial analysis, the dentist can recognize a change that can then be corrected with certain types of treatments. This way, the professional will feel safer to recommend orofacial harmonization procedures and corrections, improving the prognosis and prediction of treatments [1].

The present study aimed to discuss the issue of orofacial harmonization today, and the existing indications and contraindications of this treatment modality, through a literature review.

Methods

The present study is a literature review, and to carry out this study, a bibliographic survey of articles from the last ten years (from 2012 to 2022) was carried out in the main internet databases through the Virtual Health Library (VHL/BIREME) through LILACS, SCIELO, PUBMED/MEDLINE, and GOOGLE ACADÊMICO. This study was carried out in the following languages: English and Portuguese. The keywords or descriptors used were *Orofacial harmonization and botulinum toxin Type A. Aesthetic*. The inclusion criteria for this study were that only articles that respect the topic addressed, the time of relevance of ten years, and the aforementioned keywords are included. However, exclusion criteria do not include articles that do not in any way respect the time of relevance of ten years, the theme of the study, or the keywords mentioned.

Literature Review

Facial analysis

When talking about facial analysis, it must be taken into account that it is a diagnosis that implies the success of dental treatment, playing an increasingly

important role. This exam was used by specialties such as orthodontics and oral and maxillofacial surgery; it should now be available to any specialty. With the regulation of the aesthetic use of botulinum toxin and hyaluronic acid for dentistry in Brazil, many professionals are increasingly seeking this knowledge [3].

Guidelines Versus Rules in Facial Assessment

There are no rules for a facial assessment, all analyses described serve as guidelines based on classical, Renaissance, and neoclassical canons of proportion; modern anthropometric and cephalometric data of population norms; results of attraction perception studies, are information to help the professional understand the morphological and structural characteristics of the patient's craniofacial complex as a whole, with a thorough clinical inspection containing a trained eye that can be gleaned from the keen observation and analysis of countless patients and their diagnostic records. To do this, you need to base yourself on *Observation: to contain consistent information through detailed observation of the patient at rest and in movement; *Palpation: manual palpation of the craniofacial region, helping to relate the surface anatomy to deeper structures, numerous bony prominences, and the overlying soft tissue layer can be palpated; *Analysis of diagnostic records: handling clinical diagnosis requires the ability to accurately describe the morphological characteristics and structural relationships of the craniofacial complex [4].

Types of Facial Analysis

Facial analysis according to temperament can be subjective or objective, in subjective analysis it is necessary to have experience and sensitivity, after the clinical consultation the dentist defines your diagnosis and also carries out treatment planning; objective analysis requires examinations or video and photographic records [5].

Table 1. Temperaments.

Strong or Choleric Temperament	Objective, practical, bold, explosive, intense, dynamic, decisive, has leadership power, fearless, emotionally stable, strong and authoritative will.
Dynamic or Sanguine temperament	Extroverted, expansive, communicative, jovial, enthusiastic, optimistic, active, emotionally unstable and dynamic, but unfocused.
Sensitive or Melancholic Temperament	Organized, kind, meticulous, perfectionist, shy, reserved and has a great ability to think abstractly, has strong emotional sensitivity and is systematic.

Peaceful or Phlegmatic Temperament	Diplomatic, stable intellectually and emotionally, acts slowly and carefully, has a smooth verbal expression with caution and thoughtfulness in words, tends to accept the will of others more easily, linked to spirituality, tends to be apathetic and conformist.
Strong / Wrathful	Rectangular, triangular or hexagonal face with a straight base, with well-defined angles, especially in the jaw; horizontal and vertical lines demarcate the forehead and mouth. Rectangular central incisors, positioned with their long axes perpendicular to the horizontal plane and the incisal edges of the upper teeth form a straight line. Canine in vertical position and rectangular maxillary arch.
Dynamic or Sanguine	Inverted triangular, lozenge or hexagonal face with straight sides, a prominent nose and a wide mouth. The upper anterior teeth are slightly inclined distally, the central incisors are triangular or trapezoidal and the canines are inclined palatally. The maxillary arch is triangular.
Sensitive or Melancholic	Oval face with rounded or shaped features
Peaceful or Phlegmatic	by fine lines. Lower third less developed. Oval-shaped central incisors. The incisal edges of the upper teeth form a curved line and the maxillary arch is oval.

Source: Tedesco, 2019 [5].

Facial Assessment

The initial qualitative assessment involves observing the patient with their viewing position in which the patient and the professional can sit on adjustable seats according to the height of their heads, taking care to keep the patient's head in NHP (position natural head behavior in the Frankfurt Plane) maintaining a distance of about one meter. For the acquisition of preliminary data, even if it is a little subjective. However, quantitative analysis involves the collection and analysis of anthropometric and cephalometric data, which must be systematic, precise, and complete [4].

However, quantitative assessment involves complete craniofacial anthropometric and cephalometric assessment and analysis of other diagnostic records, when necessary. The purpose according to Naini et al. (2016) [4] is:

- Obtain objective data - acquire factual data such as linear and angular craniofacial measurements.
- Analyze objective data - proportional analysis, bilateral symmetry analysis, and comparison of measurements with parameters established for age, gender, and ethnicity.

The History of Botulinum Toxin

Botulinum toxins (TxBo) are part of a group of hydrophilic peptides that have high molecular mass, low diffusion capacity in tissues, high toxicity, being produced mainly by neurogenic anaerobic strains and spores and synthesized by bacteria of the genus *Clostridium* (*Clostridium botulinum*, *Clostridium butyricum*, *Clostridium barati* and *Clostridium argentinensis*) [6].

However, botulinum toxin type A is a neurotoxin used for treatments in different fields, such as: dental, ophthalmological, and neurological, but what is in evidence is its use in aesthetic treatments. The application of TBA is a non-surgical, minimally invasive, temporary therapeutic aesthetic procedure, dose-dependent, powerful, and effective, indicated for easy rejuvenation, improvement of the gummy smile, control of hyperhidrosis, scrotal rejuvenation and reduction of keloids and hypertrophic scars, with a high rate of effectiveness and patient satisfaction, whose effect lasts up to 6 months. The Botox brands approved by the National Health Surveillance Agency (ANVISA) are Botox®, Xeomin®, Prosigne®, Dysport®, and Botulift®. Botulinum toxin type A is administered intramuscularly/intradermally according to the technical protocol for the area to be treated. The effect lasts from 6 weeks to 6 months, achieving best results between 2 and 3 months [7].

From a structural point of view, botulinum toxin is a simple polypeptide chain of 150 kDa composed of three portions, called BONTOXILYSIN, with a mass of 50 kDa each. The two heavy chains (Hc and Hn) together total 100 kDa, contain two domains, the binding, and the translocation, and are responsible for adhesion to extracellular receptors (Hc) and internalization (Hn) of botulinum toxin in the nerve cell, in addition to help the translocation of the light chain to the cytoplasm of the neuron. The light chain (L) is long, can vary between 422 and 445 peptide segments, has a mass of 50 kDa, is responsible for the zinc-dependent metalloprotease activity that prevents the release of neurotransmitters, by blocking pre-synaptic fusion vesicles and as a result, it develops different roles in the process of cellular intoxication and consequent functional blockage [7].

A study carried out by Scott in 1981 presented the characteristics of botulinum toxin as well as its preparation and results of the use of this toxin in the extraocular muscles of monkeys and humans, as a therapeutic modality [8]. From then on, botulinum toxin became better known for its use in aesthetic medicine and therapeutic properties [9]. The use of the toxin occurred in the 90s, when it was applied to patients with Blefarospasm1, from then on it was adopted in aesthetic procedures, however, it was only in the year 2000 that it received consent from the National Health Surveillance

Agency (ANVISA) for use in aesthetics in Brazil, and it was already used in other countries under the brand Botox®. Over the years, there was also approval for the use of the brand Dysport® in 2003 and Prosigne® in 2005 [10].

However, the effectiveness of botulinum toxin was only proven thanks to the success of Dr. Scott's studies, as the Food and Drug Administration (FDA), a regulatory agency linked to the US government's health department, authorized Dr. Scott to administer the toxin in human beings and highlight the changes that would occur in the body. These studies took place between 1977 and 1978, with the result obtained by generating relaxation of the muscles in the place where the substance was applied. Scholars at the time observed that muscular inhibition occurred, that is, the movements of the muscles when receiving the toxin were interrupted [11].

It was due to the tragic episode that occurred in the 18th century, several studies began with the aim of finding the cause of the deaths. At the time, scholar Justinus Kerner stood out for identifying a strange substance present in deteriorated sausage, naming it "fatty acid", a toxic effect of botulism. The identification of the acid gained prominence with the emergence of the first treatment theory for muscular hyperactivity disorders, which in 1960 had its therapeutic effectiveness proven by Allan Scott. Studies continued and only in 1981, Allan confirmed that botulinum toxin has resulted in therapeutic modality in the extraocular muscles of monkeys and humans. Since then, this toxin has been used in aesthetic procedures and therapeutic use [12].

However, the discovery of botulinum toxin occurred by chance in the 18th century during the Napoleonic wars in southern Germany. The historical context of war at the time contributed to the population consuming sausage contaminated with the bacteria *Clostridium botulinum*, causing several deaths from food poisoning [13].

The Mechanism of Action of Botulinum Toxin

It is known that the L (light) chain of botulinum toxins is long, varying, depending on the type of neurotoxin, between 422 and 445 peptide segments called "residues". It has several homologous segments concentrated in the central and amino-terminal portions. The most conserved segment is found in the central portion and contains the main connections for zinc endopeptidases with proteolytic activities at the axon terminal. Each neurotoxin molecule contains one zinc atom, except BoNT/C (Botulinum Toxin C) which contains two zinc atoms. The proportion of the number of molecules with zinc (potentially active) and without

zinc (inactive) will depend on the temperature and incubation time of the bacterial culture [14].

When BTX-A is injected into the body, the substance is identified by the immune system as a foreign element, which can lead to the development of an immune response against the neurotoxin. This phenomenon is common, especially when repeated and constant applications are made, which causes the desired effect to fail. This immunological reaction can, in some cases, occur during the first application, characterized as a primary non-response. In general, the lack of response to the product occurs in situations of several repeated applications, in this case characterized as a secondary non-response. One way to avoid such resistance is to use small and effective doses, increasing the interval between one application and another as much as possible [7].

It can be said that the mechanism of action of botulinum toxin is triggered by several steps through peripheral nerve endings. It is known that nerve transmission in the cell occurs from the release of neurotransmitters, including acetylcholine. The toxin will act by inhibiting the release of this neurotransmitter at the skeletal neuromuscular junction, thus causing local paralysis in the muscles between the second and fifth day after administration of the toxin, reaching full effectiveness around ten to fifteen days [7].

Botulinum Toxin Dilution Methods

Type A and B botulinum toxins, as they have important properties, are manipulated in laboratories for therapeutic and aesthetic use. Type A is most used because it has favorable characteristics, such as crystallizing in a stable form, being exotoxin, and having an easy culture and conservation process. Furthermore, it is diluted in a saline solution, so that it goes through the purification operation when bound to the human albumin protein, being lyophilized and then released for use [15].

It must be taken into account that professionals must follow a protocol for therapeutic and aesthetic use but in different ways for each situation. The standards to be followed in therapeutic procedures will require larger amounts of toxin powder diluted in a small amount of serum, which prevents any secondary muscles from receiving toxin. The standards for aesthetic procedures require a medium amount of serum, between 1 mL and 2 mL, and a smaller amount of toxin. However, it is worth noting that the trained professional will know the exact amount of the substance by evaluating the patient's clinical characteristics and age group. However, at least two applications per year are required to ensure efficacy and safety [15].

It should be remembered that type A toxin is sold in powder form, so the professional must dilute it in a sterilized, preservative-free 0.9% saline solution to be administered. This process is not difficult, but special care must be taken during the dilution phase, as the content should not present bubbles when injected into the serum because of the risk of rendering the toxin inactive, as they are large and the formation of bubbles fragments the toxins molecules due to the breakdown of disulfide bonds [16].

Indications for the Use of Botulinum Toxin and its Application Points on the Face

The application sites for botulinum toxin A on the face are vast, as it can be applied to various muscles for an aesthetic treatment, such as the zygomaticus major and minor, corrugator *supercilii*, *frontalis*, *levator labii superiors*, and nasal muscles, *orbicularis oculi*, nasal muscle, *procerus*, *buccinator*, *levator labii*, *orbicularis labii*, *mentalis muscle*, *levator anguli oris muscle*, *depressor anguli oris*, *depressor labii inferioris* and *risorius muscle* [16].

With the desire to achieve a standard of well-being associated with aesthetic beauty, they have awakened in people the desire to seek, more frequently, less complicated and less invasive methods than traditional plastic surgeries. From this perspective, botulinum toxin type A has become, nowadays, a relevant technique that can avoid the need for surgical means. With increasingly effective treatments for facial dystonia made with toxins, which can block the release of acetylcholine (Ach) at the neuromuscular junction and peripheral cholinergic synapses, thus causing muscle paralysis [2,3].

However, botulinum toxin type A is the injectable medicine most used in the practice of facial harmonization, but studies prove that its use is not limited to the area of aesthetics. Its use also includes the treatment of various pathologies, thus it is prescribed in different specialties, such as dermatology, neurology, plastic surgery, ophthalmology, physiotherapy, etc. In the area of physiotherapy, it is widely used in the treatment of spasticity, sequelae of facial paralysis, and mainly in lumbar spasms. However, in ophthalmology, its use is for the correction of strabismus, blepharospasm, hemifacial spasm, acquired nystagmus, oscillopsia, and benign ocular fasciculation. In neurology, it is applied to cervical and facial dystonia, tension headaches, and even tremors [4].

The main muscles that are subjected to the application of TBA are the *frontalis muscle*, *corrugator supercilii*, *orbicularis oculi*, *procerus*, *nasal muscle*, *elevator of the upper lip* and *wing of the nose*, *elevator of the lip*, *zygomaticus minor*, *zygomaticus major*,

elevator of the angle of the mouth, *buccinator*, *risorius*, *orbicularis labii*, *depressor anguli oris*, *depressor labii inferioris* and *mentalis muscle* [12].

Contraindications for the Use of Botulinum Toxin

Drug interactions can be highlighted as they may end up interfering with neuromuscular transmission. The application of botulinum toxin type A should be avoided when medications such as aminoglycosides, quinidine, lincosamides, cyclosporines, magnesium sulfate, D-penicillamine, and amino quinolones are consumed [7].

Practical knowledge of how botulinum toxin type A works makes it easier to understand contraindications, side effects, and even treatment to correctly deal with adverse situations. The administration of this toxin is well tolerated, but it cannot be used in patients who have certain conditions, such as i) allergy to albumin or egg proteins; ii) pregnancy (the toxin can cross the placental barrier); iii) lactation (the toxin can be eliminated through breast milk); iv) neuromuscular diseases (such as myasthenia gravis). v) infections at administration sites, vi) use of medications that enhance the effect of the toxin, such as aminoglycoside antibiotics and magnesium sulfate [7,8].

However, adverse effects resulting from the use of procedures with botulinum toxin A are classified based on inadequate administration of the product or location and form of application to the patient. Among them, we can mention eyelid and eyebrow ptosis, diplopia, changes in facial expression, asymmetry, and intense or generalized muscle weakness. The treatment of these effects consists only of the use of eye drops, in the case of dry eye in diplopia, and laser therapy to undo the effect of the asymmetry. As for effects caused by the method of application, we can experience erythema, bruising, headaches, and nausea. However, all of these factors resolve spontaneously, in around 2 to 3 days, and there is no need for therapeutic interventions, causing only temporary discomfort. In addition to being very low frequency [8].

Discussion

After a theoretical survey, it can be seen that to carry out the facial or orofacial harmonization procedure, it is necessary not only to know but also to understand the importance of using appropriate materials, as well as good knowledge of anatomy, physiology, and knowing how to evaluate and plan each step of this procedure.

According to Naini et al. (2016) [4] reported that historically there have been different types of explanations for the definition of beauty, which is not unanimous. Authors described that physical beauty was

related to goodness and ugliness due to a lack of ethical principles. However, these definitions were separated in the Renaissance, where the Egyptians reported great interest in art and beauty, as an example we have Queen Nefertiti, who was the standard of beauty at the time, her facial proportions were harmonious and symmetrical. Other authors reported that Plato described physical beauty as inferior to spiritual beauty. Finally, Aristotle, a disciple of Plato, ended up declaring that the individual can be pleasant in the eyes of others, and with this the first laws of geometry were created for facial harmony and balance, attributing order, proportion, and magnitude [5,6].

According to the CFO (2019) [3], orofacial harmonization is a specialty in dentistry that refers to the set of procedures responsible for the aesthetic and functional balance of the face. Facial analysis implies the success of dental treatment. However, Naini et al. (2016) [4] described that there are no rules for a facial assessment, all the analyses described serve as guidelines based on proportion, anthropometric and cephalometric data, and perception of attraction, which help the professional understand the morphological and structural characteristics of the craniofacial complex of the patient as a whole. However according to Tedesco (2019) [5] he ends up adding that facial analysis can be subjective or objective, subjective analysis requires experience and sensitivity, and objective analysis involves photographic records and videos.

However, Tedesco (2019) [5] stated that in an assessment the face can be divided into three thirds: upper, middle, and lower. The upper third is linked to the intellect; the middle third, is to emotion, and the lower third is to intuition. It is also essential for lip evaluation, where you must pay attention to factors related to teeth and gums to better define your approach.

When talking about the use of botulinum toxin type A, one must take into account how the product is diluted as it has already been said that it is sold in powder form, another point that must be taken into consideration is the places where Botulinum toxin will be administered as it can have adverse effects. Before carrying out the procedure, it is necessary to know whether the patient uses medication such as botulinum toxin or Botox can cause drug interactions [4].

Any procedure that is to be carried out is necessary to have a good evaluation, from the aesthetic issue to even the biomechanical factors related to chewing, good planning helps to understand how to carry out the procedure and also the amount of product to be used, the patient must follow Take all precautions after the orofacial harmonization procedure, so as not to have any problems in the future [4-7].

Conclusion

Through this study it is possible to understand all the issues that are related to the orofacial harmonization procedure, from its planning to its execution with the use of botulinum toxin type A., it must be taken into account that as any treatment is of the order aesthetic or even therapeutic, it is necessary to have a good evaluation, to know the problems that this patient has so that there are no future problems, as it is known that one of the contraindications of botulinum toxin is the issue of drug interactions, apart from the issue of application errors. of this in the face region. However, the dental professional must be up to date and also have good experience regarding orofacial harmonization before doing it.

Acknowledgement

Not applicable.

Ethical Approval

Not applicable.

Informed consent

Not applicable.

Funding

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate®.

Peer Review Process

It was performed.

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References

1. Mendes ACN. The influence of aesthetics on oral health, Course Conclusion Article (Graduation in Dentistry) - Centro Universitário São Lucas, 2018. 22p. Advisor: Prof. Ma. Geruza Corrêa do Amaral Ribeiro.

2. Alves ALS. The influence of the media on the perception of Dental aesthetics, Course Conclusion Paper (Graduation in Dentistry) - Federal University of Santa Catarina, 2018. 76p. Advisor: Prof. Dr. Beatriz Álvares Cabral de Barros.
3. CFO. FEDERAL COUNCIL OF DENTISTRY. Resolution No. 198, of January 29, 2019. DOU of 01/31/2019 (no. 22, Section 1, page 91). 2019.
4. Naini FB. et al. Facial Aesthetics Concepts and Clinical Diagnoses. São Paulo, SP: Elsevier Editora Ltda, 2016.
5. Tedesco A. Facial harmonization: the new face of dentistry. Nova Odessa, SP: Napoleão, 2019. c. 2, p. 52-59.
6. Smith TJ, Hill KK, Raphael BH. Historical and current perspectives on Clostridium botulinum diversity. Res Microbiol. 2015, 166:290-302.
7. Bratz PDE, Mallet EKV. Botulinum Toxin Type A: health approaches. Revista Saúde Integrada, v.8, n3,15-16, 2015. Available at: <http://local.cneccsan.edu.br/revista/index.php/saude/article/view/232>.
8. Barbosa CMR, Barbosa JRA. Botulinum Toxin in Dentistry. 1st ed. Rio de Janeiro: Elsevier, 2017.
9. Matos BM, Valle LSMB, Mota AR, Naves RC. The use of botulinum toxin to correct gummy smile - literature review. Braz J Periodontol - September 2017.
10. Santos CS, Mattos RM, Fulco TO. Botulinum toxin type a and its complications in facial aesthetics. Episteme Transversalis. 2017, vol. 6, no. 2, p. 73-84.
11. Mosconi PM, Oliveira RCG. Study of botulinum toxin and its dilution. Uningá Magazine. 2018, vol. 55, no. S3, p. 84-95.
12. Oliveira CCA, Fernandes EC, Medeiros KDO, Maia MCB, Seabra EJG, Santo PC. Botulinum toxin: historical, molecular context and practical application in healthcare. Brazilian Journal of Education and Health. 2020, v. 10, no. 2, p. 1-10.
13. Campos JR, Aguiar KSG, Simão LC. Orofacial harmonization in the treatment of bruxism with the use of botulinum toxin. Cathedral Magazine. 2021, vol. 3, no. 3, p. 19-27.
14. Duarte MJS. Botulinum Toxin beyond cosmetics. Dissertation (Integrated Master's Degree in Pharmaceutical Sciences) – Faculty of Science and Technology of the Algarve – UAIG. FARO/Portugal, 2015. Available at: <https://sapientia.ualg.pt/bitstream/10400.1/7804/1/fim.pdf>.
15. Bishop LB. Botulinum toxin as an alternative therapeutic arsenal in dentistry. Journal of Dentistry of the City of São Paulo University. 2019, vol. 31, no. 1, p. 74-87.
16. Cruz AI, Lima JMCSR, Araújo LF, Silva MS, Lima PCCSR, Ferreira RVVL. The use of botulinum toxin in pregnant and breastfeeding women: literature review. Research, Society and Development. 2020, vol. 9, no. 11, p. 1-15.