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AMANDA MIKI OKAMOTO

GUIA DE APLICAÇÃO DE TOXINA BOTULÍNICA PARA O TRATAMENTO DE CEFALEIA TENSIONAL

BOTULINUM TOXIN INJECTION GUIDE FOR TENSION-TYPE HEADACHE TREATMENT

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Trabalho de Conclusão de Curso apresentado à Faculdade de Odontologia de Piracicaba da Universidade Estadual de Campinas como parte dos requisitos exigidos para obtenção do título de Cirurgião Dentista.

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Orientador: Prof. Dr. Paulo Henrique Ferreira Caria

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RESUMO

As cefaleias são classificadas em primárias e secundárias. Cefaleias primárias ocorrem sem doenças subjacentes e dividem-se em enxaquecas, dores de cabeça e dores de origem tensional. Para obter sucesso no tratamento das cefaleias primárias com toxina botulínica do tipo A (TXB-A) é fundamental conhecer detalhes anatômicos do músculo temporal (MT) e das estruturas adjacentes a ele. Esse projeto visou propor diretrizes anatômicas para distinguir a posição do ventre muscular do MT, de seu tendão e de vasos sanguíneos e nervos, proporcionando maior segurança e eficácia para aplicação da TXB-A em uma amostra brasileira. Foram analisadas 20 hemifaces do MT pertencentes a FOP-UNICAMP seguindo dois métodos diferentes: obtenção de medidas morfométricas do MT e do seu tendão com auxílio de um paquímetro digital e confecção de uma estrutura de quadrantes em um filme plástico transparente, o que permitiu observar a distribuição do tendão temporal e de vasos e nervos na região. Os resultados demonstraram que o tendão temporal está localizado acima do arco zigomático e possui forma retangular. O Método I avaliou a extensão horizontal do tendão temporal e permitiu sua classificação em três tipos: Tipo I (35,29%), tipo II (58,82%) e tipo III (5,88%). As distâncias verticais entre a linha horizontal LH e o tendão temporal ao longo das linhas de referência foram L0: 30.9 ± 5.5 mm, L1: 48.5 ± 3.8mm, L2: 39.2 ± 7.8mm, L3: 44.9 ± 11.6 mm, e L4: 34.2 ± 2.3mm. Segundo o Método II, o tendão temporal estava disposto nos quadrantes Pl, Ml e Al. As fibras tendíneas do MT estavam dispostas na maioria dos casos no compartimento Al (63,4%). Nenhuma porção tendínea alcançou os quadrantes Au e Pu e somente algumas fibras posteriores ocuparam o compartimento Pl, cuja mensuração ficou comprometida pela presença da orelha externa. Em todos os casos analisados, a artéria temporal superficial teve seu ponto de bifurcação no compartimento Mm. A veia temporal média teve seu trajeto majoritariamente horizontal ou levemente inclinado para cima em sua extremidade, no limite superior dos quadrantes Al e Ml. Ambas as metodologias forneceram diretrizes anatômicas capazes de garantir segurança e eficácia para a injeção de TXB-A no MT em uma amostra brasileira.

Palavras-chave: Cefaleia do tipo tensional. Toxinas botulínicas. Músculo temporal.

ABSTRACT

Headaches are classified into primary and secondary. Primary headaches occur without underlying diseases and are divided into migraines, headaches, and tension-type headaches. To be successful in the treatment of primary headache disorders with botulinum toxin type A (BTX-A), it is essential to know anatomical details of the temporalis muscle (TM) and the structures adjacent to it. This project aimed to propose anatomical guidelines to distinguish the position of the belly of the TM, its tendon and blood vessels and nerves, providing greater safety and efficacy for the application of BTX-A in a Brazilian sample. Twenty sides of TM belonging to FOP-UNICAMP were analyzed using two different methods: by obtaining morphometric measurements of the TM and its tendon with the aid of a digital caliper and by making a structure of quadrants in a transparent plastic film, which allowed observing the distribution of the temporalis tendon and vessels and nerves in the region. The results showed that the temporalis tendon is located above the zygomatic arch and has a rectangular shape. Method I evaluated the horizontal extension of the temporalis tendon and allowed its classification into three types: Type I (35.29%), type II (58.82%) and type III (5.88%). The vertical distances between the horizontal LH line and the temporalis tendon along the reference lines were L0: 30.9 ± 5.5 mm, L1: 48.5 ± 3.8mm, L2: 39.2 ± 7.8mm, L3: 44.9 ± 11.6 mm, and L4: 34.2 ± 2.3mm. According to Method II, the temporalis tendon was arranged in the quadrants Pl, Ml and Al. The tendon fibers of the TM were arranged in most cases in the Al compartment (63.4%). No tendon portion reached the Au and Pu quadrants and only a few posterior fibers occupied the Pl compartment, whose measurement was compromised by the presence of the outer ear. In all cases analyzed, the superficial temporal artery had its bifurcation point in the Mm compartment. The middle temporal vein had its course mostly horizontal or slightly tilted upwards at its end, at the upper limit of the Al and Ml quadrants. Both methodologies provided anatomical guidelines capable of ensuring safety and efficacy for the injection of BTX-A into the TM in a Brazilian sample.

Key words: Tension-type headache. Botulinum toxin. Temporal muscle.

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1 INTRODUÇÃO

As dores de cabeça são algumas das queixas mais frequentes em consultórios médicos, sendo responsáveis por diversos tipos de impactos negativos na vida de quem as sofre, causando até mesmo incontáveis dias de trabalho perdido. Possuem intensidade e características variáveis e carregam consigo uma morbidade significativa, além do seu impacto socioeconômico.

As cefaleias podem ser classificadas em primárias e secundárias. As cefaleias primárias ocorrem sem associação à processos patológicos, doenças ou injúrias traumáticas e dividem-se ainda em enxaquecas, cefaleias trigêmino-autonômicas e dores de origem tensional (Mier e Dhadwal, 2018). A cefaleia tensional é o tipo mais comum de dor de cabeça crônica, apresentando uma prevalência de 30% a 78% na população em geral (Wieckiewicz et al, 2017). Frequentemente associada à fatores musculares e psicológicos, pode ser causada pela contração de músculos da região da cabeça e do pescoço (Rollnik et al, 2000), pois a sensibilização de fibras aferentes musculares por mediadores locais, leva à sensibilização central, ocasionando as dores de origem tensional, que se não tratadas, resultam na cronificação da cefaleia tensional (Silberstein et al, 2006; Bendtsen, 2000).

A toxina botulínica (TXB) tem sido amplamente empregada no tratamento das dores tensionais, pois ela age sobre o sistema sensorial miofascial, o que ajuda a interromper a via de transmissão da dor na cefaleia tensional episódica, prevenindo sua progressão para cefaleia tensional crônica (Silberstein et al, 2006; Bendtsen, 2000). Além disso, seu uso no tratamento da cefaleia tensional é uma alternativa extremamente vantajosa e eficaz, apresentando menos efeitos colaterais e efeito de maior duração quando comparada aos fármacos comumente usados, podendo durar até 5 meses (Patil et al, 2016).

A toxina botulínica é uma neurotoxina produzida pela bactéria Clostridium botulinum que possui 7 sorotipos diferentes (Montecucco e Molgó, 2005), sendo os tipos A e B os mais usados em aplicações clínicas (Bellows e Jankovic, 2019). O uso de injeções de toxina botulínica do tipo A (TXB-A) como uma alternativa para o tratamento de dores de cabeça foi proposto pela primeira vez após observar que pacientes que receberam injeções cosméticas da TXB-A apresentaram melhora das dores de cabeça, levando a uma série de investigações que sugeriram seu benefício (Binder et al, 2000; Evans e Blumenfeld, 2003; Pascual, 2004).

A Food and Drug Administration (FDA) reconheceu a segurança e a eficácia da TXB-A no tratamento das dores de cabeça ao aprovar 31 locais de injeção para a TXB-A em 7 músculos da cabeça e do pescoço, dentre eles, quatro locais de injeção em cada lado do músculo temporal (Blumenfeld et al, 2010). O mecanismo de ação da TXB-A no alívio da dor baseia-se em impedir a liberação do neurotransmissor acetilcolina das terminações dos axônios na junção neuromuscular, o que causa paralisia muscular (Montecucco e Molgó, 2005). Isso significa que para obter melhores efeitos farmacológicos usando a TXB-A, essa deve ser aplicada visando atingir as terminações nervosas (Choi et al, 2020), por isso a compreensão das terminações nervosas que atuam no músculo alvo é fundamental.

A coloração de Sihler permite a visualização da distribuição neural nos músculos que contêm fibras nervosas mielinizadas, podendo ser considerada a melhor ferramenta para observar a distribuição nervosa dentro dos músculos esqueléticos (Won et al, 2011), entretanto o músculo temporal possui uma fáscia fibrosa e um tendão destacado, o que dificulta a aplicação da técnica.

A experiência clínica tem demonstrado que a compreensão insuficiente da anatomia e função dos músculos da cabeça e pescoço pode levar a resultados indesejáveis e eficácia reduzida (Blumenfeld et al, 2017). Diante de tal importância do conhecimento anatômico da região, o presente estudo realizou uma análise morfológica detalhada do músculo temporal, do seu tendão e dos vasos adjacentes a ele, a fim de atingir o alvo e produzir maior eficácia clínica usando concentrações mínimas de TXB-A.

2 ARTIGO: COMPARISON OF BOTULINUM TOXIN APPLICATION GUIDELINES FOR HEADACHE TREATMENT IN A BRAZILIAN POPULATION

Submetido no periódico Clinical and Laboratorial Research in Dentistry (Anexo 5)

Comparison of botulinum toxin application guidelines for headache treatment in a Brazilian population

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ABSTRACT

The present study compared two different methods in order to provide anatomical guidelines on how to differentiate the temporalis muscle, its tendon and main vessels in the region, allowing a safe botulinum toxin type A (BTX-A) injection into the temporalis muscle for primary headache disorders treatment. Twenty sides of temporalis muscle belonging to the Biosciences Department of FOP-UNICAMP were analyzed using two different methods. The first method consisted of obtaining morphometric measurements of the temporalis muscle and its tendon with the aid of a digital caliper. The second method evaluated the distribution of the temporalis muscle belly, its tendon and adjacent vessels and nerves after dividing its surface into nine quadrants of equal size. The temporalis tendon is located above the zygomatic arch and has a rectangular shape. Method I evaluated the height and length of the temporalis muscle and its tendon. The posterior border of the temporalis tendon was classified into three types: Type I (35.29%), type II (58.82%) and type III (5.88%). According to Method II, the temporalis tendon was arranged in the quadrants PI, MI and AI. Both methodologies provided anatomical guidelines capable of ensuring safety and efficacy for the injection of BTX-A into the temporalis muscle in a Brazilian sample.

KEYWORDS: Primary headache disorders. Botulinum toxin type A. Temporalis muscle.

INTRODUCTION

Primary headaches occur without underlying organic diseases and can be further classified into migraines, headaches, and tension-type headaches. Chronic headaches are disabling and significantly burden patients, being common in the population [1]. Migraine is a primary neurological condition characterized by recurrent episodes of headache with other associated symptoms, such as nausea, vomiting and sensitivity to sensory stimuli. Without effective treatments, migraine can reduce the quality of life, increase the economic cost, and decrease the productive capacity of the individual. Recent studies have shown significant benefit in treating chronic migraine (CM) with botulinum toxin [2]. This led to a new way of treating migraine.

Tension-type headache (TTH) is another condition with an extremely high socioeconomic impact, hence the importance of its study [3]. TTH occurs in up to 38% of adults, 2% have headaches almost daily, classifying them as tension headaches [4]. The underlying causes of headaches are often nervous and muscular disorders, which is why botulinum toxin type A (BTX-A) has been gaining prominence because of its effect [5,7]. Likewise, BTX-A produces fewer side effects than some drugs that are commonly used for headaches. In addition, treatment with BTX-A can last up to 4 months, in contrast to the short-term effects of the drugs administered and lidocaine injections [8,9]

The Food and Drug Administration (FDA) recognized the safety and effectiveness of BTX-A by approving 31 injection sites for BTX-A. Among them, four injection sites were suggested on each side of the temporalis muscle. These injection sites were approved after analyzing the clinical results of the BTX-A injections designed to treat tension-type headache. The hypothesis about muscle tension relief is based on suppression of the neurotransmitter acetylcholine release by the peripheral nerve [10]. This mechanism promotes peripheral and central sensitization, providing relief for patients suffering from primary headaches. Since the BTX-A acts on nerve endings, knowledge of the nerve endings that act on the muscle is essential to obtain maximum relief with the minimum concentration of BTX-A.

Invasive procedures may be limited by the lack of anatomical knowledge of the affected site, reducing the effectiveness of the BTX-A injection, in addition to the risk of damaging the muscle and local nerve endings. Therefore, the best option is to know the morphology of the temporalis muscle, its tendon, and adjacent structures. The aim of this study was to compare the effectiveness of two different methods for identifying locations for a safe and effective injection of BTX-A into the temporalis muscle in a very mixed population such as the Brazilian one.

MATERIAL AND METHODS

Twenty sides from ten Brazilian cadavers (eight men and two women - average age, 46.8 years) fixed in glycerin were evaluated. This study was submitted to and approved by the University of Campinas Research Ethics Committee involving human beings and respected all ethical principles defined in the WMA Declaration of Helsinki. The skin and the underlying subcutaneous tissue were removed, then a careful dissection of the temporal region was performed for better visualization and distinction of the anatomical structures. The limits of the temporal fossa used as limits for this study were: Anterior: posterior border of the frontal process of the zygomatic bone; superior: temporal line; posterior: supra-mastoid crest; lower: zygomatic arch. For the evaluation of the muscles, two different methodologies were used, the one described by Won-Kang Lee at al. (2017) [11], and the one by You-Jin Choi et al. (2016) [12].

Method I

With the aid of a digital caliper (CD-15 CP, Mitutoyo, Kawasaki, Japan), morphometric measurements of the temporalis muscle were performed in the 20 sides. All measurements strictly followed the analysis proposed by Choi et al. (2016) [12] which consists of dividing the surface of the temporalis muscle, using several anatomical points as a reference, to measure its height and length. The Jugale point and the zygomatic arch were used as fixed structural anatomical markers to morphologically outline the muscle. (LH: horizontal line that passes through the Jugale point, L0: vertical line that passes through the Jugale point, L1: vertical line that equally divides the distance between points L0 and L2, L2: vertical line that passes through the anterior outer margin of the ear. L3: vertical line that equally divides the distance between points L2 and L4, L4: vertical line that passes through the posterior outer margin of the ear) (Figure 1).

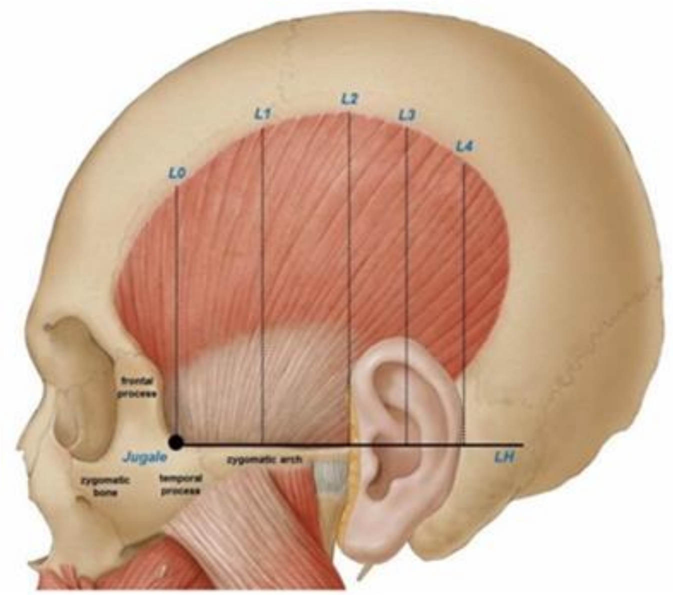

Figure 1- Schematic drawing of points and reference lines based on anatomical surface structures (Choi et al., 2016) [12].

Method II

The second analysis was described by Lee at al. (2017) [11] and consists of dividing the surface of the temporalis muscle into nine quadrants of equal size. In our study, we used a transparent and resistant plastic sheet as shown in figure 2. The reference lines that delimit each quadrant presented the same conditions for all. Therefore, the position of an anatomical structure could be marked in its natural position and perceived at first glance. As described in the study by Lee at al. (2017) [11], the lateral canthus of the eye (C), the tragus (T), the posterior outer margin of the ear (E) and the most anterior (A), superior (S) and posterior (P) points of the temporalis muscle were used as reference points. The quadrants were named according to their location (Figure 2). Then, the plastic lamina was positioned over each muscle in question, allowing to identify in which quadrants there was a prevalence of blood vessels and other important anatomical structures.

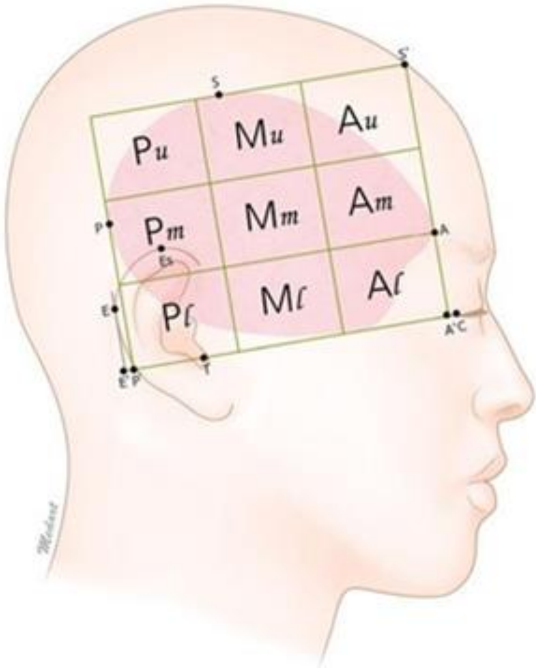

Figure 2 - Reference lines and anatomical landmarks for measurements in the temporal region. C lateral canthus of the eye; T tragus (most prominent point of the tragus); Line C-T: Reference line; A: Most anterior point of the temporalis muscle; A': contact point between the reference line and the perpendicular line from A; P: most posterior point of the temporalis muscle; P': contact point between the reference line and the perpendicular line from P; S: most superior point of the temporalis muscle; S': contact point between the perpendicular line of A and the horizontal line from S; E: most posterior point of the ear lobe; E': contact point between the reference line and the perpendicular line from E; Es: Most superior point of the ear lobe; A'-P': width of the temporalis muscle (TM); A'-S': vertical height of the TM; A'-S'/ A'-P', ratio between the height and width of the TM; A'- C, distance from the canthus of the eye to the anterior margin of the temporalis muscle; T-P', distance between the tragus and the posterior margin of the temporalis muscle. The nine compartments are labeled using two letters that describe their coordinates: A anterior, M middle, P posterior, l lower, m middle and u upper (Won-Kang Lee at al., 2017) [11].

RESULTS

Method I:

1. Posterior border of the temporalis muscle tendon

According to Method I, the posterior extension of the temporalis muscle (TM) tendon was evaluated. This horizontal measurement was performed using the distance between the Jugale point and the reference lines L2, L3 and L4 as reference. The posterior border of the temporalis tendon was then classified into the following categories: Type I, the posterior border of the temporalis tendon is located in front of L2. The distance between the Jugale and L2 was 48.5 ± 0.32 mm (mean ± SD) and occurred in 7 of the 20 case cases (35.29%). Type II, the posterior border of the TM tendon is located between L2 and L3. In this type, the distance between Jugale and L3 was 71.4 ± 0.62 mm (mean ± SD), and occurred in 11 of the 20 cases (58.82%). Type III, the posterior border of the TM tendon is located between L3 and L4. In this type, the distance between Jugale and L4 was 91.2 ± 0.5 mm (mean ± SD), occurring in 2 of the 20 cases (5.88%). There were no cases where the tendon reached or exceeded L4. (Figures 3, 4 and 5).

2. Vertical length of the temporalis tendon and the temporalis muscle

These analyzes consist of the measurement of the vertical distance between the horizontal line that passes through the Jugale point (LH) and the superior border of the zygomatic arch, up to the temporalis tendon (measure 1) along the lines (L0 to L4); and the vertical distance between the horizontal line that passes through the Jugale point (LH) and the superior border of the zygomatic arch, up to the superior border of the TM (measure 2) along the lines (L0 to L4). In measure 1, the captured values were: L0: 30.9 ± 5.5 mm, L1: 48.5 ± 3.8 mm, L2: 39.2 ± 7.8 mm, L3: 44.9 ± 11.6 mm and L4: 34.2 ± 2.3 mm. Measure 2 presented the following values: Lo: 56.9 ± 13.3 mm, L1: 76.2 ± 11.0 mm, L2: 73.1 ± 16.1 mm, L3: 56.4 ± 15.2 mm and L4 : 48.8 ± 12.3mm (table 1).

Table 1. The vertical distance of the temporalis tendon from LH (1) and the vertical length of the temporalis muscle (2).

Points	Measure 1	Measure 2
L0	30.9 ± 5.5	56.9 ± 13.3
L1	48.5 ± 3.8	76.2 ± 11.0
L2	39.2 ± 7.8	73.1 ± 16.1
L3	44.9 ± 11.6	56.4 ± 15.2
L4	34.2 ± 2.3	48.8 ± 12.3

Values are expressed in millimeters (mm).

Method II:

Temporalis muscle (TM) dimensions

In this analysis, the values related to the dimensions of the TM were obtained. The measure relative to its average height (A0-S0) was 98 ± 1.22 mm (range 73–113 mm). The average width of the TM (A0-P0) was 120.4 mm (range 88–134 mm). The average lateral distance between points A' and C was 4 mm, (range -4–8 mm). The average distance between P' and T was 27.8 ± 2.32 mm (range 22–38 mm). The average distance between T and E' was 32 mm (range 29–35 mm). The distance between T and P' was 2.8 mm and the average distance between T and E' was 2.6 mm.

Position of the superficial temporal artery (STA)

The STA bifurcation in all cases (100%) occurred above the reference line (line C-T). In all 20 cases analyzed, the bifurcation point was inside the Mm compartment of the TM rectangle. The average distance above the reference line was 41 mm (range 35-44 mm). Only in 6.2% of the cases, the STA bifurcation occurred at the limit between the Mm and Pm quadrants. The most vertical position of the STA before bifurcation was 23.3 mm (17-38 mm) from the reference line. Still about the more vertical position of the STA in relation to the reference line, it was placed within 1/3 higher of the Ml compartment in 34.7% of the cases, closer to the tragus than to the anterior border of the Al quadrant.

The middle temporal vein (MTV)

The horizontal (anterior) segment of the MTV passed through the TM 23.7 mm (range 19–27 mm) above the reference line. The MTV had its path mostly horizontal or slightly tilted upwards at its end, at the upper limit of Al and Ml compartments and then a slight inclination until its junction with the main trunk, at the 1/3 posterior of the reference line (line C-T). In all cases analyzed the junction of the MTV with its trunk occurred within the Mm and MI quadrants.

The temporalis tendon

After the total exposure of the muscle fibers and tendons, it was possible to determine the limits of the TM and its tendon in relation to the temporal line, the superior limit of the temporal fossa, the zygomatic arch and the lower limit. The tendon was arranged in the quadrants Pl, Ml and Al, that means, anterior, central, and posterior portion of the TM. Percentually, it is possible to affirm in relation to the tendon fibers of the TM that most of the cases were in the posterior part of the quadrant Al with 63.4% (range of 57-68mm) and in the posterior part of quadrant Am in 13.8% (range 2-17mm) of the cases. In the anterior region, tendon fibers never crossed the Am compartment and occupied the posterior half (55% of the total) of the Al compartment. Medially, the tendon filled the entire Ml compartment and part of the Mm, with 66.2mm (range 58.1-67.2mm), but never reached Mu. They corresponded to more than 57% of the height of the TM. In all cases analyzed, the superior margin of the medial tendon fibers was higher than the STA bifurcation. No tendon portion of the TM reached the Au and Pu quadrants. Finally, only a few posterior fibers occupied the Pl compartment, whose measurement was compromised by the presence of the outer ear.

DISCUSSION

BTX-A has been used for the treatment of bruxism [13], with some success [14], as well as for the treatment of migraine. Another option for migraine treatment is the use of oral medications whose prolonged use represents a risk of side effects for patients who have cardiovascular, cerebrovascular, liver diseases or who are pregnant, in addition to not having evident benefits [15,16]. Alternative treatment for bruxism is palliative, with the use of interocclusal plaques and physical therapy [17]. Although the mechanism of action of BTX-A in migraines is still unclear, there is empirical evidence of its success without side effects. On the other hand, the use of BTX-A for bruxism treatment has established clinical evidence [18].

The US Food and Drug Administration (FDA) has approved 31 sites for BTX-A injections for the treatment of migraines. However, they used as reference only the places of greatest pain relief, without considering the risks. As a result, there is a need of more accurate information on the safest points for BTX-A injection in similar procedures such as bruxism and tension-type headaches. Choi et. al (2016) [12] conducted a study on the nerve endings of the temporalis muscle to ensure safety for clinicians when performing such procedures. Although methodological standards have been established to assist clinicians in the injection of BTX-A [11,12], these have been performed on samples of Asian people. Methodologically, they were well performed, but the profile of the population evaluated in these studies represents only 1.1% of the Brazilian population. On the other hand, nearly 20% of all dentists in the world are in Brazil and there are 2.18 doctors per thousand inhabitants here [19], what justifies the need for anatomical references related to the local population, which has a significant index of miscegenation. Therefore, the present study was motivated by the need to analyze the topography of anatomical structures around the TM, in order to establish reasonable guidelines for safe injections of BTX-A in a Brazilian sample.

Injections of BTX-A into the TM should prevent damage to the surrounding blood vessels, reducing the occurrence of undesirable side effects after injection. The analysis of the anatomical arrangement and shape of the TM tendon can be easily established by observational study of the anatomical parts (specimens). There is anatomical evidence that supports that the injection of BTX-A should avoid the tendon of the temporalis muscle [20] Thus, by avoiding the injection of BTX-A into the muscle tendon, where there are few motor nerve endings, the clinicians will increase the effectiveness of the toxin, and also reduces events of post-injection tendonitis or laceration of tendon fibers by the needle tip.

The evaluations related to the disposition of the TM tendon, carried out in the present study, when compared to the study carried out by Choi et al. (2016) [12], indicated some similarities, but also differences. There was a prevalence of Type II (58.82%), in our study with values of 71.4 ± 0.62 mm, 11 cases out of 20. Followed by Type I (35.29%), with values of 48.5 ± 0.32mm, 7 cases out of 20. The data by Choi et al. (2016) [12] also indicated prevalence of Type II (85.7%), but their values were lower (70.2 ± 5.1 mm), 18 out of 21. Followed by Type III (90.0 ± 5.3 mm) with 2 cases out of 21 (9.5%). Both analyzes did not show Type IV cases. These results indicate that the head of the Asians is slightly smaller than the Brazilians, which is a very miscegenated population, but this aspect does not influence the professional's conduct for the application of BTX-A.

In the other analysis on the TM tendon, based on the study by Lee et al. (2016) [11], the tendon was arranged in the quadrants PI, MI and AI, therefore anterior, central, and posterior. Most of the cases (63.4%) were in the posterior part of the AI compartment, and the minority of the cases (13.8%) were in the posterior part of the Am compartment. The anterior fibers never exceeded the Am quadrant, but occupied half (55% of the total) of the AI compartment. The results of the study by Lee et al. (2016) [11], were similar to those of our study, with the posterior distribution of the TM tendon prevailing in the posteroinferior part in most cases. The prevalence of the tendon occurred in the Mm compartment. The tendon corresponded to 55.4% of the height of the TM and, in all specimens, it had a fan shape. The extension of the tendon fibers was similar in both samples, because no tendon was observed in the upper third (Au, Mu and Pu) of the temporalis muscle. The analysis of the results of the tendon arrangement in the three studies allows us to state that small differences occur between different races, however, some patterns do not change as mentioned above.

The average height of the TM in the Brazilian sample was 98 ± 1.22 mm and the average width was 120.4 mm, while in the Asian population (Won-Kang Lee at al., 2017) [11] it was 96 mm and 117,6 mm, respectively. The dimensions and proportions were almost identical, with little difference between races. Like the height and width, the other measurements were always greater in Brazilian specimens. Regarding the superficial temporal artery (STA), there were also small differences, as its bifurcation occurred above the reference line (line C - T) and within the Mm compartment in all specimens, while in the Asian population it occurred in 94.7 % of cases and in the same quadrant. The other measurements and analyzes also indicated slight differences between the two races, always with higher values related to the Brazilian race.

The horizontal (anterior) segment of the middle temporal vein (MTV) passed through the MT 23.7 mm above the reference line. Slightly below the average of the values obtained in the Asian sample. However, in both cases the route was mostly horizontal. All specimens reached the Al and Ml compartments and with few variations reached the main trunk at the rear 1/3 of the reference line (C-T), in the Mm and Ml quadrant.

In the methodology proposed by Choi et al. (2016) [12], Jugale is a part of the zygomatic bone that horizontally follows the upper margin of the zygomatic arch. The horizontal line LH, which passes through Jugale, coincides with the upper margin of the zygomatic arch, therefore, BTX-A can be clinically applied using the upper margin of the zygomatic arch as a reference. We conclude that the temporal tendon extends 45 mm above the upper margin of the zygomatic arch.

The recommended compartments for BTX-A injection are Am, Mu and Pm, all within the hairline, thus reducing the risk of developing a deficient temple. We have proposed safe and reproducible injection sites in the form of compartments. It would be useful to better specify the exact position of the injection site within the nine compartments described in this document, to allow the clinician to perform injections with greater confidence.

In the present study, the nervous distribution of the anterior, middle, and posterior branches of the deep temporal nerve was not evaluated. It is important to keep in mind that in order to be successful in BTX-A injection, blood vessels, tendons and nerves must be avoided, although in the present study the nervous distribution in TM was not evaluated.

Figure 3 - Arrangement of TM tendon fibers evaluated in Type I.

Figure 4 - Arrangement of TM tendon fibers evaluated in Type II.

Figure 5 - Arrangement of TM tendon fibers evaluated in Type III.

ACKNOWLEDGEMENTS

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3 CONCLUSÃO

Após a análise das duas metodologias propostas foi possível sugerir métodos para identificação das principais estruturas anatômicas envolvidas na região temporal, de modo a garantir maior segurança e eficácia clínica, minimizando os efeitos colaterais decorrentes da injeção de TXB-A para o tratamento tanto do bruxismo quanto das cefaleias primárias, em uma população miscigenada como a brasileira.

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* De acordo com as normas da UNICAMP/FOP, baseadas na padronização do International Committee of Medical Journal Editors - Vancouver Group. Abreviatura dos periódicos em conformidade com o PubMed.

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ANEXOS

Anexo 1 – Verificação de originalidade e prevenção de plágio

TCC Amanda

RELATÓRIO DE ORIGINALIDADE

20%	10%	19%	4%
ÍNDICE DE SEMELHANÇA	FONTES DA INTERNET	PUBLICAÇÕES	DOCUMENTOS DOS ALUNOS

FONTES PRIMÁRIAS

1	mdpi.com Fonte da Internet	8%
2	Won-Kang Lee, Jung-Hee Bae, Kyung-Seok Hu, Takafumi Kato, Seong-Taek Kim. "Anatomical recommendations for safe botulinum toxin injection into temporalis muscle: a simplified reproducible approach", Surgical and Radiologic Anatomy, 2016 Publicação	6%
3	You-Jin Choi, Won-Jae Lee, Hyung-Jin Lee, Kang-Woo Lee, Hee-Jin Kim, Kyung-Seok Hu. "Effective Botulinum Toxin Injection Guide for Treatment of Temporal Headache", Toxins, 2016 Publicação	1%
4	www.mdpi.com Fonte da Internet	1%
5	Brin Freund, Aruna Rao. "Efficacy of Botulinum Toxin in Tension-Type Headaches: A	1%

Anexo 2 – Comitê de Ética em Pesquisa

COMITÊ DE ÉTICA EM PESQUISA
FACULDADE DE ODONTOLOGIA DE PIRACICABA
UNIVERSIDADE ESTADUAL DE CAMPINAS

CERTIFICADO

O Comitê de Ética em Pesquisa da FOP-UNICAMP certifica que o projeto de pesquisa "**Guia de aplicação de toxina botulínica para o tratamento de cefaleia tensional**", CAAE **82061517.6.0000.5418**, dos pesquisadores **Paulo Henrique Ferreira Caria** e **Amanda Miki Okamoto**, satisfaz as exigências das resoluções específicas sobre ética em pesquisa com seres humanos do Conselho Nacional de Saúde – Ministério da Saúde e foi aprovado por este comitê em 25/01/2018.

The Research Ethics Committee of the School of Dentistry of Piracicaba of the University of Campinas (FOP-UNICAMP) certifies that research project "**Botulinum toxin injection guide for tensional headache treatment**", CAAE **82061517.6.0000.5418**, of the researcher's **Paulo Henrique Ferreira Caria** and **Amanda Miki Okamoto**, meets the requirements of the specific resolutions on ethics in research with human beings of the National Health Council - Ministry of Health, and was approved by this committee on 25th of January of 2018.

Fernanda Miori Pascon

Profa. Fernanda Miori Pascon
Vice Coordenador
CEP/FOP/UNICAMP

Prof. Jacks Jorge Junior
Coordenador
CEP/FOP/UNICAMP

Nota: O título do protocolo e a lista de autores aparecem como fornecidos pelos pesquisadores, sem qualquer edição.
Notice: The title and the list of researchers of the project appears as provided by the authors, without editing.

Anexo 3 – Relatório Iniciação Científica

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PARECER SOBRE RELATÓRIO FINAL DE ATIVIDADES

Bolsista: AMANDA MIKI OKAMOTO – RA 165613

Orientador(a): Prof(a). Dr(a). PAULO HENRIQUE FERREIRA CARIA

Projeto: *"GUIA DE APLICAÇÃO DE TOXINA BOTULÍNICA PARA O TRATAMENTO DE CEFALEIA TENSIONAL"*

Bolsa: PIBIC/CNPq
Processo: 136580/2017-3
Vigência: 01/08/2017 a 31/07/2018

PARECER

A aluna manteve seu desempenho acadêmico, sem apresentar reprovações. o relatório final demonstra os resultados obtidos bem como a discussão pertinente dos mesmos, mostrando o conhecimento adquirido pela aluna durante sua IC.

Conclusão do Parecer:
Aprovado

Pró-Reitoria de Pesquisa, 19 de novembro de 2020.

Mirian Cristina Marcançola
PRP / PIBIC - Unicamp
Matr. 299062

Anexo 4 – Declaração Iniciação Científica

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Declaração

Declaro para os devidos fins, que o(a) aluno(a) **AMANDA MIKI OKAMOTO**, RA 165613, foi bolsista junto ao Programa Institucional de Bolsas de Iniciação Científica - PIBIC/CNPq, com bolsa vigente no período de 01/08/2017 a 31/07/2018, sob a orientação do(a) Prof(a). Dr(a). PAULO HENRIQUE FERREIRA CARIA (FACULDADE DE ODONTOLOGIA DE PIRACICABA - FOP, UNICAMP) para o desenvolvimento do Projeto *"GUIA DE APLICAÇÃO DE TOXINA BOTULÍNICA PARA O TRATAMENTO DE CEFALEIA TENSIONAL"*.

Pró-Reitoria de Pesquisa, 8 de outubro de 2020.

Mirian Cristina Marcançola
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Anexo 5 – Comprovante de submissão do Artigo